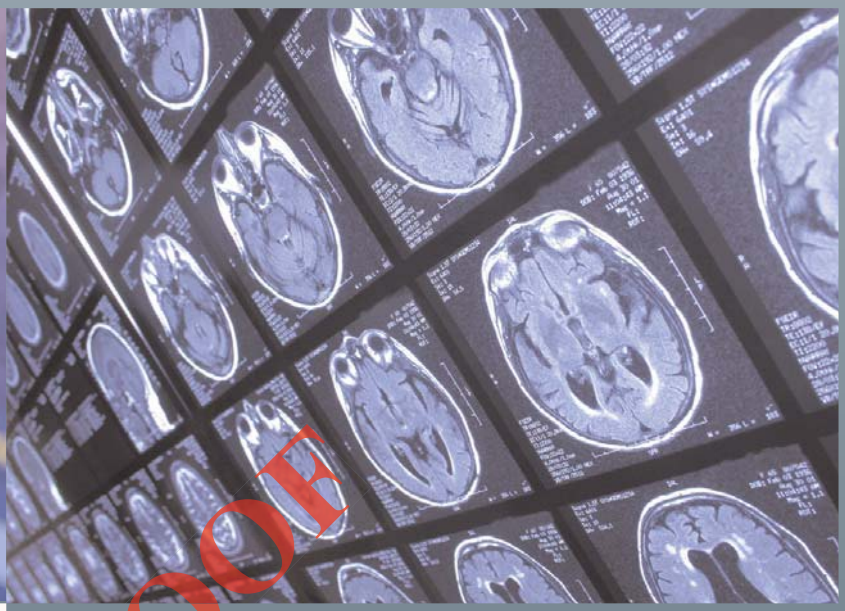

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Chapter 29

Parent Essential Fatty Acids, Oxygenation, and Cancer Prevention: A New Solution

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ABSTRACT

Despite 50 years of intensive cancer research increasingly focused on genetic causes, no single unifying cause for cancer has been universally recognized; only that there is a significant correlation between the level of tumor hypoxia and prognosis. With the exception of Nobel Laureate Otto Warburg's seminal experiments and discoveries, little work has been done to investigate and advance the causal relationship between hypoxia and cancer initiation. Over 70 years ago, Warburg (with independent confirmation by American scientists) conclusively established that cells could always be made cancerous by subjecting them to intermittent hypoxic periods, and that once done it was irreversible. While modern biochemistry does not address cancer's prime cause of cellular hypoxia, physiology does. It can now be shown that Warburg's findings of a critical 35% intermittent reduction in intracellular oxygen levels initiating cancer is linked to the incorporation of adulterated, non-oxygenating, or inappropriate polyunsaturated fatty acids, specifically termed parent essential oils (PEOs), into the phospholipids of both cell and mitochondrial membranes. Such incorporation causes physiologic changes in membrane properties that impair oxygen transmission into the cell. Trans fats, partially oxidized PEO entities, and inappropriate physiologic "parent" omega-6: omega-3 ratios are all potential sources of unsaturated fatty acids that can disrupt the normal membrane structure. A solution to protect against cellular hypoxia; i.e., cancer's prime cause is given.

Keywords: essential fatty acids, parent essential oils, EFAs, PEOs, Warburg, cancer, hypoxia

INTRODUCTION

Tragically, even with enormous budgets, brilliant minds, and an earnest desire to end the cancer plague, little of significance has been accomplished in the last 35 years to reduce cancer's spread. Today, the average American will contract cancer in his or her lifetime despite the plethora of lifestyle and nutritional changes that have been advocated by cancer specialists and eagerly followed by the public. Could the cancer research community be looking in the wrong place?

New Hope – It's Not Genetic

Most physicians currently believe cancers are caused by the activation of oncogenes – genes that predispose the individual toward cancer. That is incorrect. This theory was called into question by its discoverer Dr. Robert A Weinberg of the Massachusetts Institute of Technology (MIT). He reversed himself over 10 years ago in 1998. After discovering that "[F]ewer than one DNA base in a million appears to have been miscopied," he concluded that is not enough of a defect to mutate the cell! Weinberg's exact words: "Something was very wrong. The notion that a cancer developed through the successive activation of a series of oncogenes had lost its link to reality."[1] Nearly a decade later, in 2007, Dr. Weinberg then stated, "The connection between inflammation and cancer has moved to center stage in the research arena." He even called this discovery a "rewriting of the textbook."[2] (For other references in regard to this topic, see Lewis and Pollard,[3] Balkwill *et al*,[4] and de Visser *et al*[5]).

Furthermore, over 35 years ago, Professor Henry Harris and coworkers took normal tissue cells and fused 3 types of cancer cells to them. It was thought that the cancer cells would take over the normal cells and "convert" them into cancer. Surprisingly, they grew normally, showing cancer is genetically recessive, not dominant as everyone thought.[7] Most cancer researchers are not aware of this critically important information.

Shocking, yet unknown to many cancer researchers were statements made in 2005 by the heads of the world's largest cancer research center in Houston, Texas, when they announced that cancer's prime cause is not genetic. Dr. John Mendelsohn, president of the M.D. Anderson Cancer Center, stated:

"Any claims that this [genetic research] is going to be the key to curing cancer are not appropriate."[7] As in Dr. Weinberg's 2007 revelation detailing the inflammation/cancer connection, no genetics are required to explain cancer's prime cause. In 2008, a significant article in *Scientific American* stated: "But the oncogene/tumor suppressor gene hypothesis has also failed, despite two decades of effort, to identify a particular set of gene mutations that occurs in every instance of any of the most common and deadly kinds of human cancer."[8] Note: This includes even BRCA 1 and BRCA 2, and that in 2006, researchers actually measured the number of mutations in a cancerous cell and it was a mere "65-475 mutations per 100 million nucleotides" – not nearly enough mutations in a cell to cause cancer! This new field is termed epigenetics and theorizes that the cellular environment alone – nothing to do with genetics – is the basis for cellular disorders, such as cancer. In a 2009 article, it was made clear that precancerous stem cells can remain benign or malignant depending on the environment, and that "some sort of signal or cue from their immediate environment directs them to become benign or malignant."[9] Mina Bissell, PhD, pioneered the view that a cell's environment is as important as its genes in determining the formation and progression of tumors. Bruce Lipton, PhD, has advanced this line of reasoning focusing on the cell's bi-lipid membrane. We will bring this concept to fruition, and provide a completely epigenetic basis for cancer based on a widespread cellular environmental assault few of us are aware of that gives little notice.

The great news we can take from this announcement is that even if cancer apparently "runs in your family," there is real hope because it has nothing to do with genes. But first, some popular but clinically worthless anti-cancer recommendations need to be addressed.

Popular Anticancer Recommendations Often "Called into Question"

Many people diligently follow the experts' recommendations, hoping to beat cancer. The inability of the medical and dietary professions to curb the rising level of cancer over the last 60 years bears exploring. Although many of their recommendations may sound plausible, they aren't effective in clinical practice, nor should they be; they don't have a specific metabolic pathway directly inhibiting cancer's development. Consider the following list of recommendations along with the date of their findings being questioned or even reversed as reported in the world's foremost medical journals that many cancer researchers never saw: Fruits and vegetables protect us from cancer (called into question 2001)[10]; mammography detects initial cancer growth (called into question 2000)[11]; fiber protects against colon cancer (called into question 1999 and 2001)[12,13]; fish oil alone prevents cancer (called into question 2000)[14]; omega-3 alone prevents cancer (called into question 2006)[15,16]; soy is a positive anticancer addition to our diet (called into question as early as 1946 and 1960)[17,18]; low-fat diets are the anticancer answer (called into question 2006).[19] Are there anticancer recommendations that have withstood the test of time never having to be reversed or called into question? The answer is an emphatic *yes*.

DR OTTO WARBURG'S AMAZING ANTICANCER DISCOVERY

Nobel Prize winner, Otto Warburg, MD, PhD, has often been called the greatest biochemist of the 20th century; the sheer number and magnitude of his discoveries qualify him as the most accomplished biochemist of all time. Despite this, much of his seminal work on cancer has been overlooked. No scientist or researcher has ever disproved the validity, correctness, or applicability of Warburg's important discoveries as they relate to the prevention and cure of cancer. In fact the opposite is true – none of his findings have been called into question.

The Prime Cause of Cancer

We have become so accustomed that seemingly every discovery in the battle to defeat cancer is, after a time, called into question that the following might be hard to believe. Otto Warburg discovered, then clearly and simply stated that the prime cause of cancer is oxygen deprivation at the cellular level. "We find by experiment about 35% inhibition of oxygen respiration already suffices to bring about such a transformation during cell growth," he stated at a 1966 conference of Nobel laureates in Lindau, Germany.[20] It is that simple. Just one-third less cellular oxygen than normal and you contract cancer. Based on meticulous experiments that he and many other scientists verified numerous times, Dr Warburg discovered that the prime cause of cancer is sustaining a 35% inhibition of cellular respiration.[20] In America, seminal experiments in 1953 and 1955 confirmed that decrease of sustained cellular oxygen always induces cancer, and its converse, that cancer occurs in environments of significantly decreased

oxygen. You won't immediately feel the harmful effect of decreased cellular oxygenation, and you won't know it is happening. Yet if cellular oxygen levels can be kept above this deprivation threshold, cancer cells will not be able to form. It really is that simple.

Exercising supplies additional oxygen to the blood; however, this doesn't address transfer of oxygen through the cell membrane – the critical factor. This is why elite athletes still develop cancer. Warburg stated: "To be sure, cancer development takes place even in the presence of free oxygen gas in the atmosphere, but this oxygen may not penetrate in sufficient quantity into the growing body cells, or the respiratory apoenzymes of the growing body cells may not be saturated with the active groups." Warburg addressed the danger of impaired cellular oxygen transfer even in the presence of oxygen. We will soon see how the environments of each of our 100 trillion cells' membranes play in oxygen transfer, and in transferring this oxygen to the mitochondria, how one special factor significantly impairs oxygen transfer.[21]

Dr Warburg's discovery has been verified over and over again (never called into question), both as to how normal cells turn cancerous and in showing that cancer doesn't develop in sufficiently oxygenated areas. It is important to emphasize that two American physicians conclusively proved this in 1953, and two more investigators confirmed this finding in 1955. Goldblatt and Cameron published in the *Journal of Experimental Medicine* that once damage is too great to the cell, then no amount of oxygen will return the cell's respiration back to normal: it is forever doomed to a cancerous life.[22] However, they confirmed it is possible to prevent a "respiration impacted" precancerous cell from becoming permanently cancerous if oxygen deficiency is stopped early enough. This is wonderful news. In 1955, Malmgren and Flanigan confirmed the oxygen/cancer cause in an ingenious experiment with tetanus spores.[23] Consequently, prevention is the ultimate solution to conquering cancer.

Greater Oxygen Deprivation = Worse Prognosis

Numerous articles in cancer journals confirm the decreased oxygen/increased cancer prognosis: "Tumor hypoxia adversely affects the prognosis of carcinoma of the head and neck."[24] "[A]nalysis showed significantly lower survival and recurrence-free survival for patients with a median pO_2 of ≤ 10 mm Hg compared to those with better oxygenated tumors (median pO2 > 10 mm Hg). [M]edian pO_2 and the clinical stage according to the FIGO are independent, highly significant predictors of survival and recurrence-free survival."[25] "Tumor oxygenation predicts for the likelihood of distant metastases in human soft tissue sarcoma."[26] Greater cellular oxygen deprivation/hypoxia is directly correlated with a worse prognosis, shorter lifespan, and greater risk of metastases. The greater the cellular oxygen deprivation, the worse the patient's prognosis. There is no question…lower oxygen equals more virulent cancer.

How Can Tissue Become Oxygen Deficient? The Secret of PEO-Containing Oils

The body requires special fats, which, among other important functions, make it possible for sufficient oxygen to reach the cells via the cell membranes – the key to cancer prevention. These special fats are highly oxygen-absorbing entities called essential fatty acids, or EFAs, and must be eaten every day, because your body can't manufacture them on its own. There are two "parent" forms of EFAs that allow your body to make whatever it needs from them, i.e. the various types of EFA "derivatives." Supplemental EFA-derivatives, such as EPA and DHA are not required because the body makes them as needed in very small amounts. Parent omega-6 is termed linoleic acid (LA), and parent omega-3 is termed alpha-linolenic acid (ALA). I call these two parent EFAs parent essential oils (PEOs) in order to clearly differentiate these from the non-essential "derivatives" that are manufactured by the body "as needed."

Parent Omega-6 Increases Oxygen Transfer Like Little "Oxygen Magnets"

Campbell *et al* found that LA (parent omega-6), can associate with oxygen and dissociate the oxygen at relatively high oxygen pressure in cellular membranes. These researchers also found that fatty acids (in particular, LA) effect the permeability of cell membranes to molecular oxygen by increasing cellular oxygenation by up to 50%, thus helping you remain cancer-free.[27] They concluded that interference with the movement of oxygen can occur at any cell membrane in any tissue. That's why regardless of where the cancer occurs, the prime cause is the same – the cancerous tissue is the most oxygen impaired. This simple truth bears repeating. Warburg unequivocally showed all cancers occur for the same reason. American researchers confirmed the fact. Moreover, PEO deficiency can cause

substitution into the cell membranes of non-oxygenating fats that impair oxygen transport, exacerbating the cancer causing state. Is there more confirmation in the medical texts of PEO's oxygenating ability? Yes. Several medical textbooks and published medical papers, to name a few, all confirm oxygenating ability (Figure 1).[28-31]

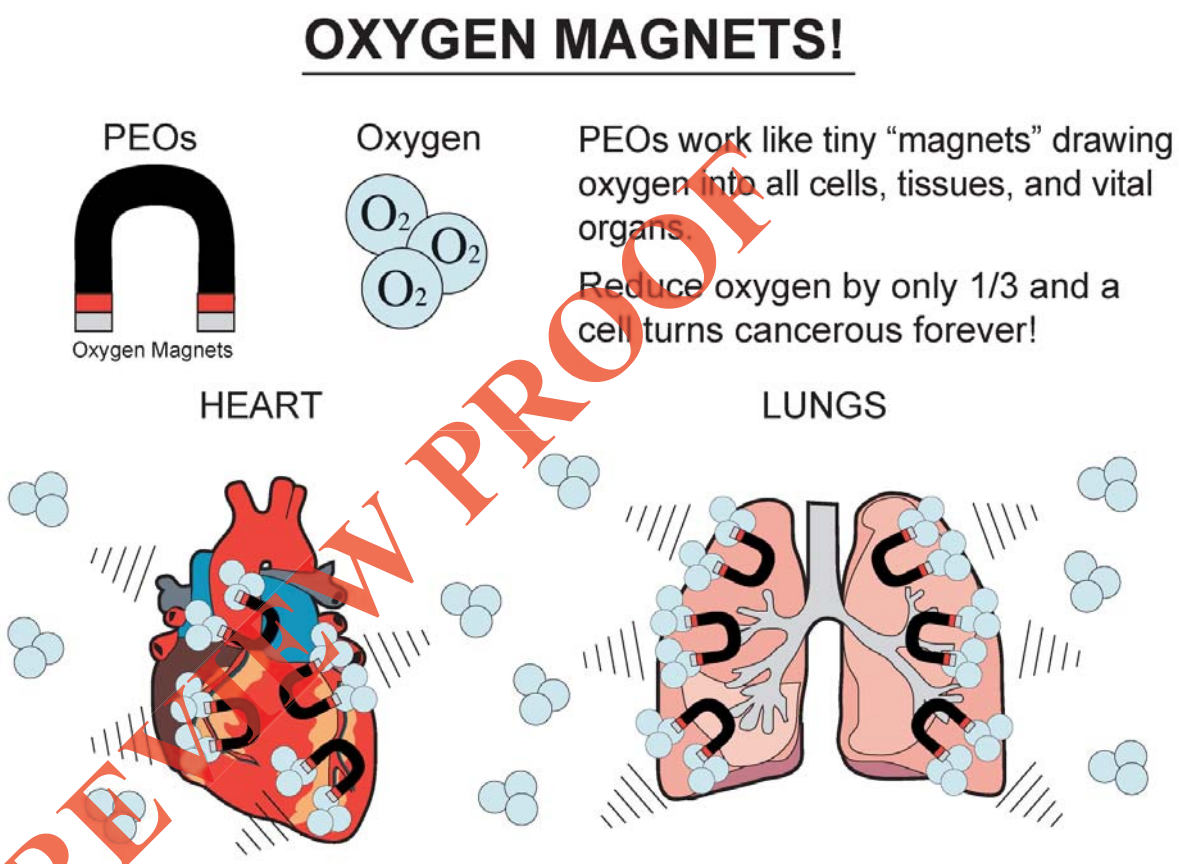

Figure 1: Parent essential oils work like tiny oxygen "magnets."

What are the Tissue Parent Omega-6/3 Ratios?

It is necessary to understand the PEO composition of various tissues and organs, such as your brain, skin, heart, and muscle, to discover the overall PEO requirement of the body. A little-known but vital fact about muscle structure is that muscle contains from 5.5 to 7.5-times more parent omega-6 than parent omega-3, depending on the degree of physical condition.[32] Extremely fit individuals require less omega-6 because their oxygen-transferring efficiency, including an increased number of cell mitochondria, is greater than in non-exercising individuals. Skin contains no omega-3, only parent omega-6, while body fat contains 20-times more parent omega-6 than omega-3.[33] Figure 2 shows the parent omega-6/-3 ratios of major organs along with the respective weights. Contrary to what many researchers think, the brain is comprised of a 100:1 parent omega-6/-3 ratio; not 1:1. Most of the plasma free fatty acid and EFAs are derived from the triglycerides stored in the adipose tissue (body fat), and organs, including the brain, use these EFAs for structural incorporation.[34]

Ratio of Tissue Composition			
Tissue	Percentage of Total Body Weight	Omega-6 PEO	Omega-3 PEO
Brain/Nervous System	3	100	1
Skin	4	1000	1
Organs and Other Tissues	9	4	1
Adipose Tissue (bodyfat)	**15-35**	**22**	**1**
Muscles	**50**	**6.5**	**1**

Reference: Spector, A.A., "Plasma Free Fatty Acids and Lipoproteins as Sources of Polyunsaturated Fatty Acid for the Brain," Journal of Molecular Neuroscience, Vol. 16, 2001, pages 159-165., "Most of the plasma free fatty acid (EFA) is derived from the triglycerides stored in the adipose tissue [bodyfat]." Note: Organs, including the brain use these EFAs for structural incorporation. "Metabolism of essential fatty acids by human epidermal enzyme preparations: evidence of chain elongation, "R.S. Chapkin, et. at., Journal of Lipid Research, Volume 27, pages 954-959, 1986, Markides, M., et al., "Fatty acid composition of brain, retina, and erythrocytes in breast- and formula-fed infants," The American Journal of Clinical Nutrition, 1994;60:189-94 and Agneta Anderson, et. al., American Journal of Endocrinological Metabolism, 279: E744-E751.

Figure 2: Tissue composition and amounts of parent essential oils.

Table 1. Percentages of linoleic acid (LA) and alpha linolenic acid (ALA) in plasma and classes of lipids. Source references[30,34]

Table 1 Percentages of Linoleic Acid (LA) and Alpha Linolenic Acid (ALA) in Plasma and Classes of Lipids				
Fatty Acid	**Plasma Unesterified**	**Plasma Triglycerides**	**Plasma Phospholipids**	**Plasma Cholesterol Esters**
LA	17	19.5	23	50
ALA	2	1.1	0.2	0.5
LA:ALA ratio	8.5:1	17.5:1	115:1	100:1

References: Sinclair HM. Essential fatty acids in perspective. Hum Nutrit 1984;38C:245-260; Spector A. Plasma free fatty acid and lipoproteins as sources of polyunsaturated fatty acid for the brain. J Mol Neurosci 2001;16:159-165.

It can also be seen in Table 1 that plasma contains significantly more parent omega-6 than parent omega-3, and that plasma cholesterol esters and plasma phospholipids contain a factor of 100 times in favor of parent omega-6 to be delivered to the cells. We also see from Figure 2 the abundance of parent omega-6 throughout. If tissues and organs are not supplied through the diet with unadulterated, fully functional parent EFAs, then either damaged EFAs or even non-EFA oils, such as omega-9 (as in olive oil), will be utilized instead causing deoxygenation of the cells.[35]

Even in the brain, LA/ALA uptake is 100-times greater in favor of omega-6.[36] Surprising, both to cancer researchers and physicians, is the fact that there is not a significant bodily storage mechanism for ALA; its main metabolic route is beta-oxidation. Even significantly raising ALA intake does not cause a significant change in adipose tissue LA/ALA storage ratios.[36]

In view of emphasis solely on supra-physiologic omega-3 recommendations that ignore the critical unadulterated parent omega-6 requirements, when the supply of PEOs, in particular, unprocessed parent omega-6, is less than the body's total requirement, the body prioritizes delivery, feeding the organs

it considers most important first: the brain, heart, lungs, and kidneys. This deprives "less important" organs, such as the breast and prostate glands from receiving adequate PEOs and oxygen. Breast and prostate tissues are predominately fat requiring lots of functional parent omega-6 EFAs. Is it merely a coincidence they are both the number one cancers worldwide for the respective sexes?

Are We Overdosing on Omega-3 and Omega-3 Series Derivatives? Surprise: Derivatives Made "As Needed"

In the study of Sinclair *et al,*[37] we discover that the major metabolic route of ALA (parent omega-3) in the body is beta-oxidation, burning for energy – not incorporation into tissue. Therefore, overdoses will be injuriously incorporated into tissue structure. In view of this, we should proceed cautiously with omega-3 supplementation, including flax oil and fish oil.

The medical journals frequently bombard us advocating supra-physiologic doses of omega-3 derivatives, such as EPA and DHA: i.e. fish oil. This recommendation is called into question because Salem *et al*[38] explains why only about 5% of the parent ALA (parent omega-3) is converted into derivatives. Pawlosky and others[39] calculate that less than a mere 1% goes to derivatives. In addition, recently in 2008, Barceló-Coblijn *et al*[40] confirmed *the effectiveness of ALA conversion* and accretion into erythrocytes. This means we all make derivatives from parents "as needed," and these authors made clear that we all do. The premise that diabetics all have impaired enzymatic ability to convert LA to GLA is called into question; no one converts much. This fact is not newly published; if anyone would have cared to look, the same conclusion was also published back in 2005.[41] Here, the conversion rates were shown to be even less; less than a mere 1%. Demmelmair and colleagues[42] also stated a significant reason why derivative-conversions were so overestimated: different residence times were not considered.

High omega-3 food sources – flax seed, fish oil, seafood, etc. – can be an overload in both parent and derivative omega-3 series EFAs. Fish, especially farmed fish, contains almost entirely omega-3 derivatives. Because of this, fish oil supplements originally thought to help prevent cancer have been called into question.[14] You need to know that supraphysiological doses of omega-3 series oils cause their abnormal incorporation into cell tissue.[35,43] Health practitioners should be terrified about the pharmacological overdoses fish oil gives to patients – approximately 10-times the amount the body makes on its own. Krill Oil simply contains fewer derivatives, but still contains no PEOs. The warning that omega-3 or omega-3 series EFAs will not prevent cancer was published in 2006 but too few physicians or health professionals took note.[15]

In light of this information we have a precise explanation for the rampant rise in skin cancer. As Figure 2 highlights, our skin has no omega-3 in its structure. Could a prime factor be the supra-pharmacological omega-3 overload that the body, in desperation, dumps into the epithelial tissue? Sunlight is required for vitamin D production so sunlight, in and of itself is a necessity. Because of wrong nutritional recommendations, your skin's cellular structure is the problem.

In spite of this fact, nutritional recommendations still often advocate consumption of quantities of parent omega-3 and omega-3 series derivatives that based on human physiology and biochemistry are far too large. The problem is compounded when they overlook recommending supplementation with unadulterated, fully functional parent omega-6. Not surprisingly, skin cancer contraction rates have increased along side of the increase in fish oil supplementation.

Food Processors Ruin PEO Parent Omega-6

My decade-long research confirms that cellular hypoxia occurs primarily from consumption of adulterated polyunsaturated fatty acids (PUFAs), which are incorporated into cell membranes and interfere with cellular oxygen transmission. Natural oils in prepared foods turn rancid over time. Likewise, so do oils used in both restaurant and commercial deep fryers. Food processors, for economic reasons, must stop the oxygen transfer that results in spoiled food. They use only two approaches: remove the oil or adulterate them into entities like trans fats and interesterified fats. Their thoughtless solution to longer shelf life is a prime cause of the unstoppable cancer epidemic. As long as food processors continue to find creative but dangerous ways to reduce cellular oxygen transfer by using adulterated PUFAs (parent omega-6 oils are exclusively used), unwitting consumers should be terrified. Bans on trans fats are not sufficient – any oil used must be non-oxygen-transferring. The only plausible choice for us is to incorporate unadulterated oils in our diets by way of a dietary supplement.

How Much Omega-6 Are We Consuming?

Many nutrition researchers state that the U.S. population is consuming 15, 20, or even 30-times more omega-6 than omega-3 in its diet. However, their analysis ignores the fact that meats, such as beef and chicken contain lots of parent omega-3 (although cooking denatures some of it). This unaccounted for parent omega-3 in foods decreases the overbalanced omega-6 ratio dramatically. For example, depending on the specific diet of the animal, steak and hamburger will contain a ratio typically between 2:1 to a high of 10:1 in favor of omega-6. A grain-fed chicken produces eggs that contain a ratio of from 1:1 to as much as 10:1 in favor of omega-6. But fish, shrimp, and shellfish (not their extracted oil) – a primary protein in many people's diets – contains more omega-3 series than omega-6, usually from 2:1 to a high of 20:1 in favor of omega-3 series EFAs. Therefore, the average American's omega-6 to -3 ratio in regard to consumption can't be above 12:1. Of the 12:1 at least half (conservatively) of the parent omega-6 in most processed foods has lost its oxygenating ability. For example, margarine and most supermarket cooking oils (even olive oil contains few PEOs) have no appreciable oxygenating ability and consequently will remain unspoiled even when kept outdoors for years. They are so unappealing that given a choice no animal will even attempt to eat them – nor will they oxidize and become rancid. Tragically, widespread commercial use of preservatives and other deoxygenating additives have become the norm.

Rethinking EFA Supplementation Ratios and Amounts

The current message to eat more omega-3 or more fish is overly simplistic. What dieticians should be telling us is to replace the adulterated omega-6 (e.g. trans fatty acids/hydrogenated fats, etc.) with unadulterated, organic, minimally processed sources, such as organically processed oils, nuts and seeds, while adding moderate supplementation of omega-3.

We are warned about "overdosing" on omega-6 in our diets and told that we must take lots of oils containing omega-3 to compensate. However, in 2009 this recommendation was changed by the American Heart Association because omega-6 series EFAs contain anti-inflammatory compounds, such as precursors including the powerful prostaglandin PGE_1, and the body's powerful "natural blood thinner" prostacyclin (platelet anti-aggregate and anti-adhesive).[44]

Because the body requires significantly less parent omega-3 than parent omega-6 overall (Figure 2), and because little of the parent omega-3 we eat is damaged (for example, we don't fry or cook with omega-3, nor do commercial food processors use it), a key to better health is to increase supplemental sources of undamaged parent omega-6 instead of exclusively taking excess omega-3 supplements, which the tissues don't want.

My research strongly supports the use of an unprocessed, organic supplement with a ratio of greater than 1:1 up to 2.5:1 of parent omega-6 to parent omega-3. With this ratio, a suggested use is 725 mg per 40 lb of body weight (e.g. a 160-lb person requires 3 g on a daily basis). For complete details of how this specific ratio is arrived at, please read *"The Scientific Calculation of the Optimum Omega-6/-3 Ratio"* available at www.BrianPeskin.com (click on "PEO Report").

How Well Does This Omega-6:3 Ratio Work?

In my research, I commissioned and directed an experiment with mice to study this relationship between cancer growth rates and supplementation with Peskin Protocol PEOs. Mice metabolize EFAs like humans.[33] The experiment showed that, in spite of tumor implantation with 2 million cancer cells at once, there was a statistically significant 24% reduction in tumor size (growth) in the longer 4-week pretreated mice compared to the control mice that received no PEO supplementation (Figure 3). In the last 10 days of the experiment, there was a 42.8% lower growth volume of the tumors in the 4-week pretreated mice compared to the untreated mice. These results clearly show the increasing value of a longer pretreatment period of PEOs.

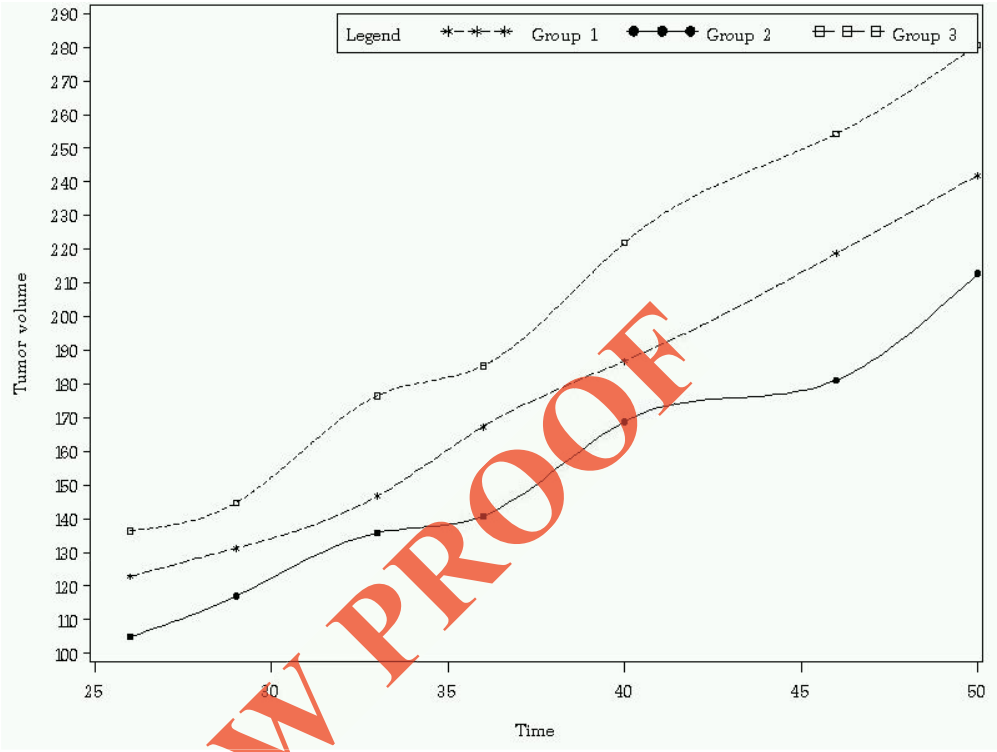

Figure 3. Tumor volumes in mice between groups from 26 to 50 days. Group 2 was pretreated with PEO formulation for 4 weeks prior to tumor implantation. Group 1 was pretreated for 2 weeks prior to tumor implantation. Group 3 was the control.

CONCLUDING REMARKS

My experiment conclusively shows that PEO-based oils are able to modify the internal structure of cells in an epigenetic fashion, thus making them more cancer resistant; the desired anti-cancer/increased cellular oxygenation solution is accomplished per Warburg's findings.

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Chapter 30

The Failure of Statins: A New Physiologic Solution to Cardiovascular Disease

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ABSTRACT

During the last half of the 1990s, almost half of all Americans and European mortalities were from heart disease. In 2006, atherosclerotic coronary artery disease (CAD) became the number one killer of Americans, with cancer running a close second. By 2010, most American deaths will be either from heart disease or cancer. If we go back in time, heart disease did not always present such a dismal picture. In the nineteenth century, heart disease was much rarer, and during the period 1910-1920, in the wards of the Massachusetts General Hospital, coronary heart disease was considered rare. As the decades passed, a variety of factors were suggested as the culprits, including the Western diet, and by the late 1970s, LDL-cholesterol was considered to be one of the primary causes of heart disease. This belief led to the development of many pharmaceutical interventions, including the statin family of drugs. Surprisingly, statins have a number needed to treat (NNT) of 100, meaning that statins fail to prevent cardiovascular disease (CVD) in clinical practice 99% of the time – an amazing 99% failure rate. The insight to prevention of CVD lies in the pathophysiology of the cholesterol structure; in particular, the esterified adulterated parent omega-6 component. A simple, clinical solution is presented.

Keywords: cholesterol, essential fatty acids, parent essential oils (PEOs), LDL

THE FAILURE OF STATINS

A medical school student getting a grade of 90% would warrant an A; a 60% grade would likely rate a D, and a 50% grade an F – failure. Shockingly, most physicians think that statins are excellent at preventing cardiovascular disease (CVD), rating them as an "A" grade medication. On the contrary, statins are anything but effective as demonstrated by their miniscule success rate of 1% in preventing CVD.

NNT (number needed to treat): The Only Effective Measure of a Drug's Success

If you treat 100 patients with a drug and all 100 improve, the drug's number needed to treat (NNT) is 1 (100 patients/100 successes). If you treat 100 patients and only 1 patient responds positively the NNT would be 100 (100 patients treated/1 positive response). This is an awful result and equivalent to a 99% failure rate. Dr. Nortin M. Hadler, Professor of Medicine at the University of North Carolina at Chapel Hill states: "Anything over an *NNT of 50 is worse than a lottery ticket*…"[1]

Study	Design	Outcomes (NNT)	Drug Failure Rate
1997 AFCAPS/TexCAPS[a]	Compared 20-40 mg lovastatin to placebo in patients on a low saturated fat, low cholesterol diet	**NNT**: acute major coronary event: 65	**98.5%**
2008 ENHANCE[b]	Compared 80 mg simivastatin + placebo to 80 mg simivastatin + 10 mg ezetimibe	Change in intima media thickness of carotid artery: 0.0058 mm (p = 0.29; not significant)	**Dual drug not Better**
2008 JUPITER[c]	Compared 20 mg rosuvastatin to placebo in patients with elevated CRP	**NNT**: Any MI: **240**; any stroke: 287; any death: 182	**99.6%**
1998 MIRACL[d]	Compared 80 mg atorvastatin to placebo in patients with unstable angina or non–Q-wave MI	**NNT: new/worsening congestive heart failure** requiring re-hospitalization: **556**	**99.8%**

Figure 1. Failure Rates of Recent Statin Trials (MI = myocardial infarction, AFCAPS/TexCAPS[2], ENHANCE[3], JUPITER[4], MIRACL[5])

Of significant importance is the fact that the 2008 JUPITER study[4] was used to try and gloss over the fact that numerous attempts to prove the "cholesterol theory" (the lower the patient's low density cholesterol [LDL-C], the greater the prevention of CVD) have failed, by attempting to make the case that the real mode of action of statin drugs was C-reactive protein (CRP) reduction. However, there is one tragic flaw: CRP is not a reliable prognostic indicator of cardiovascular events; there are better markers. An article entitled *Largest-Ever Meta-Analysis Finds CRP Is Unlikely to Be Causal for CVD*,[6] reports that scientists of the Cambridge-based Emerging Risk Factors Collaboration (ERFC)[7] found that "although CRP concentration was linearly associated with CHD (coronary heart disease), stroke, and vascular mortality, as well as nonvascular mortality, statistical adjustment for conventional cardiovascular risk factors resulted in considerable weakening of associations." Note: The JUPITER Study had an NNT of 240 (99.6% failure rate) that was not disclosed – instead, a hazard ratio (an estimate of relative risk) of 0.52 was published, thus making the trial appear much more successful than it actually was.

Statin Failures – Nothing New

Numerous medical journals have consistently published the ineffectiveness of statins to prevent or lower CVD. Here are a few examples warning of this failure. Kuhn *et al* wrote: "Blood cholesterol by itself is a poor predictor of individual risk of coronary heart disease. Few people identified purely on the basis of cholesterol levels will benefit from treatment [cholesterol lowering drugs]…"[8] Krumholz *et al* concluded: "Our findings do not support the hypothesis that hypercholesterolemia (high LDL-C levels) or low HDL-C (high-density lipoprotein cholesterol, or "good" cholesterol) are important risk factors for all-cause mortality, coronary heart disease mortality, or hospitalization for myocardial infarction or unstable angina in this cohort."[9] In 2005, on the subject of "bad" cholesterol, Colpo commented, "No tightly controlled clinical trial has ever conclusively demonstrated that LDL cholesterol reductions can prevent cardiovascular disease or increase longevity. The concept that LDL is "bad cholesterol" is a simplistic and scientifically untenable hypothesis."[10] Two years later, Mudd *et al* reiterated the pointlessness of lowering cholesterol and suggested that apolipoprotein b was a much better marker of CDV: "Despite more aggressive interventions by lowering LDL-C levels, the majority of CAD (coronary artery disease) events go undeterred [not prevented]…Measurement of apolipoprotein (apo)B has been shown in nearly all studies to outperform LDL-C and non-HDL-C as a predictor of CAD events and as an index of residual CAD risk." [11] Also in 2007 an extremely large meta-analysis of 61 prospective studies that comprised 900,000 adults found no association of cholesterol with stroke.[12] Indeed, one article wrote that the researchers seemed to be "baffled by findings indicating lower cholesterol levels were not linked to reduced stroke deaths." One of the researchers, Dr. Sarah Lewington of the University of Oxford (Britain)

was quoted as saying "I think all we can say is that we don't really understand what's going on here."[13] Even in the accompanying editorial to the research study, the two authors were puzzled: "Because most of the benefit of statins in preventing cardiovascular events can be ascribed to the LDL reduction, it is puzzling that LDL cholesterol is not associated with stroke risk."[14] At the very least these studies should constitute a big red flag: all that is statin does not glitter.

Confusion at Best – Statistics are Misunderstood by Most Physicians

If there are one million patients in each of two arms of a placebo-controlled clinical trial, and in the drug arm there is one patient contracting the illness and in the placebo case two patients contracted the illness, what is the drug's effectiveness? It is zero (1/1,000,000 = 0) calculated as (2-1)/ 1,000,000. However, according to the pharmaceutical presentation, they would claim the drug's effectiveness as not zero but amazingly as fifty percent (50%), calculated as (2-1)/2. Something is unnerving here because there is no indication of sample size.

As an illustrative example, if you earn $5000 a week, a raise of $1 a week brings total salary to $5001; hardly interesting and insignificant. However, an additional $1 per week to someone earning $10 per week would make a very significant difference. You get the same relative risk with a sample size of 10 or 1,000,000 patients. This frequently used method is termed "relative risk." When testing a new pharmaceutical, when the drug does not work well the study's director always wants to use "relative risk." However, the proper statistical analysis to use is termed "absolute risk" because it always includes sample size. Because so few drugs work well and their NNTs are often above 50, making them highly ineffective, if absolute risk was used to measure their effectiveness, no one would use them because it would be so obvious that they are failures. Relative risk or a hazard ratio disguises this failure.

Direct Effect, Not Surrogate Markers

Most antibiotics have an NNT of 1.1, meaning that for every 11 patients treated, 10 patients are cured of the ailment. This is a wonderful success rate. Insulin directly decreases the blood sugar level of each patient who takes it, thus the NNT of insulin is 1. Likewise for thyroid stimulating hormone (TSH), the NNT is 1. These drugs directly control the end result; i.e. more insulin = lower blood glucose. To the contrary, for each patient prescribed statins, the LDL-C will decrease, however, that decrease is irrelevant to decreased CVD (per above chart); hence the statin NNT of 100. Note: An NNT does not include contraindications, the negative drug side effects. That is a completely separate issue. In the case of statins, there are many contraindications. For example, cerivastatin (Baychol, Lipobay) was recalled in 2001 because of rhabdomyolysis, a potentially life-threatening condition.

NNT: Absolute Risk – The Only Correct Measure of Drug Effectiveness

NNT is the reciprocal of absolute risk. Drug companies will not often disclose absolute risk and the associated NNT unless forced to. An absolute risk of 0.01 (a highly ineffective drug) translates to an NNT of 100 and vice versa.

Focus on the Physiology

Studies are always open to (mis)interpretation and mistakes in statistical analyses. Incredibly, 50% of the world's top medical journals used incorrect statistics, which wrongly favor drug effectiveness, reporting overstated conclusions concerning effectiveness.[15,16] Even today, the situation has changed little.

Studies should be used only to confirm predicted effects of known physiology/biochemistry. "Studies" on lowering cholesterol and preventing CVD fail to show a cause-effect relationship time after time. Why? The consistent failure of statin drugs is predictable based on known physiology and biochemistry – not on ignoring or denying established medical science. How many cardiologists see fewer CVD-related patients in their offices? If statins truly worked, they would be seeing many fewer patients.

A NEW PHYSIOLOGIC SOLUTION TO CARDIOVASCULAR DISEASE

Cholesterol Is Anything But "Bad"

The pharmaceutical companies have apparently brainwashed physicians into thinking that LDL-C is bad. If LDL-C was truly bad, then you should not want any of it in your or your patient's body – not just less of it. No one wants anything bad in their body. However, if you eliminated all LDL-C, your patients would all die. Something is clearly wrong with this methodology. From a physiologic perspective, LDL-C is absolutely critical for the following reasons:

- All (100 trillion) cells contain cholesterol;
- All tissues manufacture and regulate cholesterol;
- LDL-C has a significant structural role in the brain, where it is required in high concentrations;
- It is fundamental in the control and regulation of fluidity in the lipid bi-layer of cell membranes;
- It enables nerve signal transmission
- Vitamin D manufacture requires functional cholesterol. (Note: There is a significant widespread vitamin D deficiency today. Could statins be an additional cause of this deficiency?);
- Bile for digestion requires cholesterol;
- Skin requires cholesterol for protection against water-soluble toxins;
- Skin requires cholesterol to protect against dehydration;
- LDL-C is a precursor for natural anti-inflammatory steroids;
- LDL-C is a precursor for all sexual steroid-based hormones (testosterone, estrogen, etc.);
- Most importantly, the body has no blood cholesterol sensor – because none is needed. LDL-C is a dependent variable that is regulated once other tightly controlled physiologic variables are set. The body does have blood sensors for physiologic functions that are critical; for example, blood glucose is automatically controlled to 70-90 mg/dL in everyone unless they are diabetic. This is a tightly controlled tolerance of 1 part in 1,000 (0.1%)! Sodium and calcium sensors control their physiologic tolerances to 3-4% in everyone. If the body required set LDL-C tolerances, it would have them. Therefore, the converse is true; no LDL sensor is needed.

The Structure of Cholesterol Itself Never Changes (But R Does!)

It is not the cholesterol structure that is the issue causing CVD; it is the component that cholesterol is "tied to." The cholesterol molecule (better termed "cholesteryl") is tied to a structure that does change - parent essential oils (PEOs) – the variable "R" shown in Fig. 2. This is where all of the insight lies. Cholesterol itself can become oxidized, but much more significant is the oxidized esterified component.[12,13] Note that the cholesterol ester portion of apolipoprotein B (as shown in Fig. 3) is huge compared to the free cholesterol or phospholipid components.

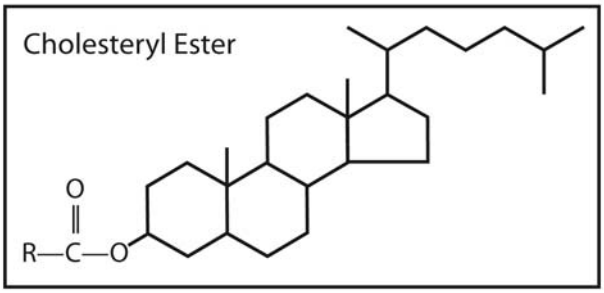

Figure 2. The Structure of a Cholesteryl Ester – An Esterol of Cholesterol

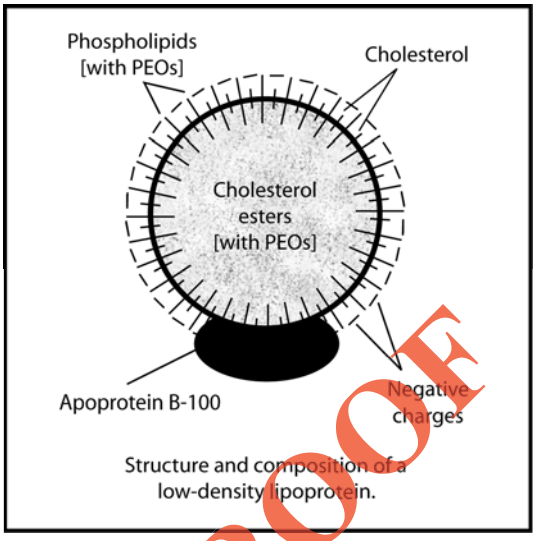

Figure 3. The Structure of Apolipoprotein B

Saturated Fat, Arterial Plaques, and Blood Lipids

There is no saturated fat in a thrombosis.[17,18] Most cardiologists are amazed when they hear this physiologic fact. Saturated fat is not causal to CVD and thrombosis, and cholesterol alone is not causal to CVD and thrombosis. Therefore, current anti-CVD recommendations of lowering LDL-C lack firm physiologic basis.

Investigators found that arterial plaques contain more than 10 different compounds, none of which are related to saturated fat. Other independent investigations confirmed this finding, but a key study in 1997 demonstrated that cholesterol esterified with nonfunctional linoleic acid (LA), a parent omega 6 fatty acid, was by far the most abundant lipid component in all types of plaque causing arterial stenosis.[19]

Percentages of Linoleic Acid (LA) & Alpha Linolenic Acid (ALA) in Plasma and Classes of Lipids

Fatty Acid	Plasma % (Unesterified)	Plasma % Triglycerides	Plasma % Phospholipids	Plasma % Cholesterol Esters
LA (parent omega-6)	17	19.5	23	50
ALA (parent omega-3)	2	1.1	0.2	0.5
Parent omega-6: Parent omega-3 Ratio	**8.5:1**	**17.5:1**	**115:1**	**100:1**

Figure 4. Percentage of Linoleic Acid and Alpha Linoleic Acid in Plasma and Classes of Lipids[20]

Approximately 70% of the cholesterol in the lipoproteins of the plasma is in the form of cholesterol esters attached to apolipoprotein B.[21] Of dietary cholesterol absorbed, 80%-90% is esterified with long-chain fatty acids in the intestinal mucosa.[22] The majority (about 55%) of the cholesteryl ester component is linoleic acid.[23] Levels of essential fatty acid (EFA) derivatives, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), made from the only 2 parent essential oils, LA and alpha linolenic acid (ALA), are insignificant and extremely low (< 2%), so are not included in this analysis because the body makes these derivatives on an as needed basis.[24-26] The n-3 series polyunsaturated fatty acids (PUFAs) makes up only 1%-2% of fatty acids in plasma.[24-26] Even in the brain, LA/ALA uptake is 100-fold in favor of LA.[25]

Surprising to most physicians is the fact that there is no significant bodily storage mechanism for ALA (parent omega-3). In fact, most parent omega-3 is oxidized for energy. Even significantly raising ALA intake does not cause a significant change in adipose tissue LA/ALA storage ratios.[25] This means that parent omega-3 has minor physiologic use and its derivatives even less, making therapeutic use of fish oil very problematic.

The Entire Problem: Oxidized Cholesterol Carries a Poison

World leading biochemist Dr. Gerhard Spiteller concludes that it is oxidized cholesterol esters that are responsible for the initial damage to endothelial cells.[27,28] LDL-C carries these toxic compounds into the endothelial walls where they cause cell damage. Injury is not significantly caused by an increase in oxidized free cholesterol but by an increase in oxidized cholesterol esters.[27,28] This is a critical issue for cardiologists and general practitioners to understand.

Inside an Artery: The Intima

The interior of the arterial lumen consists of endothelial tissue and is termed the intima. What if the cholesterol residing in the bi-lipid membrane of the intima contained significant amounts of already oxidized or nonfunctional parent omega-6, LA, before any in vivo oxidation? This line of reasoning warrants further exploration.

We know that the intima consists of a single layer of endothelial cells containing significant LA, but no ALA.[29,30] What else could cause LA in the endothelial cells to become oxidized? Could significant amounts of *LA* already defective from routine food processing, such as trans fats, hydrogenated oils, or esterified oils, transported by LDL-C be the real culprit? Yes. Consumed, processed LA deposited in arterial intimal cell membranes leads to abnormal oxidation at the vascular injury site. Note: Even food labeled as zero trans fats can actually contain up to 0.5%, which is enough to overwhelm each cell in the body by a factor of at least 100,000.[31]

EFAs and PEOs – The Essential Difference

The term "EFA" is repeatedly used incorrectly to refer to derivatives, such as DHA and EPA, and that is incorrect because there are only 2 essential fatty acids, and they must come from the diet: parent omega-6 (LA) and parent omega-3 (ALA) – both of which are essential, thus meaning that the body cannot synthesize them. DHA from fish oil is not an EFA, as it is *not essential*: the body makes it as needed, like it does many other biological substances, such as hormones from the two PEOs. EPA from fish oil is not an EFA for the same reason.

EFA Conversion Rates are Over-Estimated: New Research

Most physicians and scientists wrongly think that most, if not all EFAs are converted to their associated derivatives. It that were true, giving patients fish oil for omega-3 derivatives would be an excellent idea. However, nothing could be further from the scientific truth because there is *no* 100% conversion of parent to derivatives. Shockingly, it is less than 5% – approximately a mere 1% of all PEOs are converted into derivatives.[32-35]

A significant new finding that few physicians are aware of was published in 2008. In this study investigators evaluated the conversion rates of [U-13 C]ALA and [U-13 C]LA to their respective long-chain n-3 fatty acids. They also compared the increase of fatty acids in the RBCs from ALA with that obtained with the use of preformed EPA and DHA from dietary fish oils. The results showed that an increase in plasma n-3 fatty acid content, especially EPA (20:5n–3) and DHA (22:6n-3) was observed after consumption of fish oil-enriched supplements. Because ALA is the direct precursor of EPA and DHA it was proposed that ALA-enriched supplements such as flax oil, might have a similar effect, and indeed consuming flax oil for 12-weeks was sufficient to elevate erythrocyte EPA and DPA content, thus demonstrating the effectiveness of ALA conversion and accretion into erythrocytes. The authors noted: "The amounts of ALA required to obtain these effects are amounts that are easily achieved in the general population by dietary modification."[36] Furthermore, Hussein *et al* observed that overall conversion rates of LA and ALA, calculated from peak [13C] LCP concentrations and adjusted for dietary influences on pool sizes of LA and ALA, were low and of similar magnitude overall for AA and EPA (just 0.18% and 0.26%). Thus, we see normal PEO conversion rates of less than a mere 1%.[35] One of the reasons that earlier work overestimated the amount of conversion to derivatives was that using the area under the curve,

which is the simple, standard method of analysis**,** overestimates the conversion, because different residence times are not considered.[37]

Δ6-Desaturase and Δ5-Desaturase Enzymes Cannot Normally be Impaired

If Δ6-desaturase and Δ5-desaturase enzymes were impaired in the general population, as most physicians are told, we would see rampant epidemics of blindness in infants and youngsters, along with epidemics of mental and nervous system impairments due to inadequate DHA in both the retina and nervous system, including the brain. Because of epidemics of prostaglandin E1 (PGE1) deficiency, we should see rampant inflammation in these same populations. We do not. Therefore, the premise is false, and conversion rates are adequate, and PEO derivative supplements are not required. Derivatives such as DHA and EPA are made from the parent PEOs by the body as needed. Therefore, fish oil supplementation is not required for EPA and DHA manufacture and may provide harmful suprapharmacological and pathophysiologic overdoses of these substances.

Fish Oil is Not Physiologic and Cannot Work: It is Harmful

Fish oil supplementation to prevent heart disease was known to fail in 1995 and the American College of Cardiology stated that it was completely worthless in preventing or reversing heart disease. (Note: 6 g of fish oil supplement was used per day [38,39]) It was also known that fish oil decreases the immune response; DHA and EPA, even in low doses, do this.[40] Furthermore, it was known in 2004 that fish oil is worthless in decreasing inflammation as judged by CRP levels.[41] Other detrimental physiological effects of fish oil supplements that have been reported include possible abnormalities due to overdosing issues in brain tissue,[42-44] raising blood sugar levels and causing a blunt insulin response.[45] Therefore, fish oil supplementation is awful for a diabetic.

More recently, Nair and Connolly commented that there is insufficient evidence to recommend the routine use of omega-3 (fish oil) fatty acids, and that there is weak evidence from other meta-analyses that omega-3 fatty acids prevent ventricular arrhythmia and cardiovascular mortality.[46] As Nair and Connolly's article attests, of significance importance for physicians to understand is the fact that the GISSI-Prevenzione trial[47] was not specifically designed to evaluate sudden cardiac death, which was where the observed modest reduction in mortality occurred. Nair and Connolly go on to emphasize that Health Canada currently does not approve omega-3 fatty acids [fish oil] for the prevention of cardiovascular outcomes.[46]

An additional consideration regarding fish oil supplements is that they are highly processed, requiring ultra-high heat and chemical treatment to remove impurities, making fish oil highly adulterated with impaired functionality. Therefore, the processing negatively impacts the bioavailability and functionality of the components in fish oil. Nevertheless, even if unadulterated (if obtainable), fish oil supplementation for the general population is worthless at best and physiologically harmful at worst.

Tissue Ratio of Omega-6:Omega-3

Plasma lipids have a preponderance of parent omega-6. What about tissue? The answer is that tissue has a high predominance of parent omega-6 compared to omega-3 (11:1 conservatively).

Ratio of Tissue Composition			
Tissue	Percentage of Total Body Weight	Omega-6 PEO	Omega-3 PEO
Brain/Nervous System	3	100	1
Skin	4	1000	1
Organs and Other Tissues	9	4	1
Adipose Tissue (bodyfat)	**15-35**	**22**	**1**
Muscles	**50**	**6.5**	**1**

Reference: Spector, A.A., "Plasma Free Fatty Acids and Lipoproteins as Sources of Polyunsaturated Fatty Acid for the Brain," Journal of Molecular Neuroscience, Vol. 16, 2001, pages 159-165., "Most of the plasma free fatty acid (EFA) is derived from the triglycerides stored in the adipose tissue [bodyfat]." Note: Organs, including the brain use these EFAs for structural incorporation. "Metabolism of essential fatty acids by human epidermal enzyme preparations: evidence of chain elongation, "R.S. Chapkin, et. at., Journal of Lipid Research, Volume 27, pages 954-959, 1986, Markides, M., et al., "Fatty acid composition of brain, retina, and erythrocytes in breast- and formula-fed infants," The American Journal of Clinical Nutrition, 1994;60:189-94 and Agneta Anderson, et. al., American Journal of Endocrinological Metabolism, 279: E744-E751.

Figure 5. Omega-6/Omega-3 Ratio of Different Tissues

As can be seen, physiologically, we require at least a preponderance of 11 parts of parent omega-6 for each part of parent omega-3.

A major problem is that the majority of parent omega-6 in foods is adulterated by food processors to create long shelf life. Food processors cannot have cereal or bagels smelling like spoiled fish. Without the processing to stop the oxygen transfer, they would. At least half of all ingested omega-6-containing foods are adulterated. Therefore, we require lots of fully functional, unadulterated parent omega-6 added to our diets in the form of nutritional supplements.

Statins: A Wrong Approach

Statins do reduce the amount of LDL-C. This automatically reduces the amount of nonfunctional parent omega-6 (a positive result) from processed food that reaches cell membranes. However, statins simultaneously lower the transport of vital oxygenating functional PEOs into cells (a very bad outcome). As shown in research published in 2004, over a 24-week period in which patients were given 40 mg daily of simvastatin, mean serum parent omega-3 levels dropped 34%, and parent omega-6 levels dropped 28% – both highly significant amounts.[48]

Eicosanoid Pathways

PATHWAY SUMMARY

- **PGE1** is body's most potent anti-inflammatory.

- **Prostacyclin** is body's natural "blood thinner."*

* S. Bunting, S. Moncada, and J.R. Vane, "Prostacyclin—Thromboxane A2 Balance: Pathophysiological and Therapeutic Implications," British Medical Journal, (1983), Vol. 39, No. 3, pages 271-276.

Eicosanoids: Critical prostaglandins, etc. from parent omega-6 AND omega-3: Cell-by-cell hormone analogy (PGE1 – PGE4, etc.) - very short half-life.

Very Significant in Vascular Function

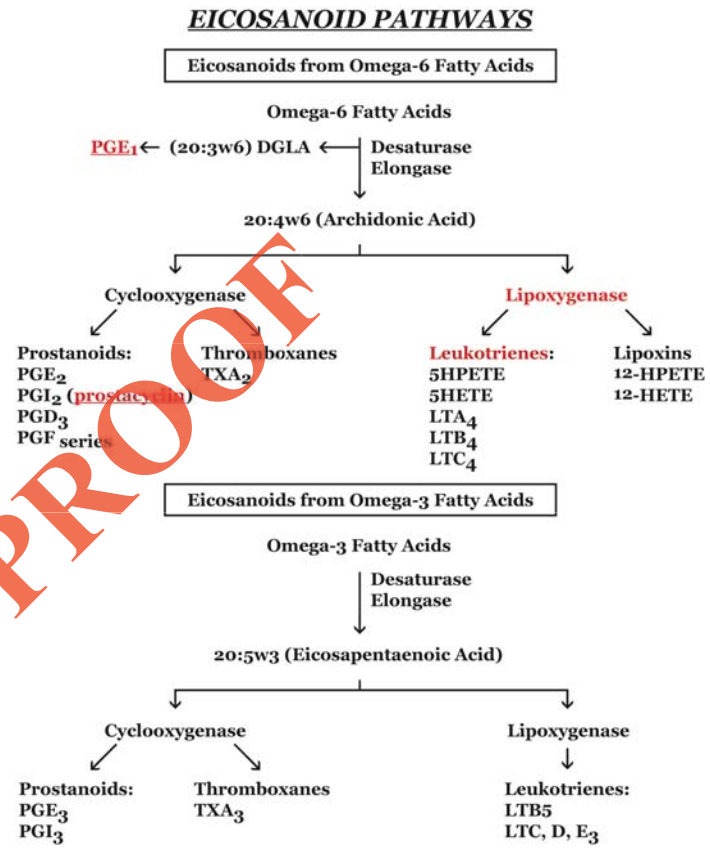

Figure 6. Eicosanoid Pathways

Note the important omega-6 pathways. PGE1 is the body's most powerful natural anti-inflammatory and prostacyclin (PGI2) is the body's natural "blood thinner," which keeps platelets separated, and stops thrombosis.

Figure 6 shows that the omega-6 series prostaglandins are more powerful than the omega-3 series prostaglandins. In the late 1980's, two significant discoveries were made. The first, was that prostaglandins are capable of limiting thrombosis.[49] The second, was that prostaglandins are capable of reversing existing thrombosis.[50] These findings are highly significant in the physiology to both reverse existing CVD and prevent patients from contracting new CVD. German physician Clause Weiss, MD, and his colleagues state: "In summary, infusion therapy with PGE1 in patients with peripheral arterial occlusive disease (PAOD) reduces thrombin formation and results in a decrease of fibrin degradation. PGE1 may thus reduce fibrin (thrombosis) deposition involved in the pathogenesis of atherosclerosis."[51] Therefore, the solution to reducing fibrin formation is adding unadulterated PEOs with a predominant LA (parent omega-6) component because they are PGE1's substrate.

It is very important to understand that PGI_2 production decreases significantly when blood vessels become hypoxic (decreased cellular oxygen levels).[52-55] Therefore, we need a powerful oxygenator to prevent cellular hypoxia. Fortunately, such a cellular oxygenator is available.

It is common knowledge that hypoxia is a direct cause of heart attack and stroke. By increasing consumption of fully functional parent omega-6, cellular oxygen increases. This was proven in 1976.[56] Fully functional, nonadulterated parent omega-6 in the phospholipids of the body's 100 trillion cells is the body's natural cellular oxygenator (if you have enough) – being utilized as substrates in both the cyclooxygenase and lipoxygenase pathways.

A Seminal Discovery: Oxidized Cholesterol Carries a Poison

The physiologic pathway of oxidization of LDL-C directly causing CVD cannot be stressed enough. As mentioned previously, world-leading biochemist, Dr. Gerhard Spiteller, concludes that it is oxidized cholesterol esters that are responsible for the initial damage to endothelial cells.[27,28] These harmful products are incorporated into LDL-C in the liver and this vehicle, basically a chemical transporter, deposits them on the endothelial cell walls of the vascular system (intima), where they initiate inflammation and familiar arteriosclerotic plaques develop as a result.

The LA (parent omega-6)/esterified cholesterol pathway is highly relevant for understanding why statins have an NNT of 100 – a 99% failure rate. Statins cannot fix the oxidized LA problem. The cholesterol structure in the arterial intima can contain significant amounts of oxidized or nonfunctional parent omega-6 (esterified) attributable largely to ingestion of foods containing oxidized LA or LA that is otherwise damaged in the course of routine food processing, before any in vivo oxidation! When these precious PEOs become oxidized, oxygen transfer stops, and CVD starts.

We know that the intima consists of a single layer of endothelial cells containing significant LA, but no ALA.[29,30] Consumed, processed (nonfunctional) LA deposited in arterial intimal cell membranes leads to abnormal oxidation at the vascular injury site, thus causing injurious inflammation. (Note: In this case, abnormal oxidation involves formation of a hydroperoxide from LA.) The real culprit is in our food supply, as ubiquitous "processed foods." Masquerading as harmless, they are the evil stealth villains in the CVD drama.

EFAs and Bio-Identical PEOs – the Essential Difference

The key to CVD prevention is PEOs – in particular, fully functional parent omega-6 in the esterified cholesterol. Not distinguishing between adulterated and nonadulterated PEOs, Brown and Goldstein, two 1985 Nobel Prize winners in physiology and medicine, stated in 2001: "How does elevated plasma LDL produce the complex lesions of atherosclerosis…The answer may lie in the unsaturated fatty acids [functional, unadulterated PEOs] of the cholesteryl esters and phospholipids of which LDL is composed…LDL can undergo oxidation [in the arteries]…."[57]

Although it was a major failure to distinguish between adulterated and nonadulterated essential fatty acids (PEOs), or realize that the two types would produce very different results (disease or health), Brown and Goldstein correctly showed that cholesterol itself has nothing to do with atherosclerosis; it is just a transport vehicle of tremendous amounts of the often adulterated PEOs (LA, parent omega-6 and ALA, parent omega-3).

Cause of Thrombosis (Blood Clots): The LDL Connection

Cholesterol esters are the predominant lipid fraction in all plaque types, and intimal macrophages contain substantial amounts of cholesterol esters, which are rich in PUFAs (PEOs). (Note: The intima is composed entirely of parent omega-6 – with insignificant parent omega-3.[19]) What about these oils going rancid (peroxides) in the body, such as the literature often "reiterates"? To the contrary, PEOs help protect against oxidation (Fig. 7).

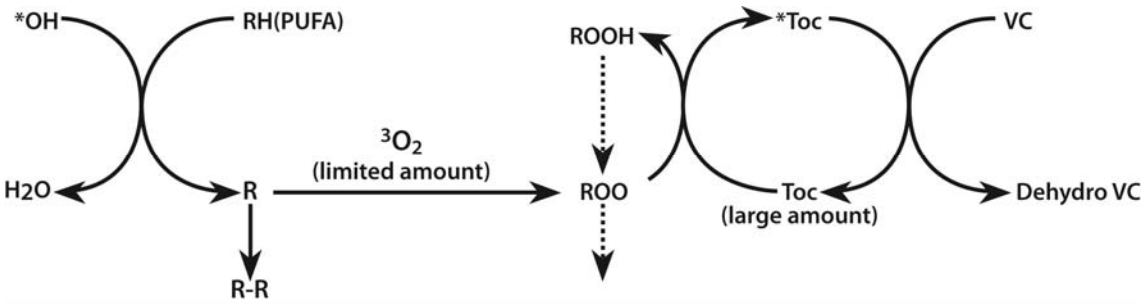

Figure 7. PEOs Act as a First Stage Scavenger of Reactive Oxygen Species In Vivo

In 2009, the American Heart Association championed a major reversal regarding omega-6 fatty acids, based on a review of the evidence.[58] "A great deal of discussion in the world of nutrition has given omega-6 fatty acids a bad reputation, which, according to the American Heart Association, is unfounded. The debate came about because one of the components of omega-6 fatty acids, called arachidonic acid, is a 'building block' for some inflammation-related molecules. This had led to concern that omega-6 consumption would lead to a greater risk of heart disease. That reflects a rather naive understanding of the biochemistry." says William S. Harris, Director of the Metabolism and Nutrition Research Center of the University of South Dakota Sanford School of Medicine and the nutritionist who led the science advisory committee that issued the report in Circulation. "Omega-6 fatty acids give rise to both pro-inflammatory compounds and anti-inflammatory compounds. To say that they are bad because they produce pro-inflammatory compounds ignores the fact that they give rise to anti-inflammatory compounds as well."[59] Years earlier, Harbige had said essentially the same thing: "Finally, the view that all n-6 PUFA are pro-inflammatory requires revision, in part, and their essential regulatory and developmental role in the immune system warrants appreciation."[60]

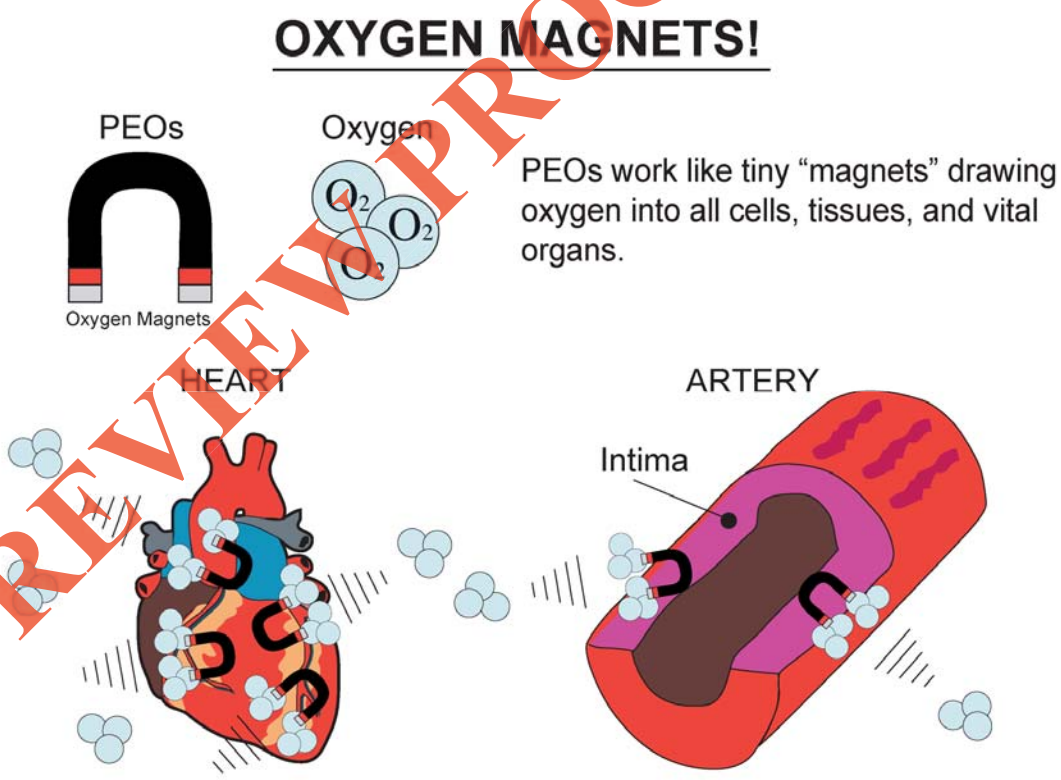

Figure 8. Parent Essential Oils Act Like Oxygen Magnets

Food processors never use omega-3 fats in frying or baking as they are far too oxygen-reactive. Most parent omega-3 in foods is, therefore, not adulterated. The problem lies exclusively in the adulterated parent omega-6 fats. This key issue needs to be properly addressed by the medical community. Because parent omega-3 oils are not processed does not mean that we don't need to understand their role in preventing CVD, as the following makes clear.

A recent cardiology journal article provides an update on the physiologic usefulness of parent omega-3. Specifically, ALA [parent omega-3] was associated with a lower risk of nonfatal acute myocardial infarction. The authors concluded: "Thus, it is possible that consumption of vegetable oils rich in α-linolenic acid could confer important cardiovascular protection in many countries where intake is low." The most significant finding was that "Fish intake was similar in cases and controls, and the variation within each group was large…. Fish or eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA] intake at the levels found in this population did not modify the observed association."[61]

It is important to note that the parent omega-3's cardio-protective result was independent of the level of fish consumption. Given all of fish oil's supposed miraculous claims, did these researchers not wonder why? However, the researchers understood that the parent omega-3 conferred benefit that the fish oil (derivatives) did not do.

There are other benefits to increased parent omega-6 (LA) consumption, such as the reduction of ventricular fibrillation (arrhythmias),[62] and for diabetic patients in terms of complications: "Erythrocyte membranes from diabetic patients show only 42% [58% *less*] of the PGE1 binding activity found in controls. These data are very important… play important roles in the long-term complications of diabetes."[63] Imagine how diabetics could be helped if more physicians, particularly endocrinologists, understood this important fact.

It is vitally important to understand that raising LA intake alone *does not* increase gamma linoleic acid (GLA), the precursor of PGE1.[64] The reason for this is likely that before widespread adulteration of cooking oils, Nature had no requirement for increasing normal physiologic rate-limited levels of PGE1. Today, that is not the case. With the widespread cooking oil adulteration, comes widespread chronic inflammation. Diabetes has become a worldwide epidemic. Unfortunately, diabetics may have impaired conversion. Therefore, any modern essential fatty acid recommendation must include gamma linoleic acid.

Don't We Get Too Much Omega-6 In Our Food?

This is true, but most, greater than 50%, is adulterated. If this were not the case, all packaged foods would quickly oxidize regardless of added antioxidants. Therefore, a substantial portion of dietary LA needs to be counted as zero because it is nonfunctional and hazardous. Some physicians wrongly think that LA promotes tumors. That conclusion is correct if the typical processed, adulterated oil is used in both human and animal studies. Furthermore, these results are often measured *in vitro* (outside the body), leading to the misunderstanding, whereas *in vivo* experiments are required.[41]

What PEO Ratio is Best?

What PEO ratio is best? A balanced physiologic blend of PEOs that allows the body to make derivatives as needed. Organic flax oil is fine for parent omega-3, but offers little parent omega-6. High linoleic (not high oleic) strains of sunflower and safflower are fine for parent omega-6, although high oleic strains cannot be used because there will not be sufficient LA.

The parent omega-6/omega-3 ratio must be 2.5:1 to 1:1 in favor of parent omega-6.[65] No omega-3-based derivative fish oil is to be used, and few derivative EFAs; only a conservative amount of GLA from evening primrose oil. Note: organic evening primrose oil produces approximately 15-times more arterial outflow of the powerful anti-inflammatory PGE1 from its GLA content than borage oil.[66] Clinicians can use this new physiologic approach to best prevent cardiovascular disease in their patients regardless of patient diet or existing complications.

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