

# HS-Omega-3 Index<sup>®</sup>



## Clinical Applications





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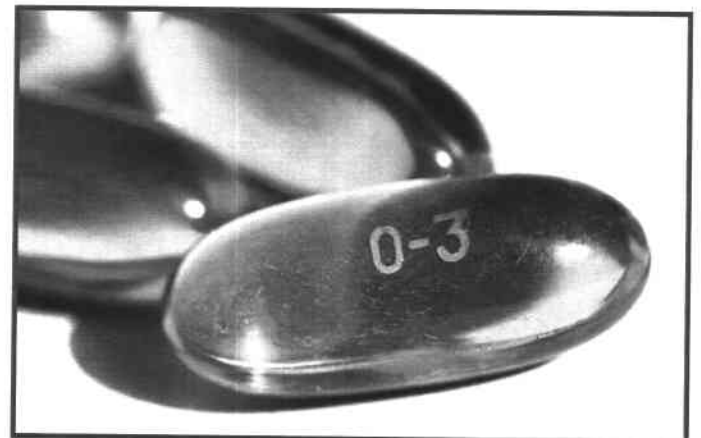
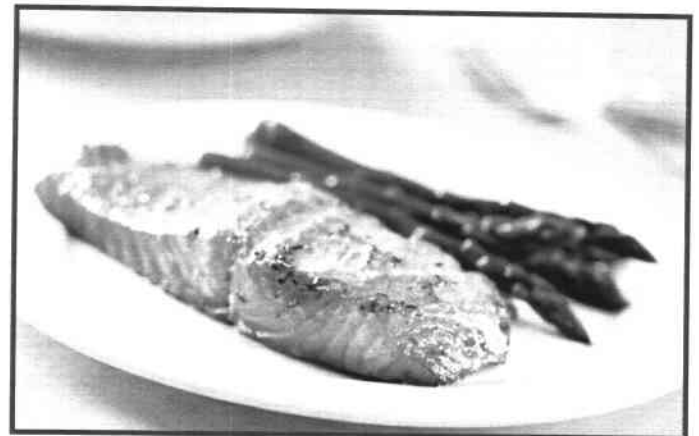
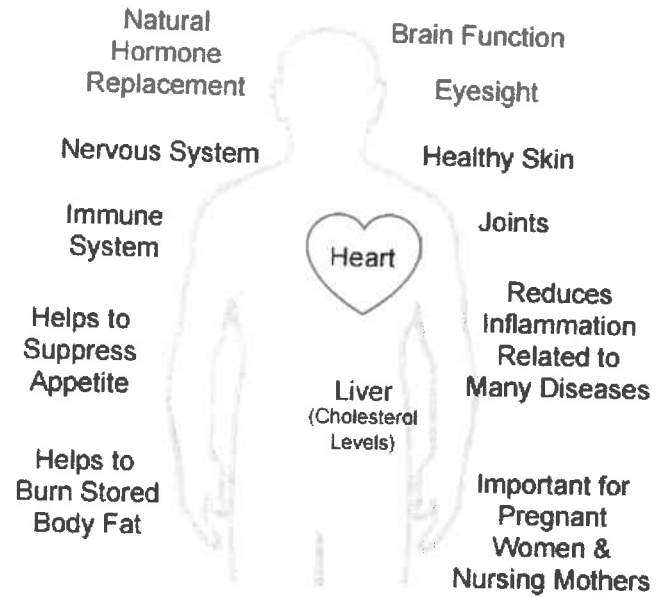
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## Health Benefits of Omega-3



# HS-Omega-3 Index®

from SpectraCell Laboratories, Inc.

## FATTY ACIDS IN THE BODY

Fatty Acid Type	Common Sources	Chemical Properties	Characteristics
Saturated	Meat, butter, coconut oil, palm oil	No double bonds	Required for healthy lung function, antimicrobial and antiviral properties
Monounsaturated	Olive oil	One double bond	Associated with favorable lipid profile
Polyunsaturated	Fish oils Vegetable oils	More than one double bond	Depending on the source, can be very healthy or very unhealthy
Trans	Hydrogenated oils and fats	Synthetic – created to make food shelf stable	Never healthy, Strongly linked with heart disease. Stiffen cell membranes

Dozens of fatty acids exist in the body, each with unique chemical properties. The major categories of fatty acids are listed in the table below, but the omega-3 fatty acids are the focus of much research today due to their incredible health properties. Since humans cannot synthesize them, it is essential that we obtain them from our diet, hence they are commonly called essential fatty acids. They are named Omega -3 because of their specific chemical properties, and the two most commonly researched omega-3 fats are DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid).

Polyunsaturated Fatty Acids	Common Types
Omega-6 Fatty Acid	Linoleic Gamma-linolenic Arachidonic
Omega-3 Fatty Acids	EPA (Eicosapentaenoic Acid) DHA (Docosahexaenoic Acid) ALA (Alpha-Linolenic Acid)

## ESSENTIAL FATTY ACIDS

Three essential fatty acids exist: linoleic acid (omega-6), arachidonic acid (omega-6) and alpha-linolenic acid (omega-3). However, the conversion of these essential fatty acids into DHA and EPA is inefficient in the human body. Nutrient deficiencies and a high concentration of other fatty acids will further interfere with this conversion so the best way to ensure adequate levels of omega-3 fats is through consumption. Ingestion of omega-3 fats via food or supplements, especially DHA, is a very effective way to increase their levels throughout the body. In most tissues,

there is a linear dose response to supplementation.<sup>982</sup>

The most common source of omega-3 fats is cold water fatty fish such as salmon, but other sources include seafood, nuts, eggs and fish oil supplements. Since genetic and lifestyle differences are so vast between patients, the best way to know whether a patient has sufficient fatty acid levels is to measure the HS-Omega-3 Index®.

## HS-OMEGA-3 INDEX®

The HS-Omega-3 Index® measures the amount of two very important omega-3 fatty acids – EPA and DHA – in a person's red blood cells. The HS-Omega-3 Index® reflects long-term intake of EPA and DHA, and the higher the content of these fatty acids, the lower the risk of a fatal heart attack and dozens of other pathologies. Several other fatty acids are also measured in this test. (see table below)

For the HS-Omega-3 Index®: Higher is better. When the HS-Omega-3 Index® is above 8%, there is a 90% reduction in risk of sudden death, whereas an index less than 4% has the most risk.<sup>996</sup> Omega-3 fatty acids influence enzyme and hormone systems throughout our entire body, and although they have gained attention primarily from their cardiovascular benefits, they alleviate symptoms of dozens of other conditions as well. They are especially beneficial for reducing inflammation and regulate many biological processes affecting the immune, respiratory, reproductive and neurological systems among others.

Type of Fatty Acid	How many of these fatty acids are measured by HS-Omega-3 Index®
Omega-3 Fats	4
Omega-6 Fats	7
Monounsaturated	4
Saturated	6
Trans	3
Fatty acid ratios	2

## OMEGA-6 TO OMEGA-3 RATIO

The HS-Omega-3 Index® will also tell a person the ratio of omega-6 to omega-3 fatty acids in their body. Omega-6 fatty acids generally contribute to inflammation while omega-3 fatty acids reduce whole body inflammation. Our Paleolithic ancestors, who were completely free of degenerative diseases like heart disease, arthritis and dementia, maintained an omega-6 to omega-3 ratio around 2:1. The modern Western industrialized diet has dramatically

changed that ratio to closer to 15:1 or even higher for the average American.

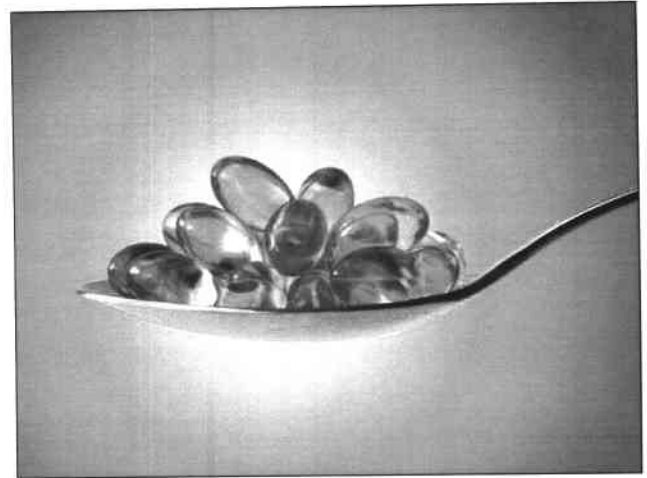
## ARACHIDONIC ACID (AA) TO EPA RATIO

The AA:EPA ratio is another indicator of the ratio of inflammatory to non-inflammatory fatty acids in the body. The higher this ratio, the more systemic inflammation that is present, which ultimately causes pain and an acceleration of degenerative disease. An increase in either the omega-6:omega-3 ratio or the AA:EPA ratio contributes to several disease states.



## WHY OMEGA-3 FATTY ACIDS AFFECT SO MANY FUNCTIONS IN OUR BODY

The answer is simple: cell membrane flexibility. Every cell has a cell membrane. When this cell membrane is rigid, it does not work well. When it is flexible, the chemicals that run our bodies – hormones, proteins, enzymes, vitamins, minerals, fats, etc – can move in and out of cells efficiently as needed, thus making the cells healthier, since the materials they need to function well are available. When the cells work well, the tissues that are made of cells work well. When tissues work well, the whole system works well and ultimately leads to overall improved health of the entire person.



For example, when there are enough omega-3 fatty acids available through either diet or supplementation, they will be absorbed into cells in the heart, making their cell membranes flexible, but strong. Consequently, the heart and arteries are stronger and therefore the entire cardiovascular system benefits. In fact, in the same way that omega-3 fats make cell membranes more flexible, the dangerous trans fats do the exact opposite – they are absorbed into the cell membranes making them stiff and unable to do their job. Just as stiff joints or stiff arteries are unhealthy, so are inflexible cell membranes. And since cell membranes are an integral part of every tissue in the body, the level of omega-3 fatty acids a person has can affect just about everything.

ADHD	Cholesterol Levels	Immunity	Psychiatry
Alzheimers	Chronic Fatigue	Inflammation	Sports Medicine
Arrhythmia	Syndrome	Insulin Resistance	Triglycerides
Arthritis	Cognitive Function	Kidney Disease	Telomeres
Asthma	Depression	Liver Disease	
Autoimmune Disease	Diabetes	Macular Degeneration	
Autism	Erectile Dysfunction	Maternal & Infant Health	
Brain Injury and	Eye Health	Metabolic Syndrome	
Concussion	Fertility	Neurology	
Cancer (breast, colon, etc)	Gum Disease	Oxidative Stress	
Cardiovascular Disease	Heart Failure	Pain	
	Hypertension	Peripheral Vascular Disease	

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## CLINICAL INTERPRETATIONS BY: PETER JAKACKI, MD

The basic unit of the body is the cell. The outer membrane of every cell has a lipid bi-layer. The fats found in our diet greatly influence the fatty constituents of every cell, particularly those parts of our body higher in fat content, such as our brain which is 60-70% fat. Essential fatty acids (EFAs) are those which must be provided by the diet and cannot be made by the human body. **Three EFAs** exist: two omega-6 fatty acids – **Linoleic and Arachidonic acids** and one omega-3 fatty acid – **Alpha-Linolenic Acid**. While these are essential to life, the ideal balance of Omega-6 to Omega-3 intake is between 1:1 to 3:1. Unfortunately, the Standard American Diet (SAD) which is full of processed foods and vegetable oils, provides an excess of omega-6 fats with a ration of Omega-6 to Omega-3 fatty acids of ~30 to 40:1. Omega-6 fats are found in abundance in processed foods and vegetable/plant oils, such as corn, safflower, sunflower, cottonseed, sesame, peanut and canola oils. Too many omega-6 fats promote inflammation, pain, cancer and heart disease.

An **HS-Omega-3 Index®** of over 8 correlates with a greater than 90% reduction in sudden cardiac death. Of the three Omega-3 fatty acids, Alpha Linolenic Acid (ALA), Eicosopentanoic Acid (EPA) and Docosohexaenoic Acid (DHA), only ALA is considered absolutely essential. A higher ALA level was found at a recent American Heart Association meeting to correlate with reduced cardiac risk. However, the body can convert only ~5% of ALA to EPA and ~0.5% of EPA to DHA. Deficiencies of zinc, magnesium and vitamin B6, in addition to hyperinsulinemia as well as high concentrations of saturated, monounsaturated and trans fats can all interfere with this critical conversion of ALA to EPA and DHA. Thus very little ALA from flax seeds, nuts and vegetables make it to EPA and DHA, which must be provided from either fish, fish oil or DHA from algae. EPA reduces inflammation, elevates mood and works positively in the blood vessels to reduce clotting. DHA comprises 11% of the weight of the brain and is extremely rich in the retina of the eye. DHA is important for cognition, memory and neurodevelopment. EPA and DHA are often found low with depression, bipolar disorder, schizophrenia, ADHD and Alzheimer's disease. They are anti-inflammatory and thus can reduce pain over time. Fish oil increases tissue and cell membrane flexibility and can thus influence cell receptor responsiveness to hormones such as testosterone, estrogen and progesterone.

**Trans-fats** are so bad for health that they have been banned from New York City restaurants since January of 2007 and stricken from many events. While the FDA now mandates that foods be labeled for their trans fat content, it allows foods to be labeled as having "No Trans Fats" if they have less than 500mg per serving. Reading the list of ingredients identifies trans fats by seeing the terms hydrogenated or partially hydrogenated. Trans fats stiffen cell membranes, potentially increase inflammation and pain, may reduce testosterone, increase ADHD and decrease cognition. When vegetable oils are cooked under high heat and/or pressure, they are often transformed into trans fats. It is critical to your overall health to eliminate or reduce trans fat intake as much as possible.

**Monounsaturated-fats** such as oleic acid can be quite healthy. Oleic acid is found in extra virgin olive oil and can be made by the human body, if one has adequate essential fatty acids and zinc. Oleic acid helps to form oleamide which is necessary for the function of the serotonin receptor. The Lyons Heart study found that the Mediterranean diet, high in monounsaturated fats, resulted in a 70-90% reduction in heart disease.

**Saturated-fats** can be produced by the human body, especially from carbohydrates. Sources of saturated fats from the diet include meat, butter, nonhydrogenated lard, palm oil and coconut oil. Saturated fats are not as bad as everyone makes them out to be. Much of the bad rap associated with saturated fats originates from the fact that trans fats have always been grouped in with saturated fats. Saturated fats serve many important functions in the body. The majority of the fats in the brain are saturated. Surfactant which lubricates the lungs and is required for healthy lung function is 100% saturated. They protect the liver from alcohol and medications, including acetaminophen.

Other important functions include being the preferred fuel for the heart, useful antiviral agents, effective anticaries, antiplaque and antifungal agents, modifiers of genetic regulation and prevent cancer; required for calcium to be effectively incorporated into bone, necessary to stabilize cell membranes and important in immune health.

The **Arachidonic Acid to EPA ratio (AA:EPA)** is one indicator of your ratio of inflammatory to noninflammatory fatty acids. The higher the AA:EPA ratio, the more likely one's fatty acid balance is off with a resultant increase in pain, menstrual cramps, heavier menstrual periods, headaches, exaggerated pain from injuries and inflammation.

**How to change your fatty acid composition:** By altering your diet. Eating grass-fed beef and buffalo as well as free-range chicken, turkey and duck, can increase omega-3 vs. omega-6 fatty acid content. Eat tree nuts, such as walnuts, pecans, almonds, cashews and macadamia nuts to increase your intake of monounsaturated fats and ALA. Eating fish will increase EPA and DHA but unfortunately, most fish have been contaminated with mercury, PCBs and many other toxins. Thus fish and/or krill oil are the best way to increase EPA and DHA. Eliminating processed foods and reducing intake of vegetable and plant oils is crucial to reducing your intake of omega-6 fats to help achieve a healthier balance of Omega-6 to Omega-3 fat intake.

	Notes	High Risk	Intermediate Risk	Optimal	High Risk Range	Intermediate Risk Range	Optimal Range	Previous Results
Indexes	HS-Omega-3 Index* (RBC EPA+DHA)*		7.0		< 4.0%	4.0% - 8.0%	> 8.0%	
	Trans-Fat Index		0.7		> 1.3%	0.7% - 1.3%	< 0.7%	

Fatty Acids	Range	Current	Previous
Omega-3 Total	0.1% - 14.1%	11.0%	
Alpha-Linolenic (ALA)	0.1% - 0.4%	0.2%	
Docosapentaenoic (DPA)	0.6% - 4.1%	3.7%	
Eicosapentaenoic (EPA)	0.1% - 2.5%	1.9%	
Docosahexaenoic (DHA)	0.1% - 8.4%	5.1%	

Fatty Acids	Range	Current	Previous
Omega-6 Total	28.6% - 44.5%	30.7%	
Arachidonic (AA)	10.5% - 23.3%	11.8%	
Linoleic (LA)	4.6% - 21.3%	14.5%	

Fatty Acids	Range	Current	Previous
cis-Monounsaturated Total	11.5% - 20.5%	16.2%	
Saturated Total	36.6% - 42.0%	41.5%	

**Comments:**

**Your HS-Omega-3 Index is below the target range of 8%.**  
 The HS-Omega-3 Index is the EPA+DHA content of RBC membranes. Increasing the intake of EPA+DHA by 1/2 to 1 gram (500 - 1,000 mg) per day, from either oily fish or fish oil supplements, should significantly improve the index. The exact amount of EPA+DHA needed will vary person to person. A re-check should be done in 3 - 4 months. Once your HS-Omega-3 Index is above 8%, it should be monitored annually.

**Your Trans-Fat Index is about average for US adults but is above the target of 0.7%.**  
 The trans fatty acids measured in this test are those that come directly from eating "industrially-produced," hydrogenated vegetable oils such as those used in commercially-baked and fried foods. Reducing the intake of trans-fat-rich foods will lower RBC trans-fat levels, and this should be detectable within 3 - 4 months. Once your Trans-Fat Index is below 0.7%, it should be monitored annually.

Analysis Performed at HDL Laboratory, Inc. / 737 N. 5th Street, Ste 103 / Richmond, VA 23219 / CLIA # 49D1100708

Spectracell Laboratories, Inc.  
 CLIA #45D0710715

John F. Crawford, Ph.D.  
 Laboratory Director



# DISEASE STATES

## ADHD and AUTISM

Researchers first linked ADHD to essential fatty acid deficiency in the early 1980s, and recent years have seen an unprecedented rise in autism and attention deficit hyperactivity disorder (ADHD). Since our nerves and brain are composed mainly of fats, poor omega-3 fatty acid status can alter neurotransmitter function and inhibit brain performance on many levels. This deficiency has a greater impact on males because their requirements for essential fatty acids are, in general, much higher – one reason why autism occurs more frequently in boys.

Brain and nerve growth throughout childhood is extraordinarily rapid, and the need for omega-3 fatty acids remains critical all the way through adolescence and into adulthood. Our brains can actually create nerve pathways in response to new experiences and learning environments. Called “neuronal plasticity,” this phenomena is crucial for long-term memory and learning and proper levels of the omega-3 fatty acid, DHA (docosahexaenoic acid) are needed for this to occur.

The ratio of omega-6 fatty acids, which differ in structure and function, to omega-3 fatty acids also affects neuronal plasticity. Scientists now agree that the ratio of omega-6 fats to omega-3 fats is as important as the actual levels, especially in autism and ADHD. A lower ratio is better and when this ratio is improved, symptoms of autism and ADHD often improve.

Stimulant drugs such as Ritalin are commonly prescribed for ADHD but studies show that supplements can be equally effective in treating symptoms of ADHD.

One Oxford University study demonstrated that fatty acid supplements given to children for 3 months who struggled with ADHD resulted in improvements in reading, spelling and behavior, which were not seen in a placebo group. When the placebo group in this study were given the same supplementation of essential fatty acids as a second part of this trial, the same improvements were eventually seen.

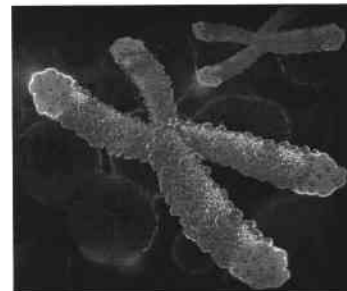
Differences in the fatty acid levels between people with ADHD and those without it are not wholly explained by differences in intake of either supplements or fatty acid-rich foods. This suggests that people with autism or ADHD are perhaps genetically predisposed to fatty acid deficiencies, and therefore metabolize fatty acids differently from normal controls. Children with low scores on behavioral assessment tests consistently have lower omega-3 fatty acids levels, and when supplemented with fish oils, the symptoms of ADHD in these children such as hyperactivity, impulsiveness and inability to pay attention – dramatically improve.

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## AGING and TELOMERE LENGTH

Omega-3 fats are certainly beneficial in slowing the aging process. There are several reasons for this – they reduce inflammation, help keep our cardiovascular system healthy, protect our brains – the mechanisms behind their protection against the diseases of aging are many. But a recent study shed light on an entirely different mechanism of action against aging: protection of telomeres.



A novel marker for biological age, telomeres are sections of genetic material that form a protective cap at the end of each chromosome in every cell of our body. When a cell divides, the telomere gets a tiny bit shorter until there is no more telomere left to protect our DNA from “unraveling” and the cell dies. This cell death causes our bodies to age, whether the cell is from heart muscle, skin or brain tissue.



A recent study on people with active heart disease showed that people with high blood levels of omega-3 fats had the lowest rate of telomere attrition. Specifically, people whose average HS-Omega-3 Index<sup>®</sup> was around 7% had a 5½% reduction in their telomere length over the course of five years. Conversely, those with an average HS-Omega-3 Index<sup>®</sup> of only 2% had a reduction of over 13% in telomere length. These findings suggest that omega-3 fatty acids protect against cellular aging.

In another study, the adoption of comprehensive lifestyle changes which included daily supplementation of 3 grams of fish oil was associated with an increase in telomeres in human leukocytes.<sup>322</sup> In animal studies, dietary enrichment of omega-3 fats prolongs life span by approximately one-third.

Although several mechanisms of protection exist, one way omega-3 fats protect telomeres is their effect on the hormone cortisol. When a group of men and women were given fish oils for six weeks, the levels of the stress hormone cortisol were significantly reduced. Cortisol is known to reduce the activity of telomerase, an enzyme that protects and even lengthens telomeres. For this reason, even stress-related cellular aging can be thwarted by omega-3 fatty acids.

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## ALZHEIMER'S DISEASE and COGNITIVE FUNCTION

Increased intake of omega-3 fatty acids from fish or marine oils lowers the risk of Alzheimer's.<sup>549</sup> In animal studies, treatment with EPA significantly improves memory, possibly from its role in regulating acetylcholine, a neurotransmitter that increases alertness. Improper function of this important neurotransmitter has been associated with the memory problems seen in Alzheimer's disease.

A high concentration of the omega-3 fatty acid EPA may decrease the risk of dementia according to a study on over 1200 people in France, especially in people who also have depression. Interestingly, the omega-3 fatty acid DHA did not show this same relationship in this particular study on older people, indicating that fatty acids may affect specific symptoms of dementia independently. For example, EPA seems to benefit depressive-like symptoms of Alzheimer's disease, whereas DHA tends to benefit cognitive symptoms. The ratio of AA (arachidonic acid) to DHA did show a direct relationship with dementia, however.<sup>466</sup> Likewise, several studies confirm the link between the ratio of omega-6 to omega-3 fats to cognitive function throughout life: the lower the ratio, the lower the risk of dementia.

In fact, evidence suggests that maintaining adequate levels of DHA in brain tissue may not only be critical for Alzheimer's prevention but that higher DHA levels improve cognitive function and memory throughout a person's entire lifespan. A recent study on adults between 35 and 54 years old showed conclusively that those with higher levels of DHA in their blood had better memory and mental flexibility.<sup>1005</sup> In some experiments, omega-3 fatty acid supplementation actually reverses age-related changes to memory decline.<sup>1086</sup>

Supplementation with DHA may protect brain tissue from the dangerous neurotoxins commonly seen in Alzheimer's patients.<sup>1017</sup> A compound called neuroprotectin D1 (NPD1) has been identified as a bioactive product of DHA that is responsible for much of the protection this omega-3 fat imparts to the brain. NPD1 represses the action of pro-inflammatory genes which are turned on by the protein deposits (amyloid plaques) characteristically seen in brain tissue of Alzheimer's patients.<sup>1242</sup> Not surprisingly, lower than normal levels of NPD1 occur in the brains of Alzheimer's patients.<sup>1305</sup>

Although the evidence suggests that DHA is useful in preventing Alzheimer's, clinical trials show that may not be effective in treating people who already have the disease. One recent study evaluated people who already had progressive Alzheimer's disease. They were given 2 grams of DHA daily for 18 months, and their rate of cognitive function did not slow.<sup>1461</sup> This suggests that knowing the levels of omega-3 fats is particularly important before other clinical symptoms develop.

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## AUTOIMMUNE DISEASES (ARTHRITIS, ASTHMA, INFLAMMATORY BOWEL DISEASE, PSORIASIS)

Fatty acids are building blocks for chemicals involved in a natural and healthy immune response. Depending on which fatty acids are available – omega-3 or omega-6 – the resulting chemicals will either promote or reduce an inflammatory response. Since omega-3 fats compete with omega-6 fats, the body will produce certain molecules (specifically, eicosanoids) with whatever is available, regardless of whether or not they damage or heal tissue. Increasing the amount of ingested omega-3 fats displaces omega-6 fats, thus alleviating many symptoms of arthritis, asthma, psoriasis, Crohn's disease and others.

### ASTHMA

Increasing the amount of omega-3 fatty acids through fish oil supplementation has beneficial effects on symptoms of asthma, especially in children,<sup>699</sup> probably because the ratio of omega-6 to omega-3 fats in asthmatics is much lower than in healthy controls.<sup>1396</sup> When a deficiency in omega-3 fatty acids exists, inflammatory hormones can decrease lung function in susceptible individuals, ultimately causing the breathing difficulties seen in asthmatics.

### ARTHRITIS

Population studies suggest both a preventative and drug-sparing effect of omega-3 fatty acids on both osteo and rheumatoid arthritis.<sup>1539,1542,1543</sup> For example, when arthritic patients were given a prescription anti-inflammatory drug combined with omega-3 fatty acids, those taking fish oils experienced less pain, stiffness and tender joints than those on the anti-inflammatory drug only. Similarly, the presence of omega-3 fatty acids appeared to enhance the effects of the pain relieving drug, indomethacin.<sup>983</sup> In addition, there seems to be a synergistic effect with glucosamine sulfate when combined with omega-3 fatty acid supplementation.<sup>1540</sup>

### INFLAMMATORY BOWEL DISEASE

Also known as Crohn's disease or ulcerative colitis, symptoms of IBD can be alleviated by fish oil supplementation, although different trials have shown varying levels of clinical benefit.<sup>1544</sup>

One study that decreased intestinal flare-ups of Crohn's disease patients used a dose of 2.7g of fish oil.<sup>494</sup> In another study on adults with irritable bowel syndrome, serum levels of omega-3 fatty acids were decreased compared to controls.<sup>1518</sup>

### PSORIASIS

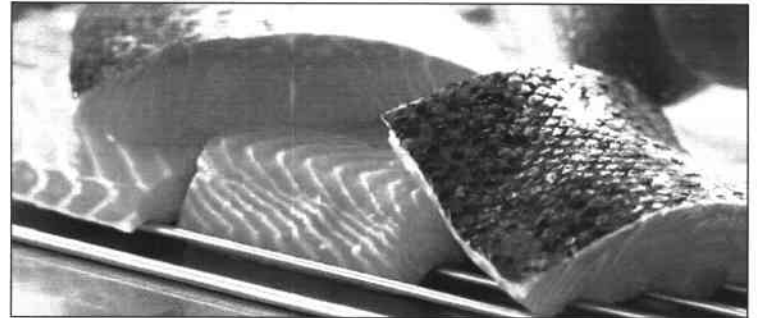
Clinical trials on omega-3 fats administered intravenously have been effective in the treatment of the autoimmune disorder of the skin, psoriasis.<sup>1528</sup> Omega-3 fats help keep the proinflammatory compounds, which are markedly elevated in psoriatic plaques, at bay. In addition, fish oil can reduce side effects of some immune suppressing drugs that are used to treat psoriasis.<sup>494</sup>

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## CANCER

Several studies support the theory that a healthy HS-Omega-3 Index<sup>®</sup> reduces cancer risk, although the mechanisms by which they accomplish this are not totally understood. Omega-3 fats have also been shown to reduce oxidative stress, a potential cause of cancer, at the cellular level.<sup>1261</sup> In reality, omega-3 fatty acids may reduce cancer risk in a variety of ways. For example, one study demonstrated how DHA favorably alters gene expression by inducing apoptosis (programmed cell death) of cancerous colon cells, thus arresting their proliferation.<sup>485</sup> A similar effect has been seen on pancreatic cells. When chemoresistant pancreatic cells were treated with omega-3 fatty acids, a dose-dependent response was seen and the cancerous pancreatic cells stopped dividing.<sup>1423</sup> Tumors of the prostate have also shown decreased growth when treated with omega-3 fats.<sup>1425</sup>



Another theory on omega-3's anti-cancer properties is that omega-3 fats compete with other, unfavorable fatty acids for a place in cell membranes. Incorporation of dangerous fats (for example, trans fats) into cell and mitochondrial membranes changes the membrane properties, making it stiffer and impairing oxygen transmission into the cell, thus disrupting normal membrane structure. Ultimately, this causes hypoxia (low oxygen) in the cell, which has been linked to cancer.<sup>1424</sup>

Reducing the ratio of omega-6 to omega-3 fats may also affect cancer risk. Chronic disease, including cancer, was virtually unheard of in our Paleolithic ancestors who typically had an omega-6 to omega-3 ratio around 1:1, while in modern industrialized nations the ratio is often 15:1 or higher. For example, a ratio of 2 1/2:1 reduced rectal cell proliferation in patients with colorectal cancer. Interestingly, a ratio of 4:1 that contained the same absolute amount of omega-3 had no effect. Reducing the omega-6:omega-3 ratio facilitates programmed death of cancerous cells.<sup>1036</sup>



Similarly, when breast tissue (which is reflective of dietary intake) was examined in a case control study, a lower ratio of omega-6 to omega-3 fatty acids was associated with reduced risk of breast cancer.<sup>1036</sup> In another study on supplement use on over 35,000 women, researchers found that the use of fish oil is associated with a significantly reduced risk of breast cancer.<sup>1249</sup>

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## CARDIOVASCULAR DISEASE

### PREVENTING HEART FAILURE

About half of heart attacks are fatal because the heart muscle goes into arrhythmia, which means it short-circuits and cannot “reset” itself, resulting in sudden cardiac arrest, or heart failure. Research shows that heart muscle containing 8% or more of omega-3 fatty acids (most Americans only have about 4%) is capable of maintaining a regular heartbeat, after a heart attack, thus lowering the heart attack death rate by an astounding 90%. Double carbon bonds are known to conduct electricity and many scientists believe this is the mechanism for preventing heart failure – that the double bonds in an omega-3 fatty acid transmit electrical impulses in heart tissue, thus enabling the heart to maintain a regular heartbeat even after a heart attack occurs. So although omega-3 fats have not been shown to reduce the incidence of heart attack, they do prevent heart attacks from being fatal.<sup>996</sup>

### HEALTHIER LIPID PROFILE

Omega-3 fatty acids lower dangerous lipid (cholesterol) levels, often more effectively than drugs. Cholesterol is carried through blood vessels by spheres called lipoproteins, and the shape and size of these lipoproteins have a huge impact on how aggressively they contribute to atherosclerosis, or clogging of the arteries. The smaller these lipoproteins are, the more easily they can penetrate the walls of our arteries causing damage, and thus the more dangerous they become. Research has shown that supplementation with the omega-3 fatty acid, DHA increases LDL (low density lipoprotein) particle size, making it less likely to damage blood vessels and cause heart disease.<sup>985, 1522, 20</sup>

High dose supplementation with 4 grams per day of fish oil increases HDL, and these benefits on HDL were not seen with statin usage in the same study.<sup>925</sup> Omega-3 fatty acids also lower triglycerides (fat in the bloodstream) at pharmaceutical doses (greater than 3 grams per day).<sup>1469</sup> However, in dosages less than 900mg they lower a very dangerous type of fat called RLP (remnant lipoprotein), which has been named by the National Institutes of Health as one of the major risk factors for heart disease.<sup>726, 727</sup> Even intakes as little as 200mg daily of DHA can protect LDL from oxidation.<sup>994</sup>

### BLOOD PRESSURE LOWERING EFFECT

Omega-3 fats demonstrate a dose related response in hypertension and DHA appears to impart the most effective benefits, at least when compared to EPA. Studies have shown that eating coldwater fish three times weekly is as effective as high dose fish oil supplementation in reducing blood pressure.<sup>1065</sup> An immediate benefit on blood pressure is also seen with omega-3 fatty acid consumption. In one study, eating a meal high in omega-3 fats reduced arterial stiffness for up to six hours, compared to a control meal.<sup>1029</sup> Since omega-3 fats are so intimately involved in cellular signaling, their blood pressure lowering effect may stem from an improvement in endothelial function of blood vessel walls. Omega-3 fats also reduce thrombotic agents and improve arterial plaque fragility, indicating that their cardiovascular benefit is truly multi-factorial.<sup>FP256</sup>

### HS-OMEGA-3 INDEX® – A CARDIOVASCULAR RISK MARKER

According to the Physician's Health Study, blood levels of omega-3 fatty acids was one of only two cardiovascular risk factors that were statistically significant for sudden cardiac death after adjusting for controlling factors like smoking and age. (C-reactive protein was the other one.) Some propose that the HS-Omega-3 Index® may be more informative than any other cardiovascular disease risk factor since it is physiologically relevant, easily modified, independent of other risk factors and demonstrates outstanding clinical utility.<sup>986, 1019</sup>

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## CHRONIC FATIGUE SYNDROME

Although the causes of chronic fatigue syndrome (CFS) are multi-factorial, low levels of essential fatty acids seem to be a common finding in patients with this disease. Some researchers theorize that viruses, which are often implicated in the etiology of CFS, reduce the ability of a cell to manufacture certain essential fatty acids. In one study, a group of post-viral CFS patients reported that after three months supplementation with omega-3 fatty acids, their symptoms of fatigue and achiness were significantly improved.<sup>1229</sup> In another study, the ratio of omega-6 to omega-3 fatty acids was much higher in CFS patients compared to normal controls and this ratio was significantly and negatively correlated to the severity of the disease.<sup>141</sup>

Stress related hormonal changes have also been suspected of promoting chronic fatigue syndrome. In one small study, levels of cortisol and epinephrine which are typically elevated in response to stress were measured on a group of people exposed to thirty minutes of mental stress (math test). Both hormones showed a spike after the stressful period. Then the groups were given fish oil for three weeks and once again given a mental stress test while hormone levels were measured. After fish oil supplementation, the spikes in cortisol disappeared and the spike in epinephrine was significantly blunted. EPA and DHA lower the stress hormone norepinephrine as well.<sup>1232</sup>

Evidence also suggests that CFS is typically accompanied by lowered antioxidant status and increased systemic inflammation.<sup>157</sup> Specifically, CFS patients have higher levels of a protein called NFkB (nuclear factor kappa beta) that acts as a switch to turn inflammation on and off throughout the body. Omega-3 fatty acids inhibit the production of NFkB, thus alleviating many symptoms of CFS.<sup>156</sup>

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## DEPRESSION and PSYCHIATRIC ILLNESS

Since the majority (about 60%) of our brain and nerves are composed of fats, it is well documented that poor fatty acid status contributes to both the incidence and severity of depression.<sup>1151</sup> EPA and DHA are the most predominant omega-3 fatty acids in our brains and consequently, the most biologically relevant when it comes to mental health.<sup>251</sup> Since they are a key structural component of the cell membrane, they largely determine the biological properties of nerve and brain tissue cells.

Although both EPA and DHA generate neuroprotective metabolites, their mechanisms of action differ. The anti-depressive effects of EPA may be due to its conversion into prostaglandins, leukotrienes and other chemicals necessary for proper brain function.<sup>1139</sup> By increasing the fluidity of cell membranes, DHA enhances serotonin receptor activity, a feel-good hormone that gives a sense of well being.<sup>FP22</sup>

The levels of omega-3 fatty acids, especially DHA, profoundly affect a woman's susceptibility to postpartum depression. Several studies have confirmed a strong negative association of omega-3 fatty acid status with postpartum depression rates, even after controlling for other confounding factors. This effect appears to influence maternal depression rates both immediately and for up to 10 months after delivery.

Impaired mental focus, disturbed sleep patterns and other common depressive symptoms often respond well to fatty acid supplementation.<sup>283</sup> In many cases, fatty acids are successful in patients with treatment-resistant depression, although there is some debate as to whether the fatty acids simply augment the actions of anti-depressant drugs or have anti-depressive properties independent of medication.<sup>FP22</sup>

The ratio of omega-6 to omega-3 fatty acids (n6:n3) is equally important. Studies show that the more severe the depression, the higher the n6:n3 ratio typically is,<sup>495</sup> but also the more effective fatty acid (or fish oil) supplementation can be. In other words, the benefits of fatty acid treatment tend to be more pronounced when the patient has a diagnosed depressive disorder.<sup>1030</sup> Since depression and psychiatric disorders are often associated with increased lipid peroxidation, fatty acid supplementation may be particularly beneficial in these cases.<sup>213</sup>

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## DIABETES

Diabetes is a pathological condition associated with increased inflammation and decreased insulin sensitivity. The anti-inflammatory effects of omega-3 fatty acids exert insulin-sensitizing effects via various mechanisms. For example, omega-3 fatty acids bind to specific proteins in our cells, thus turning on the signal for anti-inflammatory chemicals. Recent in vivo studies show that the metabolic by-products of DHA play a role in the long-term resolution of inflammation, which resulted in improved systemic insulin sensitivity.<sup>1296</sup>

Another way in which omega-3 fatty acids protect against diabetes is by altering the level of triglycerides in our blood. In one animal experiment, a diet containing the essential fatty acids EPA, DHA and ALA (alpha linolenic acid) prevented the dangerous metabolic changes that were seen when an insulin resistance state was induced.<sup>483</sup> Fish oil supplements have also been shown to improve renal function in type 2 diabetics.<sup>984</sup>

In children with an increased genetic risk for type 1 diabetes, dietary intake of omega-3 fatty acids significantly reduced this risk. In the same study, this trend was confirmed when the percentage of omega-3 fatty acids in erythrocyte membranes (HS-Omega-3 Index<sup>®</sup>) was examined.<sup>43</sup>

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## EYE HEALTH

The retinal tissue in our eyes are constantly subjected to major environmental stresses such as intense light and high oxidative stress. Recently, a compound called neuroprotectin D1 (NPD1) has been identified as a by-product of DHA that exerts powerful protection of nerve and eye tissue against this oxidative stress. Retinal cells respond to oxidative stress by synthesizing NPD1, which turns on genes that regulate cell survival, thus protecting retinal cell integrity.<sup>1307</sup> This is one reason why the photoreceptor membranes in eye tissue contains the highest amount of DHA of any cell in our body – to protect against the lipid peroxidation that is implicated in the diseases of the eye where retinal damage occurs.<sup>1305</sup>



Since adult human retinal cells do not replicate, their preservation is particularly important. Omega-3 fatty acids help ensure proper blood vessel function in the retina, and the DHA derivative NPD1 blocks the expression of pro-inflammatory proteins as well.<sup>1308</sup>

Recent randomized controlled trials has confirmed that DHA levels are critical to proper eye function in both the very young and very old. For example, a study on infants where two groups were compared: one had formula with 1% DHA and one had formula with 0.3% DHA.

The higher DHA group showed visual acuity about 1 ½ times/150% better than the lower DHA group as early as four months of age.<sup>531</sup>

In the Age-Related Eye Disease Study (AREDS), where over 4500 people between the ages of 60 and 80 were studied for omega-3 fatty acid intake, results showed that dietary intake of omega-3 fatty acids, and specifically DHA, was significantly and inversely associated with the rate of age-related macular degeneration.<sup>11</sup> In animal studies, treatment with NPD1 protected eye tissue in rats after injury to the nerves in their retina.<sup>1309</sup>

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## FERTILITY and ERECTILE DYSFUNCTION

The fatty acid composition of sperm, especially DHA may be an important determinant in male fertility. Studies suggest that DHA can restore fertility by increasing sperm count and sperm production in some cases. In fact, one animal study showed DHA was capable of restoring male reproductive capacity when supplemented for sixteen weeks.<sup>1072</sup>

In another study, the HS-Omega-3 Index<sup>®</sup> was measured on a group of fertile and infertile men, and the HS-Omega-3 Index<sup>®</sup> of the infertile men was significantly lower. In fact, a strong correlation exists between DHA and EPA levels compared to other fatty acids and sperm count, motility and morphology. Similarly, the ratio of omega-6 to omega-3 fatty acids was significantly higher in infertile men compared to fertile controls – around 15:1 for infertile men and around 6:1 in fertile men.<sup>1073</sup>

Omega-3 fats can also have clinical benefit for men with erectile dysfunction since omega-3 fats stimulate the release of nitric oxide in the endothelial lining of our blood vessels. This nitric oxide release helps to dilate the blood vessels, thus improving systemic vascular health and improving symptoms of erectile dysfunction.<sup>1210</sup>

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## INFLAMMATION and OXIDATIVE STRESS

Although the inflammatory response is certainly useful in times of injury or wound healing, when it changes from an acute to a chronic state, the unfortunate result is tissue damage and disease. Inflammation and oxidative stress are closely linked – both cause and are caused by the other. Omega-3 fatty acids can act both as a powerful antioxidant and potent anti-inflammatory, facilitating a break in the cycle of inflammation and oxidative stress.

When cells are treated with omega-3 fatty acids, inflammatory chemicals are subdued, largely because they are the building blocks for hormones called eicosanoids that are responsible for monitoring inflammation in all tissues of our bodies.<sup>1115</sup> EPA and DHA compete with other fatty acids as a substrate for enzyme production. The net effect is that anti-inflammatory compounds are produced from downstream products of DHA and EPA instead of pro-inflammatory compounds that are made from omega-6 fatty acids, when the omega-3 fats are not readily available.<sup>1425</sup>

Because of their chemical structure (they contain several double bonds), omega-3 fats are known to be quite susceptible to oxidation. In fact, despite their benefits in reducing the risk for so many diseases, concern remains that they may increase lipid peroxidation due to their increased potential for oxidation. Interestingly, the opposite appears to be true. In one study, both EPA and DHA reduced a compound called isoprostanes by as much as 24% in patients supplemented with EPA and DHA.<sup>1261</sup> Isoprostanes are prostaglandin-like compounds formed when fats in the body are oxidized, and their presence indicates damage to cell membranes has occurred.

In addition, omega-3 fats can actually affect whether or not certain genes that produce inflammation are expressed.<sup>997</sup> Clinical evidence suggests that symptoms of inflammatory diseases such as psoriasis<sup>494</sup> and chronic fatigue syndrome<sup>156</sup> are alleviated by increasing the amount of omega-3 fatty acids in our bodies, due to their potent anti-inflammatory properties.

Omega-3 fatty acids are particularly beneficial in patients with active inflammation. The amount of omega-3 fatty acids in tissues is independently associated with higher levels of anti-inflammatory markers such as interleukin 10 (IL-10) and lower levels of the following pro-inflammatory markers: IL-6 (interleukin 6), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and CRP (C-reactive protein).<sup>1036,1255</sup> Recently, a group of compounds derived from DHA that exhibit potent anti-inflammatory properties have been identified. In one study performed in vitro, liver cells were supplemented with DHA. The result was a significant reduction in hydrogen peroxide induced DNA damage of the cells. Animal studies mimicked these results in vivo.<sup>1311</sup>

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