The groundbreaking omega-3 antidepression diet and brain program

THE OMEGA-3 CONNECTION

- Why omega-3s are essential for mental health
- The remarkable antidepressive powers of fish oils, flax oil, and omega-3 supplements
- Safe and effective supplements for pregnancy and postpartum depression

ANDREW L. STOLL, M.D.

DIRECTOR, PSYCHOPHARMACOLOGY RESEARCH LABORATORY, McLEAN HOSPITAL

FACULTY, HARVARD MEDICAL SCHOOL

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Introduction

For twenty-three years, the swings of bipolar disorder wreaked havoc for one of my female patients, now a forty-five-year-old woman who worked as a research scientist. Despite her expert knowledge of science and medicine, she was unable to find adequate treatment for her condition, marked by dangerous peaks of mania and dark valleys of depression. Her wild swings, especially manic episodes and uncontrolled bouts of anger, could be quelled by two conventional medications effective against bipolar disorder, or manic depression: lithium and Depakote.

But for this patient, the cure was almost as devastating as the disease. Dull and depressed and perpetually overweight, she had trouble focusing on her work, enjoying her life, and maintaining relationships with friends. Anxious for a treatment that might balance her mood swings without the cloud of depression, she was fascinated to hear we were testing a natural therapy based on fish oil at Brigham and Women's Hospital in Boston, Massachusetts.

Participating in our controlled, double-blind study, in which neither the doctor nor the patient is told who is receiving the real fish oil or who a placebo (an inert look-alike), she nevertheless insisted she "knew" just two weeks into the trial. She knew because not only was her mania gone, but for the first time in decades, the depression had lifted too. She kept taking fish oil—consisting of fatty acids in the omega-3 category—long after the study was complete. As of this writing, she has been in full remission for three years.

Rome is a wonderful city for culture, but if you're in the throes of mania, you're better off at home. One of my sickest patients suffered his first bout of bipolar disorder in Italy, where he became so manic and disruptive that he wound up in jail. When the police realized he was suffering from a psychiatric disorder, he landed in the locked ward of an Italian hospital. He subsequently escaped, only to endure a second arrest. This time the authorities couldn't wait to get him on an airplane and send him back to the United States. It is a testament to the severity of his symptoms that he was taken from Logan Airport in Boston directly to my office at Brigham and Women's Hospital.

Although conventional treatment based on lithium alone could not act quickly or thoroughly enough for this patient, he did fairly well when we added a powerful antipsychotic medication to the mix. But the side effects were unacceptable, and we were loath to continue the antipsychotic drug for very long. Yet every time he stopped this treatment, his mania returned. This patient did not want to enter our research study. However, based on my theory that omega-3 fatty acids found in fish oil could help bipolar disorder, he began to eat salmon—a lot of it—at least four ounces a day. It clearly helped,

but who can eat that much salmon? He could not keep it up, and without the fish, the symptoms returned.

Fortunately for this patient, we found an answer in fish oil supplements delivering concentrated doses of omega-3 fatty acids including EPA, or eicosapentanoic acid, which circulates in the blood producing powerful hormones and DHA, or docosahexanoic acid, an important component of cell membranes. By adding fish oil to his lithium therapy, this patient was able to keep his mania at bay without resorting to harsh and risky antipsychotic drugs. Today his bipolar illness is in remission, without the burden of medication side effects.

Suffering severe, untreated bipolar disorder, this next patient was subject to violent rages and crime sprees. Although dynamic and articulate when well, he had already been to prison as a consequence of his illness. Without any relief from the spectrum of available mood-stabilizing drugs, he had one of the most treatment-resistant cases of bipolar disorder I had ever seen. When given the opportunity to participate in our fish oil study, he was eager indeed. The fish oil was a charm. Participating in our double-blind study, he had no way of knowing whether his capsules contained fish oil or placebo, yet he announced almost immediately that whatever we were giving him, it worked!

His mood swings and rages stopped abruptly, and he felt well for the first time in his life. He has remained on fish oil supplements for three years. These uplifting stories reveal a behind-the-scenes look at my recent study of omega-3 fatty acids and bipolar disorder, published in The Archives of General Psychiatry in May 1999. More powerful than these anecdotes to the research scientists, however, are the data. They show that a group of safe and essential natural oils—the omega-3 fatty acids—have therapeutic value in the treatment of bipolar disorder. Even more extraordinary perhaps are the emerging findings that omega-3 fatty acids are useful not just in bipolar illness, but perhaps also in depression, postpartum depression, attention deficit–hyperactivity disorder, perhaps stress, and even schizophrenia and autism—in other words, a whole spectrum of psychiatric disease.

Because the omega-3 oils are a major constituent of brain cell membranes and are converted to crucial brain chemicals, they are needed for normal nervous system function and seem to be involved in mood regulation, attention and memory, and psychosis. Future studies may link omega-3 deficiency to eating and anxiety disorders as well. In fact, because these oils are essential for the efficient function of every cell in the body, there is established and emerging evidence of therapeutic benefit for the treatment of heart disease, arthritis, diabetes, autoimmune disease, and perhaps even cancer. The seeming ability of the omega-3s to serve as global brain and body healers reveals not some magical quality, but how incredibly essential

the omega-3s are as a foundation for our health and well-being. Deficient, we develop numerous disease states. Repleted, our bodies move to wellness.

The clinical and healing power of the omega-3s are backed by hundreds of research studies in well-regarded scientific journals. Taken altogether, these studies establish that our species evolved with a much higher dietary consumption of omega-3 fatty acids than we receive today. These studies have proven oils from fish are safe to consume, even in large dosages and even for the very young and very old. These is no question that omega-3 fatty acid deficiency is widespread in the United States and much of the rest of the developed world, and that we need adequate amounts of this nutrient for optimal health from the moment of conception on.

The research shows that omega-3 deficits can lead to a range of mental and physical disorders and that replacement of the missing nutrient may often effect a cure or an amelioration of symptoms. As you read The Omega-3 Connection and its informational guide, the Omega-3 Renewal Plan, you will come to understand the pivotal role omega-3 fatty acids play in physical and mental health. If you live in the United States or anywhere else in the developed world, you can be at risk for omega-3 fatty acid deficiency and all the health problems that entails. In the pages that follow, you will learn how to overcome this sometimes devastating deficit.

By following the road map I provide, the Omega-3 Renewal Plan, you can maintain appropriate levels of omega-3, which research suggests can help protect you against many of the most devastating illnesses of our time: heart disease, arthritis, and other major physical problems, as well as depression, bipolar disorder, attention deficit–hyperactivity disorder, and other forms of psychiatric disease.

Part I THE OMEGA-3 DEFICIT

1 Nature’s Mood Enhancers

During the course of reading this book you will learn about exciting research into a remarkable group of natural substances: the omega-3 fatty acids. Omega-3 fatty acids are essential for the optimal function of every cell in our bodies, yet we cannot manufacture them internally. Instead, along with vitamins, these essential oils can be obtained only in the diet. Over the past century, people in developed countries, particularly in the United States, have largely eliminated omega-3 fatty acids from their diet. There is considerable evidence that this has had a very negative impact on the inner workings of many bodily systems, most notably the heart and the brain.

We are learning that restoring the body’s natural balance of omega-3 oils may

improve a multitude of medical disorders, including coronary artery disease, major depression, and bipolar disorder (also called manic-depressive illness). My personal journey toward discovery of the omega-3 oils began in 1987, when I finished medical school and launched my career in psychiatric neuroscience with a residency and fellowship at Harvard Medical School and McLean Hospital in Belmont, Massachusetts. The focus of my clinical work and research was (and still is) bipolar disorder, one of the most complex, dangerous, and fascinating medical disorders—and one of just a handful of afflictions that occur only in humans.

The prevalence of bipolar disorder suggests that it is not merely some random unlucky mutation, but that the genes involved might have been preferentially selected during the evolution of the human species. Without bipolar illness, our species would, at best, be uninteresting, even boring; at worst, the human race might not have survived the challenges of our evolutionary and society history at all. Why would such a life-threatening disorder be necessary for our species? Viewed through the lens of history, some people believe its evolutionary value is clear.

Kay Redfield Jamison, professor of psychiatry at Johns Hopkins University, has written extensively on the creative and leadership qualities of the many people throughout history who have been retrospectively diagnosed with bipolar disorder. From Winston Churchill and Ted Turner to Vincent van Gogh, Georgia O'Keefe, Virginia Woolf, and Charles Mingus, some of the volatile, grandiose individuals with this affliction have launched and dismantled empires, revolutionized cultures, and rendered hauntingly beautiful works of art. Bipolar disorder, characterized by alternating cycles of melancholy and mania, is especially prevalent among those in leadership and creative fields.

A long list of writers, artists, and musicians—Ernest Hemingway, Michelangelo, and Cole Porter, to name a few—have produced visionary work, despite the crests and valleys of their mood states. According to Jamison, many prominent poets of our century have suffered from bipolar disorder, including Sylvia Plath and Hart Crane, and in the years before the advent of effective treatments, many killed themselves. The occurrence of bipolar disorder is not limited to the arts. It is highly prevalent in the computer, biotechnology, and high finance fields, where some of the most creative and globally transforming work is currently being done.

Most people with bipolar disorder, of course, are not celebrities, but the wide swings between highs and lows disrupt their lives just as much, devastating relationships, school, jobs, and quality of life. Between 10 percent and 20 percent of bipolar patients will die of their illness, usually through suicide. My career as a psychiatrist has been dedicated to relief and prevention of pain and suffering from these mood disorders. As a physician-neuroscientist,

understanding and treating bipolar disorder has provided me with a profound yet still embryonic view of the biochemistry of the brain. In medical school, I was taught that if you can understand diabetes, you will understand all of medicine because those with diabetes fall prey to many other disorders, from cardiac disease to kidney failure to stroke. Similarly, if you understand bipolar disorder, you will have special insight into psychiatry because those with bipolar disorder manifest a wide variety of psychiatric symptoms.

In the full-blown disorder, periods of suicidal depression alternate with episodes of mania: euphoria, irritability, increased energy, decreased need for sleep, and racing thoughts accompanied by impulsive behaviors and grandiose ideas. Symptoms of anxiety and even psychosis may occur during different phases of the illness. As devastating as bipolar disorder can be, it is treatable with drugs. But working with patients who have bipolar illness at McLean and Brigham and Women's Hospitals, I sometimes found the standard pharmaceutical agents ineffective or so harsh that they produced temporary discomfort or caused permanent medical problems of their own.

Ongoing psychiatric symptoms, serious side effects, and noncompliance with medication therapy were the frequent results. These outcomes are even more pronounced in teaching hospitals like McLean and Brigham and Women's, where many of the patients have more severe or treatment-resistant conditions. The long-term treatment of patients with bipolar disorder relies on the so-called mood stabilizers such as lithium and valproate. These often produce dramatically good results long term and have saved thousands of lives. Unfortunately, patients using lithium often experience weight gain, tremors, increased urination, drowsiness, and acne.

Some 15 percent suffer reduced thyroid function, and as many as 5 percent develop kidney problems. Often the biggest problem for these innately creative individuals on lithium can be a loss of the creative spark. While their manias are under control, their emotions are frequently flattened, and they are, to use a clinical term, "cognitively dulled." What is more, one mood stabilizer used alone is often not effective over the long term. In an effort to control recurrent manias or depressions, patients might end up taking two or more mood stabilizers at once, increasing their risk of side effects and drug interactions.

As a psychopharmacologist (a psychiatrist specializing in medication treatments) and researcher with responsibility for treating these desperately ill people, my mandate was clear: to find newer medications with fewer side effects that worked as well as or better than the ones already in use, and to increase our understanding of the disorder. Working with the German researcher W. Emanuel Severus, M.D., I started the hunt for a better treatment in 1993. Our strategy was to conduct extensive computer searches

of medical research papers to identify substances whose biochemical properties were similar to the standard mood stabilizers, lithium and valproate.

Reviewing hundreds of papers in search of a candidate molecule (one that had never been used in psychiatric disorders), we pulled up one match time and again: omega-3 fatty acids, or common fish oil! At first our reaction was surprise and disbelief. We had no evidence that omega-3 fatty acids would be helpful in bipolar disorder, yet it made sense. Already used by some physicians in the treatment of heart disease, Crohn's disease, and rheumatoid arthritis, these oils are precursors to important signaling molecules in the body and are essential components of the healthy cell membrane—the same membranes that appear to mediate the activity of lithium and valproate in the brain.

The omega-3 fatty acids are found in unusually high concentration in the brain. Although almost nothing in the literature connected them with bipolar disorder, the possibility that they might act to stabilize mood was very real. Our subsequent clinical study, ultimately published in The Archives of General Psychiatry, suggested that these safe and natural oils had therapeutic value in the treatment of bipolar disorder. In this one study, looking at thirty patients over four months, omega-3 fatty acids, used alone or with other medications, enabled a few seemingly incurable patients to lead normal lives and enhanced mood stability for those already gaining some benefit from other medications.

Omega-3 fatty acids were also safer than valproate and lithium: they had few side effects, and, in my practice, at least, they have become one of the most frequently used "medications" for patients with mood disorders. But there is more. While our discovery emerged from a search for a new treatment of bipolar disorder, evidence points to far wider applications for omega-3 fatty acids in the care and nurturing of the brain. Studies now under way indicate considerable potential as an antidepressant in the more common type of mood disorder, termed unipolar major depression.

Other research suggests that omega-3 fatty acids may yield new treatments for postpartum depression, schizophrenia, attention deficit–hyperactivity disorder, and possibly many other disorders as well. They may be very appropriate for children and the elderly, whose bodies often cannot tolerate conventional psychiatric medications. Furthermore, it is possible that omega-3 fatty acids may actually prevent these disorders from developing at all. For those of us engaging in neuroscience research, the possibility of global healing power for this natural lipid makes sense.

Until the twentieth century, omega-3 fatty acids, derived largely from cold

water oily fish from the ocean or freshwater lakes and rivers, as well as wild animals and plants, were common elements of the human diet. Today, with the advent of processed foods and the reduction of omega-3 fatty acids in the typical Western diet, that has changed. We often think of depression and bipolar disorder as purely hereditary in nature, but research on the omega-3 fatty acids indicates that some of what is inherited may not be in the genes. In studies of omega-3–deprived mice, scientists learned that it may take several generations for offspring to deplete their brains of omega-3 fatty acids.

This is because the body tenaciously holds on to the omega-3s throughout life, and also because most of the omega-3s in young animals come from what their mother (and her mother) have consumed and stored. Over time, of course, depletion occurs. Could this possibly be one reason that depression and other mood disorders are on the rise in the United States, or be a factor in the apparently low rate of depression in Japan and other countries where the consumption of fish has remained high for generations?

Researchers in psychiatric epidemiology have found that the prevalence of depression varies as much as sixty-fold from country to country. In a fascinating study from Joseph Hibbeln, M.D., of the National Institute on Alcohol Abuse and Alcoholism, data shows that the international pattern of major depression corresponds strongly to cross-national differences in coronary artery disease, suggesting similar dietary risk factors. Of all the dietary variables, fish consumption appears to be the most significant, with fish-eating nations at lower risk for both major depression and heart disease.

There is evidence that omega-3 deficiency may play a role in postpartum depression as well. The developing fetus and newborn require high amounts of omega-3 fatty acids and receive them through the placenta and breast milk, respectively. The baby's ability to import and incorporate omega-3 oils outweighs the typical Western mother's ability to replace what she has lost. It is well-documented that infants and toddlers who were breast fed rather than bottle fed score higher on cognitive and visual system tests. It has been determined that one reason is the high levels of long-chain omega-3 fatty acids in breast milk. (There are none in U.S. formula.)

If the mother does not maintain sufficient levels of omega-3 fatty acids in her diet, she puts her body at risk of depletion during the pregnancy and breast-feeding period. Low levels of omega-3 in her brain and body may put her at greater risk for depression and possibly other disorders. In studies of children with attention deficit–hyperactivity disorder (ADHD), meanwhile, Jay R. Burgess of Purdue University has found that some 40 percent showed evidence of omega-3 fatty acid deficiency. Research into use of omega-3 supplements as an adjunctive treatment for ADHD is currently under way. Although the results of the ADHD studies are not yet in, research with healthy

populations indicate that omega-3 fatty acids may indeed play a role in attention as well as cognitive abilities like memory and response time.

In a fifty-day study of 285 normal women, with a particular focus on EPA, David Benton, Ph.D., a researcher at the University of Wales Swansea, found that omega-3 fatty acid supplements improved measurements of memory, vigilance, and mood. The jury will remain out on many of these treatments and applications until controlled clinical studies are completed and replicated. In the meantime if you are already receiving drug therapy for a psychiatric disorder and would like to start taking omega-3 fatty acids, it is important that you continue current treatment and consult with your clinician.

In most cases, the omega-3 fatty acids are used “adjunctively”; that is, added to what you already take. There are some patients with mood disorders doing very well on omega-3 fatty acids alone but until more data are in, I do not recommend treatment based solely on omega-3 fatty acid therapy, except for the mildest forms of depression or bipolar disorder, or for the general population, to enhance well-being, mood, and health. If you think you might have a mood disorder, you should consult a mental health care professional to review your treatment options.

The chapters that follow present the latest findings on omega3 fatty acids and mood enhancement—not just for those who suffer from bipolar disorder, but possibly for everyone. And because the use of this supplement in psychiatry is so new, I’ll deliver a road map for use in my Omega-3 Renewal Plan. What foods are especially rich in omega-3 fatty acids, and how much should you eat? What should you look for in a supplement? What can labels tell you? How much should you take and when? I understand that some readers may be skeptical. Who is to say this is not just another supplement flavor of the month, another bogus claim in the continual stream of magic elixirs and miracle cures?. Who is to say that fish oil is not really snake oil, a fad that will pass as others have before? Well, it may.

The case we present to you is not yet solid. Many more studies are needed. But serious scientists at many prestigious institutions like Harvard Medical School, Oregon Health Sciences University, Purdue University, the University Hospital of Ghent in Belgium, and the University of Sheffield in the United Kingdom are impressed enough to be dedicating themselves to the study of the omega-3 fatty acids. Every so often, scientists really do discover a substance of transformative power, one with the ability to cure the previously incurable and improve the quality of life for the rest of us. Omega-3 fatty acids —a component of simple fish oil, once so prevalent in our diet but now largely absent—could be such a substance.

2 The Fat of Life: A Nutritional Guide to Fatty Acids

One of the great medical myths of the past fifty years has been the notion that fats (more properly called lipids) are evil. Of course, like all other enduring myths, there is a grain of truth at the core. Literally thousands of studies over the past half century have traced high-fat diets to increased risk of heart disease. The most famous of these, the Framingham Heart Study, followed a representative sample of 5,209 adults in Framingham, Massachusetts, to examine the circumstances and risk factors associated with heart disease.

The Framingham study was an epidemiological study designed to learn how those who develop cardiovascular diseases differed from those who remain free of the diseases over a long period of time. Epidemiology is a branch of medical science devoted to the large-scale study of populations and disease; epidemiologists search for risk factors and causes of illnesses through statistical associations and other methods. Along with such culprits as smoking and sedentary lifestyle, the Framingham scientists found danger in diets high in fat.

This study and many others over the past few decades have driven the point home: diets high in fatty foods, from bacon to butter to red meat, greatly increase our chances of acquiring cardiovascular disease, reducing not just the length but also the quality of life. The problem is not simply excessive amounts of fat or cholesterol clogging arteries or adding inches to our waistlines. Certain fats, like the omega-6 and omega-3 fatty acids act as powerful hormone-like agents, playing many roles in health and disease.

The Framingham scientists, with their focus on cholesterol and saturated fats, overlooked the damaging effects of another type of fat, the omega-6 fats. With a genuine paradigm shift, we must develop an accurate view of the diversity of fats, with a range of health benefits and risks. Although some dietary fats are implicated in heart disease, others may reduce the risk of these illnesses, and even treat or prevent a range of other diseases, such as arthritis, depression, and diabetes. Some lipids suppress inflammation, others promote it. Some fats raise cholesterol, others lower it. Some make cell membranes rigid, others render them flexible.

The Essential Fats

The data from the medical literature are clear: do not lump all types of dietary fat together in a single, negative category. Excessive consumption of saturated fat and cholesterol certainly can cause disease and a greater chance of early death. But other fats, termed the essential fats, are necessary for optimal health. In the yin and yang of proper physiological balance, the essential fatty acids—the omega-3 and omega-6 oils—are health enhancers.

I want to stop here to point out my use of the term oil. We have used the term fat in a general way, but oils and fats (both lipids) differ in their chemical structures. Oils (olive, canola, and fish oil, for instance) are liquid at room temperature; fats (butter and lard) are solid. These subtle chemical differences produce vastly different chemical effects in the body. The role of the essential fatty acids in the body and brain can be best understood in terms of what we know about lipids—fats as well as oils—and their impact on health and disease.

The Cholesterol Issue

Researchers investigating risk factors in the Framingham study initially homed in on not so much the total consumption of lipids, but on detection of high blood levels of one particular lipid: cholesterol. A soft, waxy substance found among other lipids in the bloodstream and in the body's cells, cholesterol is needed to form cell membranes, certain hormones, and specific tissues.

Like other lipids, cholesterol cannot dissolve in the bloodstream, which is mostly water, and must be transported throughout the body by carriers in the blood called lipoproteins. Two lipoproteins are particularly important. The low-density lipoproteins (LDLs), when carrying cholesterol, are sometimes called "bad" cholesterol, and high-density lipoproteins (HDLs) are also known as "good" cholesterol when combined with cholesterol. Too much LDL cholesterol circulating in the blood within a pro-inflammatory environment can promote atherosclerosis ("hardening of the arteries"), which is the buildup of a thick, hard coating called plaque within the walls of the arteries.

Just like a clogged pipe, if arterial walls accumulate too much plaque, blood flowing through them will be blocked. Arterial plaque can block flow of blood to the heart, leading to heart attack (myocardial infarction), or block the flow of blood to the brain, causing a stroke (cerebrovascular accident). About a quarter of all cholesterol is carried through the body by HDLs, thought to be beneficial. The data suggesting that HDLs promote health come from two sources: epidemiological studies linking high levels of HDL to lower rates of heart disease and laboratory studies examining exactly what HDL does to cholesterol at a cellular or molecular level.

The latest studies indicate that HDL's role is complex, but that one of its actions is to carry cholesterol away from the arteries and back to the liver, where it is passed from the body. Some experts believe that HDL cholesterol can even break down the cholesterol in plaque, potentially leading to a reopening of partially clogged arteries. According to the American Heart Association, excess cholesterol in the body comes from two sources: (1) the liver, which produces about 1,000 milligrams of cholesterol a day from other

substances; (2) dietary saturated fat and cholesterol of the sort that are found in animals and dairy products.

Grouping the Fatty Acids: Essential and Nonessential Fats

Researchers today realize that not all fats are created equal. Anyone who does supermarket shopping is likely to know there are four major categories of fat listed in the labels of the foods we eat: cholesterol, saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids. Of the three fatty acid categories, only one—the saturated fats found in animal and dairy products—have been implicated in raising LDL, or bad cholesterol. Most foods contain a combination of all three fatty acids in differing proportions. Nutritionists assign foods to a general fat category based on the proportions of each fatty acid contained in the product (see Table 2–1).

What You See Is What You Get: Fatty Acids Function Based on Their Chemical Form

Like other biochemicals, fatty acids function based on their chemical structure. Essentially chains of carbon atoms with hydrogen atoms attached off to the side, the various fatty acids differ based on the number of carbon atoms in the chain and the types of bonds they share with each other (see Figure 2–1).

Fat in 3D: The Chemical Structure of the Fatty Acids

In essence, chemical bonds are created when electrons are shared between two atoms. This sharing of electrons makes atoms stick together (a bond). Carbon atoms found in nature always have four bonds available to link up with other atoms. Since the carbons are in a chain, it makes sense that two of those bonds are usually taken up with links to adjacent carbon atoms. That leaves two bonds open for other atoms, usually hydrogen. If two hydrogen atoms attach to each carbon atom in the chain, that chain is said to be “saturated”—it contains as much hydrogen as possible, with each carbon-carbon bond consisting of a single, shared electron.

Saturated fatty acids are very stable chemicals. They are also solid or stiff at room temperature. In fact, the processed foods industry uses so much saturated fat precisely because of its chemical stability and solid, pliable form. When fatty acids are “unsaturated,” it means that some of the carbon atoms in the chain have double bonds with each other and less hydrogen is present —hence the term unsaturated. The carbon-carbon double bond is the chemical signature of an unsaturated fat. Monounsaturated fats have a single double bond, and polyunsaturated fats have two or more.

Solid, Liquid, and in-Between

The differing chemical structures of the fatty acids lead to a useful variety of attributes in the physical world. The saturated fatty acids are generally solid in form, like butter, even at room temperature, and are the most chemically stable. Most of the time we consume saturated fatty acids in meat, dairy, and processed food products, including beef, veal, lamb, pork, lard, poultry, butter, cream, milk, cheese, cookies, and crackers. Coconut and palm oil (known as the tropical oils) contain a high proportion of saturated fatty acids.

Because of their specific fatty acid composition, the tropical oils are liquids at room temperature. The tropical oils are used widely in food processing because, as liquids, they are easy to handle, and because of their saturated fat content, they extend the shelf life of many foods. While useful to the food industry, however, these fats and oils can contribute to coronary artery disease.

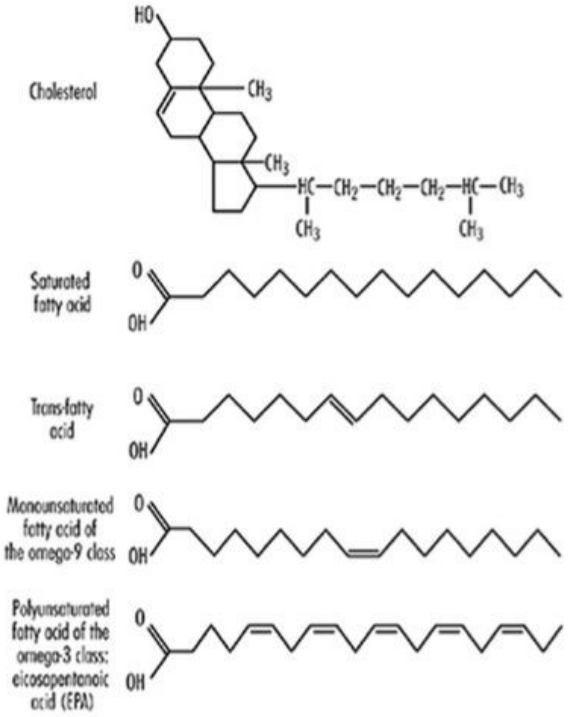

FIGURE 2–1:Chemical Structures of Cholesterol and Examples of Saturated, Trans-, Monounsaturated, and Polyunsaturated Fatty Acids

Note the large difference in the chemical structures between cholesterol (a sterol) and the fatty acids. Among the four fatty acids in the figure, the superficial similarity of the chemical structures is misleading because the presence of carbon-carbon double bonds (denoted by the double lines in the chemical structures) gives rise to fatty acids with vastly different biochemical properties in the body. For example, only the polyunsaturated fatty acids (omega-3 and omega-6 fatty acids), with their multiple double bonds are

converted into crucial signaling molecules in the body and brain, known as eicosanoids (prostaglandins are one example of an eicosanoid).

There are other consequences of multiple double bonds in the chemical structure of a fat. Every double bond produces a separate “kink” in the carbon chain, leading to many potential three-dimensional configurations, which leads to greater mobility of the polyunsaturated molecule. It is this enhanced mobility that keeps polyunsaturated fats liquid at room temperature and which may produce healthy, fluid cell membranes at body temperature. The greater membrane fluidity or possibly some other effect of the polyunsaturated fatty acids alters the function of neurotransmitter receptors and other important signaling proteins embedded in the cell membrane.

TABLE 2–1: Lipid Composition of Various Plant Oils and Animal Fats

The lipids (fats and oils) in most foods are a mixture comprised of all three fatty acid categories as well as cholesterol in various proportions. Also hazardous to health are the so-called trans-fatty acids, found in margarine and other synthetic foods. Created in the laboratory, trans-fatty acids result when manufacturers add hydrogen to unsaturated vegetable oil. Due to the configuration of the new chemical bonds—different from those found in most naturally occurring saturated fatty acids—trans-fatty acids are even more stable than those of saturated fatty acids. The advantage is longer shelf life without spoiling for processed foods.

The disadvantages, according to a spate of recent studies, include risk for coronary heart disease in excess of that associated with saturated fat. The American Heart Association (AHA) has put its stamp of approval on unsaturated fatty acids in both monounsaturated and polyunsaturated categories as healthier substitutes for saturated fats. Generally liquid at room temperature but prone to solidify when refrigerated, oils containing high amounts of monounsaturated lipids derive from canola, olives, peanuts, and avocados.

Oils containing high amounts of polyunsaturated lipids—found in safflower oil, fish oil, flax, and sunflower seeds, among numerous other sources—remain as liquids, whether refrigerated or not. Referring to extensive scientific evidence, the AHA literature today emphatically states that monounsaturated and polyunsaturated fatty acids may not only be healthier than saturated fatty acids, but may actually reverse the latter’s devastating effects. By increasing the body’s supply of HDL cholesterol, monounsaturated and polyunsaturated fatty acids can keep blood cholesterol levels down and reduce cholesterol deposits in artery walls.

The problem is that the Framingham Study and the AHA do not differentiate

between the two major types of polyunsaturated fatty acids: omega-3 and omega-6. A diet based on vegetable oil (high in omega-6) will produce a vastly different state of health than one balanced with omega-3 oils. The AHA also strongly recommends a low-fat diet, with no more than 30 percent of calories from fat of any sort. The reasoning is rooted in the findings of the Framingham Heart Study. With obesity a major risk factor for heart disease, it makes sense to limit calories, no matter how beneficial the source. And fat of any sort is calorie-rich.

The Fat Wars

Representing the mainstream, the AHA is not the only game in town. One alternative approach, pioneered by California heart researcher Dr. Dean Ornish, calls for intensive daily exercise and a diet allowing no more than 10 percent of the daily calories to come from fat. Studies show that the Ornish approach can actually reverse the ravages of heart disease without drugs or surgery. In practice, however, many people might find it difficult to adhere to such a rigorous program over the long term. Taking an opposite tack, others argue for diets high in fat.

The best-known figure promoting a high-fat diet for weight loss is Dr. Robert C. Atkins, whose best-selling Dr. Atkins' New Diet Revolution argues that carbohydrates, not fat, are the true villains in the battle of the bulge. The Atkins diet permits as much fat as desired as long as carbohydrates are kept at bay. The diet can lead to marked weight loss, but without motivation, it is difficult to maintain. In addition, the long-term health consequences (if any) of this "unnatural" proportion of fat to carbohydrate is unknown.

The Mediterranean Diet

Yet others, such as physician and nutrition scientist Artemis Simopoulos, M.D., advocate the Mediterranean Diet, based on the eating habits of Mediterranean regions like southern Italy, Greece, and Crete. The Mediterranean diet includes staples of fruits, vegetables, and grains, drawing as well some 30 percent of its calories from olive oil and other mono- and polyunsaturated fats. The first inkling that the Mediterranean diet might bolster health came in the 1970s, when Dr. Ancel Keys and colleagues at the University of Minnesota examined the relationship between diet and heart disease in seven countries.

They found that those who lived by the Mediterranean Sea suffered a fraction of the heart disease found in the United States and other Western nations. Keys noted that Mediterranean populations consumed dietary fat largely derived from fish and vegetables, as opposed to the highly saturated animal and dairy fats typical of the West. The subject of intense debate, Keys's

findings have nonetheless been confirmed in numerous prominent studies over the past ten years. Most notable is the recent research conducted by Dr. Michel de Lorgeril and colleagues in Lyon, France. In that study, 30 percent of the calories in the experimental Mediterranean diet came from fat, but only 8 percent from saturated fat. In a control group, 34 percent of the calories were from fat, with almost 12 percent from saturated fat. Lorgeril observed that the group on the Mediterranean diet had far lower rates of cardiac disease. And in a boon for the omega-3 fatty acid camp, participants with the highest blood levels of omega-3 fatty acids were at lowest risk of all.

Essential Fatty Acids and the New Fat Paradigm

In the midst of all this brouhaha, a new series of studies has quietly reframed the high-fat/low-fat debate. Although not yet extensively covered in the popular press, the latest research shows that polyunsaturated fatty acids, long grouped with monounsaturated fatty acids as enemies of cholesterol, are more complex and diverse than previously thought, with many unique and important roles in the body and brain.

Already known to lower the risk of having a heart attack and protecting against sudden death during a heart attack, polyunsaturated fats of the omega-3 class may also be responsible for protecting against arthritis, diabetes, and some psychiatric disorders. The reason is their ability to control many of the most basic functions of the cell. Omega-3 fatty acids are vital nutrients controlling energy production within each cell. They are also converted throughout the body to myriad messenger molecules essential for influencing a host of physiological functions.

The essential fatty acids are also the major building blocks of cellular membranes surrounding every cell in the body. Known as lipid bilayers (because they are made of two layers of fat), cell membranes serve as an effective barrier to unwanted substances and also function as highly selective molecular portals to the inside of each cell. These fatty acid walls help control the opening and closing of the cell's channels to a diversity of compounds, thus influencing the most basic cellular functions. Like vitamin C, calcium, and a host of other essential nutrients not manufactured by the body, most polyunsaturated acids must be consumed as a regular part of the diet for us to thrive.

Most fats, of course, are manufactured by the body, as anyone on a weight-loss program is likely to learn. Eat too much protein or carbohydrate and your body will all too readily convert these nutrients for storage as fat. For many years, nutritionists thought that polyunsaturated fats were created in the body as well. But in 1929, George M. Burr and Mildred M. Burr of the University of Minnesota reported that rats fed a fat-free diet failed to grow, lost weight,

developed scaly skin and kidney damage, and died prematurely. These conditions could be prevented and reversed only with the addition of one type of polyunsaturated fat: linoleic acid, an omega-6 oil. At that time, omega-3 fatty acids could not be isolated.

Today, it is clear that both omega-6 and omega-3 fatty acids are necessary for optimal health. This study and others caused nutritionists to group the polyunsaturated fats with the essential nutrients—those required for survival but not produced by the body—and to name them essential fatty acids (EFAs). We now know that EFAs come in two basic categories: omega-6 fatty acids and their counterparts, the omega-3 fatty acids, both named for the position of the first double bond in the carbon chain. As polyunsaturated lipids, both omega-6 and omega-3 fatty acids have multiple double bonds. The first double bond in the omega-6 class begins at the sixth carbon atom from the end of the chain. Omega-3 fatty acids differ in a subtle yet crucial way, in that they have their first double bond at the third carbon position (see Figure 2–2). This one difference—the absence of only two hydrogen atoms—is what makes the omega-3 fatty acids unique and essential for optimal health.

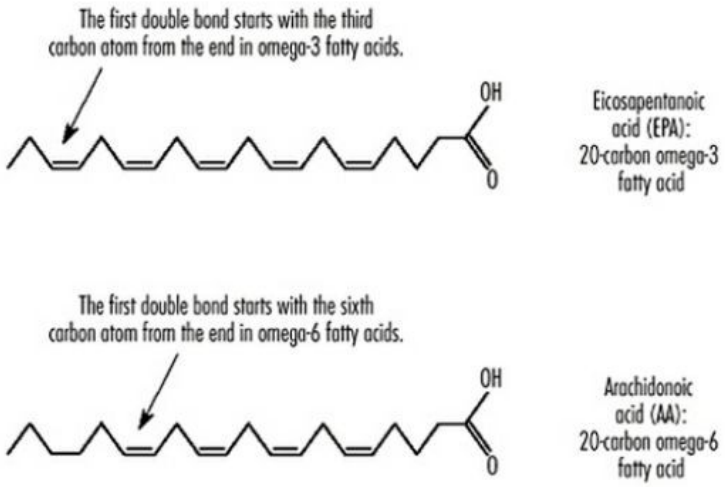

FIGURE 2–2:Chemical Structures of the Omega-3 and Omega-6 Fatty Acids

The omega-3 and omega-6 fatty acids have very similar chemical structures—both are long chain and polyunsaturated. The terms of omega-3 and omega-6 indicate where the first carbon-carbon double bond is located, counting from the end of the carbon chain opposite the acid group. The most amazing feature of the polyunsaturated fatty acids is that the subtle difference in chemical structure between EPA (omega-3) and arachidonic acid (omega-6)—just two hydrogen atoms—produces profound differences in what the omega-3s and omega-6s do in the body. Omega-3 fatty acids are found mostly in oily fish and some uncommon but edible plants.

The source of omega-6 fatty acids are most often vegetable and seed oils, which are very common in our diet. The most current data suggest that humans evolved eating a balance of omega-3 and omega-6 fatty acids. There is now a considerable amount of evidence that this shift in our diet away from omega-3s has resulted in higher rates of many medical illnesses, particularly heart disease and depression. In fact, a recent international conference recommended an ideal ratio of omega-6 to omega-3 to be 1 to 1.

Contrast that with the prevailing current U.S. ratio of omega-6 to omega-3 of 10 or 20 to 1. The challenge is getting sufficient quantities of omega-3 fatty acids. In the United States and many other developed countries, the modern food supply is low in omega-3 oils. This omega-3 deficiency, evidence now suggests, may underlie a multitude of health problems in both children and adults. The omega-6 oils are also essential nutrients required for health, but modern diets contain more than enough to meet our needs. The implications of omega-3 deficiency on the brain are profound and span the entire human life cycle.

Beginning in pregnancy, premature birth and its potential neurologic complications may result from omega-3 deficiency. Babies who are bottle-fed or born from omega-3-deficient mothers will lack the omega-3 fatty acids necessary for optimal cognitive and visual development. Children deprived of omega-3s may have less ability to pay attention and control impulsive behavior and may be at higher risk for depression. Teenagers and adults with omega-3 deficiency may be more prone to hostility or violence. In aging, the loss of omega-3 fatty acids in the brain may result in a higher risk of stroke, memory problems, or dementia. Individuals of any age without adequate amounts of omega-3 fatty acids in the brain and body may also be at higher risk for depression, bipolar disorder, and possibly other psychiatric disorders.

The Yin and Yang of Fat Science

There is balance in nature, and one example of its elegant expression is the tightly linked biochemistry of the two essential fatty acid groups, the omega-6 and omega-3 oils. Unlike other lipids, neither is made in the human body; rather, these essential fatty acids are synthesized in the chloroplasts of plants. The chloroplast, the green, chlorophyll-containing structure in plant cells, converts sunlight and carbon dioxide into oxygen and a range of complex organic molecules, including sugars, proteins, and lipids. Only chloroplasts within certain plants (e.g., marine and freshwater algae) produce high quantities of long-chain omega-3 fatty acids.

We derive omega-6 fatty acids from a commonly available range of vegetable and seed oils, including corn oil, olive oil, sunflower oil, and safflower oil. The long-chain omega-3 fatty acids are more difficult to obtain through the modern

Western diet and most often come indirectly, through the oils of fish that have received omega-3 fatty acids through the food chain, ultimately from omega-3-producing algae and other water-based plants. A shorter-chain omega-3 fatty acid is available in walnuts, flaxseeds, and some other plant sources. Once in the body, omega-3 and omega-6 fatty acids follow parallel pathways, continually competing with each other for chemical conversion to various structures and molecules inside and outside of cells.

Given this mechanism, it makes sense that the two fats might be required in approximately equal amounts. Hoping to reach a consensus on the issue, the National Institutes of Health recently sponsored an international conference for omega-3 researchers across a range of disciplines, from psychiatry and cardiology to nutrition and immunology. It is notable that despite the diversity of their backgrounds, the researchers agreed virtually unanimously: for optimum health, omega-6 and omega-3 fatty acids should be eaten in approximately equal proportions—a ratio of 1 to 1.

This stands in stark contrast to the modern Western diet, where that ratio is often highly skewed to ten to twenty times more omega-6 than omega-3 (a ratio of 10 or 20 to 1). Our dietary imbalance has shifted crucial biochemical pathways toward the more abundant omega-6 fatty acids, leading to negative changes in numerous body systems, possibly including the brain regions contributing to mood. Medical science is only beginning to comprehend the power and complexity of omega-6/omega-3 balance.

Pathways to Health

Once eaten and absorbed by the body, omega-6 and omega-3 fatty acids go through a series of biochemical conversions. This metamorphosis can be divided into two major pathways. In the first pathway, the omega-6 and omega-3 fatty acids become incorporated into cell membranes. Without access to sufficient quantities of omega-3 and omega-6 fatty acids, cell membranes will incorporate saturated and other types of fat instead. Membrane walls rich in the omega-3 fatty acids will be more fluid because polyunsaturated fats have lower melting points than saturated fats.

(Remember that polyunsaturated fats are liquid even at low temperatures.) Among the health benefits that may result from a diet high in omega-3 oils and the ideal fluidity of cell membranes, according to scientific reports, are superior cognition and visual development in babies and lower risk for cardiovascular disease in adults. In the second pathway, the essential fatty acids are converted to a series of intermediate molecules and then ultimately to hormonelike substances called the eicosanoids, an umbrella term for several classes of cell-signaling molecules, most notably the prostaglandins.

The prostaglandins mediate the “inflammatory process,” a crucial and finely tuned mechanism that fights infection, heals tissue injury, and performs a multitude of other functions within the immune system, the cardiovascular system, and even the brain. Omega-6 fatty acids produce strongly inflammatory or “reactive” eicosanoids while omega-3 fatty acids produce less inflammatory or even anti-inflammatory eicosanoids. One can begin to see the profound health implications here. When in balance, essential fatty acids promote optimal health perhaps by their fluidizing effect on cell membranes or by the proportions of various eicosanoid derivatives. When out of balance, they can throw the body into chaos.

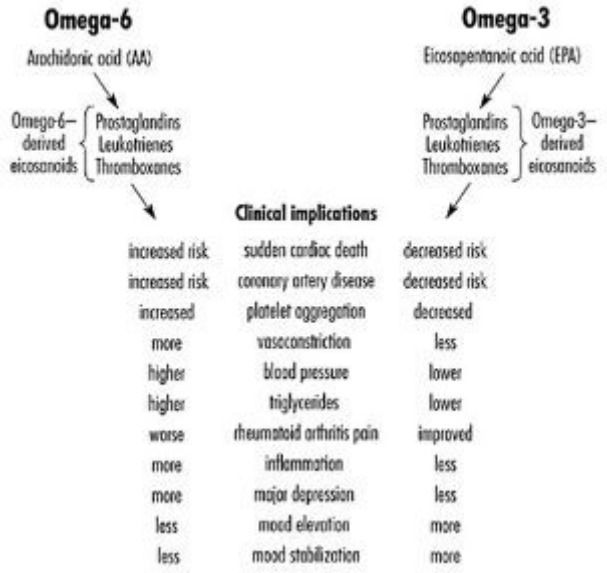

FIGURE 2–3:The Omega-6–Omega-3 Balancing Act

The Essential Difference

Although EFAs are cousins to saturated fatty acids, they live in stark contrast to those rigid, relatively inert molecules. The root of the difference is chemical structure. The carbon chain in saturated fat is straight and rigid, in contrast to the bent, twisting, and flexible structure of the polyunsaturated fatty acids. Every double bond in an EFA produces a separate kink in the carbon chain, leading to many potential three-dimensional configurations, which leads to greater mobility of the polyunsaturated molecule.

It is this enhanced mobility that keeps polyunsaturated fats liquid at room temperature and produces healthy, fluid cell membranes at body temperature. Ideally, omega-6 fatty acids work in tandem with the omega3s (see Fig 2–3). When in balance, eicosanoid derivatives of the omega-3 fatty acids keep the omega-6–derived eicosanoids in check. For example, pro-inflammatory eicosanoids (prostaglandins) derived from omega-6 fatty acids enable the immune system to fight serious infection and also set the stage for labor and

delivery at the end of pregnancy. Omega-3 fatty acids prevent these processes from spinning out of control. Women deficient in omega-3 fatty acids, for instance, have, on average, shorter pregnancies, presumably because the overabundance of omega-6–derived prostaglandins promotes earlier labor and delivery.

Tipping the Balance

This elegant design, honed to perfection through eons of evolution, has gone awry. With the gradual phasing out of traditional foods and the advent of modern methods of food production in the past century, the Western diet has changed. Our bodies and minds evolved to use roughly equal parts omega-6 and omega-3 fatty acids, and the current overabundance of the omega-6 class has altered our internal physiology in ways we are just now beginning to understand. The good news is that this trend can most likely be reversed through dietary changes or supplements.

Populations maintaining historic omega-6 to omega-3 ratios (approximately 1 to 1) are protected from many of the scourges of the modern age. Greenland Eskimos eating their traditional diet of fish, whale, and seal, for example, have extremely low rates of heart disease. Their blood tests reveal a biochemical signature for cardiac health, including high levels of protective HDL cholesterol, low levels of LDL cholesterol, low levels of triglyceride, and low levels of platelet aggregation (stickiness), a risk factor for heart attack.

Likewise, researchers have found that the fish-eating inhabitants of a typical Japanese fishing village had far lower rates of heart disease and arterial plaque than residents of a typical farming village who ate less fish. Trends in major depression parallel those seen in cardiac disease. Another recently published study shows that in Japan, Hong Kong, and Taiwan, where fish consumption is high, rates of depression are extremely low—some ten times lower than in the United States. Even when one considers underreporting of psychiatric illnesses in some Asian cultures, major depression appears to be extremely rare in Japan, where omega-3 fatty acids in fish are consumed in great abundance.

Fat Brains, Healthy Minds

What happens to your brain when you change the balance of omega-6 to omega-3 from 1-to-1 to 20-to-1? Well, there are many ways a deficiency in omega-3s could affect mood, starting first with a change in the overall composition of the brain. In fact, the findings associating omega-3 consumption with depression and mood make sense in light of the brain’s requirement for more omega-3 fatty acids than any other system in the body. Indeed, while the musculoskeletal system is rich in protein and minerals, the

major structural component of the brain and its cells (other than water) is fat.

The dry weight of an adult human brain is about 600 grams of lipid per kilogram, or an astounding 60 percent. Indeed, while other organ systems can function (if not optimally) on an omega-6 to omega-3 ratio of some 4 to 1, the brain may work best when fueled with equal quantities of the two essential fats. The brain's needs are further complicated by its inability to use some forms of omega-3 fatty acids commonly found in the diet. Some organ systems can incorporate the shorter, eighteen-chain omega-3 precursor, called alpha-linolenic acid (ALA), found in green leafy vegetables, flaxseed, canola oil, and walnuts.

But the human brain has an absolute requirement for the longer-chain omega-3 fatty acids: eicosapentanoic acid and docosahexanoic acid, both found primarily in fish oil. The studies have been somewhat mixed, but it appears that adult humans cannot convert enough ALA to EPA and then to DHA. Newborns appear to be better able to transform ALA to the longer-chain omega-3s, but these conversions may still be inadequate to fill the huge need of young children for omega-3 fatty acids. Thus, some nutritional scientists believe we must consume the fish and fish oil–derived long-chain omega-3s directly for optimal brain health.

Strict vegetarians likely have lower levels of the long-chain omega-3 fatty acids, EPA and DHA, than nonvegetarians, but may in the future be able to purchase both EPA and DHA supplements derived directly from algae. With sufficient quantities of EPA and DHA in the diet, the membranes surrounding our brain cells perform their crucial functions normally. In addition, the eicosanoids, the circulating hormones derived from omega-3 and omega-6 fatty acids, appear to have a vital, though still poorly understood, role in the brain, particularly in areas regulating mood.

It is possible that high levels of EPA circulating in the blood or incorporated into membranes may be necessary for normal brain function, thus sustaining mood and possibly preventing or mitigating the symptoms of psychiatric disorders. Without sufficient quantities of EPA and DHA in the diet, brain cells use substitute lipids such as omega-6 and monounsaturated fatty acids, which have vastly different properties from the omega-3s. Brain cells without sufficient quantities of omega-3 fatty acids in membranes have been shown to be dysfunctional in animal studies.

Showing how and to what extent this deficiency compromises the health of the human brain will be an important goal for neuroscientists over the next few years. The membrane is also an electrical regulator, controlling the movement of charged ions such as sodium and potassium into and out of the cell. Finally, the lipid bilayer serves as a doorway to the cell, controlling the

movement of molecules and information in an organized fashion. Lipid bilayers composed of proper amounts of omega-3 fatty acids appear to function best.

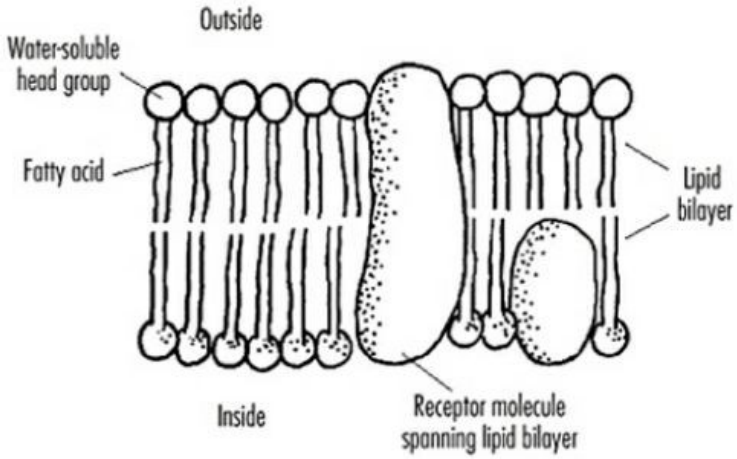

FIGURE 2–4:The Cell Membrane

The neuron, or brain cell, like all other cells, is enclosed by a membrane. The cell membrane is comprised of a double layer, or bilayer, of fats linked to other compounds that act as a highly selective barrier, preventing the contents of the cell from mixing with the rest of the body. The composition of the fats in the lipid bilayer have an enormous influence over the function of the cell. Neurons are intended to have very high levels of omega-3 fatty acids in their membranes.