

# Reducing Pain and Inflammation Naturally

## Part I: New Insights into Fatty Acid Biochemistry and the Influence of Diet

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PAIN AND INFLAMMATION ARE NEUROCHEMICAL MANIFESTATIONS of physiologic imbalances which originate biochemically, structurally, and/or neurologically. Beyond the obvious relevance to the treatment of conditions associated with pain and inflammation, the implications of the data presented will provide therapeutic insight for doctors treating a wide range of complex chronic illnesses. Given the strength and momentum of this research, combined with the public's increasing interest in alternatives to dangerous, expensive, and often ineffective pharmaceutical treatments, the time has come for the chiropractic profession to assume a more empowered leadership position in the provision of healthcare and the prevention and treatment of most chronic health problems.

### INTRODUCTION:

Since its inception, the chiropractic profession has recognized and affirmed the importance and benefits of whole-patient healthcare.<sup>1,2</sup> In contrast to the medical model of disease, which generally seeks to use synthetic drugs to target isolated biochemical pathways, the holistic model of health and disease appreciates that a multifaceted approach including physical (structural, biomechanical, anatomical), biochemical (nutritional, hormonal, neurochemical), and psychoemotional assessments and interventions is commonly safer, more effective, and less expensive in the long-term for the restoration and preservation of optimal health.<sup>3</sup> Extensive documentation in support of these concepts and their clinical applications has recently been compiled by the current author in a 486-page manuscript.<sup>4</sup>

While the benefits, safety, and cost-effectiveness of physical medicine and spinal manipulation have been well established in journal articles and commissioned reports,<sup>5,6</sup> it is only within the past few years that we have seen a literal explosion of high-quality research supporting the concept that skillful phytonutritional interventions can have a powerful and beneficial influence on patient outcomes for a wide range of health concerns. Thus, as the only nationally-licensed healthcare providers with training in nutrition, chiropractic physicians should claim their proper position of leadership in the management of chronic health disorders.

The research increasingly points to inflammation as a common determinant of many diseases, including cancer, cardiovascular disease, neurologic conditions, diabetes, arthritis, and the so-called autoimmune diseases such as rheumatoid arthritis, lupus, and multiple sclerosis. Additionally, new research is also documenting the powerful influence of nutrition on optimal cell membrane dynamics, neurotransmitter/hormone receptor function, and modification of gene expression. The most powerful, cost-effective, and fundamental means for effectively addressing all of

these processes—1) inflammation, 2) cell membrane dynamics, 3) neurotransmitter/hormone receptor function, and 4) gene expression—is with skillful nutritional intervention: dietary improvement and phytonutritional supplementation. In particular, modulation of fatty acid metabolism by supplementation with nutritional oils is the most efficient means to achieve all four of the above-mentioned goals.

### FOOD AND INFLAMMATION:

The adage “One man’s food is another man’s poison” finds particular relevance when we are dealing with patients experiencing pain and inflammation. Although dietary recommendations must always be customized for each individual patient, we can confidently make certain general recommendations to help these patients overcome their health problems and to feel and function better. Conceptually, we can organize our ideas about foods into the following categories: 1) foods to avoid, 2) foods to consume, 3) customized recommendations with regard to allergies, sensitivities, and intolerances.

**Foods to Avoid:** Many doctors and patients are unaware of the pro-inflammatory nature of many commonly eaten foods.<sup>7</sup> As long as patients continue to consume pro-inflammatory chemicals in their foods on a daily basis, then they will continue to fight an uphill battle against pain and inflammation. Generally speaking, eating is itself a pro-inflammatory event, with sugars and fats inducing more inflammation than protein-containing foods.<sup>8</sup> Therefore, simple sugars and high-fat foods should be avoided. Two fatty acids in particular, linoleic acid (LA) and arachidonic acid (ARA) from the n-6 family should be reduced or eliminated from the diet to the extent possible. LA increases inflammation by several mechanisms, one of which is activation of NF-kappaB.<sup>9</sup> (Phytonutritional modulation of NF-kappaB<sup>10</sup> will be reviewed in upcoming articles in this series.) Therefore, rich sources of LA should be avoided as much as possible. LA is abundant in most nut, seed, and

vegetable oils such as canola oil (21%), safflower oil (76%), sunflower oil (71%), corn oil (57%), soybean oil (54%), and cottonseed oil (54%). Similarly, ARA is the direct precursor to the isoprostanes—chemicals that are formed from the non-enzymatic oxidation of ARA and which exacerbate pain and inflammation. ARA is the precursor for and increases the production of inflammatory and noxious chemicals, particularly the prostaglandins and leukotrienes. Additionally, laboratory research has found that ARA also promotes activation of NF-kappaB and can cause a 400% increase in superoxide production in Kupffer cells.<sup>9</sup> The most obvious method for *reducing production of chemicals derived from ARA* is to *reduce dietary intake of ARA*; this means avoiding the richest sources of ARA such as whole milk, beef, liver, pork, lamb, and to a lesser extent turkey and chicken. Additionally, many of these problematic foods, especially beef, liver, pork, and lamb, are also major sources of dietary iron, which promotes joint inflammation independently from its contribution to iron overload and hemochromatotic arthropathy. Indeed, as I have discussed in this journal<sup>11</sup> and elsewhere<sup>12</sup>, all patients with polyarthropathy should be tested for iron overload. In summary, patients with inflammatory conditions should avoid foods that are high in fat, simple carbohydrates, linoleic acid, arachidonic acid, and iron. Artificial and processed foods should also be avoided since they are commonly rich in *trans*-fatty acids and are depleted of antioxidants.

**Foods to Consume:** Fruits and vegetables are rich sources of health-promoting nutrients such as vitamins, minerals, fiber, fatty acids such as squalene, and—perhaps most important—a wide range of phytochemicals including limonoids, carotenoids, terpinoids, isothiocyanates, flavonoids, proanthocyanidins and other polyphenols. Dietary antioxidants have important anti-inflammatory benefits that extend beyond their abilities to quench free radicals. Additionally, components of whole foods, such as the sterols and sterolins found in vegetables, have significant immune-modulating effects and have shown benefit in alleviating the inflammation of rheumatoid arthritis. Fruits and vegetables contain over 5,000 different phytochemicals that act additively and synergistically to maximize antioxidant protection and to protect health.<sup>13</sup> Vegetarian, vegan, and plant-based whole-foods diets are naturally low in fat, linoleic acid, arachidonic acid, iron, and *trans*-fatty acids. Extra virgin olive oil contains oleic acid, squalene, and phenolic compounds which work synergistically to reduce inflammation, pain, and cardiovascular disease. Whey, soy, and cold-water fatty fish provide health benefits in addition to the provision of high-quality protein. Green tea shows anti-inflammatory, antioxidant, and anti-cancer actions. Diets with a strong foundation of whole fruits and vegetables help patients increase their intake of antioxidant and

anti-inflammatory vitamins, minerals, fiber, and phytonutrients while helping to reduce intake of pro-inflammatory iron and fatty acids. Lastly, a significant portion of the health benefits and anti-inflammatory effects of increased consumption of fruits and vegetables is due to favorable alterations in gastrointestinal microflora<sup>14</sup> rather than the direct nutritive values of foods.

### **Customized Recommendations and Food Allergies:**

We are all aware that, in certain patients, specific foods and combinations of foods may exacerbate joint pain and inflammation.<sup>15,16</sup> Therefore the diet must be customized for each patient with regard to food allergies, food sensitivities, and food intolerances. Not only must problematic foods be avoided, but patients' gastrointestinal and immune status must be evaluated and improved.<sup>4</sup> Although many doctors are aware of the elimination-and-challenge technique, most doctors do not direct sufficient attention to improving gastrointestinal status and immune function so that the immune system is no longer hyper-responsive to benign food constituents.<sup>4</sup>

## **AN INTRODUCTION TO FATTY ACID METABOLISM**

We can think of the major biologically active fatty acids as originating from three major categories or “families” based on their molecular configuration and thus their physiologic properties. We can then ascribe general properties to these families and the individual members within each group. The most clinically important fatty acids are “unsaturated”, meaning they have one or more carbon-to-carbon double bonds rather than carbon-to-carbon single bonds, the latter being “saturated” with the full number of hydrogen molecules. Double bonds strongly influence the biochemical and clinical effects of fatty acids, making these fatty acids more reactive and biologically active than their saturated counterparts, as well as more prone to oxidation, rancidification, and hydrogenation.

Within each family, fatty acids progress from predecessors to progeny by a series of enzymatic steps catalyzed by desaturase and elongase enzymes. The desaturase enzymes are very slow in their conversions compared to the elongase enzymes, and the clinical relevance of this difference will become apparent as this article and series of articles progresses. We also note that fatty acids never change from one family to another: e.g., an omega-3 fatty acid will always remain in the omega-3 family and will never become a member of the omega-6 or omega-9 family. This is because the defining characteristic on a molecular level is never altered: omega-3 fatty acids have their first carbon-to-carbon double bond starting at the third carbon from the methyl group; omega-6 fatty acids have their first carbon-to-carbon double bond starting at the sixth carbon from the

methyl group; omega-9 fatty acids have their first carbon-to-carbon double bond starting at the ninth carbon from the methyl group. For the sake of efficiency and accordance with nomenclature conventions, we will hereafter abbreviate “omega” as “n” for the n-3, n-6, and n-9 fatty acids, respectively.

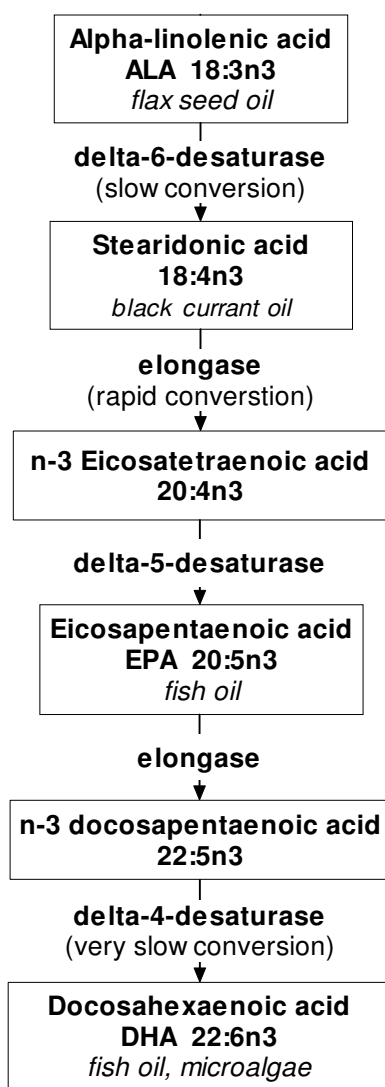
**N-3 fatty acids:** The n-3 family of fatty acids begins with alpha-linolenic acid, commonly referred to as one of the two “essential fatty acids” because it cannot be produced within the human body and must therefore be provided by the diet. Manifestations of n-3 fatty acid deficiencies are generally subtle when contrasted to those of the n-6 family and include behavioral and visual impairment, endocrinologic alterations, and a tendency toward the development and progression of several chronic degenerative diseases.<sup>17</sup>

Abundant in flax oil (~57%), alpha-linolenic acid (ALA) is converted to stearidonic acid by delta-6-desaturase. Stearidonic acid (SDA) is elongated to n-3 eicosatetraenoic acid, which is then converted to eicosapentaenoic acid (EPA) by delta-5-desaturase. EPA is elongated to n-3 docosapentaenoic acid (n-3 DPA), which is then converted to docosahexaenoic acid (DHA) by delta-4-desaturase. These substrates and conversions are illustrated in Figure 1 (modified with permission from *Integrative Orthopedics*<sup>4</sup>).

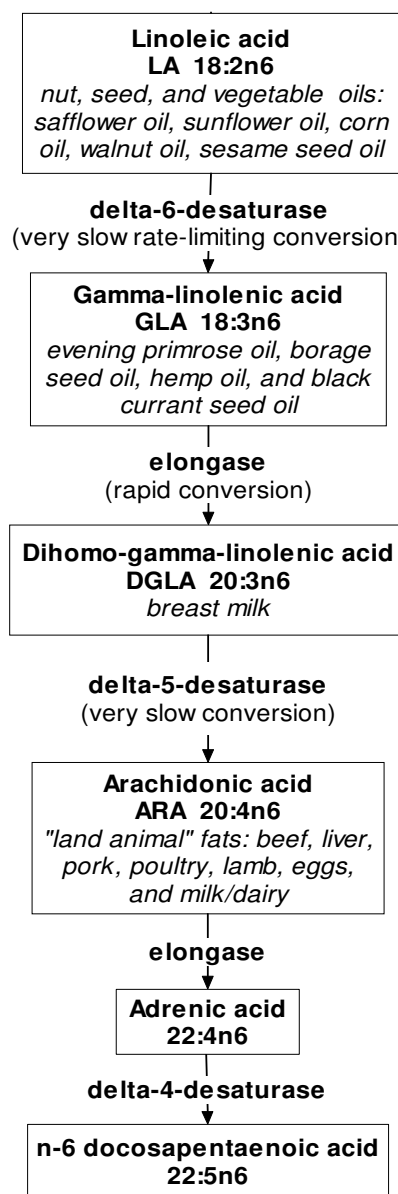
**N-6 fatty acids:** The n-6 family of fatty acids begins

with linoleic acid (LA), also referred to as an “essential fatty acid” because it cannot be synthesized *de novo* within the human body. LA is abundant in most nut, seed, and vegetable oils such as canola oil (21%), safflower oil (76%), sunflower oil (71%), corn oil (57%), soybean oil (54%), and cottonseed oil (54%).<sup>18</sup> LA is converted by delta-6-desaturase to gamma-linolenic acid (GLA), which is quickly elongated to dihomo-gamma-linolenic acid (DGLA). DGLA is slowly converted by delta-5-desaturase to arachidonic acid (ARA), which is elongated to adrenic acid, which is finally converted to n-6 docosapentaenoic acid by delta-4-desaturase. These substrates and conversions are illustrated in Figure 2 (modified with permission

**Figure 1. Metabolism of n-3 fatty acids**



**Figure 2. Metabolism of n-6 fatty acids**



from *Integrative Orthopedics*<sup>4</sup>).

Note that the term “eicosatetraenoic acid” can apply to both 20:4n6 (arachidonic acid) of the omega-6 fatty acid family<sup>19</sup> and to 20:4n3 of the omega-3 fatty acid family.<sup>20</sup> Therefore, to avoid the confusion that would result from the use of the term “eicosatetraenoic acid” by itself, “n-6 eicosatetraenoic acid” should be used when referring to 20:4n6 (arachidonic acid) and “n-3 eicosatetraenoic acid” should be used when referring to 20:4n3. Similarly, 22:5n3 of the omega-3 fatty acid family<sup>21,22</sup> and 22:5n6 of the omega-6 fatty acid family<sup>23,24,25</sup> are both referred to as “docosapentaenoic acid.” Therefore using the term “docosapentaenoic acid” will be ambiguous unless the appropriate n-3 or n-6 designation is stated. “N-3 docosapentaenoic acid” should be used to refer to 22:5n3 and “n-6 docosapentaenoic acid” should be used for 22:5n6.

**N-9 fatty acids:** The primary n-9 fatty acid in the human diet is oleic acid, the predominant monounsaturated fatty acid in olive oil. While oleic acid is certainly biologically active and therefore clinically important, due to the complexity of olive oil as the primary source of oleic acid, we are not yet able to clearly determine from epidemiological studies how much of the benefit of olive oil consumption is due to the oleic acid compared to the benefits derived from the powerful antioxidant and anti-inflammatory actions of the phenolics, the relatively high content of squalene, or other confounding variables in diet and lifestyle.<sup>26,27</sup>

## ENZYMATIC CONVERSION: CHEMICAL FLOWCHARTS VERSUS THE REALITY OF CLINICAL EFFECTIVENESS

If conversion of one fatty acid to the next proceeded as efficiently as depicted in biochemical flow charts, then n-3 ALA and n-6 LA could be supplemented to provide all of the downstream fatty acids and their metabolites, presumably in the proper ratios. However, clearly this is not the case due to intrinsic as well as genotypic (inherited) and phenotypic (manifested) defects in enzyme effectiveness. Clinicians need to understand the individual characteristics of these enzymes in order to successfully employ therapies which modulate fatty acid metabolism. Since the conversions catalyzed by elongase are quite efficient and are almost never discussed as cause for concern in the medical and nutritional literature, we will focus on the desaturase enzymes, which are noted to have significant variances in phenotypic expression and which can be adversely affected by common vitamin and mineral deficiencies.

**Delta-6-desaturase:** The first step in the n-3 and n-6 pathways is the action of delta-6-desaturase (D6D) in converting ALA to SDA and LA to GLA, respectively. Enzymatic conversions by D6D are rate-limiting due to 1)

its strong need for several vitamin and mineral co-factors, 2) its genotypic impairment, such as in patients with eczema,<sup>28</sup> 3) its phenotypic impairment in patients with diabetes,<sup>29</sup> and its impairment by trans-fatty acids,<sup>30</sup> stress neurotransmitters,<sup>31</sup> and other environmental and nutritional influences.<sup>4</sup> The slow conversions by D6D explain why, as Horrobin noted, “...it is impossible to produce any significant elevation of DGLA levels in humans by increasing linoleic acid intake.”<sup>32</sup> Similarly, conversion of ALA to the downstream and clinically desirable fatty acids EPA and DHA is unreliable, with most studies showing only a modest increase in EPA and no increase in DHA following supplementation with ALA. Cofactors required for efficient action of D6D include iron, zinc, magnesium, pyridoxine, riboflavin, and niacin; when these vitamins and minerals are deficient, D6D function will be impaired and defects in fatty acid metabolism will result.<sup>33</sup>

**Delta-5-desaturase:** Delta-5-desaturase (D5D) slowly converts n-3 eicosatetraenoic acid to EPA, and in the n-6 pathway, DGLA to ARA. Supplementation with GLA has been shown to result in a slight to modest increase in ARA that may or may not be clinically significant. Impairment of D5D is seen in patients with the blinding eye disease retinitis pigmentosa, resulting in marked reduction in retinal DHA levels.<sup>34</sup>

**Delta-4-desaturase:** Delta-4-desaturase (D4D), like the other desaturase enzymes, is also very slow-acting. While impaired conversion of adrenic acid to n-6 docosapentaenoic acid appears to be of little or no consequence, reduced bioavailability of DHA due to its slow conversion from n-3 docosapentaenoic acid has tremendous implications in the etiology of schizophrenia, a disease associated with impaired D4D activity.<sup>35</sup>

By understanding the biochemical efficiency of these enzymes, doctors are better able to understand how to implement clinical strategies for modulating fatty acid balance in their patients. In the n-3 family, supplementation with ALA increases (in order of decreasing efficiency) ALA, SDA, and EPA but does not consistently elevate DHA. Therefore, although consumption of flax oil has many important benefits and may be used to modestly increase EPA levels, it cannot be relied upon to increase DHA levels.<sup>36</sup> Supplementation with SDA increases EPA levels, but DHA is not significantly increased due to the slow conversion by D4D.<sup>37</sup> Supplementation with EPA proportionately increases EPA but does not consistently increase DHA.<sup>38</sup> DHA supplementation is the most effective and reliable means for increasing DHA levels.<sup>39</sup>

In the n-6 family, supplementation with LA does not lead to clinically significant increases in GLA or DGLA.<sup>32</sup> Supplementation with GLA greatly increases DGLA and

leads to a modest increase in ARA.<sup>40</sup> Diets high in ARA lead to increased tissue levels of ARA. Consumption of EPA lowers levels of GLA/DGLA<sup>29</sup> and oleic acid<sup>41</sup>; likewise, consumption of GLA lowers levels of EPA.<sup>40</sup>

**Overall, the implications are that when a particular fatty acid is desired for its physiologic effect and clinical benefits, it should be supplied directly from the diet or supplements.**

## CONCLUSION:

In this brief article, we have introduced and reviewed the foundational terminology and concepts which will facilitate the introduction of more advanced concepts as presented in the upcoming articles in this series. Dietary improvement and custom-tailored prescription of individual fatty acids is consistently providing patients and doctors with greater health and superior clinical results. Alleviation, prevention, and effective treatment of many diseases previously considered to be “untreatable” is now possible with fatty acid supplementation, diet modification, and the use of other vitamins, minerals, and botanical medicines. The skillful use of these interventions by the chiropractic profession, whether as adjunctive treatment to spinal manipulation or as primary therapy, is in accord with our holistic philosophy and promises to advance the prominence of our profession in the healthcare arena. Since the pharmaceutical-surgical paradigm delivers many unnecessary risks and unsatisfactory outcomes in the management of chronic disease<sup>42-49</sup>, now is the time for chiropractic physicians to step forward and deliver the safest, most effective and cost-effective therapies ever before seen in American healthcare for the management of chronic health problems.

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