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FATS OF LIFE STAFF

Editor
Joyce A. Nettleton, DSc
joyce@fatsoflife.com

Communications Manager
Angela Dansby
angela@fatsoflife.com

Sponsor
DSM Nutritional Products, Inc.,
Kaiseraugst, Switzerland
www.dsm.com

Letters and editorial comments should be submitted to Nettleton at joyce@fatsoflife.com and technical comments to Dansby at angela@fatsoflife.com. Subscribe to *Fats of Life* at www.fatsoflife.com

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Quarterly News for Consumers About Healthy Fats

HEART HEALTH

Does Fish Consumption Explain the Japanese Paradox?

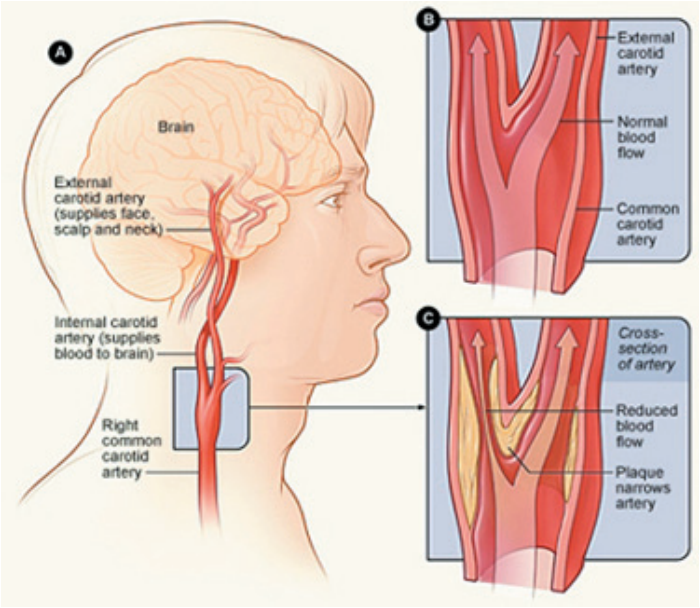
Why do the Japanese have half the chance of dying from heart disease as westerners do when their blood cholesterol and blood pressure measures are similar? In addition, they have high rates of diabetes and smoking. This is the Japanese paradox.

The Japanese have the lowest incidence of heart attack in the world and scientists have scrambled to figure out why. What makes their low occurrence of heart disease a conundrum is that the Japanese have similar blood cholesterol and blood pressure measures as people in western countries that have a higher risk of heart disease. Moreover, their cardiovascular risk factors are on the rise and they have high rates of smoking and diabetes. From everything we understand about heart disease, we would expect the Japanese to develop heart disease as readily as westerners do.

The answer to this riddle appears unrelated to genetics. Japanese who migrate to Hawaii and the U.S. have higher rates of heart disease than in Japan, but still much lower than among US Caucasians. What protects the Japanese from the leading cause of death in western countries?

One distinguishing feature between the Japanese and westerners is the high consumption of fish in Japan. Traditional Japanese eat fish as much as 8 times/week and have correspondingly higher levels of the long-chain omega-3 fatty acids (omega-3s) in their blood. A recent study comparing heart disease among Japanese men living in Japan, Japanese-Americans living in Hawaii and Caucasian men in the U.S. has reported additional differences in the heart health status among these groups.

In this study, the investigators examined blood fatty acids and the atherosclerosis status of 40 to 49 year-old men, who were Japanese living in Japan, Japanese-Americans in Hawaii and Caucasian men in the U.S. For atherosclerosis, they measured the thickness of the lining



of the carotid artery in neck and the amount of calcium in men's coronary arteries using imaging techniques.

Japanese men aged 40 to 49 years had one-third the amount of atherosclerosis as Japanese-American or Caucasian men. This observation was associated with their high blood levels of long-chain omega-3 fatty acids.

When the three groups were compared, the Japanese had significantly less atherosclerosis in their coronary arteries and in their carotid arteries compared with both the Japanese-American men and the Caucasians. In fact, the highest prevalence of carotid artery plaque and coronary atherosclerosis occurred in the Japanese-American men. Besides these striking differences in atherosclerosis, the Japanese men had twice the level of long-chain omega-3s in their blood as the other two groups. To put this in perspective, the lowest fifth of the Japanese men had higher omega-3 levels than the average levels in the other two groups. Concentrations of the main omega-6 polyunsaturated fatty acids were also significantly lower in the Japanese men than in the other groups. Omega-6 fatty acids are abundant in western diets and are found in vegetable oils and seeds. Interestingly, the levels of saturated fatty acids in the Japanese men were slightly, but significantly, higher as well, but they were not related to atherosclerosis.

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The blood omega-3 levels in the Japanese men were significantly correlated with their low levels of carotid artery thickening (plaque) and this relationship was not observed in either of the other groups. When all factors were taken into consideration in the analysis, the prevalence of atherosclerosis in the Japanese men remained significantly lower than in the Caucasians.

Because this is an observational study, the correlations reported cannot be interpreted causally. In other words, the high long-chain omega-3 levels may not be the reason why atherosclerosis is low in the Japanese men, but it is consistent with other evidence in this population and with studies where the consumption of long-chain omega-3s was associated with reduced carotid artery plaque and with low incidence of nonfatal heart events among the Japanese. This study suggests that the long-term habit of eating plenty of fish rich in long-chain omega-3s tends to counteract the development of atherosclerosis.

Women with Higher EPA Levels Have Fewer Nonfatal Coronary Events

Fish and fish oil consumption seems to protect the Japanese from nonfatal heart attacks, but has seldom been observed to do so in western populations. Is this due to the differences in fish consumption in the two populations?

For reasons we do not understand, fish and fish oil consumption, which protects against heart disease mortality and sudden cardiac death, has little effect on the occurrence of nonfatal heart events in western populations. This is not the case among the Japanese, who consume nearly 10 times as much fish as westerners. The Japanese also have half the chance of dying from heart disease. In trying to understand these striking differences, researchers have turned their attention to the long-chain omega-3 fatty acids found in fish. These fatty acids are also more abundant in the blood of Japanese fish-eaters than in most westerners. Although there is good reason to think long-chain omega-3s are at least part of the answer, a relationship between the two has not been observed in westerners.

Now the potential relationship between blood long-chain omega-3 fatty acid concentrations and the occurrence of nonfatal heart events, such as a heart attack, has been examined in a large sample of US women who were monitored for 6 years. This was a case-control study in which the investigators identified participants who incurred a nonfatal heart attack and then matched them with women having the same age and smoking status, but who did not have such an event. Blood samples were obtained from both groups of women. This study included 146 women with a nonfatal heart attack and 288 control women without a heart attack. On average, the women were 60 years old.

In this study, US women with higher levels of EPA, a long-chain omega-3, in their blood plasma had a 77% lower chance of having a nonfatal heart attack compared with similar women having low EPA levels.

When the two groups of women were compared, those who had had a heart attack weighed more, consumed less alcohol and were more likely to have diabetes, hypertension and high blood cholesterol levels, as well as a parental history of heart attack. Women who had higher levels of EPA (eicosapentaenoic acid), a long-chain omega-3 fatty acid, in their blood plasma had a 77% lower chance of having a nonfatal heart attack compared with women having lower levels. The reduced chance of heart attack was not related to their blood levels of DHA (docosahexaenoic acid), another long-chain omega-3 found predominantly in fatty fish.

The researchers also noted that women with higher long-chain omega-3s in their plasma had higher HDL levels ("good" cholesterol) and lower triglycerides (blood fats). Overall, this study provides some support in western women for fewer nonfatal heart attacks with higher levels of long-chain omega-3s in blood. The study had some other perplexing observations that are not easy to explain. For example, why was the relationship observed only for plasma omega-3s and not red blood cell omega-3s? Plasma values reflect more recent dietary intakes. It is also not clear why plasma DHA was not related to nonfatal heart attacks, as it too is associated with fish and fish oil

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consumption. What is encouraging about these findings is that they suggest that westerners may improve their heart health from a preventive point of view, just as happens in the fish-loving Japanese.

Stroke

EPA Plus Statin Lowers Chance of Second Stroke

Taking both a statin and EPA (a long-chain omega-3 fatty acid) reduced the chance of having a major heart event, such as death or heart attack. Investigators wondered whether it would also lower the risk of having a stroke.

A large study among Japanese patients with high blood cholesterol levels, who were taking statin medication to reduce their blood cholesterol levels, reported that when EPA (eicosapentaenoic acid, a long-chain omega-3 fatty acid found in fish) was added to their treatment, their chance of having a major heart event, including death, was significantly reduced. A second report from this study looked at the issue of stroke. The investigators asked the question whether taking EPA had any effect on the chance of having another stroke, if a patient had already had one. It turns out it did.

This large study included more than 18,000 participants. The occurrence of stroke was low, just over 1% in the whole sample. All the participants were given a statin to control their blood cholesterol and a portion of them was given nearly 2 g of EPA/day as well. After 5 years, the investigators looked at the incidence of stroke in the two groups. Stroke occurred at a similar rate in both the statin and statin+EPA groups.

Next the investigators examined those participants who had had a stroke when they enrolled in the study. There were 457 such patients in the statin group and 485 in the statin+EPA group. Stroke occurred in 48 patients in the statin group and 33 in the statin+EPA group, a difference that translates to a 20% lower risk with EPA and the statin. Readers should be aware, however, that statin medications by themselves reduce the risk of stroke, but this effect could not be measured in this study without a group not taking either medication. Nevertheless, the consumption of EPA boosted the preventive attributes of taking statins.

Taking both a statin and about 2 g/day of EPA significantly lowered the chance of having a second stroke in Japanese patients who had already had a stroke. The chance of a first stroke was not affected.

This is the first study to report a preventive effect of EPA plus statin treatment on the chances of having a second stroke. As has been observed with having a second heart attack, consuming long-chain omega-3s reduces the risk of having another. It has been reported previously that long-chain omega-3s reduce the risk of a first stroke, at least in some groups of people. What may seem surprising is that even with their high levels of omega-3s at the time of enrolment into the study, these Japanese patients reduced their chance of having a second stoke by taking even more EPA. In this study, more was better.

Eating Fish Often Linked to Fewer Omens of Stroke in Aging Brain

Whether a person is likely to have a stroke—the leading cause of adult disability—is difficult to predict. High blood pressure and plaque in the carotid arteries signal a greater chance of stroke from a blood clot blocking one of the brain's blood vessels. Individuals more likely to have a stroke often have brief ischemic attacks—moments of neurologic dysfunction from a temporary loss of blood flow. Other than these signs, there is no way to identify people at high risk of a stroke.

MRI imaging machine.

Researchers are adapting the power of brain imaging using magnetic resonance imaging (MRI, Illus.) to find out if there are warning signs of a stroke that can be detected before a major stroke occurs. They have observed "silent" brain infarcts, a kind of footprint left behind after bleeding in a small blood vessel. These lesions become more common as people age. People who have them experience greater loss of mental ability and are significantly more likely to have a stroke.

Because fish consumption has been linked to a reduced chance of stroke in some studies, but not all, and because consuming fish and the long-chain omega-3s they contain improves blood flow and reduces atherosclerosis, investigators at the University of Kuopio, Finland, and their colleagues at the Harvard Medical School in Boston, USA, examined the relationship between fish consumption and the occurrence of silent brain infarcts in about 3,500 individuals in the U.S. Individuals enrolled in the study had no previous history of stroke or brief ischemic episodes. Participants received brain scans when they were enrolled into the study and again 5 years later. The investigators also assessed their dietary habits and obtained information about how often and what types of fish the participants ate.

At the beginning of the study, brain infarcts were documented in 23% of the 75-year-old participants. However, when the researchers compared the lesions in people who consumed tuna or other baked or broiled fish 3 or more times/week with those in people who ate tuna less than once a month, the chance of having a brain lesion was significantly less in the fish-eaters by about a quarter.

In a large sample of adults 65 years of age or older, who had no history of stroke or brief ischemic attacks, eating tuna or other non-fried fish was associated with a 25% lower prevalence of small brain infarcts. These abnormalities are linked to a higher risk of stroke and cognitive decline.

Five years later, the prevalence of brain lesions was the same in the remaining individuals and 17% of the participants developed one or more new infarcts. For participants who ate tuna or other baked or broiled fish (i.e., not fried) 3 or more times/week, the chance of having one or more new lesions was 44% less. That suggests that eating fish often was protective against developing small brain infarcts. High fish consumption was also associated with having a better quality of brain white matter, the material that protects nerve fibers.

What it comes down to is this: eating fish often—3 times/week or more—was associated with a significantly lower chance of having any small brain infarcts or of developing a new one. It was also linked to having a higher quality of brain white matter. These odds are suggestive of protective effects of fish consumption in maintaining brain structure and function and of reducing the risk of developing a stroke. It remains to be seen if brain imaging can provide insights into maintaining cognitive function as we age.

Ventricular Arrhythmias

Heart Failure Patients with ICDs and Higher Omega-3s Have More Ventricular Arrhythmias

The rapid uncontrolled beating of the lower chambers of the heart is what happens in sudden cardiac death, the underlying cause of nearly half of all heart deaths. If the beating of these chambers becomes erratic and rapid, it is called ventricular tachycardia. If this type of heartbeat is not brought under control quickly, it can lead to uncontrolled ventricular fibrillation and sudden death. Providing an electric shock usually restores the normal rhythm. For that reason, patients susceptible to irregular ventricular beats are often provided an implantable cardioverter defibrillator (ICD). This device sends a mild shock to the ventricle should it develop rapid irregular beats.

Studies of long-chain omega-3s in patients with ICDs have yielded mixed results, ranging from potential help to no effect to possible harm.

The consumption of fish and long-chain omega-3s has been associated with a significantly lower chance of sudden death in several studies. Because these fatty acids improve the electrical properties and rhythms of the heart, it was thought that patients with ICDs might benefit from them. However, studies of long-chain omega-3s in patients with ICDs have yielded mixed results, ranging from potential help to no effect or possible harm. Thus, doctors have been cautious in counseling their ICD patients about taking fish oil supplements. However, the underlying disease in the

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patients studied so far differed widely, making it impossible to reach a general conclusion about the potential benefit of long-chain omega-3s in ICD patients.

To better understand which type of ICD patient might benefit from consuming omega-3s, a group of German investigators studied the relationship of these fatty acids to the need for electric stabilization in a sample of patients with heart failure and ICDs. In heart failure, the ventricles are unable to pump all the blood from the heart with each beat and this reduces cardiac output. The investigators assessed the patients' current omega-3 status by measuring the long-chain omega-3s in their red blood cells. They monitored the ICD patients for a year, noting the number of times each patient's ICD was triggered and compared the overall findings with individuals not having structural heart disease or an ICD.

Patients with ICDs had a significantly higher omega-3 index compared with controls not having an ICD. After one year, just over half the patients with the highest omega-3 index experienced ventricular arrhythmias, whereas only 12% of those with a lower omega-3 index had such episodes. Caution remains the watchword for omega-3s in ICD patients.

At the beginning of the study, the patients with ICDs had a significantly higher omega-3 index (the sum of EPA and DHA, the main long-chain omega-3s, as a percent of the total red cell fatty acids) than the heart patients without ICDs, 5.1% vs. 4.2%. This difference may be meaningless in terms of protecting the heart, however, because the omega-3 index is protective mainly in the range of 8% or more. After a year, just over half the patients with the highest omega-3 index experienced ventricular arrhythmias, whereas only 12% in the lowest quarter of omega-3 index scores experienced such episodes. This pattern of events occurred throughout the course of the study, not just at the end.

This surprising result suggests that heart failure patients with ICDs actually fare worse having higher levels of omega-3s than patients with low levels. How could this be? One explanation could be the altered way the failing heart handles fatty acids. We know that in heart failure, fatty acids are conserved and are less used for energy. If the heart were trying to conserve its omega-3s, it might take them from the circulation, leaving less available to reduce the excitability of the heart. Interestingly, though, the ICD patients had a slower type of heart rhythm, which is less harmful. In this regard, the omega-3s would be protective.

It is also possible, of course, that the higher levels of omega-3s increased ventricular arrhythmias in these heart failure patients. Having a higher omega-3 index in heart failure might actually signal greater risk, rather than the lower risk observed with ischemic (low oxygen) heart disease and heart attack. But this idea was not tested well in this study, because the omega-3 index was comparatively low in all the patients. Having a more uniform type of ICD patient in this study helps clarify the possible effects of long-chain omega-3s, but a greater range of omega-3 index is needed to determine whether these fatty acids actually increase risk or not. In the meantime, caution remains the watchword for recommending long-chain omega-3s in patients with ICDs and heart failure.

Higher Omega-3s Linked to Reduced Ventricular Fibrillation in Heart Attack Patients

Having higher levels of long-chain omega-3 fatty acids in one's tissues, as reflected in plasma and red blood cell measurements, has been associated with a significantly lower chance of heart disease mortality, especially sudden death. They appear to be protective in most forms of heart disease, but patients with heart failure and angina may not benefit as much or at all. One of the ways omega-3s protect heart health is to modify its electrical properties. Usually, omega-3s stabilize

abnormal heart rhythms and reduce the tendency for rapid uncontrolled beats to develop. However, this may not always be the case in patients with a tendency for abnormal rhythms in the lower chambers of the heart. A study where this appeared to happen is described in the preceding article.

This report from Norway, however, presents contrasting findings to the preceding study in patients experiencing a heart attack. The investigators recorded the electrical events of patients experiencing a first heart attack. They watched the patients for several hours after the attack to see if uncontrolled beats or fibrillation developed in the lower chambers (ventricles) of the heart. Of 265 patients having a first heart attack, 10 developed ventricular fibrillation within 6 hours of the attack. The researchers compared these patients with other heart attack patients of similar age without fibrillation. For 9 of the 10 patients with fibrillation, this heart attack was their first sign of heart disease. The investigators measured the fatty acids in the patients' blood for the first 8 hours after admission to the hospital and determined their omega-3 index, the percent of total fatty acids in red blood cells that are EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid).

In this study of patients experiencing their first heart attack, those with lower levels of long-chain omega-3s in their red blood cells were more likely to develop ventricular fibrillation than those with higher levels.

The omega-3 index of the ventricular fibrillation patients was significantly lower (5%) than in the controls 6%. This study focused on a different type of heart patient than the preceding study. In these patients, omega-3 fatty acids have often been associated with reduced risk of heart disease mortality, especially from a second heart attack. Because the omega-3 index associated with the lowest risk of heart disease mortality is 8% or more, these patients might obtain even greater protection against heart disease mortality and sudden death by having higher levels of long-chain omega-3s in their red blood cells.

MATERNAL AND INFANT HEALTH

Mother's DHA Level Drops at Delivery Even with High Fish Intake

The transfer of DHA and arachidonic acid to the fetus in the last trimester of pregnancy results in a drop in the mother's DHA status. Only very large intakes of DHA seem able to prevent these losses.

One of the most important nutritional events for the developing fetus occurs during the last trimester of pregnancy. At that time, there is a substantial transfer of long-chain polyunsaturated fatty acids from the mother to the fetus. The two most important fatty acids transferred are arachidonic acid, an omega-6 fatty acid, and docosahexaenoic acid (DHA), a long-chain omega-3. Both are needed for the brain growth spurt that occurs in the last few weeks before birth. The result of this fatty acid transfer for the mother is a drop in her essential fatty acid status. After delivery, it can take several months for the mother's long-chain fatty acids to reach their pre-pregnancy levels. The most important of these fatty acids is DHA because it is most dependent on the mother's diet.

Women who consume fish oil or DHA supplements during pregnancy lose less DHA at delivery than women who do not. In spite of this, these women still lose DHA, but not as much as women who do not consume additional DHA. It takes the consumption of about 2 g of DHA daily during the last trimester to prevent this decline in maternal DHA. Could high fish consumption work just as well?

An excellent place to look for an answer to this question is the Seychelle Islands where people eat fish about 9 times/week. The fish commonly consumed include lean and fatty fish, much as in the U.S. and other western countries. The investigators in this study estimated

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that these women consume at least 200 mg/day of DHA. From a sample of 300 pregnant women, blood samples were obtained at 28 weeks' gestation and 1 day after delivery for two-thirds of them. Fatty acid values from both time points were used in the analysis of the results.

This study among Seychelles Island women found that even with high fish consumption, the decline in the mother's DHA at delivery was not prevented.

Comparison of the mother's blood fatty acid values at 28 weeks' gestation and delivery showed a significant decline in DHA, but not in arachidonic acid. This observation suggests that the abundant fish consumption of the Seychellois was not sufficient to prevent a drop in maternal DHA, in spite of the consumption of at least 200 mg of DHA/day. This is the amount recommended by an international group of experts in December 2007 and endorsed by several professional infant and child health groups.

There is no reason to think that DHA consumption in the Seychelles is inadequate. The study suggests that even with robust fish consumption, the type of fish consumed may be more important than the total amount. Eating fish rich in long-chain omega-3s, primarily the fatty species, will supply the greatest amount of DHA and other omega-3s. Even then, maternal status may decline after giving birth, but the decline will be less than if women avoid eating fish.

DHA Supplementation Improves Mothers' and Infants' DHA Status

Women in most western countries consume fish infrequently, if at all, resulting in less DHA (docosahexaenoic acid), a long-chain omega-3 fatty acid, in their tissues to provide to their fetus during pregnancy. For this reason, health organizations encourage women to consume fish or fish oil supplements regularly during pregnancy and to obtain at least 200 mg of DHA/day. DHA is one of the key building blocks of the brain and central nervous system and is necessary for brain structure and function. The developing infant relies on the mother for this and other long-chain fatty acids, especially during the last trimester, when there is a large transfer of these fatty acids to the fetus.

Even with abundant fish and long-chain fatty acid consumption, the mother loses DHA at delivery and it takes several weeks or months to restore her tissue stores to pre-pregnancy levels. A team of investigators in Germany examined whether 200 mg of DHA consumed during the last half of pregnancy would affect the DHA status of the mother and infant at delivery. They also looked at the DHA content of the mother's breast milk at 3 months postpartum. They recruited 144 healthy pregnant women who were carrying a single child and divided them into 3 groups. One was given a vitamin and mineral supplement, the second the same supplement plus a prebiotic for digestive health, and the third group received both supplements plus 200 mg of DHA. After delivery, 80% of the infants were exclusively breast-fed.

All groups increased the DHA content in their red blood cells during the last half of pregnancy as expected, but at 37 weeks' gestation (about term) and 3 months after delivery, only the DHA-supplemented mothers had significantly higher DHA concentrations. There was no difference between the vitamins and minerals group and those also taking the prebiotic. Three months after delivery, the DHA content of the breast milk from the DHA-supplemented mothers contained significantly higher amounts of DHA compared with the other two groups. In addition, the infants of the DHA-supplemented mothers had significantly more DHA in their red blood cells compared with the other two groups of infants.

Several aspects of this study are worth noting. The first is that German women, like those in much of the U.S., Australia and Europe, consume very little fish, so they obtain no more than 100 mg of DHA/day or less. Providing these women with the recommended amount of 200 mg of DHA daily improved the DHA status of the mother, her infant and the DHA content of her breast milk. This created a win-win situation for the mother

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Pregnant women with low fish and DHA intakes improved their own and their infant's DHA status by consuming 200 mg of DHA/day in the last half of pregnancy. Breast milk DHA also increased significantly.

and her infant, assuring an adequate supply of DHA for the infant's neurodevelopment in fetal life and early infancy. The study also showed that vitamin and mineral supplements have no effect on long-chain fatty acid status. Thus, complying with the recent international recommendations for the consumption of 200 mg of DHA/day during pregnancy, especially by women with a tradition of low fish consumption, improves the DHA status of both the mother and infant.

Omega-3s in Pregnancy Unrelated to Childhood Cognition at Age 7

Many studies have reported that infant and toddler neurodevelopment is improved when the mothers consume plenty of long-chain omega-3 fatty acids during pregnancy. Studies have also shown that infants fed formula containing these fatty acids perform better on various tests compared with infants fed unsupplemented formula. As a result, nearly all infant formulas contain these fatty acids.

An important question is how long-lasting these benefits are. Do they last a lifetime? Are there any effects in late childhood or adolescence? Do the advantages seen in early life require a life-long supply of long-chain omega-3s? Answers to some of these questions are emerging. We also know, for example, that the brain and nervous system, immune system, heart and blood vessels, and visual function depend on having long-chain omega-3 fatty acids available to maintain good performance, slow or prevent deterioration and reduce the likelihood of developing several diseases of aging.

To date, there are only a few studies that have monitored children to determine the long-term effects of maternal omega-3 consumption in pregnancy. Two studies reported that 3- and 4-year-old children of such mothers had higher intelligence scores compared with the children of unsupplemented mothers. However, another study observed no effect of maternal omega-3 supplementation on childhood cognition when the children were 4 and 7 years old.

Now, a group from Norway, who had observed a benefit from maternal omega-3 consumption on the cognitive scores of the children at age 4, has reported its findings on the same children at age 7. In this study, the mothers had been supplemented with either cod liver or corn oil from 18 weeks' gestation until 3 months after delivery. The mothers consumed over 2 grams of long-chain omega-3s/day, a larger amount than would be available from eating fish every day.

Children whose mothers consumed cod liver oil during pregnancy did not differ in their cognitive scores at age 7 from children whose mothers did not take cod liver or fish oil.

The investigators found no significant differences between the two groups of 7-year-olds in their intelligence assessments or in any of the detailed aspects of intelligence that were measured. They did find that the parents' education level affected the results and this factor needs to be considered when analyzing the data. Other circumstances, such as social environment, nutrition, drugs and diseases may have affected the results. It is also possible that the cognitive benefits seen earlier simply do not carry over this long. However, this possibility is refuted by studies reporting improved behavior and learning in children of a similar age whose mothers ate plenty of fish during pregnancy. However, fish supplies other nutrients such as iodine, iron and selenium that affect brain function, too.

These findings do not diminish the importance of long-chain fatty acids in infant and child development.

Instead, they suggest that as children develop, the situation becomes more complicated.

Beneficial Nutrients and Harmful Contaminants in Fish: Which Wins?

In spite of the fact that only a few species of fish have relatively high levels of mercury, some women shun eating all fish. Doing so deprives their fetus of several nutrients needed for the brain and nervous system.

The good news about the many health benefits associated with the omega-3 fatty acids in fish and shellfish has encouraged people to eat more seafood. Some pregnant women, however, remain fearful because of the potential harm to the fetus from the varying amounts of mercury found in all seafood. In spite of the fact that only a few species of fish have relatively high levels of mercury, some women shun eating all fish. By doing so, their developing baby misses out on the long-chain omega-3s needed for brain and nervous system development. How can you win?

There is no question that in large amounts, mercury is harmful to the developing nervous system. The catch is that most fish are low in mercury, and they have other nutrients that help blunt the damaging effects of this metal. Selenium is one of those counter-balancing nutrients rich in fish. There are now several studies that have observed higher learning and behavior scores in the children of mothers who ate plenty of fish during pregnancy compared with children whose mothers avoided eating fish. The reason for this is largely attributed to the long-chain omega-3s in fish. The mothers in these studies consumed much more fish than women in most western countries.

One of the long-term studies examining the relationship between a mother's exposure to mercury and the development of the offspring has taken place in the Seychelle Islands. Here, people eat a variety of fish about 9 times/week and mothers have much higher amounts of mercury in their tissues than they do in western countries. Nevertheless, the offspring of these mothers show no detrimental effects on a wide range of performance evaluations through 9 years of age. Some recent reports from this study have analyzed the effects on children's development of multiple nutrients considered simultaneously.

Infant neuro-development is affected by nutrients and contaminants, but the nutrient benefits outweigh the risks from modest exposure to mercury.

The investigators reported that in 9-months-old infants, long-chain fatty acids and mercury exposure had no significant effect on any of the Bayley developmental scores. At 30 months of age, the situation began to change. One of the 16 developmental scores, the psychomotor index, fell by about half a point as mercury exposure increased. At the same time, as the exposure to long-chain omega-3s increased, the psychomotor scores improved. This suggests that high levels of mercury in the mother can result in a lower psychomotor score, but that higher levels of long-chain omega-3s dampen this effect. It comes down to this: having long-chain omega-3s helps build a better brain, but if mercury levels are high, the benefits of the omega-3s are less. For most women, mercury levels are a fraction of what is observed in the Seychelle Islands and the benefits of the long-chain omega-3s and several other essential nutrients outweigh the small risks from low levels of mercury. Wise fish consumption during pregnancy and lactation is based on fish having high levels of omega-3s and low amounts of mercury. These include salmon, sardines, herring, mackerel and small young tuna. Lean white fish are usually low in mercury, but have less omega-3s. Choosing the "rich" fish, women and their infants are the winners!

MENTAL HEALTH

Attention Deficit Hyperactivity Disorder

Inattentive but Not Other ADHD Children Respond Well to LC-PUFA Supplementation

Children and adolescents with attention deficit hyperactivity disorder (ADHD) often have other behavioral

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problems, such as learning difficulties, reading or writing abnormalities, motor coordination, defiant behavior and others. In addition, it has been noted often that the pattern of polyunsaturated fatty acids in their blood differs from children without this disorder. In particular, ADHD children usually have lower amounts of long-chain omega-3s, even though they consume the same amounts as other children. A shortage of these fatty acids may contribute to the condition. For example, it has been noted by some researchers that the severity of the condition is worse as levels of red blood cell DHA (docosahexaenoic acid), one of the two main long-chain omega-3s, decrease.

The situation is more complex than simply providing more of these fatty acids. This was shown in a study comparing the responses of healthy and ADHD children when supplemented with long-chain omega-3 and omega-6 fatty acids. Both groups of children improved with the supplements, but the fatty acid deficiency was not corrected. On the other hand, trials among children with a range of ADHD symptoms who consumed long-chain fatty acids reported significant improvements in behavior and learning. It takes months, however, to observe the changes.

In a new study from Sweden, researchers wanted to see if they could obtain the same encouraging results as others had in children with diverse ADHD symptoms. The children were 8 to 18 years of age. One group of children was given a modest dose of long-chain fatty acids, mostly omega-3s, while the other received olive oil as a placebo. The study lasted 6 months.

The children generally fell into two categories; those with a combined type of ADHD with hyperactive and impulsive behavior and those who were mainly inattentive. More than three-quarters of the children had other associated difficulties, such as reading or writing problems, defiant behavior, developmental coordination disorder and the like. Nearly all were boys. Their behaviors were assessed in detail by a clinician and the parents before and after the study.

For the first 3 months, children consumed either the long-chain fatty acids or olive oil. After that, all children consumed the long-chain fatty acids for another 3 months. That study design yielded two groups of outcomes for 3 months of treatment, plus a group that received the fatty acids for 6 months.

As often happens in studies, both groups showed changes in their behaviors. After 3 months, the children taking the long-chain fatty acids showed significant improvement in their clinician-based scores compared with the placebo group. Their ADHD assessment scores also improved, but not enough to reach statistical significance. At six months, the children who had been taking the long-chain fatty acids continued to improve, as did those who had been taking the placebo, but differences between the two groups were not significantly different.

In this study, children with mainly the inattentive form of ADHD were more likely to have significant improvements in their behavior after consuming long-chain fatty acids. Treatment after 3 months continued to enhance the improvements.

Next, the investigators examined the changes in children considered to be "responders." Those children showed at least a 25% improvement in their scores, regardless of which group they were in. At 3 months, 26% of children taking the long-chain fatty acids were considered responders, whereas only 7% of the placebo children were responsive. Moreover, nearly half the responders in long-chain fatty acid group improved their symptoms by 50% or more, but none in the placebo group improved that much.

When the investigators looked at which type of ADHD the responsive children had, it was the inattentive type more than the other forms. They were also more likely to be in the 13- to 18-year age category. Further, the

children with the greatest improvement experienced enhanced daily functioning.

This study contributes new information about the responses of ADHD children to supplementation with long-chain fatty acids. It suggests that children with predominantly the inattentive type of ADHD may be more likely to respond. In addition, children continued to improve the longer they consumed the supplements up to 6 months. Thus, consumption for 6 months was more effective than for 3. Finally, the study confirms previous reports that a modest amount of long-chain fatty acids may be clinically useful in at least some children with ADHD.

Long-Chain Fatty Acids Improve Attention in ADHD Children

Children with ADHD are not all alike, some being more active, impulsive or inattentive than others. Supplementation with long-chain fatty acids may have promising effects on attention.

Children with attention deficit hyperactivity disorder (ADHD) usually have more difficulty learning, interacting with peers, paying attention and remaining calm. The disorder is most commonly found in children, but can persist into adulthood. To date, treatments for the condition have relied on drugs, which often have unwanted side effects and may be of limited help. Because the condition affects some 4% to 12% of children in western countries, it has become imperative to find gentler treatments that work without bringing undesirable effects as well. Long-chain fatty acids, especially those of the omega-3 family, may offer some encouragement, at least in some types of ADHD behaviors.

It is becoming better appreciated that children with ADHD are not all alike, some being more active, impulsive or inattentive than others. There is now emerging evidence that children who are especially inattentive may benefit from a combination of long-chain fatty acids more than others. As in the preceding article, this report describes promising findings from Australia.

Researchers at the University of South Australia in Adelaide enrolled children 7 to 12 years old who were considered to have ADHD by their scores on a widely used assessment scale for the disorder. Upon entry into the study, the children's behaviors were assessed with several tests. Each child was assigned at random to receive either vitamins and minerals plus long-chain fatty acids, long-chain fatty acids alone or a placebo without any of these components. For the first 15 weeks of the study, children consumed their assigned supplement. After that, all children received the vitamins and minerals with the long-chain fatty acids. The fatty acids contained mainly long-chain omega-3s with a small amount of one omega-6 fatty acid. At 15 and 30 weeks, all children were assessed for their behavioral scores.

After 15 weeks or nearly 4 months, both groups of children taking the long-chain fatty acids had significantly improved scores in a test of executive functioning and attention, with no difference in scores between the two groups. Thus, vitamins and minerals do not account for the outcomes. The fatty acid-supplemented children demonstrated strongly improved ability to switch and control their attention compared with the placebo children.

After the second 15-week period, scores in the executive function and attention test continued to improve for those carrying on from the first half of the study. They also improved in the rest of the children who had been taking the placebo. There were significant improvements in other tests, too, including those for learning and memory, mental processing speed and the ability to ignore distractions. The analysis of the data indicated that improvements in one area of functioning had beneficial carryover effects into other areas. For example, changes in cognition and attention improved ADHD assessment, impulsivity and inattention.

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This study provides additional evidence that long-chain fatty acids affect learning and behavior in ADHD children. They may be more effective in some children and for certain behaviors than others.

In the second 15 weeks, children switched from the placebo experienced improved behavior scores, while those with ongoing treatment continued to improve. As in the preceding study, longer treatment produced additional gains. It is possible, if not likely, that greater attention facilitated the improvements in longer reading, better vocabulary and overall cognition, even though some of these changes did not reach statistical significance.

This study provides additional evidence that long-chain fatty acids, particularly those of the omega-3 family, affect learning and behavior, but do not necessarily bring about improvements in all types of ADHD or in all problem behaviors. They appear important for improved attention, a quality that has other positive carryover effects. This study is consistent with several others suggesting that ADHD children might need several long-chain fatty acids and that long-term supplementation is important for beneficial changes.

Cognitive Function

DHA Supplementation of 4-Year-Olds Linked to Better Understanding from Listening

Much of the work exploring the relationship between long-chain omega-3 fatty acids and children's development has come from studies where the mother consumed these fatty acids during pregnancy. Overall, the results have shown that mothers with higher intakes and tissue levels of long-chain omega-3s have children with better neurodevelopmental performance compared with children whose mothers consume little of these fatty acids. These findings are of particular concern in western countries where maternal consumption of fish or fish oil supplements is low.

In one of the few studies to examine the effect of DHA supplementation on learning in preschool children, this study reported higher scores on the Peabody Picture Vocabulary test in 4-year-olds with DHA. Additional confirmation of these findings is needed.

Of the few studies focused on children's learning and intelligence related to maternal diet, several have reported a beneficial effect of higher omega-3 status of the mother and children's performance up to age 4. There are not many of these studies and not all results agree. That leaves plenty of room to examine these relationships more closely.

Stepping up to the plate on this question were US investigators who enrolled 4-year-old children in a study to compare the effect of consuming DHA (docosahexaenoic acid), a long-chain omega-3 fatty acid important for brain structure and function, with a placebo of omega-6 fatty acids. The children were assigned at random to each group. The study continued for 4 months and a variety of cognitive tests were given at the beginning and end of the study.

Of the three main tests used in the study, two turned out to be too easy for these children. There were many who scored the maximum possible score at the beginning and end of the study. However, in the Picture Vocabulary Test, which assesses listening comprehension, children who took the DHA supplement scored significantly higher than those on the placebo. These results suggest that having more DHA available in childhood may improve cognition. Without more diverse test results, the study is limited in what it suggests over a range of evaluations, but it does imply that DHA may be linked to better learning performance.

Depression

Low Dose DHA Improves Clinical Symptoms in Major Depression

The main treatments for various mental disorders rely on drugs. While these are highly useful in some conditions and in some patients, others do not respond as well. Drugs are often accompanied by unwelcome side effects that reduce the patient's willingness to take them. For these reasons, researchers continue to seek safer, effective treatments that are easy to take. Long-chain fatty acids of the kind found mainly in fish have shown promising results in some

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studies. Findings are not always in agreement and there is debate about whether each or both of the two main long-chain omega-3s, EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) are effective. The evidence currently favors EPA as being more effective than DHA. The study described here set out to confirm this understanding.

Investigators in Boston examined the effectiveness of DHA supplementation in patients suffering from major depression. Participants had not consumed omega-3 fatty acid supplements in the past 6 months and were permitted medications if needed. They were divided into three groups, each given a different dose of DHA. Doses included 1, 2 and 4 g/day and were consumed for 12 weeks.

In patients with major depression, it is generally thought that EPA alone or combined with DHA is more effective than DHA alone. In this study, low-dose DHA alone improved clinical symptoms significantly.

As often happens in studies with mentally ill patients, many did not continue the study. However, 80% of them completed at least 2 followup visits. Among all participants, 32% responded to the DHA supplementation with significantly improved symptoms. The greatest responses occurred in patients who took the lowest dose, 1 g/day. Half of the patients who completed all 12 weeks of supplementation responded. The greatest response—83% of patients—occurred among those taking 1 g of DHA/day. Significant improvements were also observed in patients taking 2 g of DHA/day, but the improvements were not as great as in the 1 g/day group. None of those taking 4 g/day showed any significant improvement.

This study is worth noting for at least two reasons. The first is that it showed that a low dose of DHA had a significant positive impact on the symptoms of major depression. The second is that more was not better. In fact, as the dose increased, the clinical improvements diminished, so that by the time a dose of 4 g/day was reached, the benefits were negligible. Another important observation is that DHA was the primary, and for most participants, the only treatment. That means the results can be attributed to DHA itself, not to other treatments or conditions. These findings provide excellent justification for additional studies with DHA among patients with major depression.

Low EPA Levels Seen in the Elderly with Major Depression

One change that might reduce the chance of developing major depression in older adults is to increase the consumption of long-chain omega-3 fatty acids. This study suggests that EPA is linked to this condition in the elderly.

Although there are many reasons why people develop major depression, the condition is more frequent in younger than older adults. Nonetheless, it is a concern in the aging population. In the elderly, depression is more likely to occur in those with impaired cognition and in certain disturbances of endocrine metabolism. Depression also occurs more frequently in people with low fish consumption or low levels of long-chain omega-3 fatty acids in their blood. Higher levels of these fatty acids have also been linked to slower loss of cognition in aging. If this link between depression and nutrition becomes firmly established, it offers a fairly simple way to lower the chance of developing this unwelcome condition.

To learn more about the link between long-chain omega-3s and major depression in aging, investigators in France examined the omega-3 fatty acid levels in elderly individuals recruited from the general population. To be eligible for the study, participants had to be at least 65 years old and living in the community. Those who were considered to have major depression had scores on a depression assessment rating above an established level for the disorder. Those free of depression served as controls. On average, the participants were 75 years of age.

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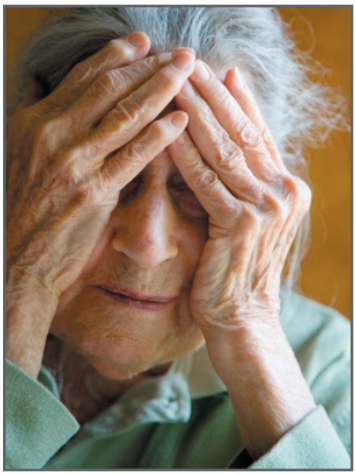

The investigators then measured the concentrations of omega-3 fatty acids in the blood of both groups. They observed that the concentrations of EPA (eicosapentaenoic acid), one of two major long-chain omega-3 fatty acids, were significantly lower in the depressed older adults compared with those free of depression. The concentrations of DHA (docosahexaenoic acid) did not differ in the two groups. Other studies, however, have reported reduced DHA levels in depression, including the DHA content of specific regions in the brain cortex.

In addition, patients taking antidepressant medications had more severe symptoms as their EPA dropped. This relationship with severity of the condition held after accounting for other variables, such as high blood cholesterol levels and the number of drugs the patients were taking.

In this study, patients taking antidepressants had more severe depressive symptoms as their EPA level dropped.

Because this was an observational study, it does not address the question of causation. We do not know whether the low levels of EPA were the result of depression or increased susceptibility to it. To date, other evidence favors the latter interpretation. There is evidence suggesting that inflammation is linked to depression. EPA is an important substance for reducing inflammation, suggesting that a connection between low EPA and major depression is plausible.

Considering the many other health benefits associated with regular fish or long-chain omega-3 consumption on heart health, visual function and cognition, it would reflect the wisdom of aging to have fish on the menu at least twice a week.

CLINICAL CONDITIONS

Alzheimer Disease

Mild Alzheimer Patients Improve Cognition with Omega-3s

People who eat fish regularly are less likely to develop Alzheimer disease as they age. Once the condition appears, is it too late to boost one's intake of long-chain omega-3s?

Most people dream of aging gracefully and keeping a lively mind. Whether we achieve our goal depends on many conditions, only some of which we can influence. We are learning quickly that a healthy diet is one habit that favors mental alertness and function. A particularly important part of a healthy diet is the regular and sufficient consumption of long-chain omega-3 fatty acids. These are found mainly in fish and shellfish, particularly in fatty fish. It has been observed in several countries that people who eat fish regularly are less likely to develop Alzheimer disease, the most common neurodegenerative disease in the elderly. Having an abundant intake of these omega-3s also slows the loss of cognition, which often accompanies aging. Further evidence that long-chain omega-3s are involved in cognition has come from the examination of the brains of individuals who died with Alzheimer disease. Their brain tissue has significantly less DHA (docosahexaenoic acid).

The association between customary fish intake and a lower chance of developing Alzheimer disease suggests that these fatty acids have some preventive effects. Does that mean it may be too late for people who have not eaten much seafood? To answer that question, scientists have provided long-chain omega-3s to older individuals and those with different stages of impaired cognition and compared them with a placebo supplement. The findings to date suggest that long-chain omega-3s may slow the loss of cognition in the early stages of decline, but not when the impairment is more advanced. Not all studies have reported improvements, however, and the severity of disease at which omega-3s are unhelpful is uncertain. As a result, the effectiveness of long-chain omega-3s in individuals with early Alzheimer disease remains to be firmly established.

In this small study of mild cognitive impairment and Alzheimer conditions, the consumption of 1.8 g/day of n-3 LC-PUFAs for 6 months was associated with progressive improvements in cognitive scores.

A recent pilot study from Taiwan examined this issue in a small sample of patients who were diagnosed with mild or moderate Alzheimer disease or mild cognitive impairment. The participants ranged in age from 55 to 90 years and were given 1.8 g/day of long-chain omega-3s or olive oil for 24 weeks. They received cognitive assessments at 6-week intervals during the study.

In participants who completed the full 24 weeks, there was a significant improvement in the clinician-based global cognitive assessments in those who took the long-chain omega-3s, but not in the placebo group. The assessments for Alzheimer symptoms did not change during the study. But the investigators observed a significant relationship between higher red blood cell EPA (eicosapentaenoic acid), a long-chain omega-3, and better Alzheimer scores. This association suggests, but does not verify, that long-chain omega-3s slow the progress of Alzheimer disease.

The virtue of small studies, such as this one, is that they may indicate connections that are worth pursuing on a larger scale. That is the case here. On their own, they are insufficient proof of what the investigators hope to establish. The downside is that if they do not show a significant effect, it may just be because the study was too small. This is often a research conundrum and is one reason why existing evidence appears conflicting.