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REPORT

Omega-3 Fatty Acids Vital to a longer, healthier life

By Dale Kiefer

The life-prolonging benefits of long-chain omega-3 fatty acids are hardly front-page news any longer. We have all heard by now that it is important to eat at least two servings of fatty fish per week for optimal cardiovascular health. After all, no less an authority than the American Heart Association recommended just such a dietary plan for all Americans in 2000, and again late last year, after reviewing years of research on the impressive health benefits of omega-3 consumption.^{1,2}



The recommendation reflects the culmination of decades of research that began in the 1950s, when scientists first examined the traditional diets and lifestyles of the Inuit (Eskimos) in Greenland in an effort to understand the Eskimos' almost startling absence of cardiovascular and other diseases. While heart and circulation disorders rank among the top killers in the industrialized world, they are virtually unknown among the hunter-fishers of the Arctic Circle. The Inuit's amazing health, scientists eventually understood, is a direct result of consistently eating large quantities of fish and marine mammals, which are rich sources of long-chain omega-3 fatty acids.

But intriguing new research from around the globe indicates that the much-heralded heart benefits represent little more than the tip of the proverbial iceberg when it comes to this versatile and utterly essential nutrient.

A 21st Century Optimal Supplement

Exciting new studies suggest that omega-3s play an integral role in overall health. When deficiencies exist, as is alarmingly common in the industrialized West, supplementation with the right omega-3s, in the right balance, has the potential to improve everything from vision to brain function. Far from simply decreasing blood pressure, and protecting against heart attack and stroke,³⁻¹⁰ omega-3s may also prevent (or play a role in the treatment of) everything from depression to autism.¹¹⁻²⁴ Certain omega-3s are crucial to the optimal development of the brain and sensory organs in preterm infants,²⁵⁻²⁸ and omega-3s have been shown to reverse the symptoms of rheumatoid arthritis and possibly to play a role in preventing Alzheimer's disease.²⁹⁻³⁴

And the list doesn't stop there, as new research suggests even more potential benefits of omega-3s. Cutting-edge research from facilities all over the world indicates that omega-3s may also prevent age-related macular degeneration, suppress cancer cell growth (while simultaneously promoting cancer cell death), decrease susceptibility to the most common form of stroke,

ameliorate complications of Type II diabetes, and even improve the health of those whose lungs have been damaged by smoking or diseases such as asthma, cystic fibrosis, and emphysema.³⁵⁻⁴⁵

But even that list fails to encompass the full scope of this essential nutrient's absolute importance to virtually every aspect of health. About 60% of the brain consists of lipids, and the omega-3s are among the most important of these. They are key components of cell membranes throughout the body, and are richly invested in neural tissue.

The omega-3s are known as essential fatty acids (EFAs) because they are necessary nutrients that must be obtained from the diet. Unlike cholesterol, for instance, the body cannot manufacture the omega-3s it needs. While certain plant sources provide the building blocks of the most crucial omega-3s, they are most readily and plentifully obtained from marine sources.



Data gathered from populations around the world paint a clear picture: societies with the lowest fish consumption have the highest rates of suicide, depression, and violence. Conversely, among populations where fish is eaten frequently, these costly social ills are dramatically lower. The jury is still out on certain promising aspects of omega-3 supplementation therapy, but one thing is clear: omega-3s play a crucial role in maintaining health. What is equally clear is that the average American does not get nearly enough omega-3 fatty acids from the diet.

Some scientists have even speculated that the lack of adequate omega-3s in the Western diet may account for escalating levels of neurological disorders such as autism, depression, bipolar disorder (manic depression), and attention deficit hyperactivity disorder (ADHD).¹¹⁻²⁴ Others are investigating the benefits of omega-3 supplementation in the treatment of everything from asthma to inflammatory bowel disease and schizophrenia.⁴⁶⁻⁴⁸ Studies have shown that omega-3s can reduce the risk of sudden death from heart attack,⁵ improve vessel elasticity,⁴⁹ lower serum triglycerides,⁵⁰ and coax an unsteady heartbeat back into a stable rhythm.⁵¹⁻⁵³ It is no fish story: Fish oil is beginning to look like a panacea for the 21st century.

Omega-3 vs. Omega-6— A Harmful Imbalance?

The human body has evolved to thrive on a roughly equal intake of omega-3 and omega-6 long-chain fatty acids. Although the important omega-3s, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) are available only from marine sources, it is not necessary to eat seal meat, as the Inuit do, to reap the benefits of these ocean-borne nutrients. They are plentiful in fatty cold-water fish such as salmon, tuna, bluefish, sardines, herring, and king mackerel. A three-ounce serving of salmon, for instance, yields roughly 3 grams (3,000 mg) of combined EFAs.

For those who do not like fish or prefer the convenience and safety of supplements, fish oil is available in capsule form. But even fish do not generate these essential polyunsaturated fatty acids. They get them courtesy of their own diets, which include marine algae or seaweed. Humans can too, of course, although it seems unlikely that the average American will be able or willing to order fresh seaweed at McDonalds any time soon.

A third essential fatty acid, alpha-linolenic acid (ALA), is available from certain plant sources, most notably flax seed, avocados, and walnuts. The body can convert ALA into EPA and DHA, but the process is slow and the rate of conversion probably varies according to age, gender, and other factors.⁵⁴⁻⁵⁶ Fish and fish oil thus remain the best sources of vital DHA and EPA.

For millions of years, humans evolved on a diet rich in natural omega-3 food sources, including

free-range game, fish, marine mammals, nuts, and fresh seaweed. In the early 20th century, however, food manufacturers in the industrialized nations began literally pouring soybean oil—a source of omega-6 fatty acids—into the food chain. A concurrent decline in fish and wild game consumption, accompanied by the heavy use of grains (another omega-6 source) as feed for livestock, conspired to drastically alter the balance between omega-6s and omega-3s in the Western diet. While an omega-6 to omega-3 ratio of roughly 2:1 is optimal, most Americans consume far more omega-6s than omega-3s, yielding a ratio skewed at least 10:1 in favor of omega-6s. Some estimates put the ratio as high as 40:1.



One researcher calculates that consumption of omega-6s has increased 1,000-fold since the early 20th century, literally changing the composition of our brains and bodies. Studies have shown that when cells are deprived of vital omega-3s, they attempt to compensate by incorporating saturated fats in cell membranes. The result is a stiff and ineffectual structure that must serve as the cell's means of "commerce" and exchange with the rest of the body. Because omega-6s break down

into arachidonic acid in the body, and arachidonic acid is converted to highly inflammatory chemicals, a huge increase in the availability of arachidonic acid translates into a huge increase in the potential for inflammatory and autoimmune diseases. Omega-3s, on the other hand, are converted by the body to series 1 and 3 prosta-glandins which serve to counterbalance the inflammatory effects of the series 2 prostaglandins, derived from arachidonic acid.

Here's a look at some of the diverse ways in which omega-3s can improve health and extend life.

Promise Shown Treating Arthritis

Arthritic complaints are rare among the Inuit, and the omega-3s in their diet are evidently the reason. Clinical trials have examined the effectiveness of omega-3 supplementation in a variety of inflammatory and autoimmune diseases, including rheumatoid arthritis, Crohn's disease, lupus erythematosus, psoriasis, multiple sclerosis, and migraine headaches. Many of these placebo-controlled trials have demonstrated significant benefits. In some cases patients have been able to reduce reliance on anti-inflammatory drugs, such as non-steroidal anti-inflammatories (NSAIDs), for relief from painful symptoms.³²



Arthritis is actually a range of diseases, all of which have joint inflammation in common. Omega-3s excel at quelling inflammation. Although experts have recognized this beneficial effect for years, recent research has shed light on the exact mechanisms involved.



A number of diseases are associated with a high level of interleukin-1B (IL-1B), a pro-inflammatory cytokine. Arthritis is associated with an increase in IL-1B and the pro-inflammatory leukotriene LTB(4), which is indirectly produced by the body from arachidonic acid. Arachidonic acid is derived from omega-6 fatty acids and gives rise to a class of immune system compounds that promote pain and inflammation. Studies have shown that when omega-3 and omega-6 fatty acids are balanced (that is, when the ratio of omega-6 to omega-

3 in the body is about 1:1 to 4:1), far less arachidonic acid is available for conversion to harmful eicosanoids and cyto-kines. Fewer of these compounds in circulation means less inflammation.

Besides "crowding out" excess arachidonic acid, the omega-3s aid the body in other ways, too. They have been shown to act on intracellular signaling pathways, to influence transcription

factor activity, and to modulate gene expression. All of these effects may combine to alleviate inflammation and disease. As one researcher noted: “Many of the placebo-controlled trials of fish oil in chronic inflammatory diseases reveal significant benefit, including decreased disease activity and lowered use of anti-inflammatory drugs.”³² Another scientist reviewed nearly two decades of published research on the use of fish oil in the treatment of rheumatoid arthritis and concluded: “Treatment with fish oil has been associated with improvement... in rheumatoid arthritis.”³⁴

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Omega-3s and Neuropsychiatric Disorders

Evidence is mounting that after several generations of omega-3 deprivation, Americans’ overall health is deteriorating. Depression, suicide, violence, and formerly rare and mysterious disorders, such as autism, are becoming increasingly common. It is impossible to quantify the exact effects of a simple but profound change in the diet of an entire nation. But some scientists believe that a move away from a balanced ratio of omega-6 to omega-3 fatty acids, which began about a century ago, has affected us in ways we are only now beginning to comprehend. And the changes have been anything but positive.

Heart disease and cancer rank among our biggest killers. It is no coincidence that most Americans consume far too few omega-3s, nor is it a coincidence that omega-3 supplementation has been shown to improve cardiovascular health and to inhibit certain types of cancers.^{37-39,44} Is there a similar connection between simple diet and the rising incidence of disorders such as dyslexia, ADHD, depression, schizophrenia, and autism? Some scientists are convinced the answer is “yes.”



And speculation regarding omega-3s’ role in neurological health does not end there. Experiments have shown that supplementation with the omega-3 fatty acid DHA increases the frequency of a particular type of brain wave that is associated with memory and learning.⁴² Other studies have shown that infants receiving adequate omega-3s develop visual acuity sooner and perform better on intelligence tests than infants deprived of sufficient omega-3s.²⁵⁻²⁸ Omega-3s are supplied naturally in breast milk, provided the mother’s intake of omega-3s from plant or marine sources is adequate. But until recently, crucial omega-3s were absent from commercial infant formulas. Even now, omega-3s are only available in special, more expensive infant formulas.

Aversion to Fish May Be Depressing

For several years, researchers have noted a correlation between omega-3 deficits and severity of depression. Patients with the lowest levels of essential omega-3 fatty acids tend to be the most severely depressed, while healthy control subjects are more likely to have normal levels of omega-3s, as measured in red blood cell membranes.¹⁷ In a recently published clinical paper, researchers in the Netherlands reported that subjects with low levels of omega-3 fatty acids (and high omega-6 to omega-3 ratios) were significantly more likely to be depressed than those whose levels of omega-3s approached a more balanced level. The study group consisted of more than 3,000 adults over the age of 60, and inflammation and atherosclerosis were ruled out as confounding factors. The finding, researchers noted, “suggests a direct effect of fatty acid composition on mood.”¹⁵



The relationship between mood and fatty acid composition in the body also has been confirmed by research conducted in the U.S. by Andrew Stoll, M.D., Assistant Professor of Psychiatry at Harvard Medical School and director of the Psychopharmacology Research Laboratory at McLean Hospital in Belmont, MA. Dr. Stoll has focused his extensive research efforts on depression (including post-partum depression) and bipolar disorder (or manic-depressive illness). In numerous medical journal articles and in his book *The Omega-3 Connection*, Dr. Stoll has documented impressive results with omega-3 supplementation among patients ranging from those with treatment-resistant major depression to

post-partum depression and bipolar disorder.^{16,18}

Other researchers also have confirmed a definitive link between consumption of omega-3s and mental health. Studies have examined either blood or adipose tissue levels of omega-3s. They have consistently revealed a correlation between low levels of omega-3s and depression.¹² Omega-3 supplementation has proven effective in the treatment of mild to moderate depression, or as an adjunct to therapy with modern drugs, especially in bipolar disorder. But there appears to be a point at which omega-3 supplementation is too little, too late. Supplementation appears to be largely ineffective in cases of major depression.¹⁹ One small but well-designed study found no significant benefit from treatment of major depression with DHA versus placebo.²⁰ Even in these cases, however, omega-3 supplementation may provide a boost to standard therapy, particularly in treatment-resistant patients.²¹

As Dr. Stoll points out in *The Omega-3 Connection*, the link between omega-3s and heart health is well established and fairly well known among the general public. But research linking mood and omega-3s is relatively new, and much remains to be explored. Some studies provide indirect evidence of the importance of omega-3s to normal brain function, but definitive work remains to be done before scientists and the public are likely to embrace the notion that something as simple as changing dietary habits can affect so many lives, in so many ways, so profoundly.

The brain-health connection is hardly surprising, however—lipids are integral to the structure and function of the brain, which comprises about 60% lipids (fat). What is surprising is that brain-lipid abnormalities are only now receiving the close scrutiny they clearly deserve. The leukodystrophies, for instance, represent an entire class of neurological disorders caused by flaws in the fatty myelin sheath, which insulates a key component of nerve cells and allows propagation of nerve signals. Some scientists are suggesting that neuropsychiatric disorders such as dyspraxia (loss of coordination), autistic spectrum disorders, ADHD, schizophrenia, and dyslexia – which often have features that overlap one another – should be re-classified under the blanket term phospholipid spectrum disorders. This new term recognizes the underlying cellular lipid abnormalities that link these seemingly disparate yet related disorders.²²



In essence, phospholipid spectrum disorders are characterized by abnormalities in the phospholipid and fatty acid composition of neural membranes. Cell membranes play a crucial role in controlling the flow of chemicals and nutrients trafficking between cells' interiors and the outside. Cell membranes are largely composed of lipids, so any abnormalities in those lipids may cause interruptions in normal communication among neurons. Traditionally, scientists have sought to improve communication by focusing on the neurotransmitters, which carry messages from cell to cell. In the case of depression, for instance, it is believed that symptoms arise when the normal flow of serotonin, a powerful mood-regulating neurotransmitter, is interrupted.

Indeed, many groundbreaking therapies, including the new class of selective serotonin reuptake

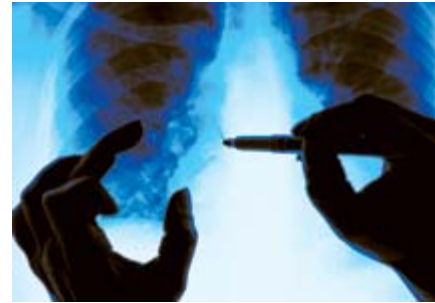
inhibitors (SSRIs), such as Prozac® and Zoloft®, have succeeded by enhancing the availability of one or more neurotransmitters. But the newer, phospholipid-spectrum-disorders approach revisits the problem by addressing underlying abnormalities in cell membranes. Because omega-3s fill an invaluable niche in cellular membrane architecture, it follows that correcting deficits in omega-3 supplies will improve cellular membrane function, thus improving intercellular neurotransmitter transport and ultimately restoring normal brain function.

Fish Oil: Protective Against Lung Disease?

Results from studies on the use of fish oil in the treatment of chronic lung diseases—such as emphysema, asthma, bronchitis, and the debilitating genetic disorder, cystic fibrosis—have been both tantalizing and inconclusive. Omega-3 supplementation in diseased subjects has produced encouraging results overall, but there are inconsistencies.

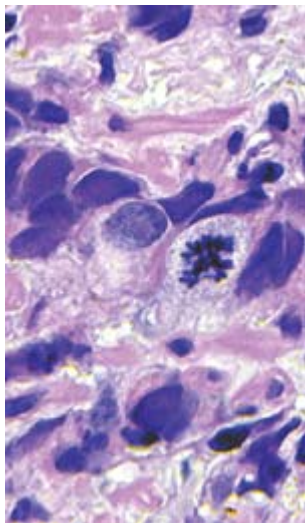
One small study on cystic fibrosis patients found significant improvement, especially decreased inflammation, among those receiving both DHA and EPA for eight months.

Patients receiving omega-3s required fewer antibiotics to control chronic lung infections and did better on tests of lung capacity. Other researchers have reported improvements in biochemical markers of disease, but little or no evidence of clinical changes. In the case of asthma, research reveals more improvement among children than adults, but further, larger studies would be required to rule out chance. Trials on smokers have indicated that omega-3s are protective against emphysema and chronic bronchitis, and yield an improvement in spirometry values (a measure of lung capacity). Another trial found a correlation between fish oil consumption and improvement in lung capacity even among non-smokers.⁴³



After reviewing published evidence from around the world, Harvard researcher Joel Schwartz concluded: "...a case can be made for why dietary intakes of PUFAs [polyunsaturated fatty acids (including omega-3s)]...might both be protective against lung disease and ameliorate the normal decline in lung function with age."⁴⁰ Schwartz notes, however, that more research is in order: "It is reasonable to study the relation between dietary PUFAs and both lung disease and the normal aging process in the lung."

Fish oil supplementation, then, holds promise not only as a health-improving strategy for those with lung disease, but also as a hedge against the normal effects of aging on the lungs of otherwise healthy individuals. As Schwartz notes, "There is clear evidence of an effect of omega-3 fatty acids on potential modulators of lung disease."⁴⁰ Clearly these intriguing results warrant further investigation and provide another example of the unexpected potential benefits of omega-3s.



Thwarting Cancer with Omega-3s

Studies have shown that omega-3s can slow the growth of experimentally induced cancerous tumors, improve the effectiveness of chemotherapy, and reduce the side effects of chemotherapy and cancer. Several mechanisms of action have been proposed to explain these multiple benefits. Omega-3s may suppress nuclear factor-kappaB activation and bcl-2 expression, allowing cancer cells to self-destruct. Omega-3s may also decrease the rapid growth of both cancer cells and the all-important blood supply that fuels the cells' unnaturally accelerated growth, by suppressing the expression of cyclooxygenase-2 in tumors. And omega-3s may interfere with the activity of two tumor-promoting genes.

Perhaps most amazing of all, omega-3s may induce cancer cells to differentiate. This is particularly significant, because cancer is a disease characterized by otherwise ordinary cells run amok. Cancer cells are undifferentiated; instead of behaving according to their specific identities (for example, a blood cell behaves as a blood cell, not as a retinal cell), cancer cells "lose their identity," so to speak. Instead of performing specific duties and following strict "rules" governing growth and dissemination, undifferentiated cancer cells are interested in unbridled growth alone, to the detriment of all else.

"It seems reasonable to assume that after appropriate cancer therapy, consumption of omega-3 fatty acids might slow or stop the growth of metastatic cancer cells, increase longevity of cancer patients, and improve their quality of life," concluded one team of researchers.⁴⁴ Another team noted: "There is both epidemiologic and experimental evidence that the long-chain omega-3 fatty acids...exert protective effects against some common cancers, notably those of breast, colon, and, perhaps, prostate."³⁷ Other researchers added skin cancer to the list, finding that DHA is more effective at preventing skin cancer than EPA, and noting that a balanced ratio of dietary omega-6 to omega-3 fatty acids may play an important role in this effect.⁴⁵ As in other areas of omega-3 research, more work needs to be done to further illuminate the potential cancer-preventing properties of omega-3s.

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Shining Eyes, Glowing Skin, and All the Rest

Fish oil shows promise far exceeding improvements in cardiovascular health. Studies show that omega-3s are vital to the proper development of vision in developing infants and that a deficiency in the nursing mother may result in insufficient milk production and breast engorgement. Research shows that omega-3s may improve vision among alcoholics who have experienced alcoholism-related vision impairment. Omega-3s also may play a significant role in preventing age-related macular degeneration.



Omega-3s are under investigation for the treatment of conditions ranging from chronic (post-viral) fatigue syndrome⁵⁷ and psoriasis to atopic dermatitis and post-menopausal bone loss.⁵⁸ Results generally have been encouraging, but further research is needed. Supplemental fish oil has even been used in the treatment of pancreatitis, a painful condition often accompanied by abnormally high levels of triglycerides.⁵⁹ Fish oil has been proven to reduce triglyceride levels, even among otherwise healthy individuals.

Getting Yours— How Much Is Enough?

Although no formal dietary guidelines have yet been established, the U.S. Food and Drug Administration has ruled that intakes of up to 3,000 mg (3 g) per day of omega-3 fatty acids derived from fish oil are Generally Recognized as Safe (GRAS). Many studies have reported positive results with as little as 2,000 mg (2 g) of omega-3s per day. For the average adult, it is probably advisable to consume at least 3 g daily of supplemental omega-3s, depending on dietary intake (fish consumption) and need. People with pre-existing disease conditions, for instance, may require higher doses than healthy individuals to achieve maximum benefits. Intake of omega-6 fatty acids should also be taken into consideration. In general, it is best to reduce omega-6 consumption while increasing omega-3 consumption to achieve a balance between these essential nutrients.

Attention also must be paid to the concentration of EFAs in a given supplement. Some supplements have such a low concentration of DHA and EPA, that seven or more capsules a day are needed to obtain minimum potencies. Higher concentrated supplements are available that provide more DHA/EPA in fewer capsules. Taking supplements with food is generally recommended for better tolerability. Omega-3s decrease blood viscosity and platelet aggregation, an action that explains at least some of the cardiovascular benefits conferred by these EFAs. Because of this, however, individuals taking blood-thinner medications should consult with their physicians before beginning supplementation in order to avoid the risk of excessive bleeding.

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