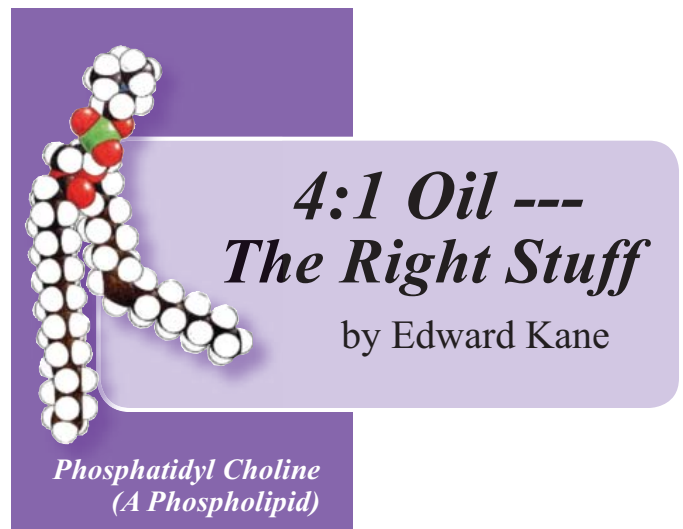
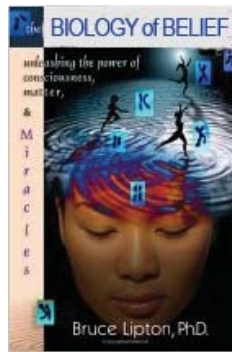


# BODYBIO *Bulletin*



## The *Membrane*

surrounds and protects every cell of every organ including the tissues of the heart and the neurons of the brain. It is a remarkable thin insulator, the protective outer skin, with a carbon copy duplicated over and over surrounding the tiny organelles inside each cell. Bruce Lipton, Ph.D., former professor of histology, University of Wisconsin Medical School, in his book, *The Biology of Belief* (2005<sup>1</sup>), puts the lipid membrane in perspective. He compares the function of the membrane to the DNA, currently the darling of medical science. Lipton calls the DNA the gonads of the cell and compares it to the hard drive of a computer, while comparing the lipid membrane to the keyboard. He describes the DNA as a storehouse of information, a personal library housing a pattern (copy) of every protein molecule specific to each of us. The DNA of each cell contains a duplicate set of genetic instructions for the development and function of every organ of our body. The basic idea we are currently led to believe is that we are controlled by our genes, by the hard drive, but that is false. The DNA, like a central processor, is a library of information. A cell can actually exist for a few weeks or even months without its DNA. Lipton performed this in a lab with cells in a petri dish. By surgically extracting the contents of the nucleolus, the DNA, and providing nourishment, the cell could last for several months. However, cell death is instantaneous after a break in the membrane. It's a bit sacrilegious to call our libraries dumb, but they are certainly not smart. Someone must extract the information and do something with it.

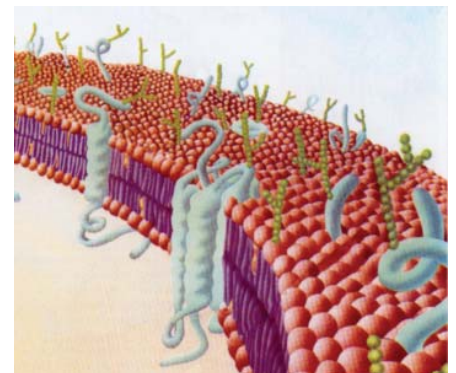


Even though the DNA holds the program for the production of all the intricate proteins we need, it acts exactly like a library. It holds all the intelligence but initiates no activity.

As the keyboard, the membrane continuously sends instructions to the DNA. In part, it has the ability to collect cellular information and to direct cellular activity.

Lipton says we should call it our mem-Brain --- and, since it is over 80% fat, our lipid membranes now take on a whole new level of importance, which is the principle focus of this issue of the BodyBio Bulletin.

The membrane of every cell and organelle is a lipid envelope, a thin fatty acid sliver that encases and protects the internal cellular components. This bi-lipid envelope is far more than isolation and protection, for linked and interlocked within the membrane are literally thousands of peptides (proteins) from the DNA, large and small, that form the windows and doors of the cell. Sixty percent of the output of proteins from the DNA are either imbedded within or positioned on the membrane where they proceed to manage our cells and our life's vital requirements (Mauritzen 2005<sup>2</sup>). Those peptides form the



Lipid biochemistry can be difficult, but if you know some of the language it eases the task. You may already know a few of the words, like omega 3, cholesterol and maybe even arachidonic acid. I have tried to lighten the task, but found it impossible without some technical words. Essential Fatty Acids are what we are made of. Analogies can help paint a picture, for example, few of us understand electricity, but that's OK, we can still turn on the lights. However, the subject of fatty acids is too important --- the lack of its knowledge will directly affect the quality of life for each of us, and if you are responsible for what others eat, their lives as well. You may have to review this paper and others more than once --- but that's OK too --- it's that important.

gates, receptors and ion channels (Corry 2006<sup>3</sup>) for ingress and egress in and out of the cell. They provide the multitudinous array of activity that trigger access and function of the cell. The lipid tails in the center of the membrane (the essential fatty acids, the EFAs) are the reservoir for the vast intercellular communication and information system through their prostaglandin regulatory activity. The prostaglandins, metabolized from the lipids we eat, may have evolved to be the basic control mechanism that permitted metazoan (which is principally what we are, a vast agglomeration of 100 trillion cells) since emerging from the primordial sea millions of years ago (Rudin 1985<sup>4</sup>). Thus the mere thought of multi-cellular activity, and especially the evolution of humankind, is, at our present level of knowledge, not possible without essential fatty acids. They are the precursors to prostaglandins, which organize the communication and control necessary for a group of cells to stay together. Before one can advance beyond unizoa (single cell organism) into multi-cell metazoan there must be both communication and a means of regulation. This is the profound world of the prostaglandins, the "local hormones" that control cell to cell interactions without which there can be no complex life form.

The membrane is the outside skin that surrounds every cell, however, there is much more membrane on the inside of the cell, actually ten times more, surrounding all the tiny organelles inside the cell. The membrane of each adult, if totaled together, is unbelievable in size. If we could unravel all the membranes of all the cells of an average person, place it all on a flat level surface --- it would cover an area of ~100 square kilometers (7.7  $\mu\text{m}^2$  times all the cells of our body<sup>2</sup>). If you'd care to jog around it, be prepared to do a marathon. The sheer volume and size of the membrane is hard to fathom --- actually impossible, there's nothing to compare it to.

Today, science has wondrous pictures of the membrane through electron microscopy, so we know what it looks like and how it's made. But its size is so small it is still unimaginable. It is so tiny you need 10,000 membranes stacked on top of each other to equal the thickness of a piece of paper. It's literally beyond comprehension. I have difficulty envisioning slicing a piece of paper 10 times let alone 10,000.

The membrane is composed of phospholipids, one of the smallest organic molecules of the body and the basic building blocks of the membrane. Approximately 70%

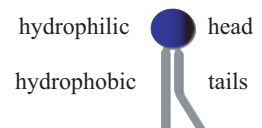
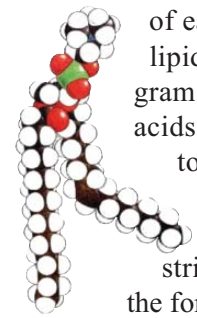
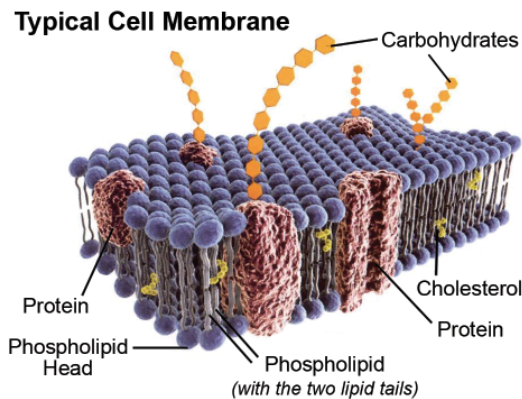
of each phospholipid is comprised of the two lipid tails (think strings of fat as in the diagram below). This is where the structural fatty acids, both saturated and unsaturated, assemble to surround and isolate each cell with its membrane, a remarkable thin protective insulator. The two lipid tails are thin strings of carbon and hydrogen that organize the formation of the bilipid membrane. The tails are hydrophobic, hate water, and scramble to line up and form a sphere, or bubble, to retreat (hide) from the watery environment.

The phospholipids assemble side by side, soldier fashion, with a duplicate line-up on the opposite side, forming a bilipid membrane, a continuous spherical closed bubble with the lipid tails comfortably in the middle of that thin line. The hydrophobic lipid tails can now safely hang out securely with water on both sides; with their head groups, who like water (hydrophilic), perfectly content to stick their heads in the water on either side of the cell. The two bilipid leaflets

of the membrane stay tightly together, but are not fastened in any way. They are actually two separate leaflets, one facing the outside of the cell (the cytoplasm), and one facing the inside of the cell (the cytosol). The leaflets are independent of each other with different horizontal fluidic motion but are physically bound together through a common hydrophobic desire to avoid the watery world on either side. It's the only way they can exist and not be washed away. It's their dislike of water that holds them in position --- forever. Inside the bubble, cellular life can now develop and grow in its own particular watery interior. Whatever specific chemistry may be needed by each cell can now be protected from the harsh sea outside.

If oil and water could get along --- we wouldn't be here. The simple characteristic of oil and water avoiding each other, refusing to mix, with the subsequent biochemical organization of a membrane, sets the stage for the beginning of life --- a marvel of biochemistry --- with an elegance that leaves you in awe of its beauty.

For all of life, the essential fatty acids (EFAs) that make up the membrane are not just essential, but, inarguably, the most essential of all nutrients. However, at the present time, the misinformation about fatty acids has so distorted our perception of fats and oils; it has undermined our ability to think clearly about how to maintain our health.

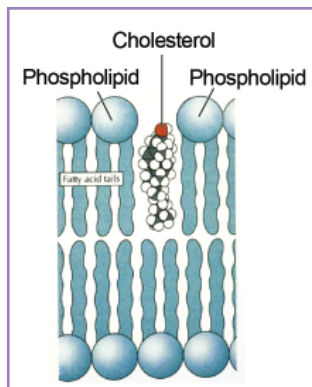


## Two Vital *FATS* That Get No Respect *Cholesterol and Arachidonic Acid*

The first, **CHOLESTEROL** --- contrary to current dogma, is an extremely important membrane structural fat, with emphasis on “**extremely**.” It is fat, not a lipid, with a wide range of body functions and a prime example of the distortion of our present perception of fats --- fats that our body needs for homeostasis. Professor Barenholz, of Hebrew University, 2002,<sup>5</sup> regarding the importance of cholesterol, “[The appearance of membrane-active sterols (cholesterol) in biological membranes of eukaryocytes is one of the major steps in membrane evolution].” (FYI, Humans are eukaryocytes, multi-cellular, as opposed to procaryocytes, single celled organisms, like bacteria.) Cholesterol is not only a vital cellular molecule, it is also a large part of us, as it occupies 30-40% of our membrane (Gurr 2002<sup>6</sup>). It is the precursor for vital hormones such as the adrenals, our fight or flight hormones, and the gonads, hormones that drive our reproductive machinery. Cholesterol is important for the metabolism of the fat soluble vitamins, A, D, E and K, and is a precursor for bile acids which manage our fatty acid intake from the gut to the cells. It is intimately involved in regulating membrane fluidity over a wide range of temperatures, as well as creating a strong membrane structure, which, incidentally, equates to a strong overall metabolism. Most individuals with high cholesterol have a strong metabolism --- and they know it.

Very little appears to impact one with high cholesterol, like airborne disturbances such as pollen with its potential for allergy, etc. “When present at high concentrations, cholesterol enhances the mechanical strength of the membrane, reduces its permeability, and suppresses the main-phase transition of the lipid bilayer” (McMullen 1996<sup>7</sup>). Mason et al 1996,<sup>8</sup> was able to detect a higher concentration of electrons that would congregate above the head of a cholesterol molecule in the membrane. He showed that ligands (peptides in the blood) flowing in the blood stream would avoid receptors positioned near the cholesterol molecule. They would simply go elsewhere on the membrane to establish contact. The resistance appears to make for a stronger, resistant cell --- and as said, individuals with high cholesterol sense it. Mason<sup>8</sup> also reported that the absorption rate of three drugs tested had an inverse ratio of absorption to the level of cholesterol in the membrane, establishing a protective relationship to the levels of cholesterol and the strength of the cell. A corollary is its association with autistic spectrum disorder. Sikora 2006,<sup>9</sup> reported that “approximately

three-fourths of the children with SLOS (Smith-Lemli-Opitz syndrome) had an ASD, and about 50% were diagnosed with Autism, the rest with pervasive developmental delay (PDD-NOS).” SLOS is an autosomal recessive condition caused by a defect in cholesterol synthesis. Tierney 2000,<sup>10</sup> demonstrated low cholesterol was associated with cognitive abilities from borderline intellectual functioning to profound mental retardation. Tierney et al, in 2006,<sup>11</sup> reporting on 19 samples of low cholesterol, “SLOS is a metabolic disorder associated with autism.” Cholesterol is



an essential element of myelin, the insulating material crucial for nerve function in the brain and central nervous system. Dr. Richard Kelley reported in 2000,<sup>12</sup> “There are heretofore unrecognized beneficial effects of cholesterol, especially in children, and that we should consider very carefully possible adverse effects that the popular war against cholesterol may have on the prenatal and postnatal development of children.”

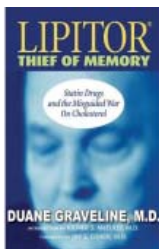
Pérez-Guzmán 2005<sup>13</sup> states that hypo-cholesterolemia is common among tuberculous patients and suggests that cholesterol should be used as a complementary measure in anti-tubercular treatment. How many more disorders, not yet studied, would respond favorably to the raising of cholesterol? Little is known or discussed about its benefits, but we see it in a number of patients with a strong cholesterol level (the value is currently debatable) that either come to our clinic or when we review their cases with their doctor (The BodyBio Blood Chemistry Report). We have long taught doctors to consider a patient’s cholesterol level when titrating a nutrient or a drug, and to prescribe less to a patient with low levels, and the reverse if high. This is not currently taught in medical schools, but should be. As noted by Patricia Kane, Ph.D., “Women who are having a difficult time becoming pregnant should first look at their cholesterol level as it is invariably low. As the diet is expanded to include essential fatty acids and phosphatidylcholine, the hormones derived from cholesterol normalize and pregnancy can more easily follow, and often does. Similarly, patients with environmental illness almost always have low cholesterol including those with sensitivity to foods, chemicals, or even frequencies, like Wi-fi, which are commonly due to the instability of the cell membrane. One patient complained that he had developed such a severe sensitivity to Wi-fi frequency that he could not travel or go into many business settings. His lab analyses revealed that he had a very low cholesterol level with a low Total Lipid Content within his red cells. The patient found relief from his symptoms after receiving high dosing with IV phosphatidylcholine and a diet high in eggs, butter, wild salmon

and balanced essential fatty acid supplementation.”  
(Patricia Kane, Ph.D. 2008).

However, cholesterol currently enjoys a label as “**Bad-Guy #1**,” which originally, may have had some semblance of logic, but is now rife with distortions, even hysteria. Here then is the question of the age --- since cholesterol is 30-40% of that vast membrane field protecting and managing critical metabolic functions, including mental acuity, sex and reproduction, why would we want to dispose of so much of it? Why indeed?

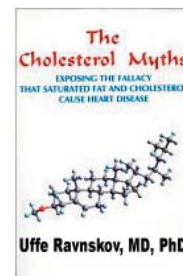
Today, the first analyte of your blood chemistry that your doctor focuses on is your cholesterol level, and if it’s elevated --- even though that value is in question --- will invariably write a prescription for a statin drug. We know the revenues generated by statin drugs to lower cholesterol are enormous, even obscene, but what is more important is the physical harm from those drugs, like transient global amnesia (TGA), liver damage or even worse, rhabdomyolysis, which, if unchecked, can cause kidney failure. Baychol<sup>®</sup>, a statin drug, was taken off the market because of its strong association with rhabdomyolysis. (Rhabdomyolysis is the breakdown of muscle fibers resulting in the release of muscle fiber contents (myoglobin) into the bloodstream, which can result in kidney damage).

In his book, Lipitor<sup>®</sup> Thief of Memory,<sup>14</sup> Duane Graveline, a medical doctor and former astronaut, details how he developed transient global amnesia (TGA), the loss of memory, after starting Lipitor<sup>®</sup>. TGA can be brief, lasting a few hours, or even twenty four hours or more. His struggle to uncover the rationale for his transient loss of memory and its association to the use of statin drugs reads like a mystery novel. Trying to find the reason for memory loss when you can’t remember whole periods is a challenge you don’t want to face. Amnesia (TGA) completely wipes out hours, even days, which, because of aging, opens thoughts about a possible beginning of mental disturbance such as Alzheimer’s. We’ve all had episodes of forgetting where we laid our keys, but when it persists it can shake up the strongest individual. The effort to unravel the missing pieces often leads to questions of one’s sanity, especially when those near and dear to you watch you struggle and begin to doubt you or just put it off as aging. Memory loss is invasive and indistinguishable from aging. If you lose it, who are you? There are recent disturbing reports of an association of statins and ALS, a devastating neurological disorder, Lou Gehrig’s Disease (Edwards 2007<sup>15</sup>). Dr. Graveline lists feedback from a number of individuals that discuss why they are frightened (Comforti 2006<sup>16</sup>) [www.spacedoc.net/ALS\\_statins.html](http://www.spacedoc.net/ALS_statins.html).



Uffe Ravnskov MD, PhD, reports in his book, The Cholesterol Myths,<sup>17</sup> that “**People with high cholesterol live the**

**longest. This statement seems so incredible that it takes a long time to clear one’s brainwashed mind to fully understand its importance.**” A shocking reversal of everything we’re led to believe about bad-guy cholesterol. Dr. Ravnskov has gathered a vast body of evidence, and, is himself, an impressive researcher. He is relentless in uncovering weaknesses in medical research and exposing flaws in some of the most touted studies that have led the medical world down a highly questionable road, one that everyone should be more aware of, especially if you are a health care professional, but even for anyone using drugs to lower their cholesterol.



Epidemiological studies have shown that an increased risk of coronary heart disease (CHD) may come from elevated levels of serum cholesterol, which may be increased from a dietary intake of saturated fats and cholesterol. Decades of large-scale tests in human and animal studies have purported to establish that link --- that’s what we were led to believe. However, in 2006, Harvard researcher Mozaffarian noted in The New England Journal of Medicine,<sup>18</sup> “that the consumption of *trans* fatty acids raises levels of low-density lipoprotein (LDL) cholesterol, reduces levels of high-density lipoprotein (HDL) cholesterol.” In addition Ascherio 2006,<sup>19</sup> also from Harvard, reported that “the intake of trans-unsaturated fatty acids (TFA) has been consistently shown in multiple and rigorous randomized trials to have adverse effects on blood lipids, most notably on the LDL:HDL cholesterol ratio, which is a strong marker of cardiovascular risk.” Zaloga 2006<sup>20</sup> also a Harvard researcher, reported that the focus on total cholesterol masked the fact that although trans fatty acids and saturated fatty acids increase low-density lipoprotein (LDL) cholesterol levels to a similar degree, *trans* fatty acids also lower high-density lipoprotein (HDL, the good cholesterol). ***These and similar reports appear to turn years of cholesterol reporting on its head --- and all the while we have been eating those funny, man made junk fats like margarine and mayonnaise, which was never considered to be a problem when they told us our cholesterol was too high, and now we are told, you must take a statin drug --- unbelievable.***

The raising of one’s cholesterol by the ingestion of foods high in saturated fats is more prevalent in today’s diet than ever before from the highly mechanized raising of beef, dairy, poultry, and now fish. We did not get here eating beef that was bunched together and fattened up in a corn feed lot before we got hold of it, and, any meat we did manage to kill was a fast moving animal like an antelope, a buffalo or a wildebeest, all of which evolve with a dramatically different fatty acid profile (Crawford 1989<sup>21</sup>). Both saturated fats and cholesterol are hard rigid fats --- and get this --- both are

essential for the health of the membrane, but not without an adequate supply of the unsaturated Essential Fatty Acids (PUFAs), which were much higher in fast moving grazing animals in our Paleolithic days. The cell membrane needs both, rigid saturated fats (the backbone) and vibrating active unsaturated lipids (the performers). Life is a balancing act. There are a large number of studies on the effectiveness of lowering cholesterol by using the primary parent EFAs, the omega-6 linoleic, and omega-3  $\alpha$ -linolenic.<sup>22-30</sup> (For a more complete review of EFA/Cholesterol abstracts visit [www.bodybio.com/abstracts/ch-efa](http://www.bodybio.com/abstracts/ch-efa)).

We are getting advice on cholesterol that is tainted. Recently, when a select group of famous doctors advised the government on new cholesterol guidelines for the public, something else most all of them had in common was not revealed. Eight of the nine were making money from the very companies whose cholesterol-lowering drugs they were urging upon millions of us. Two owned stock in them. Two others went to work for drug companies shortly after working on the guidelines. Another was a senior government scientist who moonlights for 10 companies and even serves on one of their boards (USA TODAY® 2004<sup>31</sup>). This is a picture that is repeated over and over throughout the medical world today, and not only in the USA. It is so pervasive that we can not trust the very group that we depend on for our health. Your personal doctor may not be guilty of any of this. He or she is caught up in a system that they have very little control of. They don't even have the freedom to exercise their own personal medical judgment, which, in many instances, because of our overly litigious society, may be the reverse of what they wind up writing you a prescription for. The system is broken.

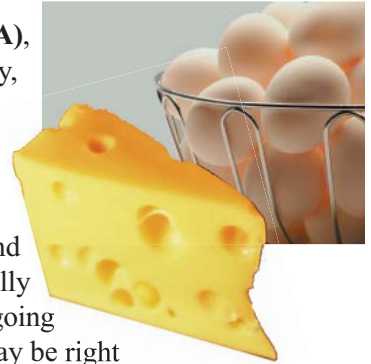
**Low cholesterol is not healthy** --- that's a statement you will probably never hear or see in print. Many studies have found that low cholesterol, in certain respects, is worse than high cholesterol. In 19 large studies of more than 68,000 deaths, reviewed by Professor David R. Jacobs<sup>32</sup> and his co-workers from the Division of Epidemiology at the University of Minnesota, low cholesterol predicted an increased risk of dying from gastrointestinal and respiratory diseases. Professor Jacobs and his group, together with Dr. Carlos Iribarren,<sup>33</sup> followed more than 100,000 healthy individuals in the San Francisco area for fifteen years. At the end of the study, those who had low cholesterol at the start of the study, had more often been admitted to the hospital because of an infectious disease. Low cholesterol and increased risk of early mortality has been well researched. (10, 34-38)

Cholesterol is a rigid fat, which can be controlled in the membrane by raising the concentration of polyunsaturated lipids, which makes the membrane more fluid. "A diet based on a high proportion of essential polyunsaturated fatty acids (fluid) would allow a higher incorporation of cholesterol (rigid) in the membranes to balance their fluidity, which

would contribute to lower blood cholesterol levels (Colin 2003<sup>28</sup>)." Colin et al also explored polyunsaturated fatty acids and the brain venturing into the subject of polyunsaturated fatty acids (PUFAs) and depression and an association of elevated omega 6 and low omega 3, which is beyond this article, but concludes with "some epidemiological, experimental and clinical data favoring the hypothesis that polyunsaturated fatty acids could play a role in the pathogenesis and/or the treatment of depression." (An interesting topic for the next BodyBio Bulletin --- Fatty Acids and the Brain).

## The Second *FAT* That Gets No Respect

is a lipid, no longer a fat, called Arachidonic Acid (AA), found in eggs, meat and dairy, which suffers the same harsh treatment as cholesterol but it's been receiving a bad rap for a much longer time. The attack on arachidonic acid and the omega 6 family, principally linoleic acid (LA), has been going on for decades. While AA may be right



behind cholesterol; the homeostatic importance of AA is on an even higher metabolic plane than cholesterol. The trumped-up case of labeling AA as "*Bad-Guy #2*" is for its role in initiating inflammation --- which it does --- but saying that alone is a one-sided statement, because it is also anti-inflammatory --- which no one mentions. There is, however, a large body of research showing the reverse, that AA and its derivatives are also anti-inflammatory.<sup>(43-52)</sup>

"Arachidonic acid (AA) is metabolized by COX-1 and COX-2 enzymes to form a mesmerizing array of biologically active products (NSAIDs, aspirin etc, block this conversion). These, in turn, are acted on by isomerases and synthases to form the Prostaglandins (PGs) and thromboxane A2" (Grosser 2006<sup>39</sup>). "Recently, our understanding of all these activated products has been transformed and is changing our perception of prostanoid biology" (Funk 2005<sup>40</sup>). NSAIDs are among the most commonly used drugs to relieve pain and inflammation by suppressing the COX function of forming PGs, which has the role of forming two opposing prostanoids, that of PGE<sub>2</sub> and prostacyclin (PGI<sub>2</sub>)<sup>40</sup> (Murata<sup>41</sup>). "The biological effects of these two prostaglandins are generally antagonistic to each other. PGE<sub>2</sub> is *pro-inflammatory*, induces proliferation, and is anti-apoptotic. In contrast, PGI<sub>2</sub> is *anti-inflammatory*, a strong vasodilator, an inhibitor of growth of vascular smooth muscle cells, and a potent inhibitor of platelet aggregation" (Garcia Rodriguez 2007<sup>42</sup>). \*Emphasis by author.

In effect, arachidonic acid can metabolize in both directions, either promote inflammation (PGE<sub>2</sub>), or, promote

anti-inflammation --- (PGI<sub>2</sub>), but we only hear of the inflammatory side, the one that tells you to buy ibuprofen, or aspirin, or even get a prescription for steroids, which also block AA metabolism. In effect, calling arachidonic acid inflammatory is a lie --- or a half-truth, which is really a whole lie.

## ***The Anti-Inflammatory Side of AA***

**Prostacyclin (PGI<sub>2</sub>)** is one of the most prominent prostaglandins, often considered a hormone by endocrinologists. PGI<sub>2</sub> is a potent anti-inflammatory agent, a vasodilator and blood pressure and pulmonary regulator. Long-term treatment with intravenous prostacyclin improves exercise capacity, hemodynamics (blood flow) and survival in most patients with primary pulmonary hypertension (PPH), and may be currently considered as the “gold standard” therapy for severe PPH patients (Sitbon 2002<sup>43</sup>). Prostacyclin is an estrogen mediator (Arnal 2007<sup>44</sup>) and is also cardio-protective. Suppression of prostacyclin (PGI<sub>2</sub>) is implicated in the cardiovascular hazard from inhibitors of cyclo-oxygenase (COX-2) (one of the main reasons why Vioxx® was a medical disaster). Furthermore, estrogen confers athero-protection via COX-2-dependent PGI<sub>2</sub> in mice, raising the possibility that COX inhibitors (NSAIDs) may undermine the cardio-protection. Garcia Rodriguez et al<sup>42</sup> contraindicates the use of NSAIDs, even an aspirin-a day, as cardio-protective. Suppression of AA with NSAIDs lowers PGI<sub>2</sub>, the principle anti-inflammatory agent derived from AA.

An increase in prostacyclin can facilitate pregnancy in women with fertility problems (Saldeen 2004<sup>45</sup>). It is a potent vasodilator (Oviedo 2004<sup>46</sup>) and inhibits platelet adhesion and cell growth (Nagaya 2005<sup>47</sup>). Prostacyclin therapy, delivered via continuous intravenous infusion, has been demonstrated to be effective in patients with severe Pulmonary Arterial Hypertension (PAH) (Launay 2006<sup>48</sup>). These are but a sample of research discussing the anti-inflammatory side of AA which extends also to a group of AA derivatives such as PGJ<sub>2</sub> which are not only anti-inflammatory (Abdelrahman 2004<sup>49</sup>), but also anti-tumorigenic (Harris 2002<sup>50</sup>, Kim 2007<sup>51</sup>, Kapadia 2008<sup>52</sup>).

Prostacyclin Pathway: COX-1 or COX-2 oxygenates AA producing PGH<sub>2</sub> --- then by prostacyclin synthase to PGI<sub>2</sub> --- or by PGH<sub>2</sub> to PGE<sub>2</sub>.

AA is a 20 carbon lipid chain with 4 double bonds (see Tech Notes), one of three eicosanoids (eico is Greek for 20), of which AA is the largest. The two other eicosanoids are DGLA, also an omega 6 lipid, and EPA, the only omega 3 eicosanoid. Of the total, AA comprises ~89%<sup>61</sup> of the three by volume, so it is the largest by a wide margin, overwhelmingly so. Oxygenation of eicosanoids by Cox 1 and 2 into PGs become the metabolic force of cellular life.

A review of the research concerning AA could easily fill a wall of medical textbooks. The activities of AA are so vital it is not possible to think of life at our level of complexity without arachidonic acid.

## **Non Steroidal Anti-inflammatory Drugs**

NSAIDs inactivate (do away with) a small percentage of each of the COX-1 and COX-2 enzymes with each dose. It is presumed that we can spare a few. If all of those vital enzymes were knocked out we would not survive since COX-1 and COX-2 initiate the formation of prostanoids from AA, DGLA and EPA. NSAIDs are not selective. In our attempt to suppress arachidonic acid and PGE<sub>2</sub> (The Bad Guy [?]), we are also blocking all prostaglandins including PGE<sub>1</sub> (from DGLA, a good guy) and PGE<sub>3</sub> (from EPA, also a good guy). The entire prostaglandin system of the body is suppressed.

Blocking a percentage of prostanoid production lowers activity throughout the body --- not just the portion under distress. If you have a tooth-ache or a headache and take an aspirin or acetaminophen, etc., the NSAID lowers metabolic function with the hope the individual problem will go away as the whole body's activity slows, and it does, sometimes. When we are in pain trying to preserve total function takes on a low priority, but taking aspirin, acetaminophen, or ibuprofen or any NSAID in excess is rife with metabolic disturbances, starting with the gut since we usually take them orally. Repetitive tempering of gut function when you need to maintain digestion is not an intelligent drug application. Acetaminophen is particularly toxic, and the principal ingredient of Tylenol® and other medications. “It is the most common drug-induced cause of liver failure from the depletion of hepatic glutathione.”<sup>53</sup> Glutathione is a vital sulfhydroxyl cellular molecule and the principle detoxifying agent throughout the body. Repeated use of an acetaminophen type NSAID may deplete the stores of glutathione and rob the body of protection, which, in our current toxic environment should be avoided. Listen up --- we need glutathione. If you are determined to use an NSAID, there is a wide choice available. However, consider that you are suppressing all the life supporting prostanoids. A healthier

alternative would be to balance the diet with the essential fatty acids so that the prostaglandins fall in balance, they are truly running the show.

**Resolvins** A whole new world of anti-inflammatory aids from AA, EPA and DHA called **Resolvins**, are a recently discovered natural anti-inflammatory hormone-type prostanoids. They search out the specific inflammation, such as asthma or arthritis and directly reverse the inflammation. Resolvins resolve it directly, hence the name --- the asthma or arthritis is relieved. It's a natural and direct action derived from the body's own lipid reservoir of AA, EPA or DHA, which is far more desirable than an indirect (body wide) NSAID or steroid form of relief. Resolvins have recently been synthesized in a medical laboratory from DHA and, oddly enough, by employing the services of a common yeast most of us are familiar with, candida, *C-albicans* (Haas-Stapleton 2007<sup>54</sup>). It appears promising that we may have a non-drug solution for inflammation in our future --- maybe (Serhan 2002-7<sup>55-57</sup>, Bannenberg 2004,<sup>58</sup> Schwab 2006<sup>59</sup>). If ... the current pharmaceutical establishment will promote or permit a natural competitive answer for inflammation ... don't hold your breath. Resolvins were discovered by Harvard researcher Charles Serhan in 1984, over 20 years ago.

The objective of labeling arachidonic acid as a huge biochemical boogie-man could be, in part, to enhance the marketing of NSAIDs and steroids as the anti-inflammatory solution. However, the media, by association, extended the negative press to the entire omega 6 fatty acid family and included linoleic acid --- *the* prime omega-6 Essential Fatty Acid. All omega-6s were branded as Bad-Guys. Little doubt, it was monetarily effective, but it was also nutritionally unconscionable, not to mention the years of misdirected research by the entire medical community. However, casting blame on AA is probably more the result of a lack of fatty acid knowledge, which, as you can tell by now is a complex subject. Branding cholesterol and arachidonic and the omega 6 fatty acid family *as bad* has set back our knowledge of health for a quarter-of-a-century. Suffice it to say there is no animal life on the planet possible without either cholesterol or arachidonic acid. How did we get so far off track --- better yet --- how do we get back?

Medline, the internet medical library of the world, provides instantaneous access to research at our fingertips. Type in "Arachidonic Acid" and you will be overwhelmed with 36,100 research studies from every university in the world --- enough to keep you occupied for half a lifetime. In spite of all the negativity, AA is the premier fatty acid in the body comprising ~12% of total brain lipids (Attwell et al., 1993<sup>60</sup>) and ~14% of the membrane of the red cells (Johns Hopkins, Red Blood Cell Fatty Acid Test<sup>61</sup>).

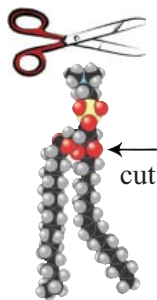
## To help view AA as a key player

let's take a brief walk with a few lipid researchers: (**Yiin and Lin**, 1998<sup>62</sup>) arachidonic acid is preferentially wasted in states of heavy metal toxicity; (**Kane**, 2002<sup>63</sup>) and has been observed to be sharply suppressed in red cell fatty acid analysis in states of heavy metal toxicity; (**Grandjean** 2003<sup>64</sup>) in particular, inhibition of desaturase activities by PCBs may affect the maintenance of arachidonic acid (AA) status during development. Because AA is of key importance for growth and development, these results suggest that this possible mechanism for PCB toxicity deserves to be explored; (**Bilak**, 2004<sup>65</sup>) arachidonic acid is a crucial precursor that is neuroprotective, an unexpected neuroprotective effect mediated by PGE<sub>2</sub>; in which activation of its EP<sub>2</sub> and EP<sub>3</sub> receptors protected motor neurons from chronic glutamate toxicity; (**McGiff**, 1991<sup>66</sup>) inadequate stores of AA can compromise detoxification. (**Wang** 2007<sup>67</sup>) AA and its derivatives are bioactive lipids that play an important role in regulating cell proliferation, apoptosis, tissue repair, blood clotting, blood vessel permeability, inflammation, and immune cell behavior; (**Koletzko** 1991<sup>68</sup>) arachidonic acid may have a growth-promoting effect which could be related to its role as an eicosanoid precursor or to its structural function in membrane lipids; (**Carnielli** VP 2007<sup>69</sup>) docosahexaenoic acid (DHA) and arachidonic acid (AA) are long-chain polyunsaturated fatty acids (LCPs) that play pivotal roles in growth and neurodevelopment; (**Papadimitriou** 2007<sup>70</sup>) AA and its COX-2 generated metabolite, PGE<sub>2</sub>, can protect beta-cells from pancreatic islets from apoptosis (programmed cell death); (**Das** 2006<sup>71</sup>) Some of these long-chain metabolites, specifically from arachidonic acid, not only form precursors to respective prostaglandins (PGs), thromboxanes (TXs), and leukotrienes (LTs), but also give rise to lipoxins (LXs) and resolvins that have potent anti-inflammatory actions. In several diseases such as obesity, hypertension, diabetes mellitus, coronary heart disease, alcoholism, schizophrenia, Alzheimer's disease, atherosclerosis, and cancer the metabolism of EFAs is altered. Thus, EFAs and their derivatives have significant clinical implications; (**McCullough** 2004<sup>72</sup>) Increased PCB exposure was associated with a modest decrease in serum AA concentrations, which is in accordance with the experimental evidence of desaturase inhibition by PCBs. Such interference with LCP utilization could attenuate the beneficial effects of the essential lipids contained in seafood. Because AA is of key importance for growth and development, these results suggest that this possible mechanism for PCB toxicity deserves to be explored; (**Hennig** 2007<sup>73</sup>) pancreatic cancer patients have an abysmal prognosis because of late diagnosis and lack of therapeutic options. Evidence that 15-lipoxygenase-1 (15-LOX-1, from AA) expression and activity may exert anti-tumorigenic effects in pancreatic cancer; (**Harbige** 2007<sup>74</sup>) Epidemiological, biochemical, animal model and clinical trial data described in this overview strongly suggest that polyunsaturated fatty acids, particularly n-6 fatty acids, have a role in the pathogenesis and treatment of multiple sclerosis (MS); (**Serhan** 2007<sup>75</sup>). Anti-inflammatory TGF-beta markedly decreased with loss of membrane n-6 fatty acids linoleic (18:2n-6) and arachidonic acids (20:4n-6). It is well-appreciated that arachidonic acid is a precursor to potent bioactive mediators, such as prostaglandins, leukotrienes, and lipoxins which is an exciting area with important roles of lipid-derived mediators in health and disease.

Getting a different picture than what we've been told? Wait --- we're not finished --- when we get to food and oil production over the last century, it's even worse. Even when faced with more than ample evidence of AA and its pro-metabolic role, no one seems willing to step up and try to set the record straight. Why? Are there food police lurking about?

NSAIDs alleviate pain by counteracting the COX-1 and COX-2 enzymes. Steroids accomplish the same suppression of AA but have no anti-cyclo-oxygenase activity. Steroids prevent the release of arachidonic acid from the membrane phospholipids by the inhibition of phospholipase A2 activity.<sup>76</sup> This comprises the second large anti-inflammatory medical option. **Steroids** are beyond the scope of this article, however, the mode of action is to specifically block **Phospholipase A2 (PLA2)**.<sup>76,77</sup> Inflammation, in itself, is part of a vast signaling network which attempts to alarm and correct simultaneously, but is often disregarded, which we may do, in part, from a misdirected lifestyle. An almost untouchable subject is the consumption of excess carbohydrates and the subsequent rise in blood sugar and its potential inflammatory effect. The physiological effect of too many carbs directly implicates AA. Excess glucose stimulates the rise of glucose and insulin which stimulates the production of phospholipase A2 (Turk 1988<sup>78</sup>).

PLA2 is a lipase, a lipid scissors. It cuts off the lipid tail at the second position of the phospholipids; recall that each PL has two lipid tails. AA resides principally on the second position. When freed by a snip from PLA2, AA will tend to initiate one or more of its vast myriad of management functions, which could include inflammation --- or, as we now know, anti-inflammation. PLA2 starts the whole process by freeing AA. Steroids block PLA2 body-wide. Reducing PLA2 reduces AA, effectively limiting function. Suddenly, with less AA available, much of normal body activity becomes null and void, which is preferred when faced with an emergency --- like fight or flight. That's what steroids do; they set you up to handle an emergency. But PLA2 is a cellular peptide (enzyme) that can be excited and overproduced. A request to the DNA to code for (produce) an excessive amount of PLA2 results in a consummate increase of AA being dumped into the milieu and the possible beginning of an arachidonic acid cascade. Too much PLA2, and it's off to the races with an excited and usually inflamed metabolism. As previously indicated, glucose can also stimulate PLA2. An analysis of the research suggests that



(Loweth 1996<sup>79</sup>) "... in pancreatic beta-cells, the rise in arachidonic acid results primarily from phospholipid hydrolysis by phospholipase A2, and activation of this enzyme has been shown to accompany glucose-induced insulin secretion." (Ma 1997<sup>80</sup>) "...the hydrolysis (freeing) of arachidonic acid from membrane phospholipids in glucose-stimulated islets appears to be mediated by phospholipase A2 (PLA2)." (Bastard 2006<sup>81</sup>--- Zawalich 1985<sup>87</sup>).

*a glucose binge* can result in an over-expression of PLA2. Our world is overloaded with processed goodies, and most of us, at times, are prone to indulge. An excess of carbohydrates stresses the body, and often, if we pay attention, will send a message such as stomach distress, mood swings, or headaches etc. Disregarding the signals, which we may do because of a preference of hanging on to our favorite **junk food**, may, for example, lead to a disturbed digestive system. This could be diagnosed as inflammation, which it usually is --- with AA then becoming the guilty party as the initiator of the disturbance, when it was just doing a management function. Should AA be charged with the crime, when in all probability, the event was the result of an irresponsible dietary venture? *He who is free from guilt has permission to cast the first stone.*



*The Answer* to the cholesterol and AA dilemma is so simple it is a challenge to know where to begin --- yet the solution is merely that cholesterol and AA, and much more, can be managed by the intake of the primary Essentials, the EFAs, which, because of the sheer volume of negative press, may seem beyond credulity. The mechanism, in part, lies in raising membrane fluidity by the omega 6 and the omega 3 essential fatty acids (EFAs). Linoleic acid and alpha linolenic acid are made only by plants --- we must eat them, and they must be in the right ratio, or we are lost in our effort to reach better health. Excessive saturated fats and cholesterol with insufficient vibrating omega-6 and omega-3 EFAs to keep the membrane stream moving creates a recipe for an aging or diseased metabolism, or even an ischemic event. *However, we must act responsibly regarding our diet for fluidity to work its magic. It can't do it by itself.*

The two lipid tails make up ~70% of membrane phospholipids and are composed of both saturated and unsaturated FAs. AA comprises ~14% of all those lipid tails --- sitting in that vast 100 square kilometer field. Science has yet to unravel the total function of AA, but what is known, is mind bending. AA, by a wide margin, is the largest concentration of lipid energy in human metabolism (more on this in tech notes). Very little function is possible without AA, including thought and motion, sensory perception, sight, hearing, touch, DNA output, sex and fetal development, the entire birthing process, wound management, including proliferation and agglomeration, restriction of blood loss, macrophage control and clean up as part of the healing process, and more. An apt description could be that AA is the CEO of the metabolic corporation --- or the conductor of a vast metabolic orchestra waving its wand continuously over that membrane field directing every



*Arachidonic Acid*



function imaginable. The functions of AA will be studied for years, possibly centuries. Venturing into the function of AA and attempting to grasp its total role is akin to understanding quantum physics, which is only partially understood, as is our present understanding of AA.

***Can you just add EFAs in the diet for better health? In a word, Yes. But for a more accurate evaluation of your fatty acids you can consult with your doctor and request a red blood cell fatty acid analysis (RBCFA), which we suggest for all neurological and complex disturbances. However, raising membrane fluidity is remarkably easy and should be standard fare for all of us.***

## Omega 3 EFAs

Alpha linolenic acid (ALA), is the beginning (precursor) fatty acid of the n-3 family. It is, therefore, **the** essential omega 3 lipid. The higher order of omega 3 lipids, HUFAs (highly unsaturated FAs), EPA and DHA, as in fish oil, can be metabolized from ALA, if you are young and healthy (females are somewhat better), but then only a few past the age of 25 are able to produce these higher order HUFAs in any reasonable quantity. EPA and DHA are then considered to be essential because all large animals (which we are) are inefficient in that metabolic process. Small mammals seem to retain that function. David Horrobin MD, PhD, a well-known lipid scientist, classed rats as 100% fatty acid efficient, while humans (and all large mammals), were, up to the age of 25, only ~5% efficient. Fish oil capsules have recently enjoyed mythical notoriety, some of it warranted. Usually, however, all things blessed with too much press tend to become overblown, and today, fish oil has reached that threshold. It is currently used as a cure-all, which it is not, but any nutrient can be problematic if taken in excess. (see BodyBio's Bulletin on Kirunal at [www.bodybio.com](http://www.bodybio.com)). The parent omega 3 fatty acid, ALA, has been somewhat forgotten under the onslaught of current attention placed on fish oils.

After a dozen years or more of close examination of detailed red cell lipid analysis at BodyBio, we have witnessed and documented repeated over-expression of omega 3 fatty acids EPA and DHA, with the ultimate suppression of omega 6 fatty acids. BodyBio analyzes the patient's complex lipid biochemistry through a computerized report, which is then forwarded to the physician. Over 90% are reporting high EPA and DHA levels most often from taking an excess of fish oil. The patients often record their fish oil (and fish intake) along with their current supplements on their medical history form. The elevated levels of EPA and DHA predominantly come from suggestions by their regular physicians to try fish oil. With the encouragement now coming from

an authority, the over-expression of EPA and DHA has reached epidemic proportions. However, the direct effect on the body is that fish oil suppresses arachidonic acid and other omega 6 fatty acids (Gurr 2002<sup>6</sup>), which further cause metabolic disturbances (see case studies). This is clearly visible in the patient's red blood cell fatty acid report, showing a distorted fatty acid profile and a disturbed metabolism, much of which is reversible with correct lipid adjustment. All nutrients should be added gently unless one is armed with pertinent information and guidance, such as a lab test showing deficiency, or by a knowledgeable professional aware of the current popular excessive use of fish oils. (The high 90% that we see of over-expression of fish oil is skewed because the individual who seeks a RBC fatty acid test is one who has read up [Google?] on the latest nutrient promotion, often taking fish oil, and then seeks a doctor that has an interest in fatty acid analysis and nutrition). (BodyBio RBC fatty acid reports are performed at Kennedy Krieger Institute - Johns Hopkins University, the premier fatty acid testing laboratory in the world).

One of the most important concepts to be gleaned from this review is to gain an appreciation of the value of a-linolenic, ALA, **the** essential n-3 fatty acid. By focusing solely on the higher n-3 fatty acids, the HUFAs, EPA and DHA, we are shifting homeostasis away from the omega 6s and also away from ALA, which is highly beneficial in its own right and discussed further below as we review the history of Budwig and Rudin. The case studies that follow will also help shed light on the subject.

## Essence

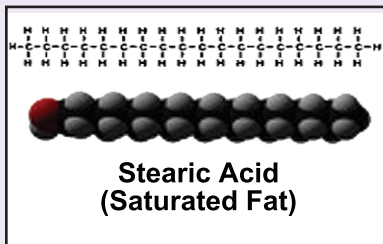
***of the essential fats:*** Fats come in two varieties, saturated (SFA) and unsaturated (mono and poly-unsaturated, M/PUFA). Membrane saturated fats are hard rigid fats. In reality they are little sticks of wax since they melt at a temperature of ~155 degrees (68C)<sup>6</sup>, in effect making the SFs solid and not liquid in the body. To be liquid in the body they must liquefy at or below 98.6 F (37C), which means that all SFs are solid. The white particles in meat are largely SF and are still a good choice for cooking; if rendered into lard as done for centuries (If collected and formed with a wick in the center, becomes a candle and can be burned to light our way, also done for centuries).

The unsaturated fats, preferably called lipids, come in two varieties as well, monounsaturated (MUFA, one double bond) and polyunsaturated (PUFA, more than one).

Both SFAs and M/PUFAS are lipid tails, strings of carbon, 16-22 long, linked together. MUFAs and PUFAs are

unsaturated lipids and are a much different kettle of fat because they are not solid in the body, they are now lipids and they move. We don't ordinarily think of oils as moving. As a liquid, oil can be poured from one container to another, but MOVING? The answer is, YES. While saturated fats are rigid sticks of wax, unsaturated lipids are in constant motion, all by themselves.

The chemistry of life gets its start by assembling strings of carbons. Each carbon (C) has two hydrogen atoms (H) attached to it all along the chain, making the string

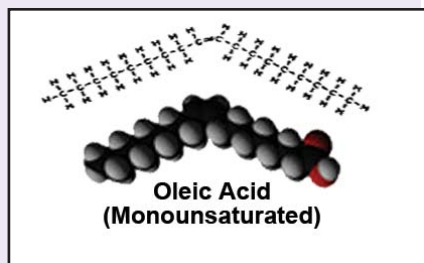


of carbons saturated with hydrogen (SF). In addition, all cells have desaturase enzymes, endowed with the ability to remove two hydrogen atoms from one side of that carbon string, making it unsaturated. A desaturase enzyme desaturates a saturated string (takes off with 2 H atoms --- steals them) making it unsaturated and forming a cis double-bond. You could say that it not only desaturated it, but in effect, destabilized it, for, from that point on, that string of carbons begins to vibrate and never stops. But read on, it gets more interesting because this is the beginning of life.

Unsaturated lipids have a gap (hole) left on one side of the carbon chain from the removal of the two Hs. The resulting cis double-bond, makes the lipid chain unstable. The carbon string kinks itself (~37°) trying to fill the gap left in the carbon chain. It tries to close the gap but is just as quickly rejected. It now vibrates back and forth --- attraction and rejection, and will literally do that dance forever. The diagram below shows a flat lipid that appears stationary, which it is anything but. It never stops vibrating --- unless oxygen

(a free radical) jumps into that gap and spoils the active PUFA chain making the lipid rancid and once again rigid.

Anti-oxidants help by blocking that pesky free radical and keep



that wondrous vibrating cis-double bond humming. Clearly there is great benefit in having vitamin E and C on hand as insurance (anti-oxidant insurance) against losing the benefits of those life-giving PUFAs. Plants and animals can further desaturate the lipid string, doing that same desaturase act again at another location on the string of carbons, making it POLY-unsaturated (more than one). This singular act propels the diversity of life. The concept of a vibrating string of fat (now a lipid) as a storehouse of life's energy is not an easy picture. It's difficult to get a glimpse of the membrane with untold millions of those vibrating lipids

responsible for controlling our flickering thoughts and movements --- but that's what they do. Armed with just a bit of the fatty acid metabolic scene, we can begin to recognize the vast importance of the omega 6 and the omega 3s, the essential fatty acids that do all the work and come exclusively from the diet. Only then can we begin to appreciate what we put into our mouths and how vital those oils are. We depend on the process industry to carefully squeeze the seeds of sunflower, safflower, canola, walnut, flax etc. We need them to take special care of how they handle such important food that influences our memory, sight, hearing, balance, love, learning, growth, reproduction ... an endless list.

The movement or frequency from the cis-double-bond generates heat in the string of carbons, making the MUFA lipid string liquid at 55° F (13C). Just that one cis-double bond has sufficient energy for the beginning of the all-important fluidity of the membrane. Before that desaturation, every carbon was filled with 2-H, making the lipid chain full, saturated and stable (non-moving). By inducing a gap in the string of a saturated fat, a gap that destabilized it, the ensuing movement creates a vibrating wonder --- because it now has the energy of life --- actually, the beginning of all life on the planet, quite possibly in the universe.

Is it that simple --- YES --- either a wax-like stationary stick (a fat) with no life-like character, or an active vibrating lipid string with a perpetual built-in source of energy. The combination of a saturated fat and a lipid are the basic building blocks that make up the two lipid tails of the phospholipids (PLs) of the membrane. That magnificent membrane is the skin of every cell and organelle. The combination of both the wax-like saturated fats and the vibrating mono and poly-unsaturated lipids combine to form the hydrophobic lipid chains of the PLs. The wax-like sticks give the membrane its strength, like a backbone, and the vibrating M/PUFAs give it the movement of life. It's an elegant combination, the essential omega 6 and the omega 3 lipid tails (if, you've eaten enough of them), along with the sticks of wax (which we seem to get too much of). Keeping those two tails plentiful and in proportion to each other is the hidden secret for good health.

We can make some of the fats and oils ourselves and do so, both the SFAs and the MUFAs, but not the PUFAs. A high percentage comes from the diet, especially those vital PUFA n-6s and n-3s, which we can not make at all. All fats and oils come prepackaged in the diet in just two varieties --- either with two lipid tails as structural PLs (phospholipids), or with three lipid tails as triglycerides, "tri" for three (TR).

The process of digestion disassembles all fat molecules (both PLs and TRs) and moves the components to the cells whereupon the carbon chains are either (1) burned for energy, or, (2) combined as phospholipids to form new cell membranes, or, (3) if we have more than we need at the moment, stored as triglycerides in adipose tissue for later use. Excess sugars are also converted into fatty acid chains and form triglycerides (3 lipid tails). When we are not careful and consume too much sugar, or grains, or fat, we will accumulate triglycerides, which may reappear around our midsection. A standard blood test usually reports both our cholesterol and TR levels, which are a measure of both our diet and our FA metabolism.

## Seed Oils

### *Edible oils come from the seeds of plants*

which are the start of the plant's next generation. The outer husk protects the oils from air, specifically oxygen, which, if exposed, will oxidize the oils and destroy the seed's ability to germinate. Oxidized EFAs are equally harmful to us. Food chemists are well aware of this, but to date there is little care or protection in the process of squeezing the oil from the seeds to avoid oxidation. There are a few small manufacturers in the health food industry that produce organic, cold pressed oils, but the huge oil processing industry totally looks the other way.



Oil seeds are pressed under high pressure with subsequent high temperature to squeeze out the oil which includes the EFAs. The increased temperature damages the seed oils but economics drives the producers to squeeze out the last drop. Heat is destructive to the unsaturated oils, the more polyunsaturated, the more fragile the oil. The vast majority of oil production from corn, soy, sunflower, safflower, cottonseed\*, walnut, etc. are pressed with chemical extraction (hexane), refined and packed in clear bottles for supermarket display. We admire the pretty clear oil, which is intended to convey the image of purity. Nothing could be further from the truth.

The preferred oils, stable enough to heat and cook with, are olive, butter, lard, coconut, and palm which are predominantly saturated fats, with the exception of olive, predominantly a MUFA, mono-unsaturated lipid. The oils from corn, sunflower, safflower, soy, flax, hemp etc., have a high percentage of the life giving polyunsaturated Fatty Acids (PUFAs) and are easily damaged by heating --- either by us in our kitchens (please do not cook with them),

\*Cottonseed oil is a byproduct of farming cotton grown with lower restrictions as to pesticides and herbicides.

or the fast food purveyors with their tasty french fries, or by our favorite restaurant cooking with total ignorance of what lipids are all about, or by the gross mishandling by the big food processors with chemicals and hydrogenation.

Seeds should be cold pressed under a blanket of nitrogen (nitrogen protects against oxygen damage), lower pressure equates to lower heat and less oil damage. Additionally, the use of dark or opaque bottles is necessary to protect the oils from light, since light is 1000 times more deleterious to the sensitive oils than exposure to air. They should also be kept cold (refrigerated) all along the process, much like the milk industry, immediately from the cow, to the homogenizing, bottling, trucking, and finally to the food store and into our homes to be stored in our refrigerators. We should treat our oils with affection; they are the beginning of life --- our life.

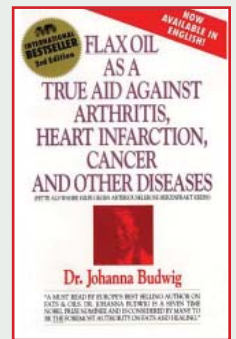
## Budwig & Rudin

### *The Cottage Cheese and Flax Oil Diet*

**Johanna Budwig (1908 - 2003)**, was a brilliant German pharmacologist, with doctorates in chemistry and physics, a seven-times Nobel Prize nominee, who worked as the chief expert-consultant for drugs and fats at the former Bundesanstalt für Fettforschung (Federal Institute for Fats Research). Dr. Budwig openly attacked the damaging processing of our food oils, and although the general public was eager for this new information, the German manufacturers of commercial dietary fats (margarine, hard shortening and vegetable oils) went to extremes to prevent her from publishing her findings. Their war against Budwig was probably instrumental in her being denied the Nobel.

Budwig railed against the use of what she calls "pseudo" fats. Those are the harmful trans-fats, principally "hydrogenated" or "partially hydrogenated," which destroys their life-giving oxygenating function (the cis-double bonds). Hydrogenation preferentially attacks the omega 3 (alpha linolenic) oils, twisting the molecular structure of the lipid molecule into a trans-fat. The cell is fooled into thinking that trans-fats are OK because a trans-fat looks normal. Hydrogenated fats can take their place on the phospholipids (PLs), but it is not the same.

What was once a phospholipid with a high energy omega-3 or omega-6 lipid is now a phospholipid with a trans-fat (liquid at 111°, now solid in the body).



The hydrogenation of PUFAs preferentially attacks the omega-3, ALA, creating a solid wax-like trans-fat, which lengthens the shelf life of any product made with that oil. The lifeless trans-fats with its longer shelf life were quickly adopted by the food processors. It's all a bad game of destruction totally hidden from view. We incorporate those distorted fats into our membranes since they appear biochemically normal. The metabolic destruction happens slowly, years later, long after we ate the bad guys. Trans-fats encourage hardening of the arteries since they are actually hard fats themselves, and more important, is the loss of the omega 3, ALA. Recently, there have been a number of reports documenting the harmful effects of trans-fats and their relation to cardiovascular disease, (discussed earlier) thus directly implicating trans-EFAs, especially trans-linoleic acid, with increased cardiovascular risk. The universities, led by Harvard Medical School, which have recently collaborated on these studies, are impressive.

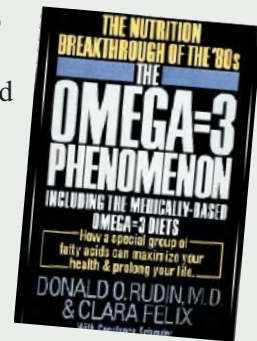
Even though the dangers of trans-fats were sung from the rooftops for decades by nutritionally minded doctors, the impressive credentialed universities were able to initiate changes and directly influence public health. There is no substitute for that. The current FDA labeling (probably triggered by the reports from Harvard) of "trans" on all foods has encouraged a number of cities and states to ban its use in restaurants. The knowledge of harmful hydrogenation was known 50-60 years ago. It is difficult to imagine the damage --- how much margarine, mayonnaise, and other funny fats in salad dressings and cooking oils did we consume in that half century?

Budwig said that the best combination is cottage cheese and linseed oil. Linseed is high in omega 3s (not the fish oil variety of n-3s, EPA and DHA --- but ALA). Budwig or Rudin (below) never used fish oil for n-3s; it was not yet in vogue. Budwig claimed that "the diet is indicated for all kinds of chronic diseases, especially heart ailments (coronary thrombosis), gall disorders, diabetes, arthritis, and malignancies. It improves failing hearing and sight. It is the ideal nutrient for children and infants."



**Donald Rudin (1923 - 2006):** In the mid 1980s', Donald Rudin, a Harvard MD and brilliant mathematician, as well as a professor at Harvard, and one of world's leading experts on omega 3 oils, followed Budwig by also using flax oil (~55% ALA) to resolve EFA deficiency in patients, but, with mixed results. Patients had positive

response initially followed by a sharp deterioration with continued use of flax oil. For 3-4 months, the diet could provide clinical resolve of psoriasis, eczema, internal bowel improvements, and a myriad of health benefits, even a marvelous smoothing of the skin on the hands and feet. Unfortunately, as Rudin reported in his manuscript, this lasted for several months, but was followed by a decline, and a return of symptoms after which he took them off the flax oil diet. By stopping the flax, the patient gained relief. Later, Rudin would retry the diet when the patients' original symptoms returned, and almost always produced periods of relief of their symptoms again. This on and off approach was not only confusing, but frustrated much of Rudin's effort at reaching a satisfactory EFA answer. Based on our current EFA knowledge about the ratio of omega 6 and omega 3 FAs, as well as Rudin's frustration, we can only presume the same to have plagued Budwig. (Dr. Rudin shared his observations and his manuscript, The Omega Factor: Our Nutritional Missing Link, with both Ed and Patricia Kane, Ph.D. and, was, up until his death in 2006, on the Advisory Board of BodyBio). Later research during the 1990s showed they were missing an important piece of the lipid puzzle. They did not realize that flax was not the answer --- the high n-3s (ALA) had created a significant problem when kept on the diet too long. The high n-3s were displacing the n-6s disturbing the EFA balance.

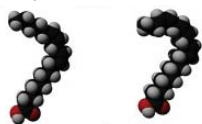


## FLAX OIL WAS NOT THE ANSWER

Both Budwig and Rudin had brilliant foresight in emphasizing the mixing of essential proteins and essential fatty acids --- especially discovering that the missing piece in our world of processed food was the re-addition of the n-3 alpha linolenic acid. Using flax and cottage cheese, Budwig and Rudin could effectively add ALA back, and temporarily heal the body. However, the research at that time was incomplete. A significant piece of the lipid puzzle came later from a group of scientists from Bar Ilan University of Haifa, Israel, and Boston University. Yehuda, Mostofsky, Rabinovitz, and Carasso have consistently shown that the most beneficial ratio of essential fats (EFA) is 4 parts of linoleic acid (LA) to 1 part alpha linolenic acid (ALA), 80% omega-6 to 20% omega-3, or a 4:1 EFA ratio. The difficulty of using flax oil is that the ratio is wrong. It contains ~17% omega-6 (linoleic) to ~58% omega-3 (linolenic). That's a 1:3½ ratio compared to Yehuda's 4:1 --- almost the exact reverse.

# The Fabulous 4:1 Ratio

EFAs play such a major part in bodily function, the blink of an eye, the wiggle of a toe --- even our flickering thoughts; it's a challenge to try to describe it. To raise fluidity (think energy) of our cell membranes we need those omega 6 (n-6) and omega 3 (n-3) oils, and we need them in the right ratio. However, the ratio between the two essential EFAs is equally difficult since they both use the same enzymes to metabolize their lipid chains to the higher order of fatty acids, the HUFAs. LA and ALA are both 18 carbons



**Linoleic**   **Linolenic**

long. Both must be elongated (add more carbons) by an elongase enzyme (to 20 and 22 carbons) and both must be desaturated by D6D and D5D. LA and ALA use those

same enzymes, which places them in competition with each other, sort of a mini-war as to which will get served. However, even though they are both the same length of carbons, 18, the omega-3s have an energy advantage over the 6s. Alpha-linolenic (n-3) has 3 double bonds compared to linoleic (n-6) with 2. The cis-double bonds are the seat of the energy of PUFAs (and of all life), giving ALA 50% more oomph than LA.

In addition, the location of the first cis-double bond on the chain is critical. This pertains not just to the base EFAs (LA and ALA), but also to all members of each family. For ALA and all the n-3s, the first DB on the carbon chain is positioned 3 carbons up from the methyl end (the methyl end is the tip of the chain). It derives the name omega-3, from the location of the first cis-DB on the carbon chain, which is at the 3rd carbon, actually between the 3rd and 4th. The destabilizing dance of the first cis-double bond of the n-3s effectively swings just 3 carbons of the chain, a much lighter load than for its competitor LA, hence a higher frequency. The n-6 first DB is between the 6th and the 7th position and has to swing 6 carbons, twice the amount, which equates to a lower frequency. Recall that the activity level of the cis-double bond of poly-unsaturated lipids is the loss of two H atoms on one side, inducing a frequency. The frequency of ALA is higher because it's swinging a lighter load --- simple. Swinging 3 carbons back and forth is easier than swinging 6. That gives the 3s an energy advantage. At a one to one ratio the 3s will win the metabolic race and subsequently suppress the 6s, which we see in the RBC Fatty Acid test results. The difference in activity level helps to visualize how life survives in extremely cold environments.

All life on the planet requires more omega 3s (higher energy) as we move away from equatorial climates towards the North and South poles. The higher frequency of the omega 3s provides a higher lipid chain movement with greater

resistance to cold. Wheat grown in central Canada has more n-3s than wheat grown in Oklahoma. The higher fluidity is a must for the sap to be able to flow as the temperature drops. All life in the frozen tundra such as polar bears, Eskimos, and especially the Emperor Penguins have a higher omega 3 content. Standing in frigid 60-70 degrees below, with gale force winds, with only their unique body chemistry, is an awesome evolutionary event, only possible with a high concentration of omega 3s. It starts with the food supply in the oceans, which is enhanced by the longer days with more sun in the Polar Regions, both north and south, contributing to an explosion of life, all with a higher omega 3 content in their tissues, a necessary fatty acid characteristic for life in that part of the world. The high frequency n-3 oils move up the food chain from the plankton to krill, salmon, seals, whales, and Eskimos. We, in the warmer climes, need omega 3s as well, but not nearly to the extent that life does in the frozen Arctics.

The discovery of the essentiality of the long-chain polyunsaturated fatty acids was made by Burr and Burr, George and his wife, Mildred, in 1929. We knew back then that both the n-6s and n-3s were essential. We also knew that a healthy cell can make as much omega 9 fats (MUFAs) as it needs, so omega 9 fats are not essential. But we definitely can not make the EFAs, the 6s or the 3s; only plants can do that --- and since they are essential, they must be part of our diet --- but that was it. Up to the 1990s, medical science did not have a clue as to how much of each, only the importance of both, but we were making headway.

An important step was made by Bourre et al from France in 1989. Along with colleagues, he discovered that feeding rats a diet containing oils that were low in alpha linolenic acid (ALA), such as corn or safflower oil, resulted in reduced amounts of docosahexaenoic acid (DHA) in all brain cells compared to rats fed a diet of soybean oil (8% ALA), or canola oil (10% ALA). A diet of corn or safflower oil, low in n-3, led to anomalies in eyesight and dramatically impacted learning. Feeding safflower oil (less than 1% omega-3) would not raise the necessary DHA, the dominant n-3 HUFA in the brain, but feeding sunflower or canola provided enough omega 3s for the small animals, since they are more proficient in FA metabolism. Bourre also recorded the rate of tissue recovery, which was rapid, in just 2 weeks in the kidney and liver, 3 weeks in the lung, 6 weeks in the retina and 10 weeks in the testes. Bourre's work on omega 3 deficiencies with its negative effects on the brain, and then the rapid reversal of n-3's in the organs, was significant.

**Yehuda:** However, before 1993, how much of each of the EFAs was still unknown. Prior to Bourre, Yehuda and Carasso from Israel had published an EFA study with

soybean oil, showing significant improvement in learning capacity (1987<sup>87</sup>), however, the more definitive testing followed in 1993<sup>88</sup> which zeroed in on the ratio of the 6s and the 3s. Yehuda, Mostovsky, Carasso, and Rabinowitz created the most thorough testing regime yet done using linoleic (omega 6) at seven different ranges, 3, 3.5, 4, 4.5, 5, 5.5, and 6, to 1 part linolenic (omega 3), however, the majority of testing encompassed the four ranges from 3.5 to 5:1. The results covered learning performance, pain thresholds, and thermoregulation, with later studies on chemical insult and speed of recovery. Even though the specific mode of action remained unresolved, the tests conclusively proved the optimum ratio to be 4:1. Quoting from Yehuda's 93 studies, "The initial hypothesis that attempted to explain these results focused on the amount of polyunsaturated fatty acids (PUFAs) in soybean oil. However, sunflower oil, which contains a higher level of PUFAs than soybean oil, failed to produce the positive effects of soybean oil. Since soybean oil contains a considerably higher level of  $\alpha$ -linolenic acid (8-9%) than sunflower oil (about 0.4%), we postulated that the relative quantity (ratio) of  $\alpha$ -linolenic acid to linoleic acid (18:2 $\omega$ 6), rather than the absolute quantities of the fatty acids, was the critical factor for brain bioavailability and the central nervous system-mediated effects."

The extensiveness of the studies was impressive, as one can judge from the range of ratios tested. Repeatedly, the 4:1 ratio was shown to be optimum. Quoting from the conclusion of Yehuda's 2005 paper on "Essential fatty acids and the brain: From infancy to aging: **Infancy and aging are two sensitive and critical periods, where adequate EFA and PUFA bioavailability is crucial for proper functioning of the brain. In addition, linoleic and alpha-linolenic acids per se have an effect on the neuronal membrane fluidity index. They are able to decrease the cholesterol level in the neuronal membrane, which would otherwise decrease membrane fluidity, which in turn would make it difficult for the cell to carry out its normal functions and increase the cell's susceptibility to injury and death. Symptoms of essential fatty acid deficiency include fatigue, dermatological problems, immune problems, weakness, gastrointestinal disorders, heart and circulatory problems, growth retardation, and sterility --- this list is not all-inclusive.**" (Yehuda, et al, 1987-2005<sup>88-100</sup>).

Yehuda et al's research has unlocked the root cause of Rudin's frustration with flax oil back in the 80s. Leaning on Yehuda's research, BodyBio began packing its Balanced 4:1 Oil. Since '97, BodyBio has been distributing this oil elixir made from organic sunflower and flax, with excellent results (see case studies). Balancing the EFAs with 80%  $\omega$ 6s will contribute to the stabilization of Arachidonic acid

(AA), which by now, as you read these words, has probably gained a bit more respect. However, the principal value of Yehuda's 4:1 ratio is the ability to raise the level of fluidity with a low risk of over-expression of either of the two families. The 4:1 oil gives the clinician a highly critical tool to safely raise EFAs and to offset the high saturated fat of our current generation.

Year after year from '93 on, in study after study, the number was the same: four parts of linoleic to one part of alpha linolenic --- 80% linoleic (n-6) to 20% linolenic (n-3). Yehuda called it SR-3 for Specific Ratio-3. We should call it the "Goldilocks" number because you can not imagine the excitement after learning of Yehuda et al's research. BodyBio advises doctors daily on nutrition, with a special emphasis on Fatty Acid analysis. Yehuda's research filled a major nutritional hole. We finally had a true scientific value for what is probably the most important nutrient in all of health science. We see and hear about the positive effects daily from clinics that employ the PK Protocol (see insert), from doctors worldwide. The genius level of Yehuda et al's work, and its contribution to humanity, is of such import to the world, to warrant consideration of a Nobel Prize.

But --- remember --- there are two levels of EFAs, and the 4:1 oil addresses only the lower level, LA and ALA, not the higher --- the HUFAs. At the present time, without a Red Blood Cell Fatty Acid analysis, there is no way of accurately assessing how much HUFAs, AA, GLA, EPA, or DHA, the body needs. For the majority, the 4:1 oil should be a staple, with the dietary addition of eggs, meat, and dairy for the n-6s, and fish or fish oil for the n-3s, which should fill in our higher EFA requirements.

The value of Yehuda and his colleagues' research to FA biochemistry is incalculable. I can not over emphasize these comments. We see it almost daily perform healing of a vast myriad of diseases that medical science seems incapable of making even the tiniest advances. After a decade of being directly involved as a teacher of the science of fatty acids in clinical applications, and seeing what can be done with simple seed oils, it boggles the mind to see the ineptness of our current state of medicine. All efforts at healing, of any magnitude, should include an attempt to rebuild the membrane (or, mem-Brain), which, I should add, is doable at any age. Please visit our website, [www.bodybio.com](http://www.bodybio.com) --- which has the Yehuda abstracts for this Bulletin published for your review. (For more information see Chapter 2 of The Detoxx Book or visit [bodybio.com/abstracts/yehuda](http://bodybio.com/abstracts/yehuda)).

BODYBIO blends the oils of sunflower and flax oils specifically to a ratio of 4:1 (see [BODYBIO Balanced Oil](#)). Hemp seed oil comes very close, since it has a ratio of 3.8 to 1.

The following case studies are selected for your review. There are many different tests from premier laboratories across the country to help doctors analyze each patient. However, the use of a Johns Hopkins Red Blood Cell Fatty Acid test\* and the BodyBio computerized medical report is paramount for each patient. There is no other way to diagnose a patient's fatty acid profile without looking into the membrane, and then carefully making adjustments of fatty acid intake.

*\*Patricia Kane, Ph.D., Neal Speight, M.D. and Domenick Braccia, D.O. Kennedy Kreiger Peroxisomal Diseases Laboratory.*

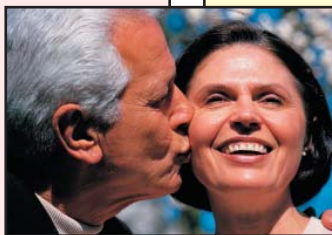
## Case Studies

### Case #1 – SCHIZOPHRENIA



Joanna had a long history of schizophrenia, spanning back into her childhood. In her parents' attempt to help her she had seen many physicians, both traditional psychiatrists and alternative practitioners; however, her symptoms remained intense and controlled only with strong medication. In her mid 40s Joanna was taken to a doctor who put her on an

extremely high dose of fish oil at 16 capsules daily. As Joanna continued the fish oil, her emotional status completely deteriorated after only a few months. Her doctor sharply increased her medication but her emotional instability was so intense that she was going to need to be hospitalized. Thankfully, Joanna's parents consulted with another doctor who tested Joanna's red cell fatty acids and found that the overdose of fish oil had caused a severe deficiency of omega 6 fatty acids. Joanna's arachidonic acid (found in butter, egg yolk, meat fat) was 186% lower than normal, her Gamma Linolenic was -41%, and Dihomogamma Linolenic acid was also depleted at -132%. The lower order omega 6 fatty acid Linoleic was quite low at -88%, and the lower order omega 3, Alpha Linolenic, was also low at -106%. Joanna was deficient in the lower order omega 3 fatty acid, Alpha Linolenic even though she had been taking fish oil, which contains only EPA and DHA. Joanna's doctor stopped the fish oil and prescribed a high dose of the SR3 balanced oil in a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic, at 2 tablespoons 3x daily. After the first week Joanna had improved, and by the second week her behavior was back to baseline and her medications were able to be reduced.



### Case #2 – LYME DISEASE AND CHRONIC PAIN

Vicky had struggled with Lyme disease and severe pain for two years without relief of her overwhelming symptoms of fatigue, sweating, joint/muscle pain, poor memory, dizziness, brain fog, headaches, mood swings, excessive thirst, eczema, and light sensitivity. Vicky had been taking fish oil, so when her red cell lipid test returned her EPA and DHA were elevated. Her base fatty acids Linoleic (omega 6) and Alpha Linolenic Acid (Omega 3) were dramatically low. Linoleic was -159% and Alpha Linolenic was -64%. Vicky was started on balanced oil in a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic at 2 tablespoons 3x daily along with an array of nutritional supplements, plus two weeks of IV lipid therapy. Within two weeks Vicky showed a great deal of improvement in pain, mood and brain fog. Over the next two months she experienced relief of her fatigue, memory problems, dizziness, eczema, light sensitivity, excessive thirst, and mood swings.

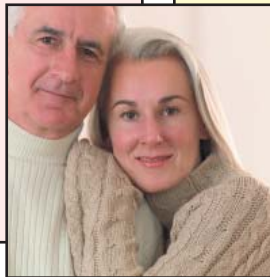


### Case #3 – CHRONIC FATIGUE SYNDROME

Ellen had a long history of severe fatigue, depression/anxiety, heart palpitations, gastrointestinal problems (vomiting, diarrhea, nausea, tan stool), dizziness, headaches and muscle weakness. Ellen had many abnormalities on her laboratory results with a very low cholesterol, hemoglobin, potassium, calcium, sodium and white cell count. Her red cell fatty acid test had gross elevation of very long chain fatty acids and a global depletion of all the essential fatty acids. Her base fatty acid Linoleic (omega 6) was 50% low. Ellen was started on balanced oil in a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic, at 2 tablespoons 2x daily, along with an array of nutritional supplements and IV Lipid therapy. Within two weeks she had some relief of her fatigue and a more stable mood. After six weeks of nutritional therapy her mood, GI symptoms, headaches, muscle weakness and fatigue were much improved.

### Case #4 – MULTIPLE SCLEROSIS

Kara developed the first symptoms of MS while she was a teenager. MS attacks followed for ten years until she was confined to a wheelchair before her 40th birthday. Kara had extreme fatigue, depression, brain fog, blurred vision, muscle cramping, swollen ankles, inability to walk, limited use of her hands, and heat intolerance. Kara was low in all the essential fatty acids – both omega 6 and omega 3. Her base fatty acids Linoleic (omega 6) and Alpha Linolenic Acid (Omega 3) were dramatically low. Linoleic was –115% and Alpha Linolenic was –51%. Kara was started on balanced oil in a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic, at 2 tablespoons 3x daily, along with an array of nutritional supplements. She received IV lipid therapy for five days, then returned home to continue oral therapy. Within three weeks Kara had less muscle cramping and fatigue, and was able to walk up the stairs holding onto the railing.



### Case #6 – STROKE LIKE EPISODES

David was a 53 year old minister who had given his Sunday sermon for 25 years. One Sunday morning David looked down at his notes but they did not make any sense to him, and he was unable to express himself coherently. His family doctor examined him and said he was not sure what was wrong, and they would have to wait and see, but David continued to struggle with similar episodes of confusion, difficulty with articulation, word-finding problems, and memory loss. His gait and balance were abnormal; he had headaches, low mood, leg weakness, insomnia, weight gain and fatigue. David's diet was high in peanut butter, and he ate 6 or more slices of bread daily. Peanut butter contains a high amount of very long chain fatty acids that are a challenge for the liver and brain to burn off, and appeared at high levels in David's red cell fatty acid test. David

was low in all the essential fatty acids – both omega 6 and omega 3. His base fatty acids Linoleic (omega 6) and Alpha Linolenic Acid (Omega 3) were especially low. Linoleic was –83% and Alpha Linolenic was –68%. David was started on balanced oil in a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic, at 3 tablespoons twice daily. Bread, pasta, peanut butter and sugar were removed from his diet, and nutritional supplements were started. Within 2 weeks David had lost 15 pounds, he had increased energy, and showed improvement in his memory, word finding, mood, muscle strength and speech. His headaches, insomnia and confusion slipped away. After six weeks David had lost 30 pounds, and felt comfortable once again at the pulpit giving his sermons. Most of his symptoms were sharply reduced or resolved completely, much to his delight and that of his family.

### Case #5 – MILD AUTISM

Alex, at age 8, had anxiety, sensory sensitivity (sound), muscle weakness, difficulty expressing himself, poor initiative, fatigue, night sweats, flat expression and learning problems. Diagnosed with autism at age 3, Alex had a long history of natural and drug interventions with some improvement but did not resolve his autistic symptoms. Alex's red cell fatty acid test revealed that he had a depletion of all the essential fatty acids with his lower order omega 6 Linoleic very low at –209% and omega 3 Alpha Linolenic quite low at –50%. He was started on balanced oil in a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic at 2 tablespoons twice daily along with an array of supplements. Alex had a dramatic response to lipid therapy (he also received IV lipids) in the first month of therapy with increased expression, less anxiety, more independence, learned to ride his bike, understands 'cause and effect,' more verbally expressive and understands humor – is able to 'get' a joke and delighted the staff by being able to tell them a joke as well.

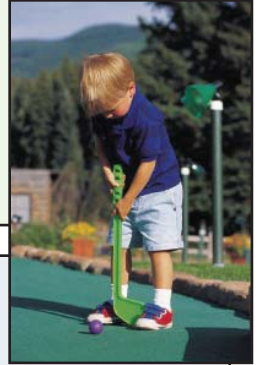
### Case #7 – EPILEPSY

Jeremy started having seizures at 14 months of age, and now, at age 4, his seizures were grand mal, the most severe stage, even with strong medication taken on a daily basis. Jeremy could not talk or walk. He had been given very high doses of fish oil for the past two years. Red cell fatty acid testing revealed a gross deficiency of omega 6 Linoleic acid at –183%, with a sharp elevation of EPA (+462%) and DHA (+162%). Jeremy was fed frequently, so 1 tablespoon of the SR3 Balanced oil in a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic was added to his food 5x daily. Within three weeks of using high dose lipid therapy Jeremy had fewer and milder seizures, and he attempted to talk and walk.



## Case #8 – MUSCULAR DYSTROPHY

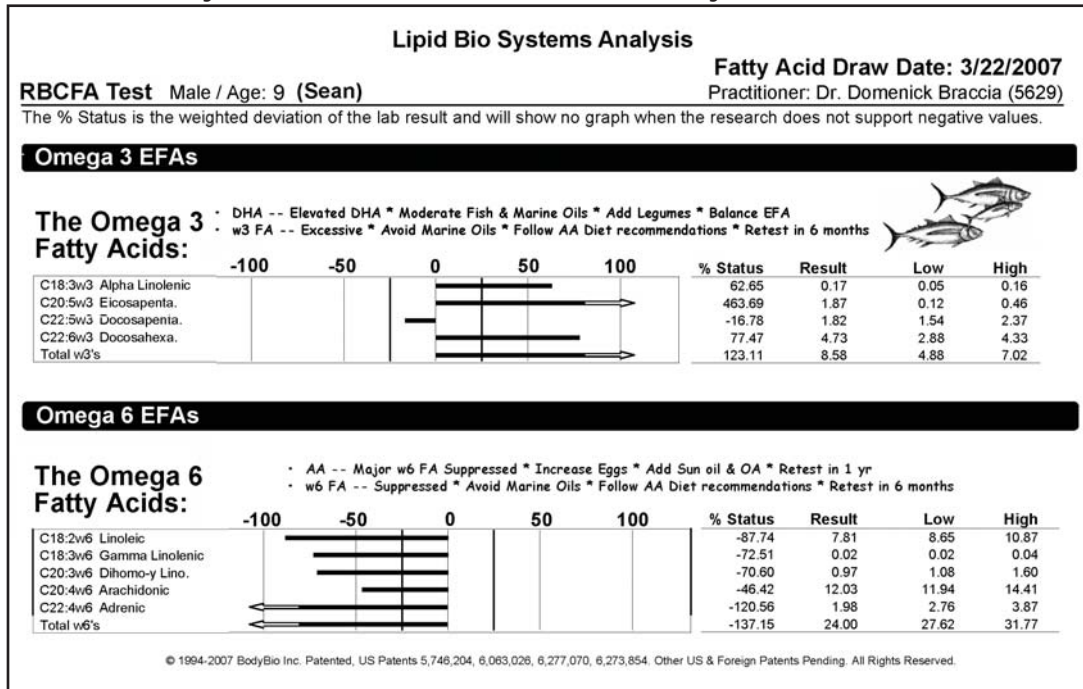
Christopher was diagnosed with muscular dystrophy at age 4, and over the next four years slowly deteriorated, much to his parents' dismay. His symptoms included a severely abnormal gait, muscle stiffness/pain/atrophy, weight loss, nose bleeds, back pain, anxiety, poor coordination, and frequent falls. A delightful child, Christopher was well aware of his body's failure to function, and was willing to try any of the nutrients his alternative doctors suggested. Christopher had been on SIX tablespoons of fish oil daily for two years, thus, when his red cell fatty acid test returned, he had a gross elevation (actually the highest recorded) of EPA at +3888% and DHA +312%. His omega 6 fatty acids were sharply depleted, with Linoleic acid -209%, Dihomogamma Linolenic acid -190% and Arachidonic acid -356%. His lower order omega 3, Alpha Linolenic, was low at -48%. Christopher was prescribed a high dose of the SR3 Balanced oil in a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic, at two tablespoons 3x daily, accompanied by 6 egg yolks and evening primrose oil. Fish oil was stopped completely. After the first week Christopher started to recover from hypotonia, with less stiffness in his leg muscles, more normal movement, and his gait was more fluid.



## Case #9 – DEVELOPMENTAL DELAY AND AUTISM

Sean was unable to speak at age nine. He had frequent outbursts, had difficulty sleeping, severe learning difficulties, hyperactivity, very dry skin, digestive problems, tan stool, anxiety, poor coordination and memory problems. Sean's MRI results revealed that he had enlarged ventricles (open areas in the middle of the brain filled with cerebral spinal fluid) in his brain, which may indicate a breakdown of phospholipids. Sean's red cell fatty acid test revealed that he had a depletion of all of the omega 6 fatty acids and elevated levels of EPA and DHA from taking cod liver oil. He was also taking flax oil, which was reflected in an elevated omega 3 Alpha Linolenic, at +62%. Sean was started on an oil regimen with a 4:1 ratio of four parts Linoleic to one part Alpha Linolenic 2 tablespoons twice daily. The cod liver oil was stopped. Evening primrose, butter and eggs were also added to his supplement regimen, with an array of vitamins, electrolytes and liquid minerals. Within the first month Sean made dramatic progress in his behavior, learning, and sleeping pattern. His skin began to soften, and his digestion and elimination improved. Speech began to emerge after two months of balanced fatty acid therapy.

### Red Cell Fatty Acid Test Results on Case Study #9:



Statements made in this article have not been evaluated by the Food and Drug Administration. Any reference to product's is not intended to diagnose, treat, cure, or prevent any disease.

## Tech Notes:

**Essential Fatty Acids (EFA):** Animals (including humans) cannot produce EFAs, the polyunsaturated lipids, which have more than one double bond. Omega 6 EFAs, linoleic acid (LA), and Omega 3 EFAs, alpha linolenic acid (ALA), are produced by plants on land and in the oceans. All of our cells require these two EFAs and must be included in sufficient quantities in the diet. However, the science of fats and oils is as yet unclear regarding the functions of the membrane of the cell, however, their importance is paramount. There is probably no dietary requirement more critical than the ingestion of the correct ratio of EFAs, which research has shown to be 4 parts LA (n-6): to 1 part ALA (n-3).

**PUFA** oils originate from seeds, nuts, grains and green leafy vegetables as LA, n-6 in ...Safflower 78% / Sunflower 68% / Corn 57% / Soy 53% / Walnut 56% / Sesame 43%, and as ALA, n-3 in ...Flax (linseed) 55% / Hemp 20% / Walnut 16% / Soy 8% / Canola 10% (canola also contains 5% erucic acid, a very long chain FA -- should be avoided) .

**HUFA** oils are the higher order of EFAs and include GLA, n-6 ...in Primrose 10% / Borage 23% / Blackcurrant / 17% / Hemp 2.6% / and Arachidonic Acid (AA), n-6 ...in eggs, meat, dairy and shellfish, and EPA and DHA, n-3, from cold water fish and fish oil capsules.

**PUFA** (poly-unsaturated), poly = more than one, however, we prefer to separate the EFAs and reserve PUFAs for the lower order, and HUFAs (highly-unsaturated) for all their offsprings. PUFA refers to just LA and ALA, the beginning FAs of each omega family. HUFA refers to the higher metabolites of both families, n-6 (Gamma LA (GLA), DiHomo gamma LA (DGLA) and AA) and n-3 (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)).

**LA and ALA** technically, are the only essential fatty acids. All large animals, including us, have enzyme capability to produce HUFAs from LA and ALA. We are, however, inefficient in doing so. David Horrobin classed humans as being able to produce ~5% of required HUFAs, but generally, only if young and healthy, which is further degraded with aging and disease. Since HUFAs are paramount for good health, HUFAs should also be considered as essential EFAs.

**Omega 6 HUFA** (GLA, DGLA, AA) are the premier FAs of all metabolism influencing growth, motion, digestion, heart rate, blood pressure, reproduction etc. There is much confusion today concerning fatty acid knowledge, specifically regarding n-6 Arachidonic Acid (AA). AA is considered to be inflammatory, which it is. However, inflammation is a life preserving event. AA is not only inflammatory, but also anti-inflammatory. Its metabolic influence and function is so vast, and as yet, incompletely known, it will be studied for generations. BodyBio encourages the use a Red Blood Cell FA test from Johns Hopkins University, the premier fatty acid testing laboratory, to enhance the analysis of EFA balance of each individual. Testing the n-6 and n-3 FA levels permit more precise dietary and supplement adjustment --- all else is guesswork.

**Omega 3 HUFA** (EPA and DHA), in part, modulate AA to more accurately control growth, gestation, birth delivery, heart rate, and nerve response including sight and brain function, etc. and as suggested, EPA and DHA should be considered as essential oils.

**The 2 levels** of EFAs, the base PUFAs and higher, the HUFAs, may be supplemented for proper EFA balance. LA and ALA are necessary for membrane fluidity and body function, especially heart, reproduction and CNS, etc. The ratio of each is paramount. Best long term ratio of base oils is 4:1 (LA: ALA). Supplements such as primrose and marine oils are highly desirable; however, dietary considerations for FA nutrient additions should always be under the advice of a competent Health Care Professional.

## References:

1. Lipton BH, The Biology of Belief, Unleashing the Power of Consciousness Matter and Miracles. 2005, Mountain of Love/Elite Books, Santa Rosa, CA 95404.
2. Mouritsen OJ. Life-As a Matter of Fat, The Emerging Science of Lipidomics. Berlin Heidelberg: Springer-Verlag, 2005.
3. Corry B, Chung SH. Mechanisms of valence selectivity in biological ion channels. *Cell Mol Life Sci.* 2006 Feb;63(3):301-15.
4. Rudin DO. Unpublished manuscript: The Omega Factor: Our Nutritional Missing Link, 1985, Chapter 7.p.18.
5. Barenholz Y. Cholesterol and other membrane active sterols: from membrane evolution to "rafts". *Prog Lipid Res.* 2002 Jan;41(1):1-5.
6. Gurr MI, Harwood JL, Frayn KN. Lipid biochemistry: An Introduction 5th Edition London, UK: Blackwell Publishing, 2002, reprint 2004.
7. McMullen, TPW, McElhane RN. 1996. Physical studies of cholesterol-phospholipid interactions. *Curr. Opin. Colloid Interface Sci.* 1:83-90.
8. Mason RP et al, Chapter 6: Lipids, Health, and Behavior. 1996, Ed: Hillbrand M and Spitz RT. American Physiological Assoc Washington DC 20090.
9. Sikora DM, Pettit-Kekel K, Penfield J, Merckens LS, Steiner RD. The near universal presence of autism spectrum disorders in children with Smith-Lemli-Opitz syndrome. *Am J Med Genet A.* 2006 Jul 15;140(14):1511-8.
10. Tierney E, Nwokoro NA, Kelley RI. Behavioral phenotype of RSH/Smith-Lemli-Opitz syndrome. *Ment Retard Dev Disabil Res Rev.* 2000;6(2):131-4.
11. Tierney E, Bukelis I, Thompson RE, Ahmed K, Aneja A, Kratz L, Kelley RI. Abnormalities of cholesterol metabolism in autism spectrum disorders. *Am J Med Genet B Neuropsychiatr Genet.* 2006 Sep 5;141(6):666-8.
12. Kelley RI. Inborn errors of cholesterol biosynthesis. *Adv Pediatr.* 2000;47:1-53.
13. Perez-Guzman C, Vargas, MH, Quinonez, F, et al. A cholesterol-rich diet accelerates bacteriologic sterilization in pulmonary tuberculosis. *Chest* 2005; 127: 643-651.
14. Graveline Duane, 2004 Lipitor®, Thief of Memory: StatinDrugs and the Misguided War on Cholesterol.
15. Edwards IR, Star K, Kiuru A. Statins, neuromuscular degenerative disease and an ALS-like syndrome. *Drug Saf.*2007;30(6):515-25.
16. Conforti A, Magro L, Moretti U, et al. Fluvastatin and hepatic reactions: a signal from spontaneous reporting in Italy. *Drug Saf.* 2006;29(12):1163-72.
17. Uffe Ravnskov. 2002 The Cholesterol Myths: Exposing the Fallacy that Saturated Fat and Cholesterol Cause Heart Disease. New Trends Publishing.
18. Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans fatty acids and cardiovascular disease. *N Engl J Med.* 2006 Apr 13;354(15):1601-13.
19. Ascherio A. Trans fatty acids and blood lipids. *Atheroscler Suppl.* 2006 May;7(2):25-7.
20. Zaloga GP, Harvey KA, Stillwell W, Siddiqui R. Trans fatty acids and coronary heart disease. *Nutr Clin Pract.* 2006 Oct;21(5):505-12.
21. Crawford, Michael and Marsh, David. The Driving Force: Food, Evolution and The Future by, 1989, Harper & Row (New York).
22. Binkoski AE, Kris-Etherton PM, Wilson TA, Mountain ML, Nicolosi RJ. Balance of unsaturated fatty acids is important to a cholesterol-lowering diet: *J Am Diet Assoc.* 2005 Jul;105(7):1080-6.
23. Sato M, Yoshida S, Nagao K, Imaizumi K. Superiority of dietary safflower oil over olive oil in lowering serum cholesterol. *Biosci Biotechnol Biochem.* 2000 Jun;64(6):1111-7.
24. Sunitha T, Manorama R, Rukmini C. Lipid profile of rats fed blends of rice bran oil in combination with sunflower and safflower oil. *Plant Foods Hum Nutr.* 1997;51(3):219-30.
25. Gupta SV, Yamada N, Fungwe TV, Khosla P. Replacing 40% of dietary animal fat with vegetable oil is associated with lower HDL cholesterol and higher cholesterol. *J Nutr.* 2003 Aug;133(8):2600-6.
26. Sanders TA, Oakley FR, Miller GJ, et al. Nutrition, Food Influence of n-6 versus n-3 polyunsaturated fatty acids. *Arterioscler Thromb Vasc Biol.* 1997 Dec;17(12):3449-60.
27. Yang L, Leung KY, Cao Y, et al. Alpha-linolenic acid but not conjugated linolenic acid is hypocholesterolaemic in hamsters. *Br J Nutr.* 2005 Apr;93(4):433-8.
28. Colin A, Reggers J, Castronovo V, Anseau M [Lipids, depression and suicide] *Encephale.* 2003 Jan-Feb;29(1):49-58.
29. Ristic V, Ristic G. [Role and importance of dietary polyunsaturated fatty acids in the prevention and therapy of atherosclerosis] ed: *Pregl.* 2003 Jan-Feb;56(1-2):50-3.
30. Koba K, Liu JW, Bobik E, Sugano M, Huang YS. Cholesterol supplementation attenuates the hypocholesterolemic effect of rice bran oil in rats. *J Nutr. Sci. Vitaminol.* 2000 Apr;46(2):58-64.
31. USA TODAY Health and Behavior Cholesterol guidelines become a morality play, Posted 10/16/2004.
32. Jacobs D et al. Report of the conference on low blood cholesterol: Mortality Associations. *Circulation.*1992 Sep;86(3):1046-60.
33. Iribarren C, Jacobs DR Jr, Sidney S, Claxton AJ, Feingold KR. Cohort study of serum total cholesterol and in-hospital incidence of infectious diseases. *Epidemiol Infect.* 1998 Oct;121(2):335-47.
34. Volpato S, Leveille SG, Corti MC, Harris TB, Guralnik JM. *J. Am. Geriatr Soc.* 2001 Sep;49(9):1142-7.

## References (cont.):

35. Ives DG, Bonino P, Traven ND, Kuller LH. Morbidity and mortality in rural community-dwelling elderly with low total serum cholesterol. *J Gerontol.* 1993 May;48(3): M103-7.
36. Schalk BW, Visser M, Deeg DJ, Bouter LM. The Longitudinal Aging Study Amsterdam. *Age Ageing.* 2004; Mar;33(3):266-7
37. Obialo CI, Okonofua EC, Nzerue MC, Tayade AS, Riley LJ. *Kidney Int.* 1999 Sep;56(3):1058-63.
38. Bologa RM, Levine DM, Parker TS, Cheigh JS, Serur D, Stenzel KH, Rubin AL. *Am J Kidney Dis.* 1998 Jul;32(1):107-14.
39. Grosser T, Fries S, FitzGerald GA. Biological basis for the cardiovascular consequences of COX-2 inhibition: therapeutic challenges and opportunities. *J Clin Invest.* 2006 January 4; 116(1): 4-15.
40. Funk CD. Leukotriene modifiers as potential therapeutics for cardiovascular disease. *Leukotriene Nat. Rev. Drug Discov.* 2005; 4:664-672. [PubMed].
41. Murata T, et al. Altered pain perception and inflammatory response in mice lacking prostacyclin receptor. *Nature.* 1997;388:678-682. [PubMed].
42. García Rodríguez LA, Egan K, FitzGerald GA. Traditional nonsteroidal anti-inflammatory drugs and postmenopausal hormone therapy: a drug-drug interaction? *PLoS Med.* 2007 May;4(5):e157.
43. Sitbon O, Humbert M, Simonneau G. Primary pulmonary hypertension: Current therapy. *Prog Cardiovasc Dis.* 2002 Sep-Oct;45(2):115-28.
44. Arnal JF, Douin-Echinard V, Tremollières F, Terrisse AD, Sié P, Payrastr B, Guery JC, Bayard F, Gourdy P. *Arch Mal Coeur Vaiss.* 2007 Jun-Jul;100 (6-7):554-62.
45. Saldeen P, Saldeen T. Women and omega-3 Fatty acids. *Obstet Gynecol Surv.* 2004 Oct;59(10):722-30.
46. Oviedo PJ, Hermenegildo C, Cano A. Raloxifene increases the capacity of serum to promote prostacyclin release in human endothelial cells: implication of COX-1 and COX-2. *Menopause.* 2004 Jul-Aug;11(4): 430-7.
47. Nagaya N, et al. Gene transfer of human prostacyclin synthase ameliorates monocrotaline-induced pulmonary hypertension in rats. *Circulation.* 2000 Oct 17;102(16):2005-10.
48. Launay D, Humbert M, Hachulla E. Pulmonary arterial hypertension and systemic sclerosis. *Presse Med.* 2006 Dec;35(12 Pt 2):1929-37.
49. Abdelrahman M, Collin M, Thiemermann C. The Peroxisome Proliferator-Activated Receptor-[gamma] Ligand 15-Deoxy D12,14 Prostaglandin J2 Reduces the Organ Injury in Hemorrhagic Shock. *Shock.* 22(6):555-561, December 2004.
50. Harris SG, Padilla J, Koumas L, Ray D, Phipps RP. Prostaglandins as modulators of immunity. *Trends Immunol.* 2002 Mar;23(3):144-50.
51. Kim HK, Choi H. Anti-inflammatory lipid mediator 15d-PGJ2 inhibits translation through inactivation of eIF4A. *Lipids.* 2001 Dec;36(12):1331-6.
52. Kapadia R, Yi JH, Vemuganti R. Mechanisms of anti-inflammatory and neuroprotective actions of PPAR-gamma agonists. *Front Biosci.* 2008 Jan 1;13:1813-26.
53. Salgia AD, Kosnik SD. When acetaminophen use becomes toxic. Treating acute accidental and intentional overdose. *Postgrad Med.* 1999 Apr;105(4):81-4, 87-90.
54. Haas-Stapleton EJ, Lu Y, Hong S, Arita M, Favoretto S, Nigam S, Serhan CN, Agabian N. *Candida albicans* Modulates Host Defense by Biosynthesizing the Pro-Resolving Mediator Resolvin E1. *PLoS ONE.* 2007 Dec 19;2(12):e1316.
55. Serhan CN, Hong S, Gronert K, et al. Resolvins: a family of bioactive products of omega-3 fatty acid transformation circuits initiated by aspirin treatment that counter proinflammation signals. *J Exp Med.* 2002 Oct 21;196(8):1025-37.
56. Serhan CN, Arita M, Hong S, Gotlinger K. Resolvins, docosatrienes, and neuroprotectins, novel omega-3-derived mediators, and their endogenous aspirin-triggered epimers. *Lipids.* 2004 Nov;39(11):1125-32.
57. Serhan CN. Lipoxins and new lipid mediators in the resolution of inflammation. *Anesthesiol Clin.* 2006 Jun;24(2):341-64.
58. Bannenberg GL, Aliberti J, Hong S, Sher A, Serhan C. Exogenous pathogen and plant 15-lipoxygenase initiate endogenous lipoxin A4 biosynthesis. *J Exp Med.* 2004 Feb 16;199(4):515-23.
59. Schwab JM, Serhan CN. Lipoxins and new lipid mediators in the resolution of inflammation. *Curr Opin Pharmacol.* 2006 Aug;6(4):414-20.
60. Attwell D, Miller B, Saantis M. Arachidonic acid as a messenger in the central nervous system. *Seminars in the Neurosciences* 1993;5:159-169.
61. Kennedy Kreiger Peroxisomal Insitute Fatty Acid Laboratory of Johns Hopkins University, Baltimore, MD USA.
62. Yiin SJ, Lin TH. Effects of metallic antioxidants on cadmium-catalyzed peroxidation of arachidonic acid *Ann Clin Lab Sci.* 1998 Jan-Feb;28(1):43-50.
63. Kane PC, Foster JS, Braccia D, Kane E. *The Detox Book: Detoxification of Biotoxins in Chronic Neurotoxic Syndromes.* Millville, NJ USA: BodyBio, 2002
64. Grandjean P, Weihe P. Arachidonic acid status during pregnancy is associated with polychlorinated biphenyl exposure. *Am J Clin Nutr.* 2003 Mar;77(3):715-9.
65. Bilak M, Wu L, Wang Q, Haughey N, Conant K, St Hillaire C, Andreasson K. PGE2 receptors rescue motor neurons in a model of amyotrophic lateral sclerosis. *Ann Neurol.* 2004 Aug;56(2):240-8.

## References (cont.):

66. McGiff JC. Cytochrome P-450 metabolism of arachidonic acid. *Annu Rev Pharmacol Toxicol.* 1991;31:339-69.
67. Wang D, DuBois RN. Measurement of eicosanoids in cancer tissues. *Methods Enzymol.* 2007;433:27-50.
68. Koletzko B, Braun M. Arachidonic acid and early human growth: is there a relation? *Ann Nutr Metab.* 1991;35(3):128-31.
69. Carnielli VP, Simonato M, Verlato G et al. Synthesis of long-chain polyunsaturated fatty acids in preterm newborns, etc. *Am J Clin Nutr.* 2007 Nov;86(5):1323-30.
70. Papadimitriou A, King AJ, Jones PM, Persaud SJ. Anti-apoptotic effects of arachidonic acid and prostaglandin E2, etc. *Cell Physiol Biochem.* 2007;20(5):607-16.
71. Das UN. Essential Fatty Acids - a Review. *Curr Pharm Biotechnol.* 2006 ec;7(6):467-82.
72. McCullough L, Wu L, Haughey N, Liang X, et al. Neuroprotective function of the PGE2 EP2 receptor in cerebral ischemia. *J Neurosci.* 2004 Jan 7;24(1):257-68.
73. Hennig R, Kehl T, Noor S, et al. 15-lipoxygenase-1 production is lost in pancreatic cancer and overexpression of the gene, etc. *Neoplasia.* 2007 Nov;9(11): 917-26.
74. Harbige LS, Sharief MK. Polyunsaturated fatty acids in the pathogenesis and treatment of multiple sclerosis. *Br J Nutr.* 2007 Oct;98 Suppl 1:S46-53.
75. Serhan CN, Lu Y, Hong S, Yang R. Mediator lipidomics: search algorithms for eicosanoids, resolvins, and protectins. *Methods Enzymol.* 2007;432:275-317.
76. Gryglewski RJ, Panczenko B, Korbut R, et al. Corticosteroids inhibit prostaglandin release from perfused mesenteric blood vessels, etc. *Prostaglandins* 10, 343-355 (1975).
77. Tashjian AH, Voekel EF, McDonough J, Levine L. Hydrocortisone inhibits prostaglandin production by mouse fibrosarcoma cells. *Nature* 258, 739-741 (1976).
78. Turk J, Hughes JH, Easom RA, Wolf BA, Scharp DW, Lacy PE, McDaniel ML. Arachidonic acid metabolism and insulin secretion by isolated human pancreatic islets. *Diabetes.* 1988 Jul;37(7):992-6.
79. Loweth AC, Scarpello JH, Morgan NG. A specific inhibitor of cytosolic phospholipase A2 activity, AACOCF3, etc. *Biochem Biophys Res Commun.* 1996 Jan 17;218(2):423-7.
80. Ma Z, Ramanadham S, Kempe K, et al. Pancreatic Islets Express a Ca2+-independent Phospholipase A2 Enzyme, etc. *J Biol Chem.* 1997 Apr 25;272(17):11118-27.
81. Bastard JP, Maachi M, Lagathu C, et al. Recent advances in the relationship between obesity, inflammation, and insulin resistance. *Eur Cytokine Netw.* 2006 Mar;17(1):4-12.
82. Fujimoto WY, Metz SA. Phasic effects of glucose, phospholipase A2, and lysophospholipids on insulin secretion. *Endocrinology.* 1987 May;120(5):1750-7.
83. Hirano T, Fukuyama S, Nagano S, Takahashi T. Involvement of phospholipase A2 and arachidonic acid in cholecystokinin-8, etc. *Endocrinol Jpn.* 1984 Oct;31(5):549-55.74.
84. Metz S, VanRollins M, Strife R, et al. Lipoxygenase pathway in islet endocrine cells, etc. *J Clin Invest.* 1983 May; 71(5):1191-205.
85. Simonsson E, Karlsson S, Åhrén B. Involvement of phospholipase A2 and arachidonic acid in cholecystokinin-8-induced insulin secretion in rat islets. *Regul Pept.* 1996 Sep 9;65(2):101-7.
86. Tadayyon M, Green IC. Pharmacological interference with phospholipase A2 activity reveals mechanistic differences, etc. *Diabete Metab.* 1993 Jan-Feb;19(1):36-43.
87. Zawalich W, Zawalich K. Effect of exogenous phospholipase A2 on insulin secretion from perfused rat islets. *Diabetes.* 1985 May;34(5):471-6.
88. Yehuda S, Carasso RL. Effects of dietary fats on learning, pain threshold, thermoregulation and motor activity in rats, etc. *Int J Neurosci.* 1987 Feb;32(3-4):919-25.
89. Yehuda S, Carasso RL. Modulation of learning, pain thresholds, and thermoregulation in the rat, etc. *Proc Natl Acad Sci USA* 1993; 90:10345-10349.
90. Yehuda S, Carasso RL, Mostofsky DI. Essential fatty acid preparation (SR-3) raises the seizure threshold in rats. *Eur J Pharmacol* 1994 Mar 11;254:1-2:193-8.
91. Yehuda S, Carraso RL, Mostofsky DI. Essential fatty acid preparation (SR-3) rehabilitates learning deficits induced by AF64A and 5,7-DHT. *Neuroreport.* 1995 Feb 15;6:3:511-5.
92. Yehuda S, Brandys Y, Blumenfeld A, Mostofsky DI. Essential fatty acid preparation reduces cholesterol and fatty acids in rat cortex. *Int J Neurosci.* 1996 Sep;86:3-4:249-56.
93. Yehuda S, Rabinovitz S, Carasso RL, Mostofsky DI. Essential fatty acids preparation (SR-3) improves Alzheimer's, etc. *Int J Neurosci.* 1996 Nov;87:3-4:141-9.
94. Yehuda S, Rabinovitz S, Mostofsky DI, et al. Essential fatty acid preparation improves biochemical and cognitive functions, etc. *Eur J Pharmacol* 1997 Jun 5;328:1:23-9.
95. Yehuda S, Rabinovitz S, Carasso RL, Mostofsky DI. Fatty acids and brain peptides Peptide 1998 19:2:407-19.
96. Yehuda S, Rabinovitz S, Mostofsky DI. Essential fatty acids are mediators of brain biochemistry and cognitive functions. *J Neurosci Res.* 1999 Jun 15;56:6:565-70.
97. Yehuda S, Rabinovitz S; Carasso RL, Mostofsky DI. Fatty acid mixture counters stress changes in cortisol, cholesterol, and impair learning. *Int J Neurosci* Jan 2000;101:1-4: 73-87.
98. Yehuda S, Rabinovitz S, Carasso RL, Mostofsky DI. The role of polyunsaturated fatty acids in restoring, etc. *Neurobiol Aging.* 2002 Sep-Oct;23:5:843-53.
99. Yehuda S, Rabinovitz S, Mostofsky DI. Mixture of essential fatty acids lowers test anxiety. *Nutr Neurosci.* 2005 Aug;8(4):265-7.
100. Yehuda S, Rabinovitz S, Mostofsky DI. Essential fatty acids and the brain: From infancy to aging. *Neurobiol Aging.* 2005 Dec;26 Suppl 1:98-102.