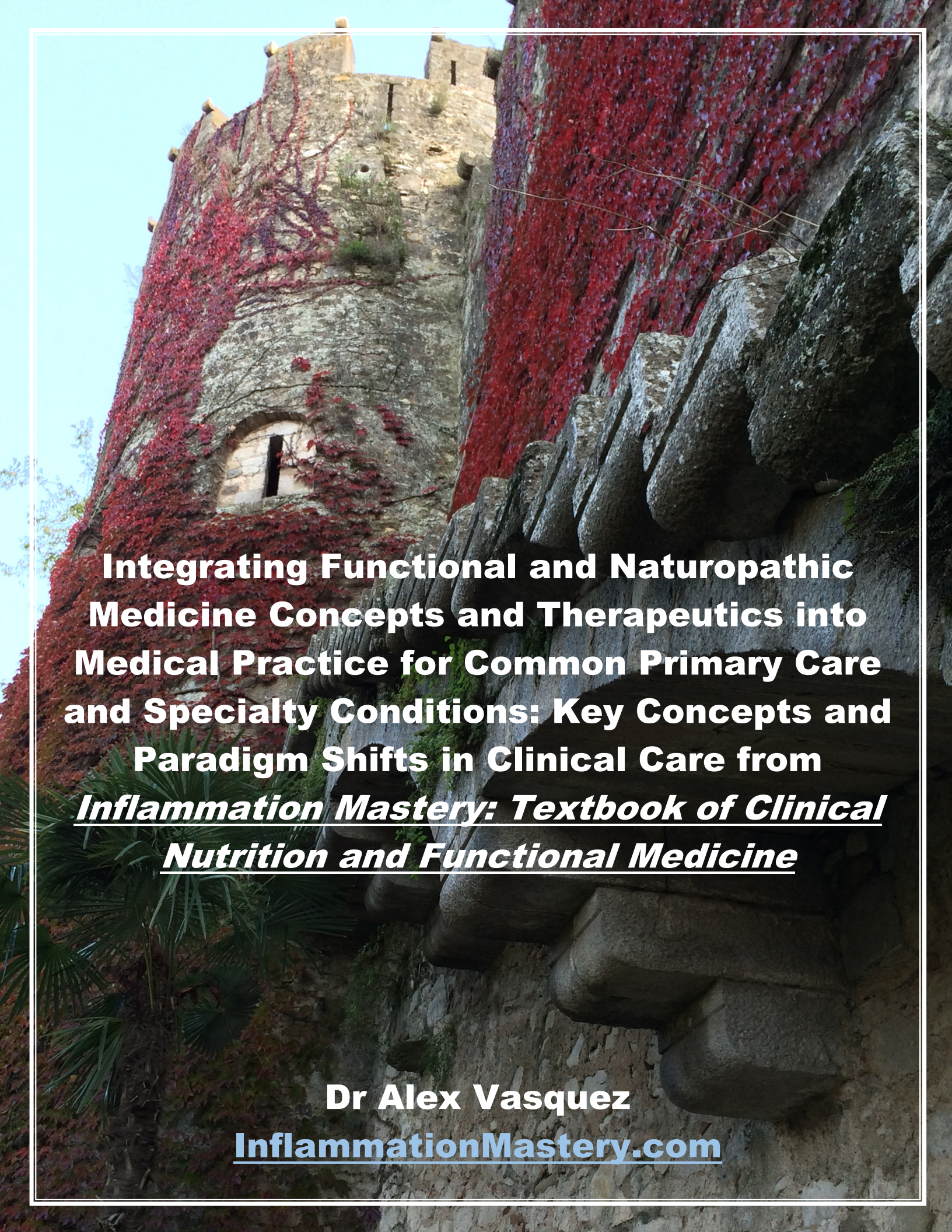

# Integrating Functional and Naturopathic Medicine Concepts and Therapeutics into Medical Practice for Common Primary Care and Specialty Conditions: Key Concepts and Paradigm Shifts in Clinical Care from *Inflammation Mastery: Textbook of Clinical Nutrition and Functional Medicine*

**Dr Alex Vasquez**

InflammationMastery.com

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**Orientation**: This is the edited transcript of a video presentation available for viewing and purchase at InflammationMastery.com/medical. The video presentation contains at least 136 slides or "pages" that include the scientific citations, additional commentary and notes, as well as illustrations, diagrams, and excerpts from other publications, especially my 1,200-page full-color *Inflammation Mastery 4th Edition*, published in a two-volume set as *Textbook of Clinical Nutrition and Functional Medicine*. Please see those complete published works for the complete list of citations, additional illustrations, case reports and detailed clinical implementation of the protocols that are structurally outlined here. Because the scientific/research citations are provided within the video presentation, which is available for free viewing, I do not feel any need to repeat those citations here except when 1) I am quoting directly from another author's work, or 2) when the citation is of particular importance or has been added retrospectively. Finally, in certain instances wherein the original presentation (combination of words and illustrations) does not convey well to transcription—such as for example in the case of tables or particular illustrations—I will embed the original page/slide into this transcript. For the obvious reasons that the original presentation was performed and edited in English and that all of the original sources are in English, which is widely considered the official language of science, the edited English-language transcript of this considered the final and official version of this presentation; translations into other languages are performed by language-translation professionals (Russian) and experienced multilingual doctorate-level healthcare providers (French, Spanish). Any updates/edits to this document (printed May 18, 2020) will be available via https://ichnfm.academia.edu/AlexVasquez and/or InflammationMastery.com/medical

**Major Sections**:



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## Introduction

Hello, everyone! Dr Alex Vasquez here, and today's presentation is titled "Integrating Functional and Naturopathic Medicine Concepts and Therapeutics into Medical Practice for Common Primary Care and Specialty Conditions."

I will touch upon some key concepts and paradigm shifts in clinical care which I believe have taken place over the last 15 to 20 years. I will start with an introduction, and then I will discuss some of the major clinical paradigms (for example: functional medicine and naturopathic medicine *versus* drug-centered so-called standardized or "conventional" medicine) and I will also contrast those clinical paradigms so you can see the advantages and disadvantages of each of those.

Then I will introduce and outline a protocol that can be used from a functional medicine and naturopathic medicine model for the understanding, management, and treatment of inflammatory conditions. I will divide those conditions into four categories: 1) metabolic inflammation, 2) allergic inflammation, 3) autoimmune inflammation, and 4) neuroinflammation or "brain inflammation" including the concept of the gut-brain axis.

## This Work is Important for Your Life, Relationships, Profession

I think that you will find this work relevant for your life if you are a clinician, researcher, teacher, or if you simply inhabit and maintain a human body. I think this protocol will show you some of the major checkpoints that we need to attend in order to optimize health and prevent disease. Also, if you have any friends or family who may have any of the conditions that I discuss in this presentation, I am sure you will find the presentation to be all the more relevant.

## Limitations

Some of the limitations that apply to this presentation include the fact that this is a single presentation of approximately two hours, and so that timeframe will not provide me a lot of opportunity to go into ***deep detail*** as I would if this were a graduate course of 20-30 hours or extended weekend seminar of 9-15 hours.

## Intellectual Structure

Within the constraints of this 2-hour timeframe, I will provide you an overview and an ***intellectual template*** that you can use for the understanding, study, and management of various clinical conditions.

## Paradigm Shifting

The two major themes of this presentation include starting with an introduction that includes an analysis of different clinical paradigms, and thereafter and most importantly, the bulk of my time is going to be spent outlining a clinical protocol, then using some examples of how to implement that protocol clinically, and how you can use it as a model to study other conditions.

Anytime we are learning new information, we may have to discard old information and anytime we are learning a new paradigm, we need to appreciate how that new paradigm contrasts with an old paradigm that we *consciously learned* or *unconsciously accepted* previously and see what we might use and what we might need to discard. Learning *new information* that fits into an *old paradigm* is simple and rapid, because the mental template has already been constructed, whereas learning new information that ***gives structure to a new paradigm*** takes a bit more time and effort; to assist that process, everyone is invited to review the video 2-3 times to allow the new model to "sink in" to enhance or replace previous models.

## Introduction to Presenter and Author

Again, I am your host for this presentation Dr. Alex Vasquez. I am a Doctor of Chiropractic—graduate of University of Western States, Doctor of Naturopathic Medicine—graduate of Bastyr University, and Doctor of Osteopathic Medicine—graduate of University of North Texas Health Science Center in the United States. Several other accomplishments are listed here, including some of my clinical experiences, teaching experiences, also editing, writing at least 25 books, and also writing at least 100 articles and various scientific and specialty journals and professional magazines. You can see some of those locations where I have published my work listed here. And I have also not only worked within three or four different professions (ie, chiropractic, naturopathic, osteopathic, medicine and functional medicine), but I have also lived within different cultures and on three different continents including in the United States, Latin America and Europe—each of these cultures has different perspectives, priorities, and opportunities regarding health and healthcare.

## Copyrights, Notices, Format

This page provides an overview of some of my copyrights, disclosures, trademarks, etc. Anytime I talk about dosages, within this presentation, I am talking about dosages for adults who are not lactating, not pregnant, and who do not have kidney or renal disease. Each of my slides, of course, is going to have a title at the top, and a little bit of information here in the corner. Then I will have an index to the left-hand side to kind of provide some orientation, then the bulk of the information will be of course in the center of the slide. When I need to provide a summary, I will do that within a mauve or purple colored text box like this. And then you will see the use of certain images from my books such as *Inflammation Mastery*, and another book I will discuss later called *Brain Inflammation*. Again, the two major themes of this presentation are number one to discuss the medical paradigm and contrast that with functional medicine and naturopathic medicine and then I am going to spend the most of the time of today's presentation, discussing a clinical protocol, certain clinical examples and how to implement that protocol in clinical practice.

## Moving Beyond the Limited and Outdated Medical Paradigm and Medicalization Routine

Learning new information that is consistent with a previously-learned model or paradigm is easy: just "plug and play" new data into an old mainframe. However, learning *new information* within a *new model* requires that we first create some space for that new information. If people are rigidly adherent to the

medical paradigm, then the mind is not open to a new way of seeing things. Being open to a change in paradigm does not indicate that a person thereafter ignores previous information, or to the extreme "stops using drugs to treat patients", but rather has more options and can use drugs within a framework of **cognitive flexibility**, *rather than* ***blind obedience*** *and* ***repetitive routine****.*

The clinical employment of nutrition, naturopathic principles, and functional medicine involves a paradigm shift—a completely different (relative to the drug-centered medical model) way of looking at disease and treatment, not simply the employment of different treatments that replace drugs within a medical model. Using nutrients to replace drugs is sometimes called "**green medicine**", such as when we substitute a pharmacologic HMG-CoA-reductase inhibitor (i.e., lovastatin or any of the other "statin" drugs) with a natural cholesterol-lowering supplement such as red yeast rice, niacin or policosanol. Using nutrients to replace drugs is not equivalent—neither in terms of conceptualization, efficacy, clinical acumen, nor global impact—to either naturopathic medicine or functional medicine; however, it is a common and understandable entry point for doctors transitioning from one paradigm to the other. Ironically, many medical physicians and organizations especially in the United States insult the use of nutritional supplements without knowing that the prescription drug lovastatin was originally sourced from the natural product monacolin K from red yeast rice, and the substances are chemically identical[1]; such is the potency of indoctrination and the nonstop antinutrition barrage from medical journals and pro-drug imbalanced news sites which constantly repeat—in error and voluntary ignorance in service of their pharmaceutical sponsors—that "Vitamins and supplements are a waste of money."[2]

I think most of us are aware that the entire process of medical training from the education in medical school[3] to the textbooks[4] to postgraduate education[5] is highly influenced by the pharmaceutical industry. You can see that discussed here in an editorial published in *The Lancet*, and I have also provided additional commentary and details on this page [see presentation]. I would hope that by now most of us are aware that the medical journals are highly controlled and influenced by the pharmaceutical industry as well—see the classic article by Smith, 2005.[6] In fact, last year I published an editorial on that topic cowritten with Dr Joe Pizzorno—see our "Concerns About The Integrity of The Scientific Research Process-Focus On Recent Negative Publications Regarding Nutrition, Multivitamins, Fish Oil And Cardiovascular Disease" published in the February 2019 issue of *Integrative Medicine—A Clinician's Journal*.[7]

Because of the heavy-handed influence of the pharmaceutical industry in medical education and in scientific publications, we of course then see that influence translated into how doctors think and practice clinically. So you will notice that most doctors in clinical practice focus on the disease, the drug, the diagnosis and the management, but they do not really think outside of that box into what actually might be causing the condition that their patient is presenting with.[8] To think of ***what is causing a condition that a patient presents with*** [patient-centered model] is very different from thinking ***what drug do I need to use in order to treat or alleviate this condition*** [drug-centered model].

"**Treating the cause**" as we do in naturopathic medicine is very different from asking oneself, "How do I manage this condition? And what drugs do I use to treat this condition?" So what I am going to show you in today's presentation is how we can shift that paradigm to focus more on **the cause** *that we*

*can correct*, rather than thinking how can we simply medicate these numbers and medicate these symptoms so that the condition is therefore "successfully medically managed."

Let us look at some characteristics of the pharmacocentric medical paradigm. First of all, it is disease-centered and—secondarily—drug-centered. If a condition has no drug, it is usually ignored within so-called standardized or so-called conventional medicine. A good example of a common disease with lethal effects is hemochromatosis, a genetic cause of iron overload; the condition is common—affecting approximately 1 per 200 persons with a severe form and 1 per 7 with a milder form of the disease—and potentially deadly—increasing the risk for diabetes, heart failure, liver disease and arthritis—but because no drug exists for it, doctors do not often think of it and therefore do not diagnose and treat it.

Thirdly, the medical paradigm, as most of us know is very self-affirming. Drugs, surgery, radiation and vaccination are the *assumed* or *presumptive* solutions to all health problems, regardless of their dangers, costs, inefficacy, or the existence of better options not taught in medical school and residency. Nutrition is belittled *categorically* and that belittlement is not based on knowledge, but rather ignorance.

I think we also know that the medical profession is also very exclusive in many ways, socially and conceptually. If a better solution is *not a drug* then it is usually not considered a "realistic" solution. Again, nutrition is excluded categorically, even though nutritional therapy has been shown to provide benefit even for purely genetic disorders such as sickle cell anemia.

Another aspect of the medical paradigm is that "the ends justify the means." This is what I call *illogical proportionality*: serious diseases require serious—that is expensive and risky—treatments. And I think this model of ends justifying the means also accounts for some of the abusiveness that we see in medical education.

Also within the medical paradigm is hierarchy of command and thinking, the deference to specialists, which of course at sometimes is highly appropriate. However, generally speaking within medicine, most of the decisions are made by authoritative groups and published in major journals. And so doctors have to comply with the so-called "standard of care" and so-called "approved" treatments. So again, medicine is very hierarchical. It is decided upon by authoritative groups, then implemented by physicians, and then followed by "compliant" patients and students. Very little deviation, very little customization, and very little independence of thought—this contributes not to *better healthcare*, but to healthcare that is *uniformly mediocre* even by the medical profession's own low drug-centered standards.[9]

And number seven, finally for this page, the medical paradigm is very fatalistic. When a person has a disease, the disease has the person and fate is pretty much predictable and certain. So we say, for example, that "a person has diabetes" and many articles even in modern times have been published saying that diabetes is "irreversible" and must be managed by medical therapy—drugs and surgery. In contrast, in the naturopathic and functional medicine paradigm, we see that the same diabetes described as *irreversible* in medical textbooks is described as "**curable"** and "**reversible"** in specialty journals.[10]

So what I will do on this page is contrast the paradigm of **drug/disease-centered medicine** as I might call it here against functional and naturopathic medicine. So again, the so-called standardized or so-called "conventional medicine" that most of us learn in medical school is very disease-centered. In contrast, functional medicine and naturopathic medicine are patient-centered.[11]

| **Instruct**—to load, to assemble, to train | **Educate**—to bring out, nourish [the best in a person] |
|---|---|
| Noninteractive lectures, breakneck "fire hydrant" speed | Interactive lectures, human pace |
| Questions mocked by professors; students insulted | Questions welcomed by professors; students respected |
| Professors see questions and independent thought as a challenge to their authority and their persona | Professors welcome challenge and even arrogance from their students as an opportunity to further refine their expertise and to model decorum and professionalism |
| Reading assignments followed only by examination and regurgitation | Reading assignments followed by discussion, perspectivism, qualification, contextualization |
| Ultimate goals are indoctrination, obedience, conformity, dependency | Ultimate goals are knowledge, contextualization, application, appreciation of nuance, autonomy |
| Zero training in logic, fallacies, debate, and public speaking | Curriculum must include study of logic, fallacies, debate, and public speaking |
| Multiple choice exams, zero debate, little/no expression of knowledge | Fill-in-the-blank exams, essays, expression of declarative knowledge |
| Hazing, abuse, sleep-deprivation, social isolation | Respect for autonomy and well-being |
| Curriculum confined to topic | Curriculum includes skills for life |
| Training in obedience, repetition, "be like us" | Training in leadership, teamwork, cooperativity, "be one of us" |
| All questions weighed equally, no emphasis on importance | Core competencies weighed more heavily (mandatory mastery) |
| Goal: Prepare students for residency training after graduation | Goal: Prepare students for independent solo private primary care practice |

In functional medicine and naturopathic medicine, we use ***clinical nutrition interventions to change gene expression*** rather than think our patients have "irreversible genetic diseases" that we can never influence. Obviously, some diseases are do originate genetically (from specific gene defects); however, unknown to most medical physicians is the fact that many of these conditions can be *at least* ameliorated by functional and nutritional interventions to reduce the disease impact, reduce drug dependence, improve functional capacities, and maintain higher quality of life. I already made brief mention of the condition sickle cell anemia, which we all know is a genetic disease—commonly thought of as incurable; however, with skilled nutritional intervention, we can change gene expression with the use of selected nutritional supplements to alleviate the disease.[12]

Whereas drug-based medicine or so-called standardized/conventional medicine is drug-centered and focuses on isolated molecular targets, functional and naturopathic medicine are both nutrition-centered and lifestyle-centered for their interventions. **The goal is to improve health and function of the entire organism, not simply impact *isolated molecular targets* and *pathologized pathways*.**

The medical paradigm is very self-affirming; it affirms that its treatments are the best: drugs, surgery, radiation, vaccines. In contrast, in functional and naturopathic medicine we affirm the patient and we affirm whatever treatment is best for our patient. Whereas drug-based medicine is very self-affirming, in functional and naturopathic medicine, we affirm *what is best for our patient*, and we affirm *whatever has the best efficacy* for *improving patient outcomes*.

We all know that standardized medicine is very exclusive. It includes its own treatments but excludes everything else that is outside of medical training, most obviously nutritional interventions and nutritional supplementation. In contrast, functional medicine and naturopathic medicine are inclusive of all ideas and interventions that helped to improve the health of our patients.

In standardized medicine, we think that "serious diseases" require "serious treatments"—drugs, surgery, vaccination and radiation. In functional and naturopathic medicine, we think effective treatment requires the physician's skill and the patient's involvement. But we do not necessarily believe that "a serious disease requires serious [expensive and risky] treatments"—this is illogical, this is a clinical logical fallacy. **Serious disease requires *effective* treatment**; serious disease does not necessarily require *expensive* and *risky* treatment, nor are the four medical treatments necessarily the best option for every health problem, particularly those that result from dietary faults and toxic exposures.

In medicine, everything from the way we were trained to the way that we treat patients is based on ***illogical proportionality*** and that the *ends justify the means*. In functional in naturopathic medicine, we again believe that effective treatment requires the physician skill and the patient's involvement. The *emphasis is on clinical efficacy and maintaining patient autonomy and respect* rather than thinking that again, a serious disease has to require a complicated, risky, and expensive treatment.

Specific to naturopathic medicine is the concept of the **"hierarchy of therapeutics"** which is an especially important concept. What we do in naturopathic medicine is start with the *least invasive* intervention possible—usually botanical medicines, nutritional intervention, diet and lifestyle—before we think of going on to using drugs, or even surgery. I am sure as we all know, in so-called conventional or standardized drug-centered medicine, drugs are primary first-line "day one" therapy. A patient with a health problem can expect *to have their nutritional needs ignored* and *to have drugs prescribed on the first visit* when they see a so-called standardized or conventional medical practitioner.

Again, the medical paradigm is very fatalistic: people have their diseases and often they are told **they will always have their diseases**. In contrast in naturopathic and functional medicine we are positivistic rather than fatalistic, and we think we can change these conditions for the better. This is much less medieval thinking and thinking that is more in accord with the Enlightenment and Renaissance.

In standardized medicine, hierarchical compliance is most important. The doctor complies with the guidelines, and the patient complies with the doctor. In functional and naturopathic medicine, accuracy and effectiveness are most important.

In so-called conventional or standardized medicine, surrogate markers are commonly considered more important than patient outcomes. Whereas in functional and naturopathic medicine, patient outcomes are most important while we also responsibly manage risk factors, laboratory results, etc. A really good example of where surrogate markers are considered more important than patient outcomes was a recent publication using vitamin C in septic hospitalized patients; the study had two major findings.[13] First is that vitamin C did not change parameters of organ function—"a 96-hour infusion of vitamin C compared with placebo did not significantly improve organ dysfunction scores." Second is that patient mortality was reduced by approximately 50% (hazard ratio: 0.55) in the patients who received vitamin C—"Vitamin C–infused patients exhibited a significant reduction in 28-day all-cause mortality." The conclusion of the study was that vitamin C was *ineffective* because they focused on surrogate markers, rather than the **successful patient outcomes of reducing mortality by nearly 50% and safely reducing the number of days that patients required mechanical ventilation.**

Also, you will notice that the language of the interventions used in medicine is very different from the language that we use in naturopathic and functional medicine. In standardized medicine we emphasize ***compliance*** rather than ***autonomy***, and the drugs that we use are mostly **blockers** and **inhibitors**. We ***block*** the formation of cholesterol, we ***block*** angiotensin receptors, we ***block*** the ACE enzyme, we ***block*** HMG-CoA reductase, we ***block*** the uptake of neurotransmitters etc. In so-called conventional or drug-based medicine, we ***block*** receptors, we ***block*** enzymes and we ***interfere*** with pathways whereas in naturopathic and functional medicine we ***support*** processes and we ***improve*** physiologic function. In contrast and functional in naturopathic medicine we try to help systems work better. Especially in naturopathic medicine, we use different language such as ***support***, ***improve***, ***nourish***, we ***give people and their bodies what they need to succeed***.

Nutrition is conceptually different from drug-based medicine. Whereas drugs work on ***individual pathways*** mostly by inhibiting enzymes and blocking receptors, nutritional interventions work on ***multiple systems*** by improving enzymatic function and ***normalizing metabolism and immune function***. And on the following page, you can begin to see how some of the major body systems are interconnected and how one might influence the other.

## Transitioning to a New Model that Provides New Possibilities

I invite you to take a look at this page and contrast so-called standardized or so-called conventional medicine with functional and naturopathic medicine. In our post-graduate courses for doctors, we have seen that as doctors move from a **drug-based model** to a **functional systems-based model**, for them, they really experience a paradigm shift that changes their entire perception of clinical practice, medical care and healthcare.

For many people who are new to these concepts, they are now crossing into a new world that focuses more on **patient-centered medicine**, **systems-based medicine** rather than targeting isolated pathways. In functional medicine and naturopathic medicine, we use nutrition and lifestyle-centered interventions that are very nuanced and detailed, patient-affirming instead of drug-affirming and disease-affirming. Functional medicine and naturopathic medicine are ***inclusive***, respecting interventions based on priority, effectiveness, synergism and their ability to address the primary cause(s) of the patient's problem. Effective treatment here requires more physician skill and more patient involvement. For patients, they generally at least have to be willing to improve their diet and lifestyle. And for physicians, they actually have to think in more creative ways as they address the underlying cause of the disease, rather than simply managing the disease and manipulating surrogate numbers by using drug therapy.

For example, we all know that with patients who have hypertension or diabetes, the goal is to lower their blood pressure and to lower their glucose. In those situations, we are really just treating the numbers if we approach this problem from a drug or medical model. Now, we all respect the fact that this can be necessary and appropriate especially in certain emergency situations in patients who have acute hypertension or acute hyperglycemia. In those situations, yes, we need to get the numbers down and normalized as quickly as possible. However, we need to appreciate that the **acute management of those acute crises with fast-acting drugs** needs to be di**fferent from the chronic long-term management of those conditions**, especially if we are going to actually try to cure the condition rather than medicate it for the duration of the patient's lifetime.

## Making the Transition

Obviously, as within any other type of deep-learning experience, physicians who are beginning to integrate functional and naturopathic medicine into their practices have to go through a learning curve, but that learning curve ultimately results in their being ***more empowered*** and ***more creative and effective*** in their clinical practices.

I am going to pause just for a moment here to emphasize that we are transitioning now from 1) the introduction and 2) the contrast of different models into 3) a new model that emphasizes clinical applicability. In order to do that, we need to memorize at least two categories of items.

Number one: what are the four main types of inflammation? You will remember that I discussed these on the first page. The four main types of ***sustained*** or so-called "chronic" inflammation are 1) metabolic inflammation, 2) allergic inflammation, 3) autoimmune inflammation, and 4) neuroinflammation or brain inflammation. I want you to start categorizing inflammatory conditions into metabolic, allergic, autoimmune, and neuroinflammation or brain inflammation.

Number two: I want you to start creating some space to remember the seven main components of so-called *chronic* or what I call **sustained** inflammation. What are the seven main components or contributors to chronic inflammation? That is what I am going to discuss on the next few pages.

The more "new" these concepts are to you, the less likely that you can expect to understand, learn and memorize everything in the first viewing. But by the time you review this material two or three times, it will start becoming manageable and usable. So now, let us dive in to those seven contributors to *chronic* or ***sustained*** systemic inflammation.

**Paradigm shift**: this anonymous wood-engraving (from Camille Flammarion's 1888 book *L'atmosphère—The Atmosphère: Popular Meteorology*) depicts the **paradigm shift** from the mundane dailiness of microscopic local life to the contextualized macroscopic **awe and amazement of logical thought, scientific discovery, personal/social/spiritual liberation**. Note for example the transition from a flat finite earth to a round and boundless universe.

## Functional Inflammology Protocol

After many years of teaching functional medicine to postgraduate audiences internationally, plus teaching my graduate students how to organize a large amount of information efficiently so they could quickly transition from familiarity to understanding to memorization to implementation, I developed this functional inflammology protocol, and the accompanying acronym that I will show you in just a moment to accelerate mastery of these concepts for practical use and clinical implementation. Again, the four types of inflammation that I am going to deal with most specifically are metabolic inflammation, allergic inflammation, autoimmune inflammation and neuroinflammation.

Also in this presentation, I will make a little mention of infectious inflammation whether that comes from dysbiosis or from viral infections. You will find this information very applicable to your outpatient management of chronic conditions and also but to a lesser extent applicable to inpatient care whether that is infectious inflammation, trauma or more severe and acute systemic inflammatory conditions.

In medical training, we are taught that ***cure is impossible*** and that ***we have to manage these conditions long-term with drugs;*** in functional and naturopathic medicine, we aim for cure.

Let us revisit that diagram one more time before we dive into the details, I want you to see how the entire model works together because we are addressing the causes. With this **functional inflammology protocol**, we are addressing the **upstream contributors** to *chronic* **sustained inflammation** and the underlying **immune activation**. Rather than dealing with the long-term "management" of inflammatory consequences, what we try to do in naturopathic medicine and functional medicine is address the **upstream contributors** to that *systemic inflammation* and *immune activation* **so that the inflammatory response is dampened**, overall health is improved, and our patients can ultimately and hopefully be *liberated from their diseases* rather than having to carry those diseases throughout their lifetime.

The benefit of this **functional inflammology protocol** is that it **organizes the major causes of inflammation** into a mnemonic that helps doctors clinically apply this information in an organized manner. Thereby, this **functional inflammology protocol** *liberates mental and intellectual bandwidth*, while also liberating faculties for other purposes such as attention to patient details and needs. At the risk of being redundant, I will read that one more time: The benefit of the functional inflammology protocol is that it organizes the major causes of inflammation into a mnemonic that helps doctors apply this information in a clinically organized manner, thereby the **functional inflammology protocol** *liberates mental and intellectual bandwidth* to *reduce physician fatigue*, while also **liberating those mental and intellectual and social faculties for other purposes, such as giving more attention to patient details and patient needs**.

**Functional Inflammology Protocol—Major Success from the First Use**

Let me show you this example from my own clinical practice, my own clinical experience of a patient with severe aggressive drug-resistant rheumatoid arthritis. This patient had already been seen by several medical specialists, she had also gone to the local naturopathic medicine clinic—this was in the Pacific Northwest region of the United States, where we have two naturopathic universities with their respective teaching clinics. She had already been given all of the drugs for rheumatoid arthritis, none of them had worked for her, and she continued with severe aggressive drug-resistant rheumatoid arthritis and debilitating inflammatory pain.

In rheumatoid arthritis, one of the laboratory markers that we use for diagnosis is called CCP—blood levels of a protein called cyclic citrullinated peptide. In her case, her CCP level was actually so high that the lab could not measure how high it was—it was greater than 250. The actual level could have been 400, 600 or 700. But it was very "positive"; that means ***very bad*** in this case at more than 250. The normal level of CCP should be less than 50 or 60; so, obviously a value greater than 250 is extremely abnormal. That was her level of disease activity in March of 2012, when I was first developing and restructuring this clinical protocol.

About nine months later, we had reduced her levels from greater than 250 down to 195. I was pretty happy because we could see that we were making progress in normalizing this important clinical marker, and she was clinically asymptomatic, able to work in her garden at her farm without pain and without any anti-inflammatory drugs.

Within two more months in April of 2013, her antibody levels had almost normalized at 54. So in summary: within one year, we were able to transition her from having severe aggressive drug-resistant rheumatoid arthritis with pretty severe pain every day to being relatively asymptomatic, not taking any anti-inflammatory or anti-rheumatic drugs, and with nearly normal laboratory results. This was not simply "successful management" of her rheumatoid arthritis but rather ***successful reversal*** of her rheumatoid arthritis.

With rheumatoid arthritis, CCP antibodies are part of the disease process. So when we can achieve clinical benefit along with reduction of these antibodies, we know we are on the right track, and that we are not simply managing the disease or treating the disease, but we are actually reversing the disease. And that is what we were able to show with these results.

## Inflammation is the Major Common Theme of All Disorders of Sustained Inflammation

So now again, I want you to think of inflammatory conditions as being within the following categories:

1. **Metabolic Inflammation**: We commonly see patients who have what I call metabolic inflammation. This is cardiovascular disease, hypertension, diabetes mellitus type-2 and metabolic syndrome. Standard medical treatment for these patients is to simply lower the abnormal numbers that represent the metabolic disease process; a patient comes into the office with hypertension, and we lower their blood pressure with drugs; another patient comes into the office with elevated glucose when they have diabetes, and we lower their glucose with drugs. In both cases, when we operate from the drug-centered medical paradigm, we are addressing the abnormal numbers without really addressing the underlying metabolic-inflammatory causes of the imbalances that result in those abnormal numbers. So that is obviously treating a manifestation of the problem, not the problem itself. By now, I think all healthcare providers should know that inflammation is a major component to all major so-called chronic health problems. I prefer to refer to these as *sustained* inflammatory conditions, not *chronic* inflammatory conditions. If we say that these conditions are *chronic*, then we pretty much stop thinking and we accept the "fact" that the patient is going to have this condition or these conditions for long periods of time. Hence the title *chronic* which becomes a self-fulfilling prophecy. If we change the language slightly in our description of these conditions, and instead of calling these *chronic* inflammatory conditions, we refer to these conditions as disorders of *sustained* inflammation then we change our mental perception of the condition and **instead of accepting these as chronic, we begin to look for what are the causes of the sustained inflammatory response** and what can we do to address and eradicate those causes that are sustaining the inflammatory response.
2. **Allergic Inflammation**: Category number two is allergic inflammation, asthma, allergic rhinitis and conjunctivitis, eczema and atopic dermatitis, which has a strong dysbiotic component in it as well. Typically, these patients are having an allergic reaction to bacteria on their skin; sometimes the trigger is a food allergic response. Eczema patients also show a higher body burden of mercury, which is a toxic heavy metal known to trigger inflammatory reactions in the skin and to promote worsening of allergic reactions.

3. **Autoimmune Inflammation**: Another inflammatory type or inflammatory subtype is autoimmune inflammation. The prototypes include rheumatoid arthritis and psoriasis also, of course other conditions such as inflammatory bowel disease and multiple sclerosis. The standard medical treatment is just to provide those patients with a buffet of anti-inflammatory drugs but not to address the underlying cause of the inflammation. We simply treat the inflammatory **response**, not the inflammatory **trigger**, and that is an important distinction.
4. **Brain Inflammation**: And category number four, as I have already mentioned, is neuroinflammation or brain inflammation. This includes depression, brain injury, autism, schizophrenia and bipolar disorder, neurodegenerative conditions such as Alzheimer's and Parkinson's, hyperphagia, obesity and insulin resistance, multiple sclerosis, PANDAS, brainstem, encephalitis, migraine and fibromyalgia.

So now let us dive into this clinical protocol that we can use to treat these disorders of *chronic* inflammation or *sustained* inflammation. If you call these conditions *chronic*, you are setting yourself up to believe that these are going to be long-term conditions. **If you call these conditions disorders of *sustained* inflammation, then your task becomes to identify what is causing or triggering this sustained inflammatory response.**

## Inflammation is Always in Response to One or More Triggers; Prolonged Inflammation is Due to Prolonged Exposure to One or More Inflammation-Generating Causes (Inflammogens)

Inflammatory responses should be acute and short term and responsive to a specific trigger or small number of triggers. Chronic inflammation is not physiologically normal, even though we have been taught to accept it as normal because we see so many conditions characterized and labeled as chronic inflammatory conditions. But we need to see that that is *not normal*. Chronic inflammation is *not normal*. **Inflammation exists as a response to resolve problems**, not to sustain and perpetuate those problems or engage in a long-term relationship with those problems. We as clinicians need to try to identify what is triggering this ***sustained inflammatory response***.

## Naming the Demons: Identifying the Most Common and Most Important Triggers that result in Sustained Inflammatory Responses that underly so-called "Chronic Inflammatory Diseases"

What are the common causative themes among obesity, hypertension, diabetes, metabolic syndrome, allergy, asthma, autoimmunity, and neuroinflammation? In this section, I will help you identify the major inflammatory triggers on this page and to differentiate those which we can correct from those which we cannot. You will see that we can nearly always correct or at least ameliorate the inflammatory triggers, and that this also applies to so-called "genetic diseases."

0. **Genes—the ultimate scapegoat**: Clearly, a few disease have legitimate genetic causes; in some rare cases, specific gene defects result in the production of abnormal proteins that fail to function properly, and the result can be an impaired process that affects the brain, muscles, or other organs and systems such as the immune system. Much more commonly, undefined "bad genes" are blamed for lifestyle-

generated and food-promoted illnesses so that doctors will prescribe a lifetime of drugs to various patient populations so that

1. **Food and Diet**: We also need to look at dietary excess, especially carbohydrate excess, sometimes food allergies, nutritional deficiencies and imbalances and other conditions that have a positive response to skillful nutritional intervention. I call those conditions, **diet-responsive disorders** or **nutrition-responsive disorders**. If a condition is dietarily responsive or nutritionally responsive, that does more than merely provide us therapeutic advantage and success—it also provides us some information about the underlying cause and the pathophysiology of that condition.
2. **Microbes**: We know that many long-term inflammatory responses are also induced by microbial exposures whether those are subclinical infections or dysbiotic relationships.
3. **Immune recalibration with nutritional supplementation**: We can also help our patients to kind of recalibrate their immune system through anti-inflammatory interventions to increase the production and effectiveness of their T-regulatory cells (Tregs) and to dampen the responses induced by pro-inflammatory Th1, Th2 and Th17 cells. I will show you how to do that in just a moment. My phrase for that is nutritional immunomodulation.
4. **Metabolic imbalances, mitochondrial dysfunction**: We need to appreciate the role of mitochondrial dysfunction in sustained inflammatory responses.
5. **Stress, sleep deprivation, lack of exercise**: Stress, sleep deprivation, psychology, sociology, social inequality, failure to construct a healthy lifestyle, failure to get enough exercise—many of the individual items that fall into category number five can be called style of living, sleep hygiene, stress management, and sociological considerations. So in my listing of these things, these start mostly with the letter S or at least the sound "S", as in psychology.
6. **Hormone imbalances**: We can also look at hormonal imbalances that promote inflammation or that result from inflammation.
7. **Toxic exposures**: Most foreign chemicals (for example: pesticides and plastic residues) are toxic to metabolic processes if the exposure or consumption of those chemicals is excessively high, excessively prolonged or if it occurs in combinations wherein two or more chemicals have an additive or synergistic effect; the same is true of toxic metals such as lead, mercury and aluminum. Foreign substances are also called "xenobiotics" and strictly this applies to chemicals, but more casually and practically we can also use this term to apply to toxic metals. Any foreign substance—whether a metal or a chemical—that might result harm to the organism is reasonably labeled a "toxin" or a xenobiotic. (Again, strictly speaking, "toxins" are produced by other organisms whereas "toxicants" are any substance such as a chemical or metal that has a toxic or harmful effect, either obvious or subtle.) Exposure to toxic chemicals and metals can promote inflammation and alter function of the immune system; this can be described as "xenobiotic immunotoxicity" because it is a toxic effect on the immune system caused by xenobiotics, whether those are metals or chemicals.

**All Medical Textbooks acknowledge "Environmental Contributions" to the most common Clinical Disorders but then Fail to Define those Contributions, thereby Promoting Drug Dependence**

We all know that the common medical textbook explanation for nearly all chronic diseases is that they "result from a combination of genetic predisposition and environmental factors." My way of looking at this is to say that we really cannot do a lot about undefined "genetic predispositions" although in certain selected cases we can influence gene expression enough to get a favorable clinical outcome.

The human genetic code is fixed and permanent, at least within our personal lifetimes; however, we can certainly alter the expression of those genes to thereby alter the course of health and disease. Genes or the genetic code can be thought of as words in a book or commands in a program; although we cannot change the words, we can to some extent select which words and commands are read, which ones get more "play time" or "air time" or repetition. For example, a person may have a genetic predisposition to excess inflammation, but with tailored nutritional intervention, those pro-inflammatory genes can be silenced or suppressed, for example though a process called DNA methylation, which reduces the readability of that section of genetic programming. Conversely, another person may have altered genetic expression due to age or trauma, and we can use nutritional supplementation to increase the readability or "open those pages of the book" to promote healing and rejuvenation, for example by promoting a process called histone acetylation.

From this point forward in this, the largest section of the presentation, I will describe the most high-impact "environmental factors" that we can address in the treatment of inflammatory disorders. Again, instead of just saying "environmental factors" and leaving these pathologic-therapeutic fulcrums unused, we need to define what those environmental factors are, and then leverage our treatment plan on these major points of influence.

Non-modifiable mechanisms include the genes that we have inherited from our parents, while the modifiable mechanisms include diet, dysbiosis, nutritional immunomodulation, mitochondrial dysfunction, psychoneuroimmunology, hormonal imbalance, xenobiotic immunotoxicity. We need to memorize those, and we need to incorporate those into a clinical strategy that we can use with great facility so that we can then liberate our mental capacities to focus on other details. Memorizing the list of categories is the first step.

Note that the standard medical evaluation fails to consider these important modifiable components other than faint lip-service to "diet and lifestyle." I want you to consider memorizing these seven items because this is going to be the focus of our clinical assessments and therapeutic interventions. You will notice that this list is actually pretty hard to memorize. For that reason, we are going to use a mnemonic (memory aid), by which we are going to simplify that complex list into something more manageable, and we are going to focus on memorizing these seven items, food, infection, nutrition, dysfunctional metabolism, stress and style of living, endocrine imbalances, xenobiotics and toxins. I have now taken a complex list and made it more simple.

Now we are going to use an acronym—words made from the first letter of each of those words—from that list to make it simpler yet, and that acronym is F-I-N-D S-E-X and I will show you how to use that in just a moment. Interestingly enough, I first presented this new model and acronym in 2012 in the city of Paris, the so-called "City of Love."

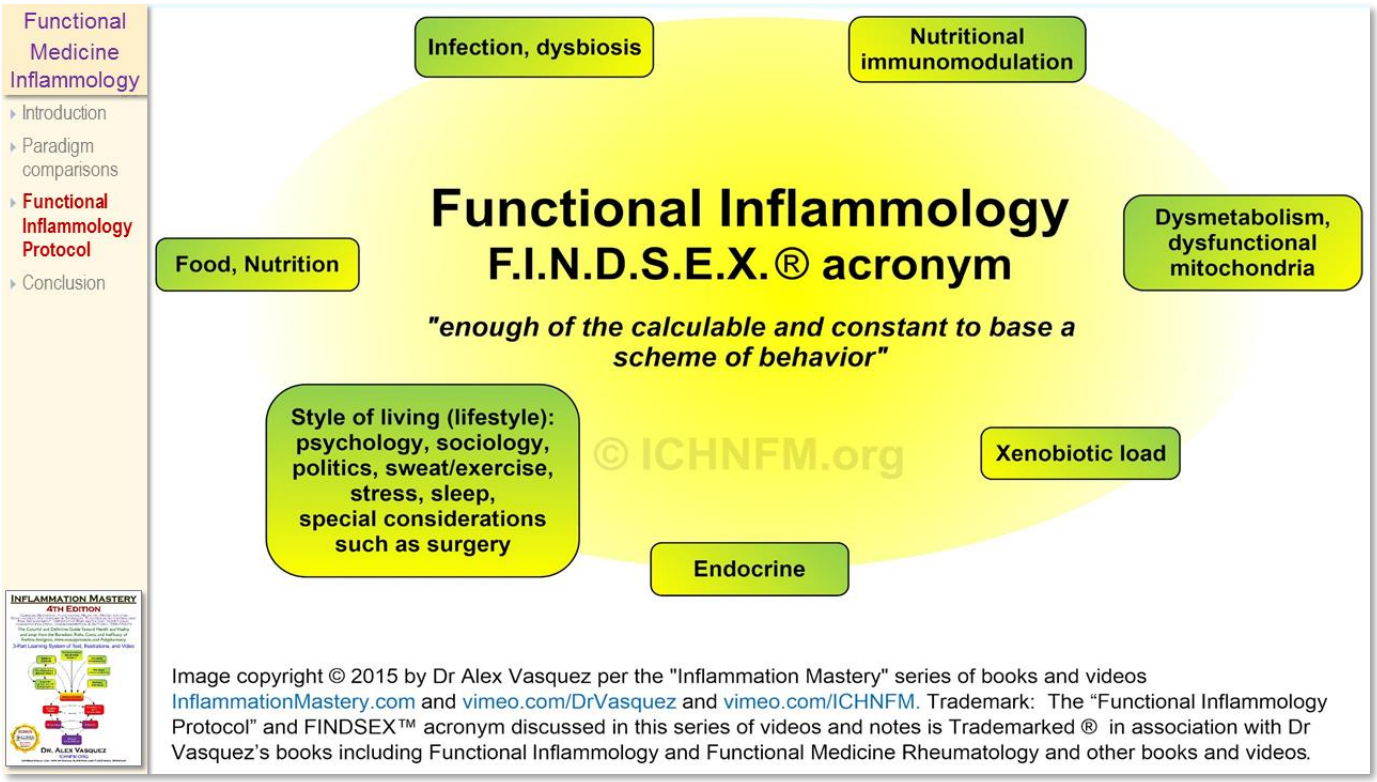

In this page of the video presentation [see video], I provide the origin of and a few updates to the functional inflammology protocol since its inception in 2012. I start with a little bit of my own personal and educational background, also my background in naturopathic and functional medicine, how I developed the functional inflammology protocol initially for my graduate students and postgraduate audiences in Europe. In an update to the protocol coincident with two publications on autism[14] and following the publication of ***Brain Inflammation in Chronic Pain, Migraine and Fibromyalgia*** in 2016, I added neuroinflammation as the fourth category of inflammatory conditions in 2017.

The benefit to using the functional inflammology protocol as a clinical tool is that it provides the clinician a memorable and structured organization of the major concepts that we need to address clinically in order to help our patients to be liberated from these so-called chronic inflammatory diseases. **The first step in liberation from these conditions is to *stop* calling them *chronic* diseases and to *start* calling them *sustained* diseases.** So, instead of repeating the medical rhetoric of "combination of genetic predisposition and environmental factors", we start asking answerable questions: **what factors are sustaining this disease process?** Is it dietary and discretion, is it carbohydrate excess? Is it insufficient exercise? Is it microbial colonization or small intestine bacterial overgrowth? Is it mitochondrial impairment, due to a

viral infection or due to xenobiotic exposure? We have to start asking different questions if we are going to get different results.

We can always fall back on prescribing drugs to meet the "medical standard of care." If all we want to do is manage high blood pressure by lowering the numbers with drugs, we can do that. If all we want to do is lower blood sugar by giving our patients so-called antidiabetic drugs, we can do that too. But if we want to liberate them from their diseases, and if we want to improve our true clinical success and the management of those conditions, then we need to ask different questions, search for other causes, and find other solutions to help these patients restore homeostasis, and metabolic health.

We can use this clinical protocol very efficiently because it is structured, well organized, easy to remember, and powerfully evidence-based. Using a logical and proven structured protocol liberates our mental capacity to be free in order to find creative solutions to these problems. You will agree that the acronym is very easy to memorize; hopefully, you have already memorized it. **What are the two words that represent these seven areas of our main clinical considerations for modifiable factors in these disorders of sustained or so-called chronic inflammation?**

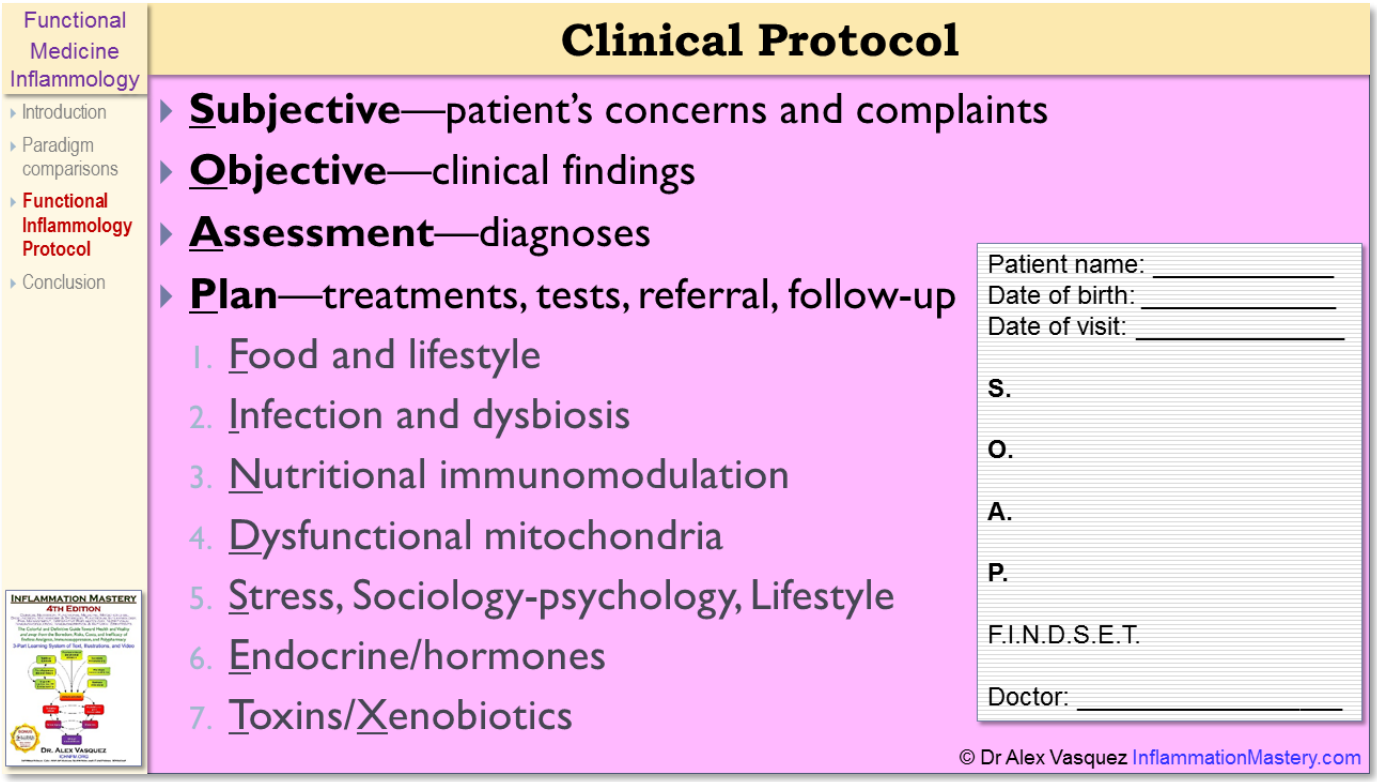



We have four categories of inflammatory conditions: metabolic, allergic, autoimmune, and neuro or brain. Now, how do we address those categories of inflammatory conditions? We do that by using this protocol, which focuses on seven areas of clinical and pathological importance, and this strategy is what guides our treatment. The pathologic triggers for these inflammatory conditions typically comes from one

or more, or all seven of these areas of focus. By addressing these seven areas of focus with individualized treatment, we can then gain better success in treating our patients.

Here is another way of visualizing these major components: food, infection and dysbiosis, nutritional immunomodulation, dysmetabolism and dysfunctional mitochondria. The acronym for those four categories is F-I-N-D.

Then we move to style of living, psychology, sociology, sweat as a metaphor for exercise, stress, sleep, specialized supplementation, and surgery. Then we look at endocrine function and balance and also xenobiotic load. Style of living and most of those special considerations start with the letter S, then we go to E for endocrine, and X for xenobiotics. So that is S-E-X. So, the complete acronym is F-I-N-D S-E-X.




That is easy to memorize, but not necessarily an acronym that you would want to write in your patient chart notes. So in category number seven, you can replace the X for xenobiotics with a T for toxins—thus changing the word "sex" into "set", and you are looking for a ***set*** *of problems* and a ***set*** *of solutions*. Again, F-I-N-D S-E-X or F-I-N-D S-E-T: food infection, nutritional immunomodulation, dysfunctional metabolism, stress and style of living, endocrine imbalances, toxins and xenobiotics. We are going to add this on to our routine way of managing and medicalizing these patients. If a patient needs drugs, they need drugs; but at the very least, especially for long-term success, we also need to address their diet, lifestyle, hormone imbalances, toxic exposures, and other keystone factors.

In American medical schools and clinical settings, we commonly use what is called a SOAP note to document our patient encounters. The S-O-A-P is a mnemonic acronym for ***Subjective***, which is the

patient's concerns and complaints, ***Objective*** are our clinical findings, ***Assessment*** is our diagnoses, and ***Plan***, which includes treatments, test, referral and follow up. What I am proposing here is that in addition to our regular clinical routine of ***Subjective***, ***Objective***, ***Assessment*** and ***Plan***, that we *simply add on a more detailed Plan* that includes addressing the seven factors previously mentioned: food, infection and dysbiosis, nutritional immunomodulation, dysfunctional mitochondria, stress, sleep, and style of living, endocrine and hormonal problems, as well as any toxic or xenobiotic exposures. And you can see that perfectly demonstrated in the amended SOAP note that I have shown on this page. So now let us see how to apply this in clinical practice.

**Protocols are the Starting Point, the Intellectual "Insurance Plan" or "Safety Net" that Ensures the Most Important Considerations are Remembered within Each Outpatient Encounter**

What exactly is a protocol? A protocol is a predetermined plan or a default mode of behavior and thought. Protocols can be *strict* or *flexible*, and I am encouraging you to use this on a rather flexible basis. If your patient comes in with a given problem, I want you to use this protocol but that does not mean that you would not address the patient's acute needs with drugs, if necessary. Protocols are a default mode of thought and behavior that can be applied with flexibility to meet the needs of the clinical situation with each individual patient. Protocols are a starting point; they serve to organize our thoughts and actions to ensure that we have an intellectual safety net—a security scaffold—that guarantees that the most important considerations are addressed or at least considered, regardless of the other distractions and details of the clinical encounter.

Of course, protocols can be abandoned altogether when circumstances call for a different course of action, such as in my clinical experience, I remember seeing a rheumatoid arthritis patient who presented with transverse myelitis. So obviously, in that case, we had to move not necessarily directly to diet and lifestyle, but to anti-inflammatory drugs to control that transverse myelitis. Again, acute exacerbations may require acute medical therapy, but we always have to maintain our focus on addressing the underlying causes of these inflammatory conditions so that we can liberate our patients from their diseases, and so that we can attain greater success in our clinical practices. Protocols provide a default plan of action that can be used reliably in most clinical situations; obviously we customize this per patient and per clinical situation.

**FOOD—contrasting Pro-Inflammatory (Western) Diets/Lifestyles versus Anti-Inflammatory (Wellness) Diets/Lifestyles**

First of all, we have to appreciate that diet can indeed induce systemic inflammation. This was a radical idea, say 20 years ago when my friend David Seaman wrote the article, "The Diet-Induced Pro-inflammatory State"[15] in 2002, stating, "The typical American diet is deficient in fruits and vegetables and contains excessive amounts of meat, refined grain products, and dessert foods. Such a diet can have numerous adverse biochemical effects, all of which create a pro-inflammatory state and predispose the body to degenerative diseases. It appears that an inadequate intake of fruits and vegetables can result in a

suboptimal intake of antioxidants and phytochemicals and an imbalanced intake of essential fatty acids. Through different mechanisms, each nutritional alteration can promote inflammation and disease."

By now, this knowledge should be pretty widespread that the **typical Western/American processed food diet does indeed contribute to sustained or chronic inflammation.** If a pro-inflammatory diet is the problem, then obviously the solution is an anti-inflammatory diet, which I have defined here as a **Five-Part Nutrition Protocol**, which I call "**the supplemented Paleo-Mediterranean Diet**"; this is a diet that emphasizes fruits, vegetables, nuts, seeds and berries, and high-quality protein, as I outlined in 2005.[16]

For each patient, we may need to customize the diet to tailor to their food sensitivities and intolerances. For example, most of us would agree that citrus fruits are a health-promoting food, but some people have allergy to citrus, so we have to help them avoid whichever foods that they are allergic to. Likewise, with beef, milk, chicken or fish—those are health-promoting foods for the majority of people; however, some people will be unknowingly intolerant or allergic, and so of course they need to avoid those foods. The fastest way to stop repetitive allergic reactivity is to cease exposure to the antigen; thereafter, we can work on (re)establishing proper immune system (and digestive and gut) function so that the exaggerated immune-inflammatory responses to these benign food antigens no longer occurs.

Again, the foundational diet is a **plant-based protein-adequate diet** of fruits, vegetables, nuts, seeds, and berries with high-quality protein. I call this the **Paleo-Mediterranean Diet**. I first published this in 2005 and again in 2011, and it is also included within my textbooks. You can also download a free copy of these articles, which I recently compiled together: https://ichnfm.academia.edu/AlexVasquez/Books

**The foundational diet is ❶ the Paleo-Mediterranean diet**, and then we add ❷ a high-potency broad-spectrum multivitamin-multimineral. We want to make sure that our patients are getting enough ❸ vitamin D, typically that is 4,000 to 10,000 international units (IU), then we add ❹ combination fatty acids and then ❺ probiotics and phytochemical prebiotics. This is the 5-part dietary plan that I recommend and that I have used personally and clinically for more than 20 years.

Again, we start with the ideal foundational diet, the Paleo-Mediterranean diet of fruits, vegetables, nuts, seeds and berries with sufficient high-quality protein, a multivitamin, multimineral supplement and vitamin D on top of that, along with fatty acids and probiotics and prebiotics. Here [in the video presentation: Revisiting the Five-Part Nutritional Wellness Protocol: The Supplemented Paleo-Mediterranean Diet. *Nutritional Perspectives* academia.edu/39751813] is the article that I published in 2011; you are welcome to download this and use it personally, but also share it with your patients because this outlines what I consider to be a good foundational diet plan—this article is available from my archives at ichnfm.academia.edu/AlexVasquez and inflammationmastery.com/reprints.

This is a plant-based diet—emphasizing fruits, vegetables, nuts, seeds, berries—but it is not necessarily vegetarian or vegan. We want to make sure that our patients eat sufficient protein, and you can categorize your patient typically as an adult recreational exerciser, and for that categorization, per pound of body weight, they would consume 0.5 up to 0.75 grams per pound of body weight. With

kilograms, that would be 1.1 to 1.65 grams per kilogram of body weight, as demonstrated in the table below from *Inflammation Mastery 4th Edition*.

| Recommended Grams of Protein per Patient Profile and Body Weight Per Day | | |
|---|---|---|
| **Patient Profile** | *Per* **pound** of weight[100] | *Per* **kilogram** of weight |
| Infants and children ages 1-6 years[101] | 0.45-0.68 | 0.99-1.4 |
| RDA for sedentary adult and children ages 6-18 years[102] | 0.4 | 0.88 |
| **Adult recreational exerciser—average for adults** | **0.5-0.75** | **1.1-1.65** |
| Adult competitive athlete | 0.6-0.9 | 1.32-1.98 |
| Adult building muscle mass | 0.7-0.9 | 1.54-1.98 |
| Dieting athlete | 0.7-1.0 | 1.54-2.2 |
| Growing teenage athlete | 0.9-1.0 | 1.98-2.2 |
| Pregnant women need additional protein | Add 15-30 grams/d[103] | Same |

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If you judge that your patient does not fit into that adult recreational exercise or category or if you need to make other changes for example for liver or kidney disease, then obviously you can do that. Again, the diet has a foundation of plants: fruits, vegetables, nuts, seeds and berries—these are the best dietary sources of antioxidants and antiinflammatory components. We add sufficient protein, and we customize for allergy avoidance. We prefer everything to be as organic, fresh and local as possible. That is the foundational diet.

If we use that as the foundational diet, we do not have to use a lot of time talking about artificial sweeteners, gluten, emulsifiers, chemicals, flavor enhancers, artificial colors, or the nutritional and physiochemical destruction that occurs to foods when they are processed into ultra-processed foods. Let us keep the diet as real as possible with real foods: fruits, vegetables, nuts, seeds, berries and adequate protein; the diet is customized for allergy avoidance per patient as necessary.

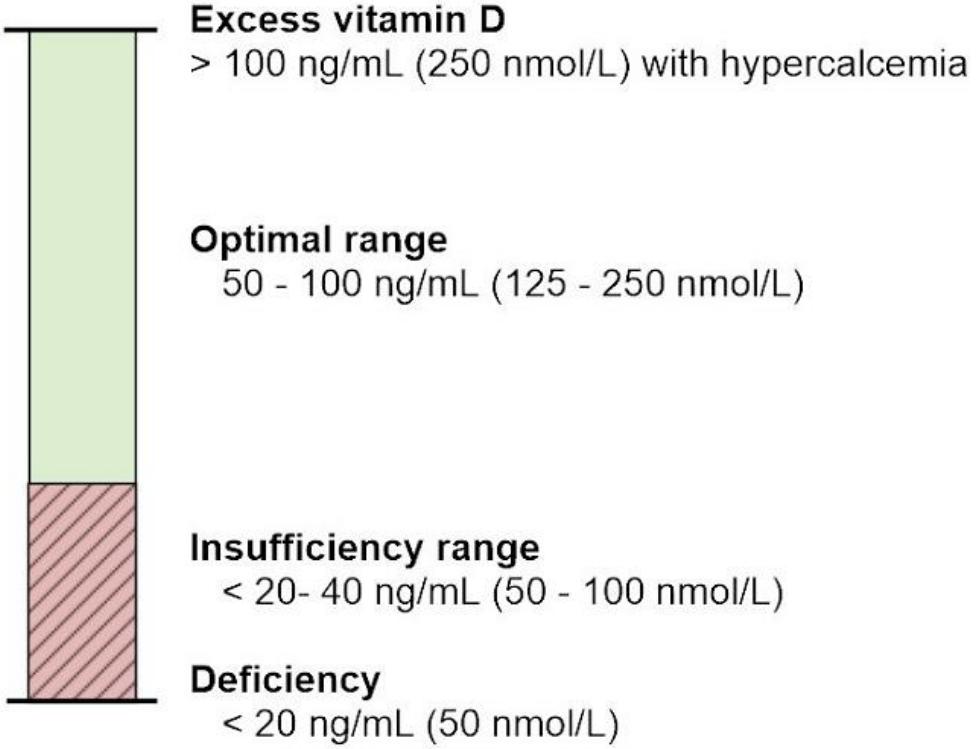
The reason we add a multivitamin on top of that diet is because "most people do not consume an optimal amount of all vitamins by diet alone." According to this article from *Journal of the American Medical Association*, "it appears prudent for all adults to take vitamin supplements. Physicians should make specific efforts to ensure that patients are taking the vitamins that they should."[17] We also notice that with multivitamin supplementation, we can see a reduction in systemic inflammation of up to 14% according to this article published in the *American Journal of Medicine* 2003 [see video presentation for citations].

Likewise, with vitamin D supplementation, we can see an additional 23% reduction in systemic inflammation as measured by CRP—the blood test for C-reactive protein, which is the most commonly used laboratory test for measuring systemic inflammation in the body. Actually in this study[18], their dose of vitamin D was quite modest, so if we were to use a physiologic dose of vitamin D in the range of 4,000 international units per day for adults, I would expect a greater reduction in systemic inflammation and therefore C-reactive protein. I have written several articles on vitamin D including a major monograph

published in 2004, and then as you can see here, two letters; one that was published on *The Lancet* website in 2005 and another letter that was published in the *British Medical Journal* also in 2005. **You may download a compilation of all of my published vitamin D articles from 2004-2019 from https://www.inflammationmastery.com/d and https://www.academia.edu/40429791.**

The goal of vitamin D supplementation is to optimize serum levels of 25-hydroxyvitamin D. And that optimal range should be no lower than 40 nanograms per milliliter. You can see that I have published that twice [demonstrated in the video presentation]: once in a textbook in 2008 for continuing medical education and also in the original article published in 2004. The minimum level of 25-hydroxyvitamin D to be considered normal is 40 nanograms per milliliter, otherwise known as 100 nanomoles per liter.

Measurement of serum 25(OH) vitamin D (or empiric treatment with 2,000 – 10,000 IU vitamin D3 per day for adults) is indicated in patients with chronic musculoskeletal pain, particularly low-back pain.[176] Optimal vitamin D status correlates with serum 25(OH)D levels of 50 – 100 ng/mL (125 - 250 nmol/L)—see our review article for more details[177]; levels greater than 100 ng/mL are unnecessary and increase the risk of hypercalcemia.

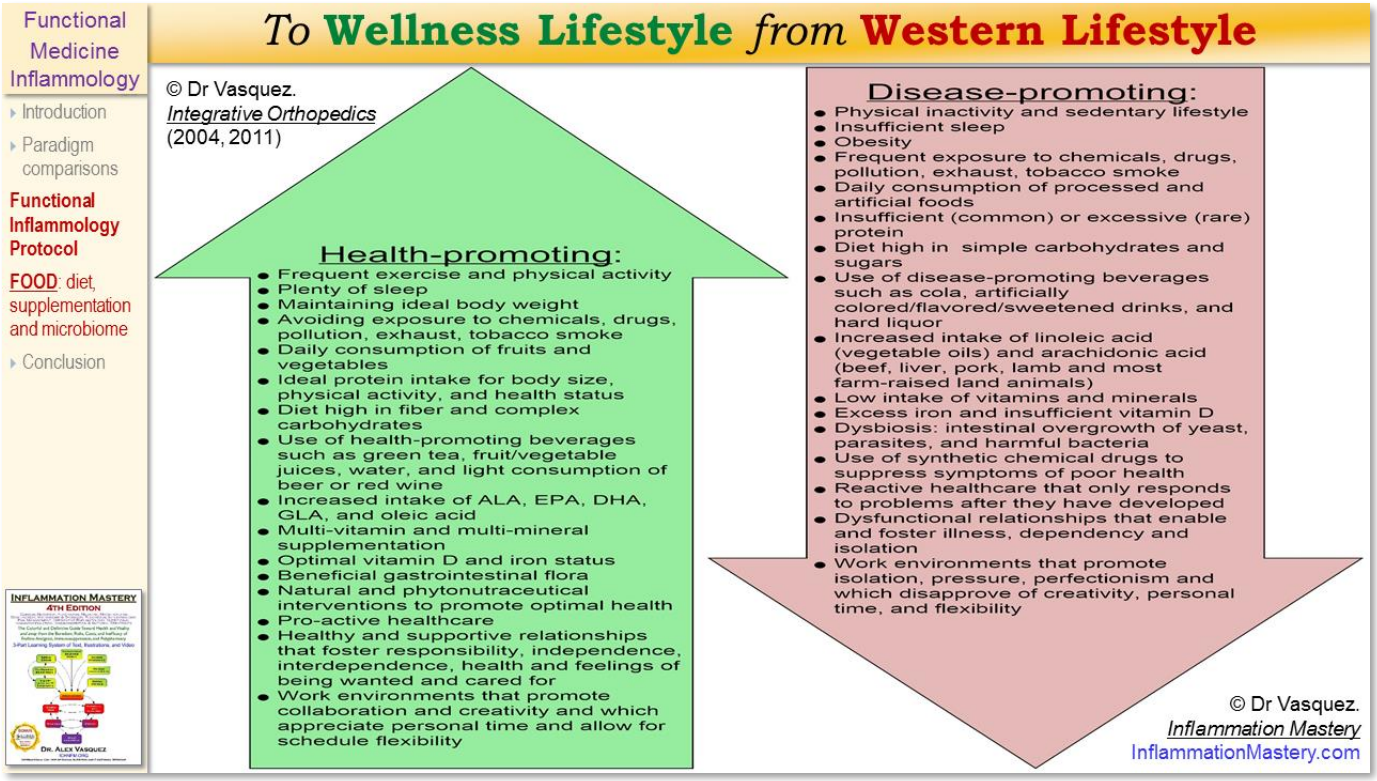



**Interpretation of serum 25(OH) vitamin D levels**. Modified from Vasquez et al, *Alternative Therapies in Health and Medicine* 2004 and Vasquez A. *Musculoskeletal Pain: Expanded Clinical Strategies* 2008.

And I will read you the conclusion from our 2004 paper[19]: "Until proven otherwise, the balance of research clearly indicates that oral supplementation in the range of 1000 international units per day for infants, 2000 international units per day for children and 4,000 international units per day for adults is safe and reasonable to meet physiologic requirements to promote optimal health and to reduce the risk for several serious diseases. [Many of those include so-called chronic inflammatory diseases or what I call disorders of sustained inflammation.] Safety and effectiveness of supplementation are assured by periodic monitoring of serum 25-hydroxyvitamin D and serum calcium."

Very briefly, let us recap the progress we have made so far. **We have defined the optimal diet as being a plant-based diet of fruits, vegetables, nuts, seeds and berries with adequate protein and allergy avoidance customized per patient.** On top of that, we add a multivitamin multimineral supplement and we want to make sure that our patients get enough vitamin D to optimize their serum 25-hydroxyvitamin D levels. These are some of the first steps we take when we are trying to transition our patients from a Western lifestyle to a wellness lifestyle.




**Transitioning our patients from a Western lifestyle to a wellness lifestyle—beyond nutrient consumption to impacts on gut flora and gene expression**

The typical pro-inflammatory Western lifestyle is characterized by ❶ consumption of processed foods—this promotes obesity, insulin resistance, and gastrointestinal dysbiosis characterized by loss of microbial diversity (defective quality) consequent with bacterial overgrowth (excess quantity), ❷ inadequate exercise and physical activity, ❸ psychosocial stress, social inequality, and mild-moderate sleep

deprivation. As clinicians, we know that on day number one we need to improve the diet and we need to begin encouraging more exercise, and that is how we begin to tip the scales ***away from*** ongoing inflammation that promotes chronic "modern" diseases and ***toward*** a wellness lifestyle that promotes health, longevity and vitality.

Our selected lifestyles and our health habits are either health-promoting or they are disease-promoting. This is a concept that I am very happy to have learned in my first year of chiropractic college, and this image [in video presentation] shows the balance of influences of those choices that we make in our daily diet and lifestyle. We also know that a health-promoting diet and lifestyle helps to improve genetic expression toward a more anti-inflammatory phenotype. The study of dietary and nutritional impacts on gene expression is called ***nutritional genomics*** or ***nutrigenomics***.

You can see the idea of nutrigenomics represented in this diagram that I published in my book, *Integrative Orthopedics* in 2004 and also in a professional journal in 2005. Here you can see that many of the nutrients we commonly think of as being anti-inflammatory actually change genetic expression to reduce the clinical manifestations of systemic inflammation. In contrast, a processed food diet, which I have partially represented here by these omega-6 fatty acids, actually promotes NF-kappaB activation and the clinical manifestations of a diseased or pro-inflammatory phenotype. NF-kappaB—nuclear transcription factor kappa beta, NFkB—enhances the expression of genes involved in inflammatory responses.

You can see more details in this diagram showing that certain stressful environmental stimuli, including oxidative stress, bacterial LPS and nutrient deficiencies lead to the activation of the transcription factor NF-kappaB. That NFkB activation leads directly to increased expression of pro-inflammatory genes resulting in the elaboration of these pro-inflammatory mediators, which contributes to the diseases that we see in clinical practice. As stated simply and clearly in the review by Tak and Firestein[20], "The activation of the NF-kappaB pathway plays a central role in inflammatory disease through its ability to induce transcription of pro-inflammatory genes."

Thus, **diet and lifestyle directly impact gene expression and that can be a positive impact or a negative impact.** We obviously want to impact gene expression in a positive manner and that is why we need our patients to adopt an anti-inflammatory diet and lifestyle and move away from their Western or Americanized lifestyle, which is inherently pro-inflammatory. Additional benefits of the anti-inflammatory diet and nutritional supplementation includes increased consumption of anti-inflammatory nutrients that inhibit the NF-kappaB pathway; these include: vitamin D, lipoic acid, green tea, grape seed extract, zinc, coenzyme Q10 and selenium, N-acetyl-L-cysteine, resveratrol, GLA, EPA, and botanical extracts such as Boswellia, Harpagophytum and willow bark. All of these nutrients have been shown to have anti-inflammatory properties and to provide anti-inflammatory benefits in clinical trials with humans.

## Characteristics and Consequences of the Pro-Inflammatory Diet and Lifestyle

The majority of people follow what we can call a pro-inflammatory lifestyle. This includes high sugar foods, high fat foods, fatty acid imbalances with insufficient omega-3 and an excess of omega-6 and trans

fats, vitamin and mineral deficiencies, and consumption of allergens even though they might not know it, insufficient intake of phytonutrients from fruits, vegetables, nuts, seeds and berries corresponding with insufficiency of fiber, excess consumption of foods that promote bacterial overgrowth of the small bowel including processed foods, sucrose, wheat, potatoes, lactose and dairy.

Dietary indiscretion promotes gastrointestinal dysbiosis, which then becomes a different problem. You will see that in my introductory review of diet, I also have to begin mentioning dysbiosis and imbalances in the gut microbiome because these are consequences of a nutrient-poor processed food Western diet. A consequence of that dietary pattern is gastrointestinal dysbiosis marked by the paradox of ***bacterial overgrowth*** with ***insufficient diversity of gut microbes***—a *quantitative overgrowth* with a *qualitative lack of variety*.

Number 10 on my list of characteristics of a pro-inflammatory lifestyle is insufficient exercise, also xenobiotic and toxin accumulation. One way that the body gets rid of chemicals and pesticides and chemical xenobiotics is through the sweat. As such, when we encourage our patients to exercise, part of what we are aiming for with exercise is to induce sweating because we know that sweating is going to help them detoxify or eliminate the poisonous chemicals that they are accumulating. For example, induction of sweating via exercise or sauna results in enhanced dermal excretion of Bisphenol A (BPA); thus, sweat can be used for laboratory assessment of body burden of certain toxicants/xenobiotics while sweating is also a means by which to reduce body burden of certain toxicants.[21]

And finally, number 12—emotional stress and toxic relationships have been shown to promote inflammation, impair wound healing, and reduce immune defenses. Again, the unhealthy diet that too many people pursue is characterized by excess consumption of grains, simple carbohydrates, lack of fruits, vegetables, nuts, seeds and berries, and therefore a lack of fiber and phytonutrients, insufficient protein, and an excess of omega-6 fatty acids. I have given you citations here to two excellent articles by my friend David Seaman, one from 2002 titled the "Diet-induced Pro-inflammatory State" and another from 2007 titled "Dietary Pursuit of Disease", which I thought was a very witty title.

## Characteristics and Consequences of the Pro-Inflammatory Diet and Lifestyle

In contrast to this pro-inflammatory diet, we want our patients to consume an anti-inflammatory diet, and that is a diet mostly composed of fruits, vegetables, nuts, seeds, berries and lean protein, phytochemicals, fiber for bulk and laxative effects, and a relatively modest intake of sodium chloride or table salt. We want this diet to be nutrient dense and to promote alkalinization to provide a urine pH of approximately 7.5 to 8; when we promote urinary alkalinization, this helps to enhance mineral retention, lower systemic cortisol levels, eliminate toxins, and increase endorphin levels—thereby improving mood and alleviating pain and depression. We want to ensure our patients get sufficient protein and omega-3 fatty acids, and either sun exposure or supplementation with physiologic amounts of vitamin D, typically at least 4,000 international units per day for adults.

You will see that basically what I have done on this page [see video presentation] is simply add more detail to the foundational diet of fruits, vegetables, nuts, seeds, berries, and sufficient dietary protein.

The most efficient way to manage this diet is to simply emphasize the proper diet, and that takes care of all of these details. But of course, those of us who are in medicine and science want to know the details. Let us look at the contrasting diet, which is a fast food diet and we see that that fits into the pro-inflammatory lifestyle that most people are living.

## Characteristics and Consequences of the Pro-Inflammatory Diet and Lifestyle—more details

This article (Increase in intranuclear nuclear factor kappaB and decrease in inhibitor kappaB in mononuclear cells after a mixed meal *Am J Clin Nutr* 2004[22]) was a very important article published in 2004 showing that a fast food breakfast of egg and sausage, muffin, sandwiches and two hash browns increased by 150% NF-kappaB activity, which we all appreciate is a major pro-inflammatory transcription factor. As you can see here, a single meal of egg and sausage muffin sandwiches with two hash browns caused an increase of 150% for NF-kappaB, which is the major pro-inflammatory transcription factor, for approximately two hours, and was associated with increase in oxidative stress and the inflammatory marker C-reactive protein. **This clinical trial provided us with direct proof that junk food diets directly promote systemic inflammation.** And for those of us who have worked in [American] hospitals, we know that this is typical of the type of food that hospital patients are fed; in contrast, what I have seen in other countries [Colombia] is that the hospital diet is comprised of healthy foods such as low-fat protein, vegetables, and whole-fruit purees. Therefore, typical American **hospital food actually promotes inflammation and immune suppression**. As a consequence of systemic inflammation, people develop insulin resistance, hyperglycemia and other complications, and they need more drugs from the medical perspective, even though we doctors are causing their inflammation by feeding them hospital food that promotes inflammation. This is horrible but is commonplace and overlooked in American medicine; in contrast, what should be occurring is that we educate patients while they are in the hospital and are a "captive audience" to learning about how to maintain a healthier diet and lifestyle.

Here is another very classic and important article again [see video], showing that simple carbohydrates found in processed foods stimulate reactive oxygen species, and we also see that these suppress immune function as well. Research shows that diet-induced inflammation correlates directly with diet-induced immune suppression. **Pro-inflammatory diets are actually immune suppressive at the same time.** This is a human clinical trial with normal healthy persons who receive 75 grams of glucose. What was shown here is that glucose challenge stimulates free radical production, reactive oxygen species generation by leukocytes. Those same leukocytes are then damaged by that free radical production, and free radical damage to immune cells causes immune suppression.

A common characteristic of the pro-inflammatory lifestyle is the consumption of processed foods, especially those containing wheat as a base. Wheat should be avoided for several reasons:

1. Wheat is nutrient-poor, supplying mostly carbohydrate and very little fiber and micronutrients.
2. Wheat is phytochemical-poor, virtually devoid of antioxidants which are abundant in fruits, vegetables, nuts, seeds, and berries

3. Wheat also correlates obviously with celiac disease, which is now believed to occur at approximately one per 140 persons.
4. Wheat allergy is different from celiac disease and wheat allergy is also very common.
5. Other problems that we see with gluten and wheat include gluten ataxia and dermatitis herpetiformis.
6. Consumption of wheat also triggers the formation of circulating immune complexes that can contribute to vasculitis and the nephritis.
7. Wheat is also a high fermentation grain, which means that it promotes bacterial overgrowth of the small bowel.
8. Wheat proteins are inherently pro-inflammatory independent of allergy or celiac disease.

Again, we want to reinforce adherence to an anti-inflammatory lifestyle and that includes a low-carbohydrate diet as you can see supported by this article in *Journal of the American Medical Association* in 2004. A low glycemic load diet reduces C-reactive protein by approximately 50%. I am sure that we all agree that is an amazing reduction in systemic inflammation, gained here simply by reducing carbohydrate intake. **Simple carbohydrates are directly pro-inflammatory within hours**, we also see a delayed and prolonged response through changes in the gut microbiome. **Simple sugars and high-fermentation sugars such as found in wheat and potatoes promote bacterial overgrowth of the small bowel, which provides a double-hit of systemic inflammation and immune suppression**.

When people consume a processed food diet—let us say of wheat and potato products—they get an acute inflammatory response within two hours. They also get a delayed inflammatory response as that diet promotes systemic inflammation via small intestine bacterial overgrowth. One of the things I have said in my presentations is that **we have to improve the diet in order to improve not simply nutrient intake, but also to encourage beneficial changes quantitatively and qualitatively in the gut microbiome**. We do not simply change the diet to change nutrient intake; we change the diet to beneficially change the microbes in the gut, and that changes immune response and systemic inflammatory balance.

As I have said before, we want patients on a good foundational diet and then we want to supplement that diet with a multivitamin-multimineral, sufficient vitamin D, and we also want to make sure that patients are getting the so-called essential fatty acids (EFA) that they need. These are ALA, EPA and DHA as the omega-3 fatty acids, and the anti-inflammatory omega-6 fatty acid, GLA. The more complete scientific names of these fatty acids are alpha-linolenic acid (ALA), gamma-linolenic acid (GLA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Olive oil provides oleic acid, which is an anti-inflammatory omega-9 fatty acid, and phytochemicals and squalene. The historical Paleolithic intake of omega-3 fatty acids was seven grams per day; the typical American or Western diet provides one gram per day. Therefore, if we were to estimate physiologic requirements based on historical provisions, we could reasonably state that most people need to consume more omega-3 fatty acids, and that is clearly born out in the clinical research using those fatty acids.

The typical supplemental/therapeutic dose of GLA starts at 500 milligrams per day. The typical dose of EPA and DHA is approximately two grams per day at least. I have published some major reviews

on this back in 2004, 2005, and you can access those articles from my archives: inflammationmastery.com/reprints and ichnfm.academia.edu/AlexVasquez. The health-promoting fatty acids, ALA GLA, EPA, DHA, and oleic acid from olive oil have consistently proven anti-inflammatory and clinical benefits in randomized, placebo-controlled trials.

The molecular mechanisms of what I call "combination fatty acid therapy" (CFAT) include the following; precursor competition in cell membranes, activation of PPAR-gamma and PPAR-alpha, (otherwise known as fatty acid receptors), and nutrigenomic effects—modulation of gene transcription via downregulation of NF-kappaB. Those anti-inflammatory fatty acids also effect their biological functions through their conversion to docosatrienes, resolvins, protectins and maresins; these fatty acid derivatives are ***active*** in the healing process and actively contribute to the resolution of inflammation—in other words: these fatty acid derivatives "put the brakes on inflammatory processes" and reverse the inflammatory phenotype. In the brain, these fatty acids promote a reduction in hypothalamic inflammation by modulation of Toll-like receptor 4 (TLR4). They also help to induce the T-regulatory cells through several different mechanisms, including the activation of PPAR-gamma by gamma linolenic acid. Omega-3 fatty acids also provide anti-inflammatory, anti-hyperlipidemic and anti-diabetic benefits through the activation of G protein-coupled receptor 120 (GPR120).

These fatty acids also provide improved cell membrane dynamics and function, and we know that many receptors are on the surface of cell membrane; so when we improve the components of that cell membrane, we improve numerous functions for example of hormone reception and intercellular communication. Further, omega-3 fatty acids optimize not simply the cell membranes, but also the membranes of the mitochondria; in this way, omega-3 fatty acids actually help to improve and support mitochondrial function.

Omega-3 fatty acids support improved neurotransmitter synthesis and reception, also support a reduction in intracellular calcium (with omega-3 fatty acids), thus lessening a pro-inflammatory phenotype. Point number 12 concluding this page, the combination of omega-3 and omega-6 fatty acids in the form of GLA has synergistic and cumulative anti-inflammatory benefits.

One of the main ways that these nutrients—fatty acids as well as vitamin D—function is by saturating cell membranes and body fat stores prior to effecting their full clinical benefits. Clinical trials that are of a duration of only three months typically do not show maximal benefit of fatty acid therapy or vitamin D supplementation because short-duration clinical interventions do not provide sufficient time for body fat stores to become saturated with the fat-soluble nutrients. More treatment time is needed in order to saturate body fat storage with those nutrients in order to gain the clinical and physiologic benefits.

Relatively recently in 2018 and 2019, a series of articles was published in leading or misleading journals stating that fish oil supplementation was not effective for prevention of cardiovascular events. Immediately thereafter, a new and prescription only and very expensive fish oil product was brought to the market at a cost of nearly $300 per month, or $10 per day. I produced a series of articles and video reviews showing that the data presented against fish oil was grossly flawed, including the fact that they

underdosed the product to create the illusion of inefficacy. The clinical trials also included failure of appropriate lab evidence to substantiate compliance and absorption of the products that they were using. They used fake placebos such as olive oil to make fish oil look in efficacious, and they also used a fake placebo in the form of mineral oil to make fish oil look miraculous; these paid researchers changed the comparator against fish oil depending on the illusion that they wanted to create. When they wanted to make fish oil look in efficacious, they compared it against olive oil, which is also cardioprotective and anti-inflammatory. When they wanted to make fish oil look great, they challenged it against mineral oil, which is known to be pro-inflammatory and to cause nutrient deficiencies by blocking nutrient absorption. Major conflicts of interest among the authors and the editors were also evident, such as descriptions of researchers as "independent investigators" when in fact they were paid and supervised by drug companies that wanted to influence the results. I invite you to take a look at those video reviews, you can find those at my video archives at vimeo.com/drvasquez and ichnfm.org/public. You can also see a review article that I published with Dr Joe Pizzorno in his journal *Integrative Medicine* in February, 2019: ncbi.nlm.nih.gov/pmc/articles/PMC6601430/

Returning to the theme of diet now, I mentioned that we want to help our patients avoid the foods to which they are allergic or allergically sensitized. Consumption of foods to which a person is sensitized is known to promote the formation of immune complexes, to trigger migraine headaches, to increase intestinal permeability, and to adversely affect the gastrointestinal microflora. The most common allergenic foods are listed here; wheat, orange and other citrus foods, especially in the form of juice because of the way that they are industrially processed with fungal enzymes. Egg allergy is also common as is sensitivity to tea and coffee, chocolate and milk, beef, corn, cane, sugar and yeast. And you can see from this study published in *The Lancet* [citation in video] that when migraine patients avoid these foods, 85% of those patients are able to become migraine-free simply by avoiding the foods to which they were unknowingly sensitized.

Patients consuming gluten-containing grains can have an increased production of antibodies that results in the formation of circulating immune complexes. Immune complexes are known to directly contribute to several inflammatory conditions including dermatitis (inflammation of the skin), nephritis (inflammation of the kidneys), and also arthritis (inflammation of the joints).

This brings us to the end of my quick overview of food, diet and lifestyle as part of the functional inflammology protocol. I will pass through the following sections a bit more rapidly because—in this first section—we needed to establish a good, healthy foundational diet and lifestyle. I am now going to discuss infection and dysbiosis, then I will talk about nutritional immunomodulation and dysfunctional mitochondria.

## Infections and Dysbiosis

I wrote a comprehensive review of dysbiosis in 2006, you can download that article for free. I also published a small book on the topic of *Human Microbiome and Dysbiosis in Clinical Disease* in 2015, and this was later included in *Inflammation Mastery* in 2016. You can see here I also published a peer-reviewed

article in the *Annals of the New York Academy of Sciences* titled "Biological Plausibility of the Gut-Brain Axis in Autism." Also in 2016, I published this letter "Neuroinflammation in Fibromyalgia and CRPS (complex regional pain syndrome) is Multifactorial" in *Nature Reviews Rheumatology*; one of the important factors in the perpetuation of fibromyalgia and CRPS is gastrointestinal dysbiosis.

**My definition of dysbiosis is that it is a noninfectious, non-acute microbial colonization or exposure that adversely affects the human host.** Again, my definition of dysbiosis: a noninfectious non-acute microbial colonization that adversely affects the human host. Important concepts include the following: **subclinical infections are common in patients with *chronic* or *sustained* inflammatory diseases, especially all types of autoimmunity**. We need to remember that the microbe alone is not the problem; we need to look at the patient's total inflammatory load (TIL) and address that, as well as promoting immune ***defense*** and immune ***tolerance*** in order to reduce the consequences of that microbial colonization. Clinical assessments include laboratory tests such as blood and stool testing; obviously what is most important is the clinical response to treatment.

Our therapeutic categories include ❶ antimicrobials, whether those are drugs or botanicals, ❷ immunorestoration, and ❸ functional immunomodulation or nutritional immunomodulation, and that is to enhance tolerance to inflammatory stimuli. **Often what we find when working with autoimmune and inflammatory patients is that they are having a pathogenic inflammatory response to a nonpathogenic microbe.** We see evidence for that in every single autoimmune disease.

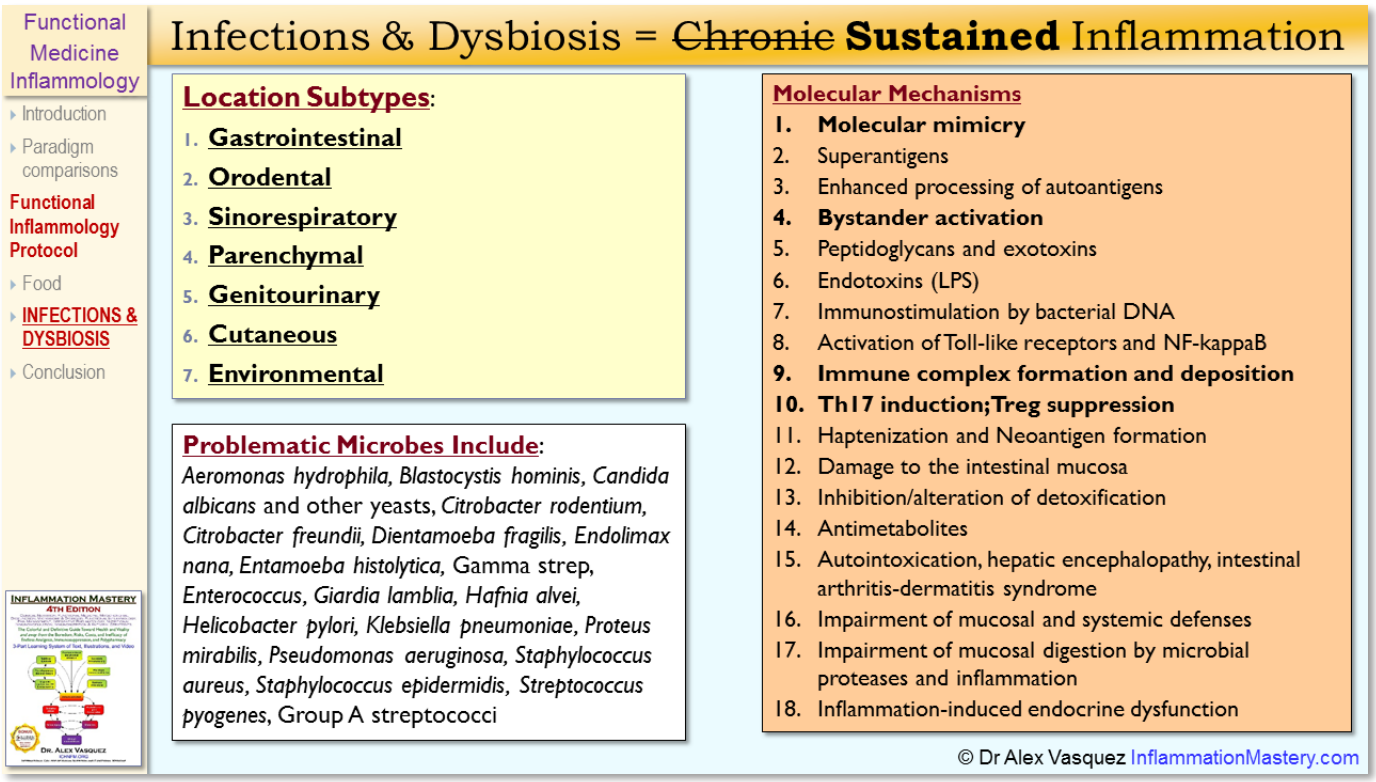
We can look at the classic prototypes of autoimmunity such as reactive arthritis and short bowel syndromes to appreciate the mechanisms and the cause-and-effect relationship between microbial dysbiosis and systemic musculoskeletal and vascular inflammation. **Remember, we are not looking for classic infection here: we are looking to determine which underlying disruptions may be exacerbating inflammation and the patient's symptomatology.** We have to look beyond the basic infection-associated characteristics of the microbe to see the patient's individualized response to that microbe. Patients can have individualized responses to particular microbes. Dysbiosis in one patient may present with dermatitis, while what appears to be the same microbial imbalance in another patient can present as peripheral neuropathy or inflammatory arthritis.

Dysbiosis occurs in various locations throughout the human body including the gastrointestinal tract, orodental cavity (mouth and throat), sinorespiratory tract, and parenchymal tissues. We see evidence of microbial dysbiosis, for example, in internal organs including the brain. Dysbiosis can also occur in the genitourinary tract—such as we see with reactive arthritis following sexually transmitted infections—and the skin, such as we see in patients who have eczema. Environmental exposure to microbial molecules can also trigger systemic inflammation.

Some of the microbes that we encounter commonly in clinical practice include *Blastocystis hominis*, *Candida albicans*, *Citrobacter freundii*, *Endolimax nana*, *Entamoeba histolytica*, Gamma strep, *Giardia lamblia*, *Hafnia alvei*, *Helicobacter pylori* (connected with triggering migraine headaches, vasculitis, and also Raynaud's syndrome), *Klebsiella pneumoniae* (classically associated with ankylosing spondylitis), *Proteus*

*mirabilis* with rheumatoid arthritis, *Pseudomonas aeruginosa* with multiple sclerosis, *Staphylococcus aureus* with psoriasis and eczema, and likewise *Streptococcus pyogenes* colonization of the tonsils with psoriasis.




Here are some of the mechanisms through which microbes can create systemic or tissue specific inflammation or autoimmunity, these include: molecular mimicry, bystander activation, Th17 cell induction and suppression of T-regulatory cells, also immune complex formation and deposition. You can see other mechanisms listed here and you can see how those mechanisms work together in this diagram originally published in my book *Integrative Rheumatology* in 2006, now updated as *Inflammation Mastery: Textbook of Clinical Nutrition and Functional Medicine* in 2016.

Let us consider a hypothetical example of a common problem; let us assume a patient has gastrointestinal dysbiosis. Gastrointestinal dysbiosis includes many different mechanisms all functioning at the same time to promote systemic inflammation or tissue-specific autoimmunity, as you can see in the diagram. Obviously, I have continued to develop this work from my original publications in 2006, most recently published in *Inflammation Mastery* 2016—see video for glimpse of updated and colorized diagram.

Some microbes actually are hosts for other microbes; therefore, the possibility exists that some microbes may be infected with smaller microbes. At the very least, we could use the example of bacteriophages, which are viruses that infect bacteria. A patient could have a dysbiotic inflammatory response against a microbe (such as a viral bacteriophage) within other microbes (such as gastrointestinal bacteria). We do see some evidence for a correlation between bacteriophages and inflammatory bowel disease.

Here I will give you a concrete example from my own clinical practice. This is a 40-year-old white male with a five-year history of idiopathic peripheral neuropathy presenting with numbness and weakness in his arms and legs. By the time he came to see me, he had basically given-up hope as he had already seen many medical specialists in neurology without any benefit. Of course, being a good naturopathic and functional medicine physician, I assumed that he had gastrointestinal dysbiosis. We performed a leaky gut test on him, and you can see here [see video or textbook *Inflammation Mastery* for laboratory images] that his lactulose absorption was very high, indicating leaky gut, and his mannitol absorption was quite low indicating malabsorption. So, he clearly has evidence of intestinal inflammation as part of his clinical presentation of this symptomatic peripheral neuropathy. Again, on the first day of consultation with him, I assumed that he had gastrointestinal dysbiosis, and here we prove that he had gastrointestinal inflammation. When we did follow-up testing for specific microbes, we found that he did indeed have gastrointestinal dysbiosis with *Pseudomonas*. We know from the research literature that *Pseudomonas aeruginosa* cross-reacts with myelin basic protein in peripheral nerves and also myelin oligodendrocyte glycoprotein. In his case, I normalized his immune system, helped him heal the gut, eradicated this bacteria, and the result was that his peripheral neuropathy disappeared within one month.

When we talk about treating gastrointestinal dysbiosis, we commonly use either drug antibiotics or botanical antibiotics. One of the botanical antibiotics that we can reach to with good reliability is oregano oil in a time-released emulsified tablet. The emulsified form of the oregano increases dispersion of the oil and the time release tablet helps to increase delivery of that oregano oil throughout the gastrointestinal tract. When oregano oil is used in the treatment of gastrointestinal parasites, the common dose is 600 milligrams per day in divided doses for six weeks.[23] Another botanical that we commonly use is berberine; this is well-studied, and a typical dose of berberine these days would be 500 milligrams, two to three times per day for three months.

So this brings us to the end of my quick but quite authoritative and complete overview of infections and dysbiosis and systemic inflammation. Next topic is going to be what I call nutritional immunomodulation. As you can see here by the index on the left-hand side, we are now on the third part of my functional inflammology protocol. I have already reviewed food, then infection and dysbiosis, and now we are at part three, which is what I call nutritional immunomodulation.

## Nutritional Immunomodulation: Improving the Number/Function of T-Regulatory (Treg) Cells to Limit Inflammation caused by Th1, Th2 and Th17 Cells

The important concept here is that **we can favorably influence the number and function of immune cell populations by using specific nutrients**. Our clinical goal is to reduce inflammation, whether that is metabolic inflammation, allergic inflammation, autoimmune inflammation or neuroinflammation. One of the ways that we accomplish that goal mechanistically is to increase the number and activity of anti-inflammatory T-regulatory cells and to decrease the number and activity of pro-inflammatory Th1, Th2 and Th17 cells. T-regulatory cells (Treg) are named "regulatory cells" because these cells regulate, counterbalance or modulate the activity of pro-inflammatory cell populations.

The traditional view has been (or was) that T-helper cells function mostly as intermediaries, supporting growth and function (as "helpers") of the true effector cells such as cytotoxic cells and antibody-producing B-lineage plasma cells. In the early decades and centuries of Immunology as a scientific field, researchers could study only what they could see (cells) and measure (antibody proteins) but were not aware of cytokines, which were discovered in the mid-1970s, far after many names and paradigms had already been established. However, with the increased appreciation of the direct effects of cytokines, we should likewise appreciate the progressive blurring of the distinction between "helper" and "effector" cells; for example, Th17 cells in the "helper" category secrete the cytokine interleukin-17 (IL17) which has direct pathogenic effects, largely by changing gene expression and inducing various other pro-inflammatory cytokines which—independently and synergistically—promote tissue destruction, especially the types noted in chronic/sustained disorders of autoimmunity.[24]

**Nutritional immunomodulation—per my use of the term—is specifically the induction of T-regulatory cells via a defined evidence-based multi-component nutritional protocol. My nutritional immunomodulation protocol reduces inflammation by enhancing endogenous physiologic control mechanisms**, contrasted against the use of antiinflammatory drugs that ***block*** enzymes, ***block*** receptors, ***block*** cytokines, or ***globally suppress immune function***.

You might ask, "Well, how does this work?" Naive, undifferentiated T-cells are called Th0 cells, and these are born in the bone marrow, move to the thymus (and possibly the tonsils), and then to the gut-associated lymphoid tissue, otherwise abbreviated as GALT. In the GALT, Th0 cells are programmed to become effector T-helper cells capable of either pro-inflammatory or anti-inflammatory actions:

- Th0 zero cells are undifferentiated and mostly inactive.
- Th1 cells participate in cell-mediated inflammation.
- Th2 cells help produce antibodies and therefore we commonly think of Th2 cells as being involved with allergy and autoimmunity.
- Th17 cells are specifically involved with autoimmune type inflammation.
- T-regulatory cells or the Tregs promote tolerance, suppress inflammation, allergy and autoimmunity.

These changes in cellular maturation-development are achieved through epigenetic mechanisms, resulting in changes in gene expression, which result in either pro-inflammatory or anti-inflammatory immune cell activity. Nutritional deficiencies, especially but not exclusively of vitamins A and D, promote a pro-inflammatory gene expression pattern, resulting in pro-inflammatory cellular behaviour and an inflammatory clinical phenotype. Gastrointestinal dysbiosis leads to peri-intestinal inflammatory signaling which is communicated via several mechanisms and pathways including the GALT, resulting in the expected pro-inflammatory programming of immune cells. Thus, gut dysbiosis and nutritional deficiencies are readily correctable causes of sustained systemic inflammation.

On this page [in the video presentation] we see examples from the research literature showing that retinoic acid or vitamin A helps to increase the production of these FOXP3+ regulatory T cells. The same occurs with vitamin D supplementation as shown in this clinical trial with human subjects. [See video for

citations.] Therefore per this evidence, by providing nutrients including but not limited to vitamin A and vitamin D, we can increase the production and function of these regulatory T cells to provide an endogenous anti-inflammatory effect through endogenous immune-modulating mechanisms.

I trust that some viewers/readers recall that I previously discussed the inclusion of probiotics in my 5-part nutritional protocol. You will recall that my **five-part supplemented Paleo-Mediterranean diet** is a plant-based diet of fruits, vegetables, nuts, seeds, berries and lean sources of protein. Those same **fruits, vegetables, nuts, seeds and berries act as prebiotics for beneficial bacteria** that we commonly (casually and not entirely accurately) refer to as probiotics (which are defined as living organisms consumed for host benefit). **Those probiotic or beneficial bacteria that we want to cultivate within the gut also help to induce these T-regulatory cells**, which suppress the inflammatory activity of Th1, Th2 and Th17 cells. So again, this is what I call *nutritional immunomodulation*, and that is the specific therapeutic induction of T-regulatory cells to help dampen and endogenously control these excessive pro-inflammatory responses. These concepts and the practical clinical protocol are detailed in Chapter 4 of *Inflammation Mastery 4th Edition*, published in a two-volume set as *Textbook of Clinical Nutrition and Functional Medicine*.

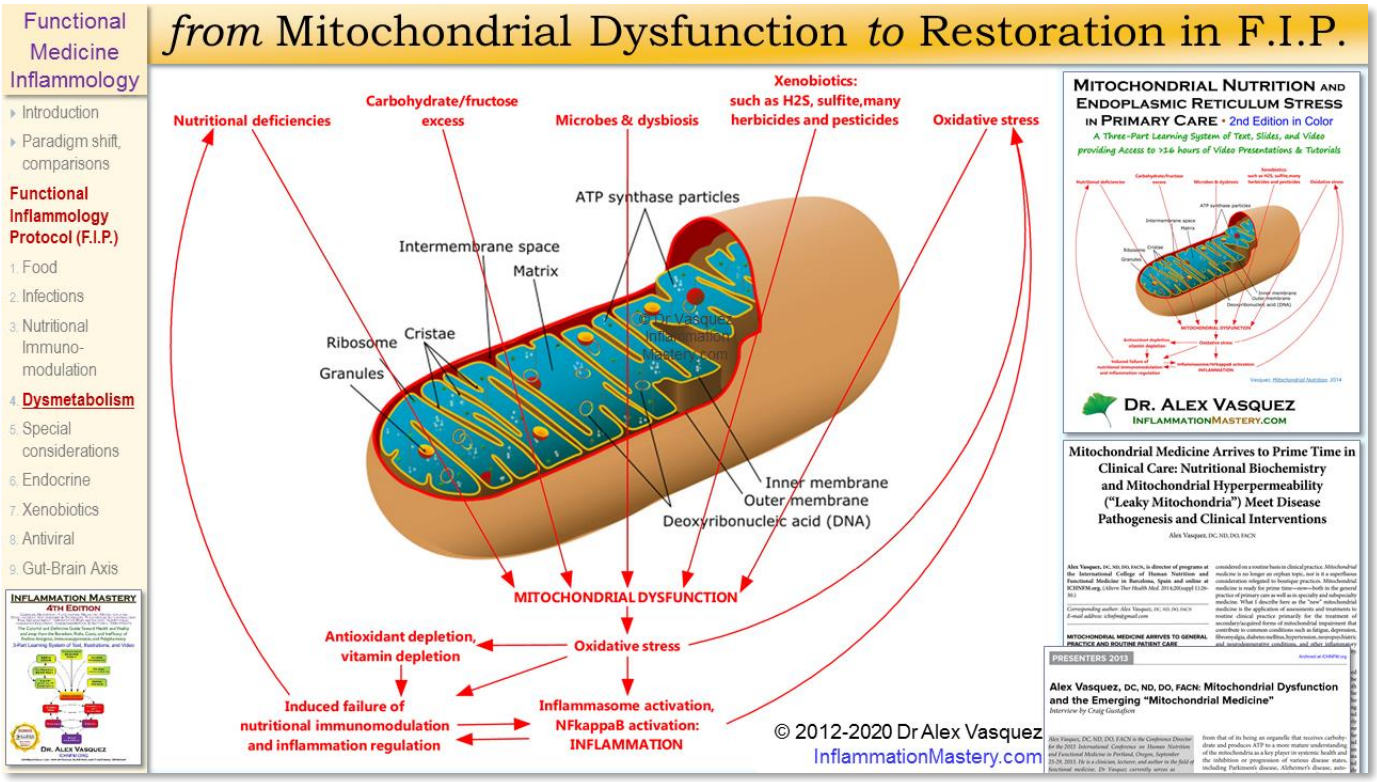
## Dysfunctional Mitochondria and Dysmetabolism—Including Inappropriate mTOR activation and Endoplasmic Reticulum Stress

Let us go on now to component number four of my functional inflammology protocol, which is dysfunctional mitochondria and also—more broadly—metabolic dysfunction. As you can see here from my diagram: nutritional deficiencies, carbohydrate and fructose excess, also exposure to microbes and dysbiosis, xenobiotics such as herbicides and pesticides and also oxidative stress—all of these contribute to mitochondrial dysfunction which then increases the production of free radicals. This increased production of free radicals leads to antioxidant vitamin depletion, which then leads to nutritional deficiencies which then promote mitochondrial dysfunction and obviously a vicious cycle here. That same oxidative stress increases the activity of the pro-inflammatory gene activator and transcription factor NF-kappaB, and that leads back to more oxidative stress to create another pro-inflammatory and free radical-mediated vicious cycle as you can see here. So what you need to understand at the very least from this diagram is that **mitochondrial dysfunction leads to oxidative stress**, and that **oxidative stress promotes systemic inflammation**. For this reason, we all need to be aware of the role of mitochondrial nutrition and what we can call mitochondrial medicine in the treatment of these primary care and specialty care conditions. You can see a review of this theme that I published in 2014 titled "Mitochondrial Medicine Arrives to Prime Time in Clinical Care: Nutritional Biochemistry and Mitochondrial Hyperpermeability Meet Disease Pathogenesis and Clinical Interventions"; this article from *Integrative Medicine: A Clinician's Journal* is available for free online: https://ichnfm.academia.edu/AlexVasquez. The major concept here is that while everyone knows that mitochondria make ATP, the cellular currency of energy, people also need to know that **damage and dysfunction to mitochondria can occur as a result of deficient diets and chemical pesticide exposures resulting in changes in mitochondrial function with consequences in gene expression, immunity and the amplification of inflammation**.

The clinical presentations associated most strongly with mitochondrial dysfunction are diabetes, insulin resistance, hypertension, migraine, fibromyalgia, also Alzheimer's and Parkinson's diseases. So the interventions we can use when we are addressing mitochondrial dysfunction include dietary intervention, especially a low-carbohydrate nutrient dense diet, nutritional supplementation, and as needed, detoxification and depuration to detoxify and remove those poisonous chemicals that are damaging mitochondrial structure and function.

A very simple example of the treatment of mitochondria dysfunction in clinical practice is the use of high-dose riboflavin at 400 milligrams per day in the prophylaxis of migraine headaches. Migraine headaches are a well-known example of mitochondrial impairment. Helping to improve mitochondrial function through nutritional supplementation—one example of which is riboflavin, another example could easily be magnesium—that helps to improve mitochondrial biochemistry improves intracellular signaling and also reduces intercellular free radical production, which then reduces the activation of these inflammatory pathways. This is a clear biochemical and physiologic explanation of the means by which "mitochondria-enhancing nutrition" can alleviate the clinical manifestation of this complex disorder that we call migraine.

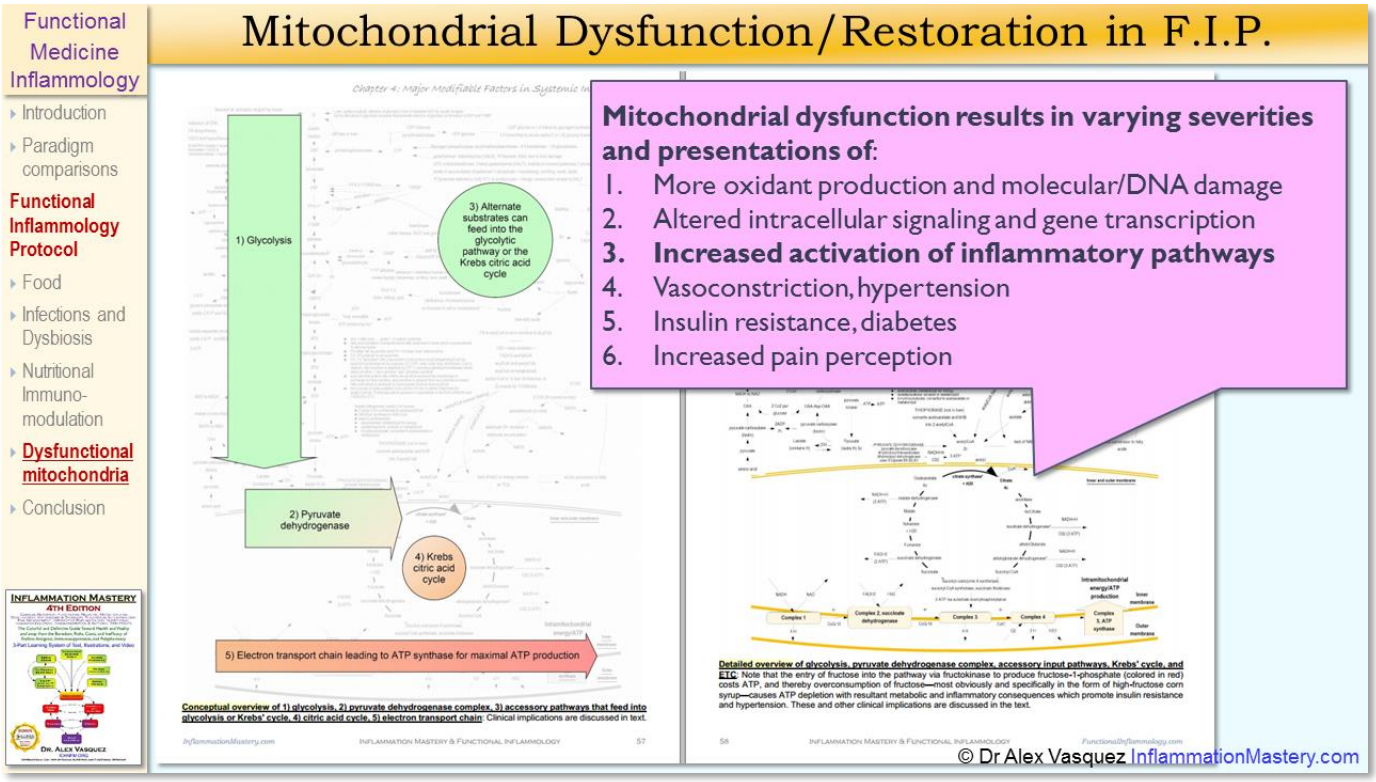



In addition to the article mentioned previously from 2014[25] is another article that I published in 2013[26] (Vasquez A, Gustafson C. Mitochondrial Dysfunction and the Emerging Mitochondrial Medicine. *Integrative Medicine* 2013 Aug; 12(4): 20-24 https://ichnfm.academia.edu/AlexVasquez) and indeed an entire textbook on this topic entitled *Mitochondrial Nutrition And Endoplasmic Reticulum Stress In Primary*

*Care* published as a second edition in 2014, and this book is included within *Inflammation Mastery* published in 2016. Let us now take a look at mitochondrial function just to provide you a quick overview.

We all know that the production of cellular energy begins with a process of **glycolysis**, then we go through the **pyruvate dehydrogenase complex**, we enter the **Krebs cycle**, and then those final remaining substrates are shuttled through the **electron transport chain**. When I am teaching this information to students, I typically introduce the topic in a rather simplistic manner as you see here, and we talk five main components to cellular energy production. Number one is **glycolysis**, number two is the **pyruvate dehydrogenase shuttle, or they pyruvate dehydrogenase complex**. **Other substrates can also enter** here [see video], but ultimately we enter into the **Krebs cycle** and then we go to the **electron transport chain**. So we then detail these five main components. Again, the five main components of cellular energy production: ❶ glycolysis, ❷ pyruvate dehydrogenase, ❸ Krebs cycle, ❹ ATP production through the electron transport chain, and obviously ❺ other fuels can also enter into the Krebs cycle.

Typically, when we talk about mitochondrial dysfunction, we are talking about defects in the Krebs cycle, but **more commonly we are talking about defects in the electron transport chain**. Again, for example, if you think of patients with migraine headache, they have numerous defects in their production of ATP because of defects in the electron transport chain. And those defects that we see in patients with migraine headaches are almost identical to the defects that we see in patients with fibromyalgia. See Chapter 5 of *Inflammation Mastery: Textbook of Clinical Nutrition and Functional Medicine* or the excerpt *Brain Inflammation in Chronic Pain, Migraine and Fibromyalgia*.

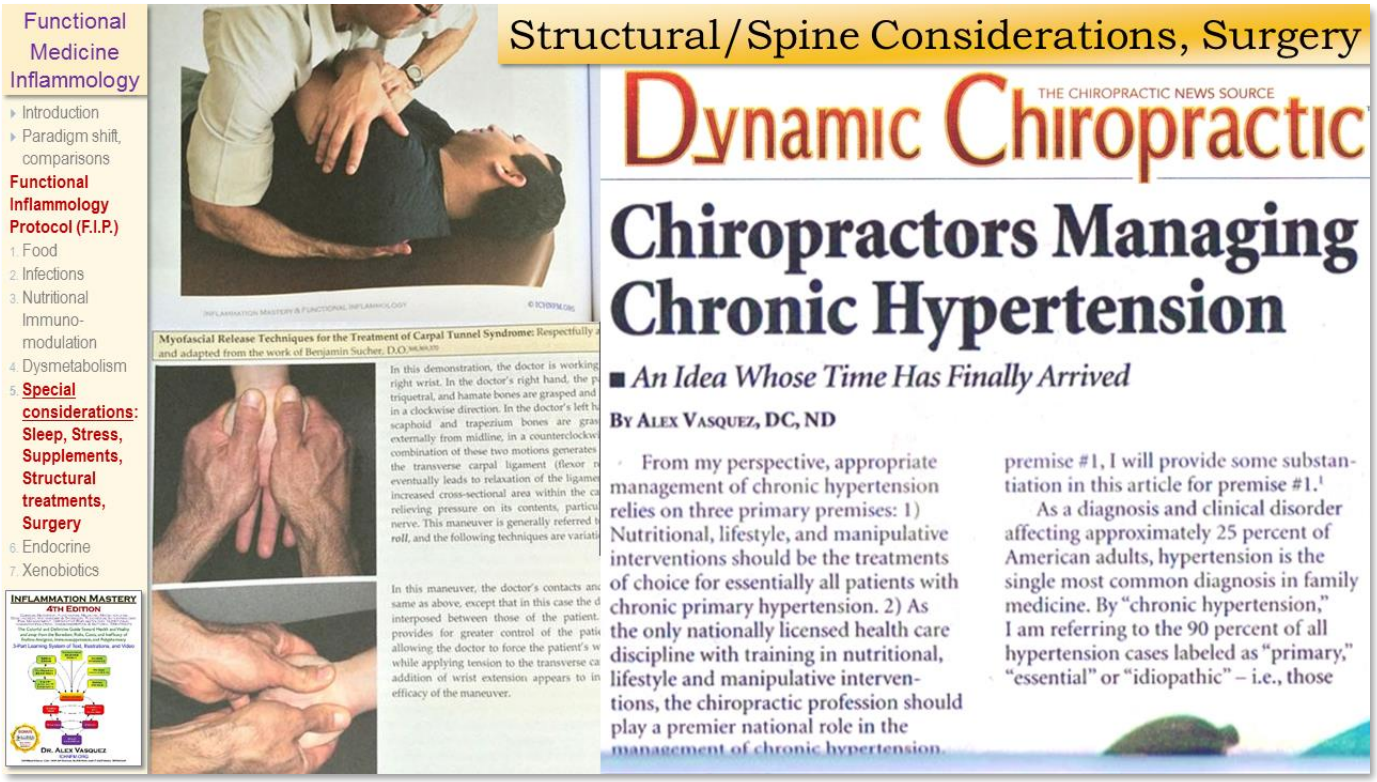


Mitochondrial dysfunction results in varying severities and clinical presentations of more oxidant production and molecular damage, including DNA damage, altered intracellular signaling and gene transcription. **Increased activation of inflammatory pathways is critical**, and that is a **common theme that we see across the board with these disorders connected with mitochondrial impairment**, insulin resistance and diabetes, and also increased pain perception.

Mitochondrial dysfunction leads to disease, we see this in inflammatory conditions, allergic conditions, autoimmune conditions, metabolic syndrome, type-2 diabetes and hypertension, heart failure, fibromyalgia, migraine and neurodegeneration, especially the prototype's Parkinson's disease and Alzheimer's disease.

**Style of Living, Sleep Hygiene, Stress Management, Special Supplementation, Spinal Manipulation/Adjusting, Social Psychology and Inequality, Surgery**

Dysfunctional mitochondria and dysmetabolism was topic number four in my clinical protocol; we are now going to talk about **stress**, **sociology**, **style** of living, and other **special** considerations including **surgery**. All of these can start with the letter S, or in the case of **psychology** the sound of the letter S.




We want to help our patients reduce their **stress**, manage it better, and obviously avoid the causes or sources of their stress. Other considerations in this category include **sociopsychology** (including politics) quantity and quality of **sleep**, **sweat** as a metaphor for exercise, **spinal** health, including osteopathic and chiropractic manipulation or adjustments, **specialized supplementation**—including

selenium for its antiviral effects, melatonin for immune and mitochondrial stimulation, B6 to lower glutamate and raise GABA levels within the brain. **Surgery** might be necessary in some cases, and sometimes people will simply need to **stamp their passport and take a vacation**. So you can see that this fifth category of the protocol helps us open our minds to additional considerations ranging from surgery to additional supplementation, to spinal manipulation, to exercise and improving people's sleep hygiene and their psychosocial situation. Let us look at a few more examples on the following page.

You will notice that I use the letter S to represent all of the items within this fifth category and that includes sweat as a metaphor for exercise. Current guidelines recommend that people get at least one hour of exercise per day, at least five days per week emphasizing aerobic exercise, and two days per week emphasizing resistance training. Another item that we can fit into this category that also starts with S is spinal health, and one of my favorites is spinal adjusting or spinal manipulation. We see that chiropractic-type manipulation also has benefit in the treatment of hypertension, as demonstrated in this clinical study that concluded, "No adverse effects were recorded. "We conclude that restoration of [vertebral] atlas alignment is associated with marked and sustained reductions in blood pressure similar to the use of two-drug combination therapy." This was published in *Journal of Human Hypertension* in 2007.[27] I also published a commentary on that article suggesting that chiropractors could manage chronic hypertension, this was published in *Dynamic Chiropractic* in 2010. You will also see from these examples from my book that I do discuss chiropractic manipulation and osteopathic manipulation as treatments you can see here for the thoracic spine and rib cage and also for carpal tunnel syndrome.

## Endocrine Dysfunction, Hormone Imbalances

Now let us talk about category number six which is hormone and endocrine function. Obviously, patients with inflammatory disease commonly have hormonal imbalances. For example, they may have **elevated prolactin**, they may have **elevated estradiol**, they may have insulin resistance and elevated fasting glucose or **hyperinsulinemia**. Meanwhile, some immune-modulating hormones may be on the lower end, and these anti-inflammatory hormones include low **DHEA**, low **cortisol** and also low **testosterone**. Of course we always want to check thyroid function with history, physical exam, several laboratory tests, and by monitoring response to treatment.

In this case from my clinical practice, you can see this young man with three different autoimmune diseases also presents with several different endocrine abnormalities; low **testosterone**, **thyroid** autoimmunity. His glucose level was acceptable, but he has slight **insulin resistance**, has a slight elevation in his TSH, also **testosterone and estrogen imbalance**, and here he also has **vitamin D deficiency**—many people think of vitamin D as being a hormone, not simply a vitamin.

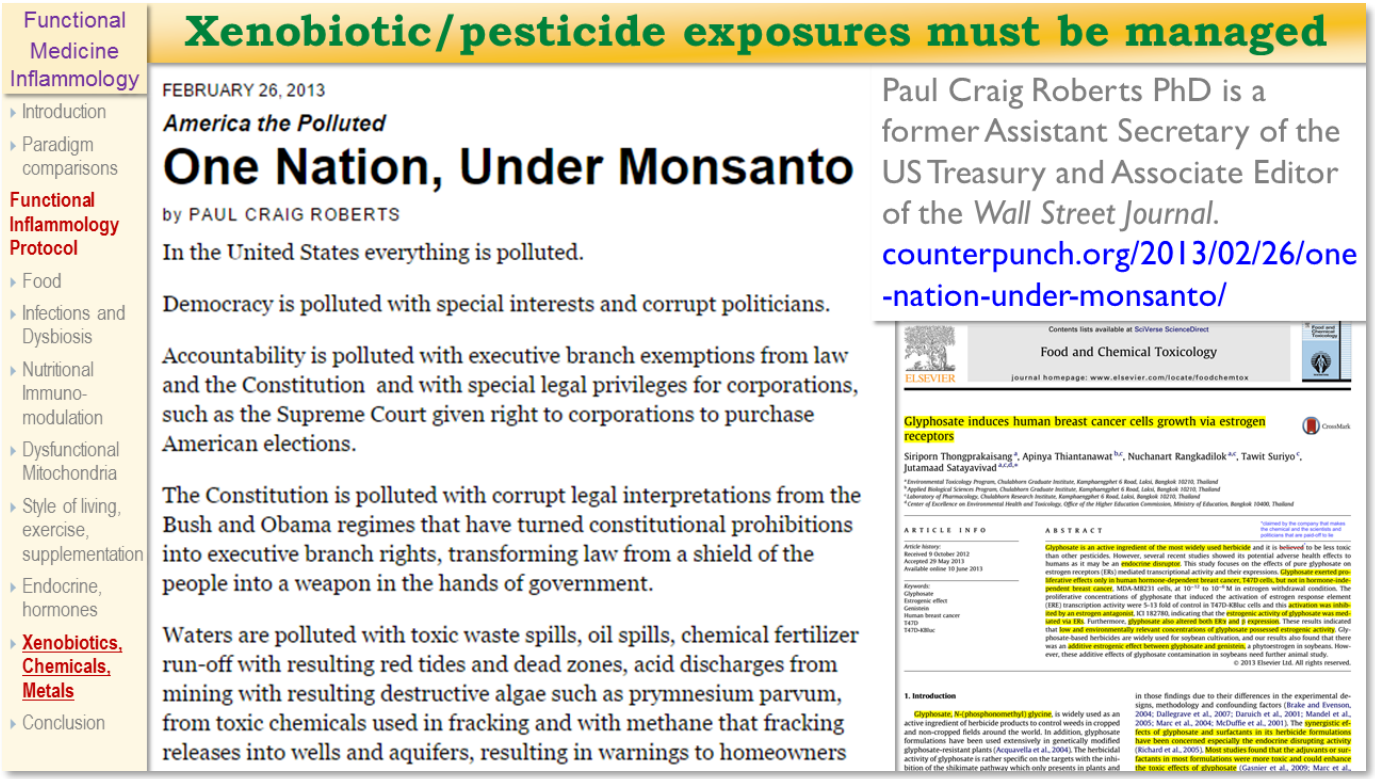
So again, when we are assessing and managing and treating these patients with *persistent* or *chronic* or *sustained* inflammatory disorders, we need to look at their hormones and either directly intervene to optimize the levels or indirectly intervene to address the underlying cause of their hormone imbalance so then they can attain better inflammatory balance overall. In other words, one of the ways that we reduce inflammation is to optimize hormone levels, and one of the ways that we optimize hormone levels is to

determine the cause of those hormone imbalances. As I have said more recently, **we have to treat not simply the cause of the disease**, but **we have to treat the *causes of the causes* of the disease**.

## Xenobiotic Exposure/Accumulation/Immunotoxicity

Now finally, let us talk about toxins and xenobiotics. The basic summary is very simple. We are all poisoned with chemicals, especially pesticides, and we need to manage that poisoning responsibly through a ***detoxification lifestyle***, not simply isolated events every other year or every year. Detoxification support needs to be a component of the daily lifestyle.

Supporting detoxification and reducing exposure may include using a water filter, getting sufficient exercise to sweat and to therefore remove those toxins from the body, eating organic foods, taking nutrients to support detoxification, and also of course engaging politically because we would not live in a poisoned environment had the politicians not allowed this to occur, and the reason they allow it to occur is because they are paid by big corporations. From a clinical perspective, xenobiotics includes chemical toxins and also includes heavy metals such as mercury, lead, aluminum; all of these including pesticides and other persistent organic pollutants (POPs) contribute to persistent inflammation.




Toxins impair metabolic function, as I said before, by impairing mitochondrial function. Mercury and lead are also known to promote hypertension. Mercury also promotes the development of drug resistance among gastrointestinal bacteria. Toxins and xenobiotics also promote insulin resistance, and this is well established in the study and pathogenesis of diabetes. A 2012 publication stated, "any effort to

reduce the external and internal exposure to POPs would be necessary to decrease the social burden of type 2 diabetes."[28]

Toxins such as pesticides can also lead to a lowering of immune function such as lower immune globulin levels, while at the same time, those same toxins can promote autoimmunity manifesting with higher levels of antinuclear antibodies (ANA). So as I have said before, toxin awareness and detoxification support are necessary on a daily basis. We have known for many years now that the typical American is loaded with at least 13 different pesticides per data published in 2004 updated in 2018[29] and certainly by now we would find even more pesticides.

These pesticides lead to metabolic impairment, systemic inflammation, and also genetic damage as you can see in this 2007 publication, "Evaluation of DNA damage in an Ecuadorian population exposed to glyphosate" from *Genetics and Molecular Biology* 2007.[30] Well, obviously this applies to anyone who is exposed to glyphosate and that includes the vast majority of the global population. Here we see that the pesticide "glyphosate accumulates in Roundup Ready genetically modified soybeans" published in *Food Chemistry* 2014[31] in an open-access publication: doi.org/10.1016/j.foodchem.2013.12.054. These soybeans are of course used as food products for humans, but these same genetically modified pesticide-laden soybeans are also used to feed livestock such as cattle. Therefore, whether these are consumed by humans to have a direct toxic effect or they are consumed by other animals which we then consume for an indirect toxic effect, the fact remains that these genetically modified soybeans are contaminated with glyphosate. Glyphosate has also been shown *in vitro* to induce human breast cancer cell growth via activation of estrogen receptors, published in *Food and Chemical Toxicology* 2013.[32] Obviously with this mechanism of activating estrogen receptors, we would expect glyphosate to contribute to a wide range of human cancers, not simply breast cancer, but also prostate cancer and colon cancer.

From a clinical viewpoint, we see that patients who have problems with fertility also have higher levels of pesticide exposures and higher levels of pesticide residues. As you can see from this study, "high pesticide residues in fruits and vegetables correlates with poor quality of semen and infertility."[33] Again, we would not have this problem of massive global pesticide exposure were it not for the politics involved. Indeed, some people have argued that the entire world is contaminated by these pesticides and that is because our entire global political system is corrupted by money from these chemical corporations.

As I said before, accumulation of persistent organic pollutants leads directly to insulin resistance and metabolic syndrome at least partly through the induction of mitochondrial dysfunction. Exposure to and accumulation of toxic chemicals leads to activation of the Aryl hydrocarbon receptor (AHr), which causes downregulation or suppressed expression of the GLUT-4 insulin receptor, thereby leading directly to insulin resistance. For all of these reasons and as I said before, **detoxification needs to be part of the daily lifestyle to combat the exposure to these toxic chemicals which also occurs on a daily basis**.

So now as you can see by the index on the left, we have now completed our overview of the functional inflammology protocol, starting with ❶ food, ❷ infections and dysbiosis, ❸ nutritional immunomodulation, ❹ dysfunctional mitochondria, ❺ style of living, sleep hygiene and stress

management, ❻ endocrine and hormone imbalances, and finally concluding with some mention of ❼ xenobiotics chemicals and heavy metals. So now you have new insight into how all of these contributors can lead to systemic, "chronic" or ***sustained*** immune activation and inflammation.

**These contributors, acting alone or in synergistic combinations, lead to the diseases that we see in clinical practice**. If we as clinicians are going to truly prevent and treat these problems effectively, then we need to ***look upstream*** to address the pro-inflammatory diet and lifestyle, the infections and dysbiosis, the immune imbalance that we address with the nutritional immunomodulation plan, dysfunctional metabolism and dysfunctional organelles, including the endoplasmic reticulum and the mitochondria, psychoemotional and physical stressors, as well as sleep deprivation, endocrine imbalances, and xenobiotic immunotoxicity. **All of those contribute to sustained inflammation and immune activation** that leads to modulation of gene transcription, the elaboration of pro-inflammatory mediators, tissue injury, oxidative stress, and that leads to a vicious cycle. **In order to break this vicious cycle, which ultimately leads to clinical manifestations, we need to look upstream at the contributors and address as many of these as possible.**

Now that I have reviewed the overall structure and some examples of clinical applications, as we arrive to the end of this presentation, I will provide a few specific insights into the gut, brain axis, neuroinflammation, and a very brief mention of my antiviral nutrition protocol.

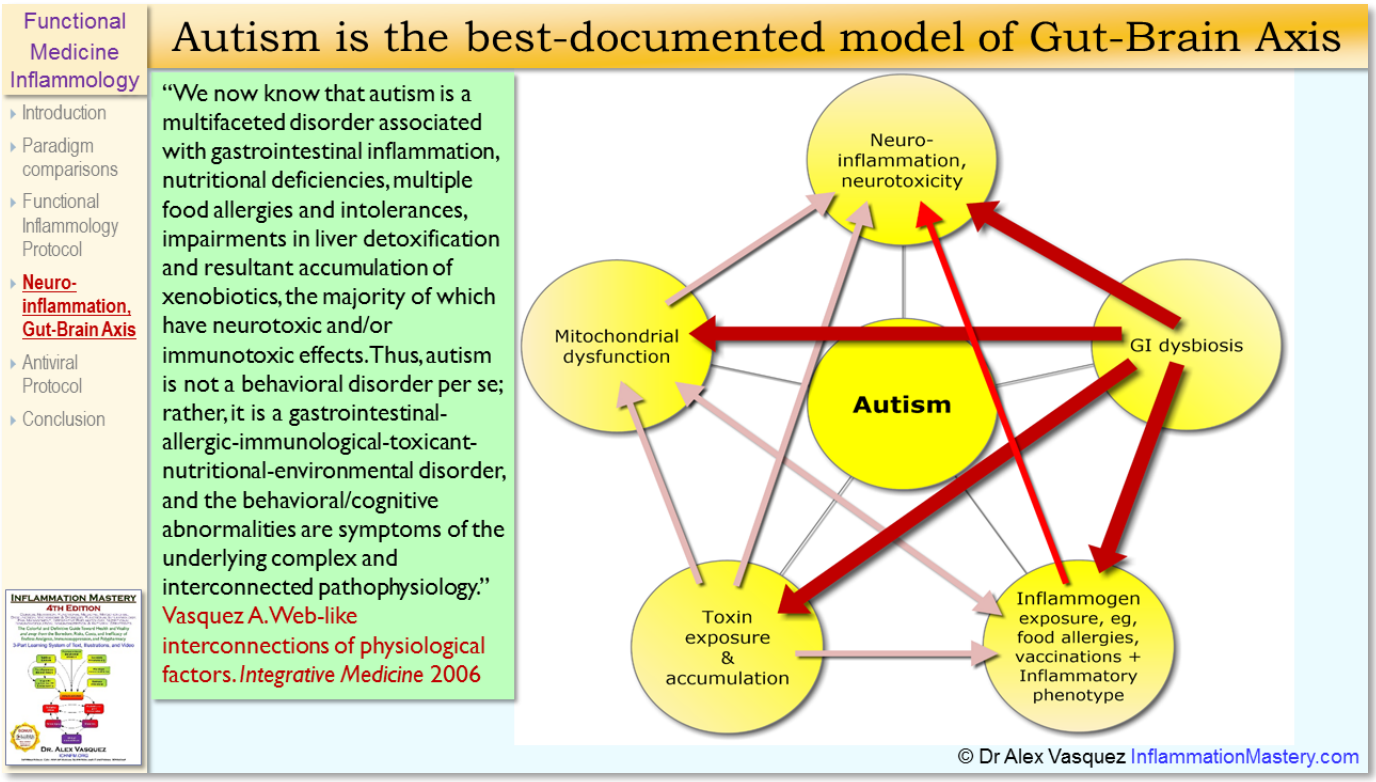
## Brief Mention—Neuroinflammation and the Gut-Brain Axis

On the next few pages, let us talk about neuroinflammation. This is relevant for depression, brain injury, autism, schizophrenia, bipolar disorder, neurodegeneration, hyperphagia, obesity and insulin resistance, multiple sclerosis, PANDAS, brainstem encephalitis, migraine, and fibromyalgia. If you are interested in this topic, you can see several of my chapters and clinical monographs, including *Human Microbiome and Dysbiosis in Clinical Disease* (2015), included within *Inflammation Mastery* (2016). Also, an article that I published in *Nature Reviews Rheumatology*, specific to fibromyalgia, which was also covered in my book, *Brain Inflammation*, and also a much shorter book on *Autism, Dysbiosis, and the Gut-Brain Axis* in 2017 coincident with my publication in *Annals of the New York Academy of Sciences*.

Some of the more important concepts to know in this conversation of gut-brain axis and neuroinflammation include the fact that some microbes within the gut produce neurotoxins, others produce inflammogens, and others produce mitochondrial toxins. When neurotoxins are combined with inflammogens and those inflammogens are also combined with mitochondrial toxins, **different combinations of toxins, neuroinflammation, and mitochondrial impairment result in different clinical phenotypes.** All of these alone or in combination lead to glial activation within the brain, and that changes glutamate neurotransmission and also increases the production of kynurenines. Neuroinflammation is exacerbated by mitochondrial impairment, and neuroinflammation also causes mitochondrial impairment—another vicious cycle. If a person is consuming a pro-inflammatory diet and following a pro-inflammatory lifestyle, obviously these impacts are going to be amplified. If a patient has strong anti-inflammatory reserve, including vagal stimulation for anti-inflammation, then of course we would expect

a milder impact on their neurocognitive and emotional functioning. Other factors that affect these pathways include genes, nutritional status, and again, stress, resilience, exercise, and age.

Autism really provides us a great example for understanding the impact of the gut microbiome, and how it can have adverse effects on neuroinflammation and neurotoxicity, mitochondrial dysfunction, toxin exposure, and impaired detoxification. All of those can synergize with other factors to lead to the activation of inflammatory pathways, systemically and within the brain.

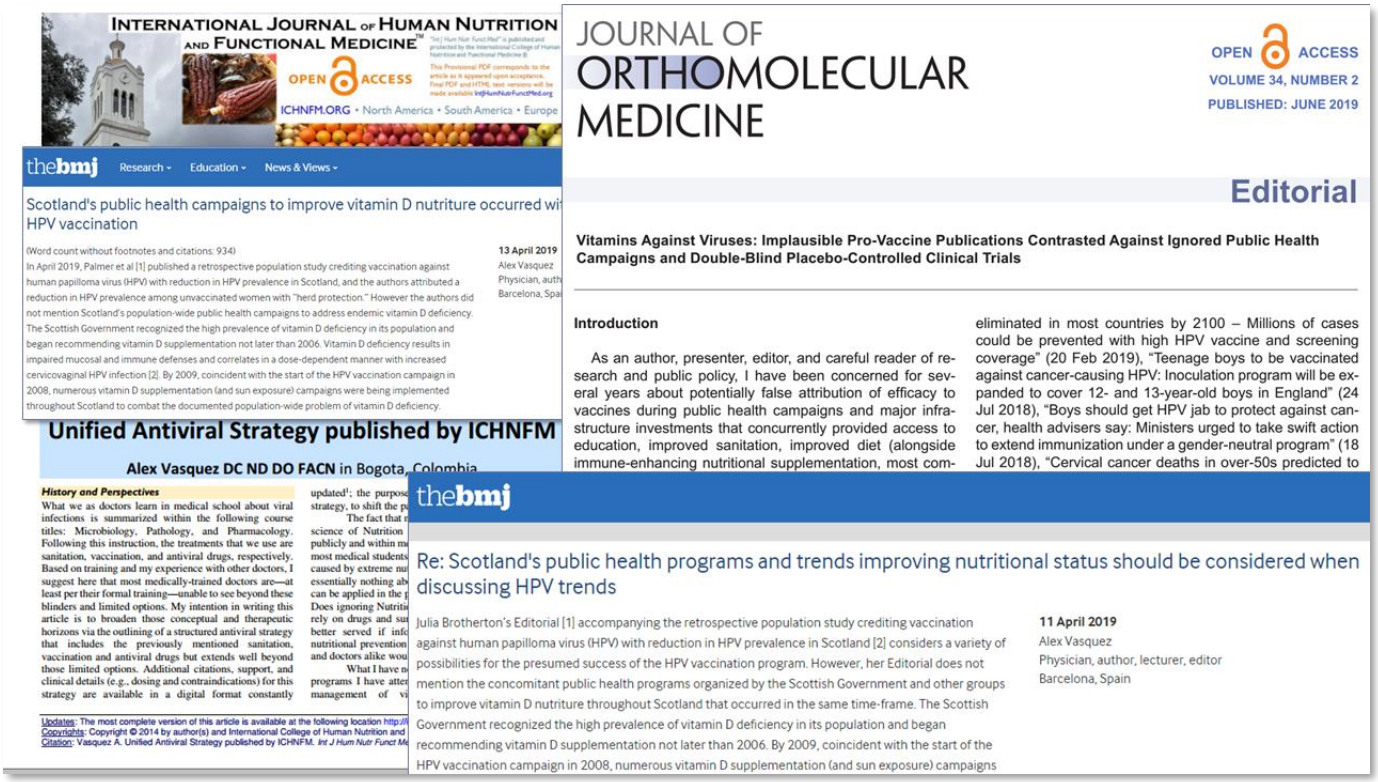



## Brief Mention—Antiviral Nutrition

Very briefly now, as we reach the conclusion of this presentation, let us talk about viral infections. Viral infections can be prevented and treated in a logical and structured manner. I published my first article on this in 2014 (https://www.ichnfm.org/antiviral5), and more recently in 2019, I published a response on the website of the *British Medical Journal* (see bmj.com/content/365/bmj.l1375/rr-4 and bmj.com/content/365/bmj.l1161/rr-8) followed by an editorial in the *Journal of Orthomolecular Medicine* (see academia.edu/39406350 and isom.ca/article/vitamins-against-viruses/), and I invite you to take a look at all of those articles, so that you can gain some new perspective on the pathophysiology of viral infections, but also how we can treat them clinically.

Let us take a look at my overall program, which has four main components. First, is addressing virus and virus acquisition. Second, is impairing viral replication. Third, is supporting immune nutrition, both defense and tolerance. Part number four of my strategy is to support cellular and systemic health.

We can view these as separate components of viral infection pathophysiology, and also treatment, and we can see how these structures overlap. Certain nutrients, for example, affect all of these pathways by inhibiting viral acquisition, inhibiting viral replication, supporting immune function, defense, and tolerance, and also supporting cellular and systemic health. Three examples include zinc, selenium, and vitamin D, which provide benefits in all four of these major areas. Other nutrients, such as vitamin A, do not provide benefit in every area, but they are nonetheless very essential. Any basic antiviral protocol must include zinc, selenium, vitamin D, and vitamin A.




I discussed this in my 2014 book, *Antiviral Strategies and Immune Nutrition*, which is now available as a PDF download, titled *Antiviral Nutrition*. And that exact same material is included in the 2016 edition of *Inflammation Mastery 4th Edition*.

## Conclusions and Closure

So, we have now reached the ending and conclusion of this presentation. As I said before, and as I have said for many years to my graduate students, **organized and declarative knowledge is the most valuable type of knowledge for intellectual pursuits and practical application**. *So again, what are the four main types of inflammatory conditions that we see in outpatient clinical care?* Metabolic inflammation, allergic inflammation, autoimmune inflammation, and neuroinflammation. *What are the seven main components that create chronic or sustained systemic inflammation?* So, I taught you to use my acronym, which is FIND SEX, or alternatively, FIND SET. F stands for Food, then Infections, Nutritional immunomodulation, and Dysmetabolism or Dysfunctional mitochondria. That is the FIND. The SEX is Stress, Social inequality,

Sweat as a metaphor for exercise, Sleep deprivation, Specialized Supplementation, Spinal manipulation, and sometimes Surgery. The E stands for Endocrine imbalances. We look for three hormones that are typically elevated, and three that are typically depressed, and we also make a complete assessment of thyroid function. And finally, the X or the T stands for Xenobiotics or Toxins.

So again, we need to follow the healthiest diet and lifestyle possible, with organic and preferably fresh and locally grown food, free of pesticides. Also, as I said at the beginning of this presentation, you cannot necessarily expect to understand, learn, and memorize everything, everything in the first viewing. But by the time you review this material two or three times, it will start becoming manageable and more useful for you in your own life, when you are helping friends and family, and obviously when you are working with patients and clients in clinical practice.

As Nietzsche said, "In order for a particular species to maintain itself and increase its power, its conception of reality must comprehend enough of the calculable and constant for it to base a scheme of behavior on it. … In other words, a species grasps a certain amount of reality, in order to become master of it, in order to press it into service." And I believe that is what we have accomplished with this protocol that I have now outlined for you.

So, think of all that you have already learned, and all that you have already suffered in your medical training. Now realize that you can add this information atop your previous experience and gain new levels of talent and success.

Thank you very much for your attention. I have been your host, Dr. Alex Vasquez, showing you how to integrate functional and naturopathic medicine concepts and therapeutics into medical practice for common primary care and specialty conditions. And again, you can apply this protocol to all conditions of *metabolic* inflammation, *allergic* inflammation, *autoimmune* inflammation, and *neuroinflammation* or brain inflammation. Thank you very much for your attention.

**Alex Kennerly Vasquez DO ND DC (USA), Fellow of the American College of Nutrition (FACN), Overseas Fellow of the Royal Society of Medicine**: An award-winning clinician-scholar and founding Program Director of the world's first fully-accredited university-based graduate program in Human Nutrition and Functional Medicine, Dr Alex Vasquez is recognized internationally for his high intellectual and academic standards and for his expertise spanning and interconnecting many topics in medicine and nutrition. Dr Vasquez holds three doctoral degrees as a graduate of University of Western States (Doctor of Chiropractic, 1996), Bastyr University (Doctor of Naturopathic Medicine, 1999), and University of North Texas Health Science Center, Texas College of Osteopathic Medicine (Doctor of Osteopathic Medicine, 2010). Dr Vasquez has completed hundreds of hours of post-graduate and continuing education (certifications) in subjects including Obstetrics, Pediatrics, Basic and Advanced Disaster Life Support, Nutrition and Functional Medicine; while in the final year of medical school, Dr Vasquez completed a Pre-Doctoral Research Fellowship in Complementary and Alternative Medicine Research hosted by the US National Institutes of Health (NIH). Dr Vasquez is the author of many textbooks, including Integrative Orthopedics (2004, 2007 2012), Functional Medicine Rheumatology (Third Edition, 2014), Musculoskeletal Pain: Expanded Clinical Strategies (commissioned and published by Institute for Functional Medicine, 2008), Chiropractic and Naturopathic Mastery of Common Clinical Disorders (2009), Integrative Medicine and Functional Medicine for Chronic Hypertension (2011), Brain Inflammation in Migraine and Fibromyalgia (2016), Mitochondrial Nutrition and Endoplasmic Reticulum Stress in Primary Care, 2nd Edition (2014), Antiviral Strategies and Immune Nutrition (2014), Mastering mTOR (2015),

Autism, Dysbiosis, and the Gut-Brain Axis (2017) and the 1200-page **Inflammation Mastery 4th Edition** (2016) also published as a two-volume set titled **Textbook of Clinical Nutrition and Functional Medicine**. "DrV" has also written approximately 100 letters and articles for professional magazines and medical journals such as *TheLancet.com*, *British Medical Journal* (BMJ: online x3, print x1), *Annals of Pharmacotherapy*, *Nutritional Perspectives* (x11), *Journal of Manipulative and Physiological Therapeutics* (JMPT), *Journal of the American Medical Association* (JAMA), *Original Internist*, *Integrative Medicine* (x4), *Holistic Primary Care*, *Alternative Therapies in Health and Medicine* (x2), *Journal of the American Osteopathic Association* (JAOA), *Dynamic Chiropractic* (x3), *Journal of Clinical Endocrinology and Metabolism*, *Current Asthma and Allergy Reports*, *Complementary Therapies in Clinical Practice*, *Nature Reviews Rheumatology, Annals of the New York Academy of Sciences,* and *Arthritis & Rheumatism*—Official Journal of the American College of Rheumatology. Dr Vasquez lectures internationally to healthcare professionals and has a consulting practice and service for doctors and patients. DrV has served as a consultant, product designer, writer and lecturer for Biotics Research Corporation since 2004. Having served on the Review Boards for *Journal of Pain Research, Autoimmune Diseases, PLOS One, Alternative Therapies in Health and Medicine, Neuropeptides*, *International Journal of Clinical Medicine, Journal of Inflammation Research, BMC Complementary and Alternative Medicine* (all PubMed/Medline indexed), *Integrated Blood Pressure Control, Journal of Biological Physics and Chemistry*, and *Journal of Naturopathic Medicine* and as the founding Editor of *Naturopathy Digest*, Dr Vasquez has recently served as Editor (2013-present) of *International Journal of Human Nutrition and Functional Medicine* and Editor (2018-2019) of *Journal of Orthomolecular Medicine*.

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[1] "Red yeast rice contains a fungus (Monascus purpureus), which was utilized in the original production of lovastatin (MEVACOR, Merck & Co, Whitehouse Station, NJ), the first marketed pharmaceutical statin, and is chemically identical to such product. Their identical properties account for the similarity in therapeutic and side effects of red yeast rice and lovastatin. The red yeast rice ingredient that blocks cholesterol production is monacolin K." Dujovne CA. Red Yeast Rice Preparations. *Am J Med*. 2017 Oct;130(10):1148-1150. doi: 10.1016/j.amjmed.2017.05.013

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*Additional articles and book excerpts have been amended to the previous publication in order to provide context and orientation to the author's main works.*

**BOOK EXCERPTS, CHAPTERS**:

- https://www.amazon.com/Dr-Alex-Vasquez/e/B00AT5764Y
- https://www.ichnfm.org/im4
- https://www.ichnfm.org/volume-1-essential-knowledge
- https://www.ichnfm.org/volume-2-inflammatory-disorders

**PDF articles**: Full-text archives of the author's articles are available per the following:

- **https://ichnfm.academia.edu/AlexVasquez (main archive/repository)**
- https://www.researchgate.net/profile/Alex_Vasquez2 (archive/repository)
- https://www.inflammationmastery.com/**reprints** (cloud-based PDF folder)
- https://www.ichnfm.org/public

**VIDEOS**: Access to public videos is available per the following:

- **Main archive: https://vimeo.com/drvasquez**
- See also: https://www.ichnfm.org/public
- And to a lesser extent: https://www.youtube.com/channel/UCPR2pgwFw9L2GUnBgupQ5Aw

**WEBSITES**:

- **Main: https://www.inflammationmastery.com/**
  - Antiviral: https://www.inflammationmastery.com/**antiviral**
  - Fibromyalgia: https://www.inflammationmastery.com/**fibromyalgia**
  - Migraine: https://www.inflammationmastery.com/**migraine**
  - Complete protocol: https://www.inflammationmastery.com/**book-nutrition-functional-medicine**
- **Main: https://www.ichnfm.org/ This is actually a very rich website with many blogs and videos**
  - https://www.ichnfm.org/antiviral2019 and the long series starting with https://www.ichnfm.org/**antiviral**, https://www.ichnfm.org/antiviral2, https://www.ichnfm.org/antiviral3, https://www.ichnfm.org/antiviral4, and continuing…
  - https://www.ichnfm.org/**braininflammation**

**SOCIAL MEDIA UPDATES**: Note that updates are made on a regular basis to the following social medial pages, with some overlap but also some topic-specific specialization, which is self-explanatory by the titles of these pages:

- **Dr Alex Vasquez 's Inflammation Mastery https://www.facebook.com/InflammationMastery**
- Migraine Headaches, Hypothyroidism, and Fibromyalgia https://www.facebook.com/MigraineHypothyroidismFibromyalgia
- International Journal of Human Nutrition and Functional Medicine https://www.facebook.com/IJHNFM
- International College of Human Nutrition and Functional Medicine (higher quality and academic news) https://www.facebook.com/IntCollHumNutrFunctMed
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# Inflammation Mastery

## 4th Edition

Clinical Nutrition, Functional Medicine, Mitochondrial Dysfunction, Microbiome & Dysbiosis, Functional Inflammology, Pain Management, Integrative Rheumatology, Nutritional Immunomodulation, Immunonutrition & Antiviral Strategies

The Colorful and Definitive Guide Toward Health and Vitality
*and away from* the Boredom, Risks, Costs, and Inefficacy of
Endless Analgesia, Immunosuppression, and Polypharmacy

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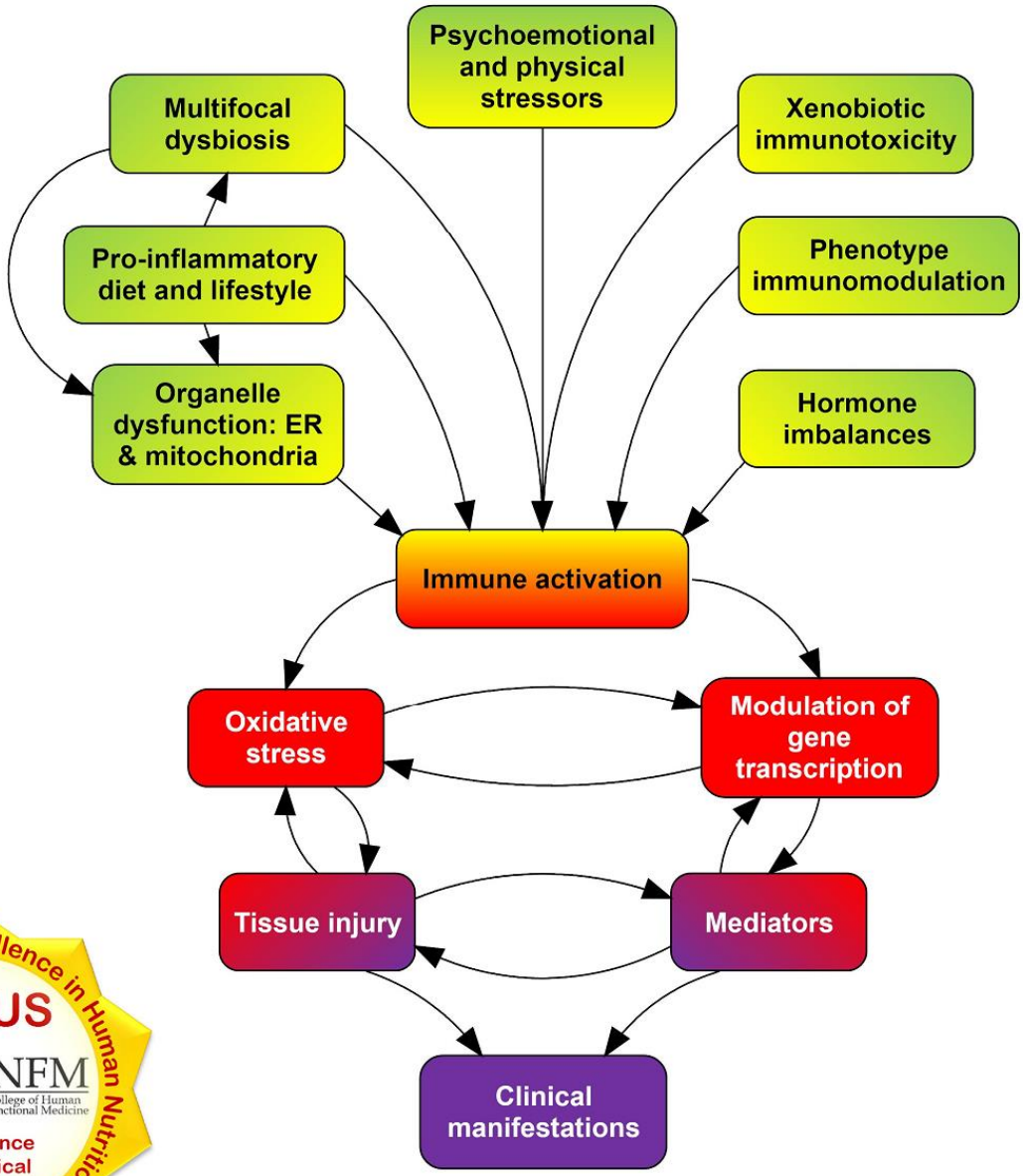




**Dr. Alex Vasquez**

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International College of Human Nutrition and Functional Medicine

# INFLAMMATION MASTERY

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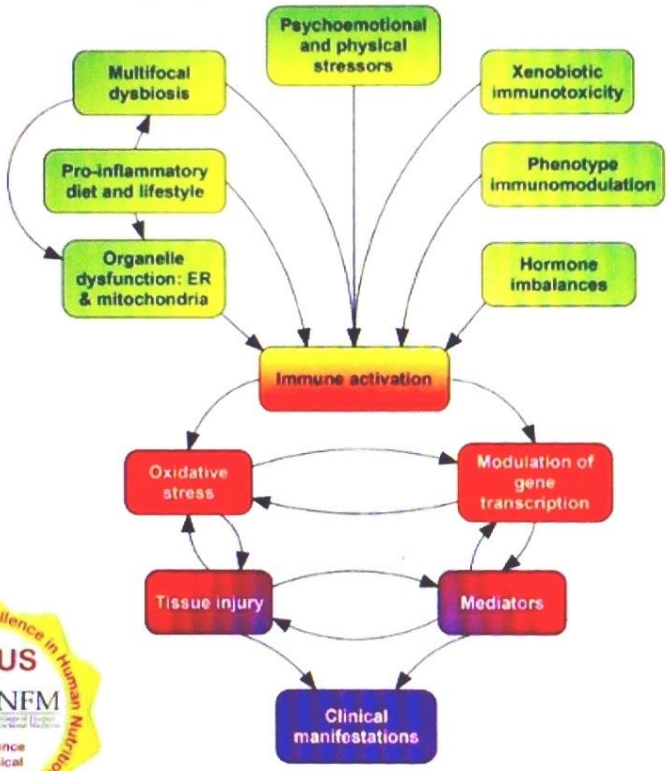


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5) Special Considerations: Sleep, Sociopsychology, Stress, Surgery
6) Endocrine Imbalances
7) Xenobiotic Immunotoxicity

**Volume 2**: Chapter 5—Clinical Applications of the Functional Inflammology Protocol

1) Hypertension
2) Diabetes Mellitus
3) Migraine & Headaches
4) Fibromyalgia
5) Allergic Inflammation
6) Rheumatoid Arthritis
7) Psoriasis and Psoriatic Arthritis
8) Systemic Lupus Erythematosus
9) Scleroderma & Systemic Sclerosis
10) Vasculitic Diseases
11) Spondyloarthropathies & Reactive Arthritis
12) Sjögren Syndrome/Disease
13) Raynaud's Syndrome/Phenomenon/Disorder

# Chapter 4:
# Introduction to DrV's Functional Inflammology Protocol: The Seven Major Modifiable Factors in Systemic Inflammation, Allergy, and Autoimmunity

**Major Modifiable Influences on Immune and Inflammatory Balance**

This section reviews clinically-relevant information related to the pathogenesis and etiology of inflammatory/allergic/autoimmune conditions. Following extensive reviews of the research literature in conjunction with the author's impressively successful clinical experience with patients with "idiopathic" and inflammatory/autoimmune disorders, the original version of this information was published in the first edition of *Integrative Rheumatology* (2006). This section is a distillation of thousands of research articles, abstracts, seminar notes, conversations with colleagues, one-on-one patient encounters and the author's own considerations and reflections.

Following my review and perusal of thousands of research articles in addition to the attentive application of my interest in these conditions throughout three doctoral programs, I have come to appreciate seven major modifiable factors that are chiefly relevant for the initial and long-term management of patients with inflammatory conditions and rheumatic diseases. These 7 factors are:

1. Food intake and nutritional status: The pro/anti-inflammatory effects of diet, including food allergies and intolerances, nutrient deficiencies and dependencies,
2. Infections and dysbiosis: Chronic exposure to microbial effectors/effects,
3. Nutritional modulation of the immune system: Nutrigenomic modification of immunocyte phenotype,
4. Dysmetabolism and Dysfunctional organelles, most notably mitochondria: Especially the pro-inflammatory, pro-oxidant, and anti-apoptotic consequences of dysfunctional mitochondria (DysMito or MitoDys); more recently the conversation has extended beyond mitochondrial dysfunction to include endoplasmic reticulum stress/dysfunction (ERS) and resultant unfolded protein response (UPR),
5. Stress, sleep deprivation vs sleep sufficiency, spinal health, social and psychological considerations: Included in this section is a collection of important considerations which—in the first draft of this acronym—started with stress management, sleep hygiene, and pSychological and social factors. Later versions have included spinal health (chiropractic model), somatic dysfunction (osteopathic model), surgery, specialized supplementation, and "stamp your passport"—sometimes we all just need to vacate for a while and implement some *geographic cure* for the sake of inspiration, life enhancement, exposure to new ideas and lifestyles, and the breaking of (dysfunctional) thought patterns and routines,
6. Endocrine imbalances: Hormones can promote or retard the genesis and perpetuation of inflammation/allergy/autoimmunity; therapeutic correction with prescription or nonprescription interventions can have a profound anti-inflammatory benefit.
7. Xenobiotic immunotoxicity: Exposure to and accumulation of toxic chemicals and/or toxic metals can alter immune responses toward allergy and autoimmunity and away from immunosurveillance against infections and cancer.

Common diseases such as psoriasis and rheumatoid arthritis are greater public health concerns and are more commonly encountered in clinical practice than are the more rare conditions; proportionate mention is made in the following section. Importantly, readers should appreciate that the information in various sections likely applies either conceptually or specifically to conditions described in other sections and that therefore the best way to understand inflammatory/allergic/autoimmune disorders in their totality is to appreciate the nuances of each and the common themes among all.

I am quite pleased to see that the original five variables that I defined in the first two editions of *Integrative Rheumatology* (2006, 2007) have stood the tests of time, science, and clinical practice: in fact, all have been strengthened in the intervening years.

**Affirmation and consistency of common themes in an interconnected reality; the importance of transitioning from reception to comprehension to conception to behavior**

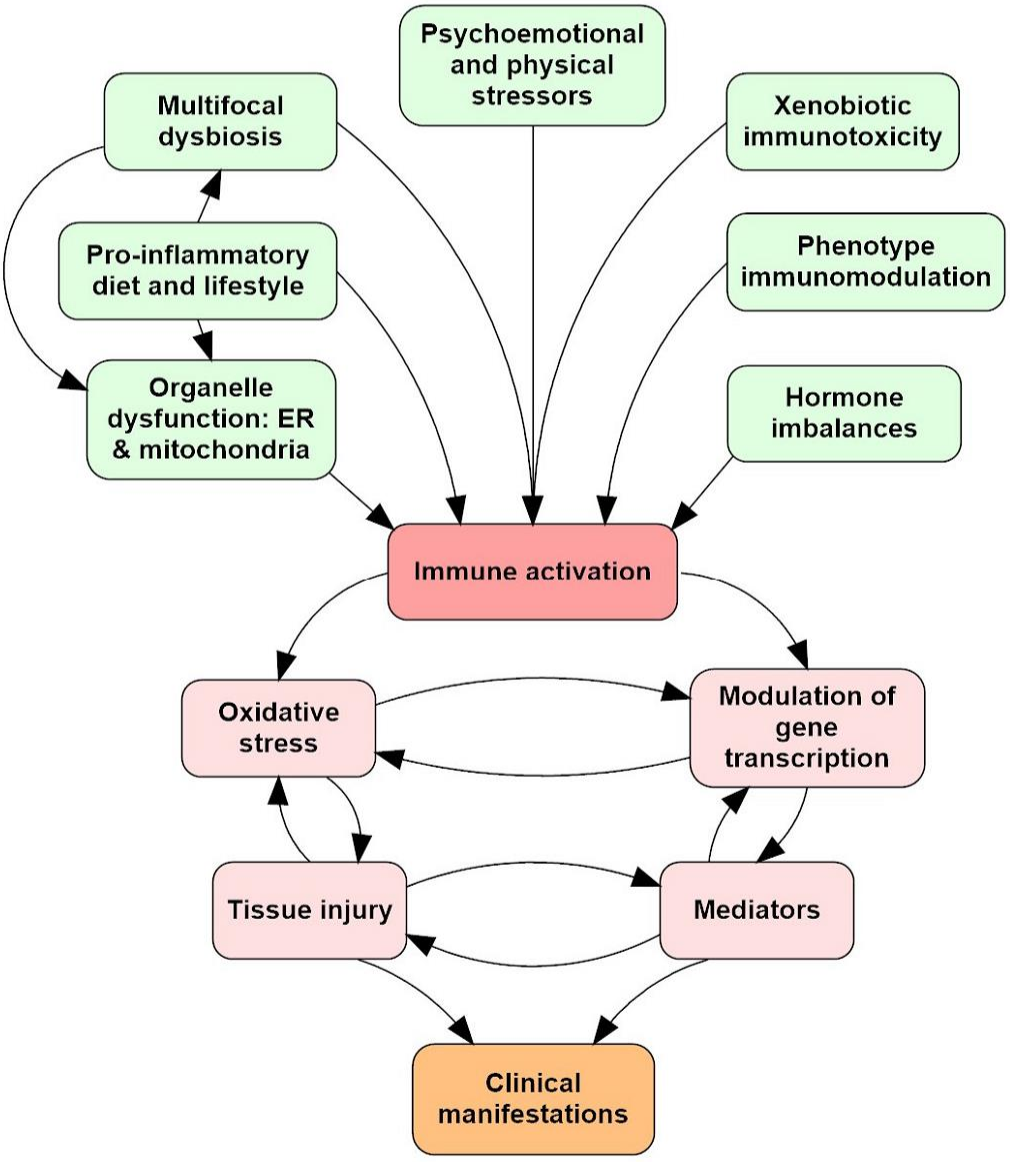
"The fact that today I still stand by these ideas, **that in the intervening time they themselves have constantly become more strongly associated with one another, even to the point of growing into each other, intertwining, and becoming *one***, that has reinforced in me the joyful confidence that they may not have originally developed in me as single, random, or sporadic ideas, but up out of common roots, from some fundamental *will for knowledge* ruling from deep within, always speaking with greater clarity, always demanding greater clarity.

In fact, this is the only thing appropriate and proper for a philosopher. **We have no right to be isolated in any way: we are not permitted to make isolated mistakes or to run into isolated truths**. Our ideas, our values, our affirmations and denials, our *if*s and *but*s—these rather grow out of us from the same necessity which makes a tree bear its fruit—totally related and interlinked amongst each other: witnesses of one will, one health, one soil, one sun."

Nietzsche FW. *On the Genealogy of Morals*, 1887, Preface essay #2

"In order for a particular species to maintain itself and increase its power, **its conception of reality must comprehend enough of the calculable and constant** for it to **base a scheme of behavior on it**."

Nietzsche FW. *Will to Power*,1901, #480




**Inflammation in a simple cause-and-effect diagram**: The major causative factors amenable to clinical implementation are represented, along with the pathophysiologic consequences and clinical effects. Molecular details, clinical assessments, and therapeutic interventions are introduced/reviewed in this chapter; in later volumes of this work, clinical protocols detail the drugs and doses, etc.

# ❶ Food: Diet and Basic Nutritional Supplementation

**Major Concepts in this Section**

"Food" is the first part of the protocol and the foundation of the overall plan, not simply for improving nutritional status, but for setting the biochemical stage for more profound improvements in immune balance, mitochondrial function, et al. Patients can and should appreciate that they have near complete control over what they consume; unfortunately and conversely, however, in countries such as the United States where much of the food supply is contaminated with pesticide residues and genetically manipulated food-type (GMO) products, consuming a health-promoting diet can present unique challenges.

Contents of this section:



## Introduction to Nutrigenomics: Pro-Inflammatory and Anti-Inflammatory Effects of Foods and Nutrients

We must look beyond the nutritional properties of foods to appreciate that dietary patterns and the consumption of specific foods can influence genetic expression and either promote or retard the development of inflammation and related clinical disorders. The purpose of this section is to help clinicians attain a more profound understanding of the value of nutrition and its critical role as a foundational component in the treatment plan of patients with inflammatory disorders. The "correct" diet for the vast majority of patients with inflammatory disorders is the "supplemented Paleo-Mediterranean diet" which I have described in several other publications. The diet is modified for the specific exclusion of allergenic foods; it is implemented on a rotation basis, and it allows for periodic fasting and vegetarianism/veganism. The implementation of health-promoting dietary modifications is an *absolutely mandatory* component of the treatment plan, upon which other treatments depend for their success. The study of how dietary components and nutritional supplements influence genetic expression is referred to as *nutrigenomics* or *nutritional genomics* and has been described as "the next frontier in the postgenomic era."[7] Various nutrients have been shown to modulate genetic expression and thus alter phenotypic manifestations of disease by upregulating or downregulating specific genes, interacting with nuclear receptors, altering hormone receptors, and modifying the influence of transcription factors, such as pro-inflammatory NFkB (NFkB) and the anti-inflammatory peroxisome-proliferator activated receptors (PPARs).[8,9,10,11] **The previous view that nutrients only interact with human physiology at the metabolic/post-transcriptional level must be updated in light of current research showing that nutrients can, in fact, modify human physiology and phenotype at the genetic/pre-transcriptional**

[7] Kaput J, Rodriguez RL. Nutritional genomics: the next frontier in the postgenomic era. *Physiol Genomics*. 2004 Jan 15;16(2):166-77. Very important article.
[8] Vamecq J, Latruffe N. Medical significance of peroxisome proliferator-activated receptors. *Lancet*. 1999;354:141-8
[9] Ehrmann et al. Peroxisome proliferator-activated receptors (PPARs) in health and disease. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2002 Dec;146(2):11-4
[10] Kliewer SA, Xu HE, Lambert MH, Willson TM. Peroxisome proliferator-activated receptors: from genes to physiology. *Recent Prog Horm Res*. 2001;56:239-63
[11] Delerive P, Fruchart JC, Staels B. Peroxisome proliferator-activated receptors in inflammation control. *J Endocrinol*. 2001;169(3):453-9

**level**. Fatty acids and their *eicosanoid*, *leukotriene*, and *isoprostane* intermediates and end-products modulate genetic expression in several ways. In general, n-3 fatty acids decrease inflammation and promote health while n-6 fatty acids (except for GLA, which is generally health-promoting) increase inflammation, oxidative stress, and the manifestation of disease. Corn oil, probably as a result of its high n-6 LA (linoleic acid) content, rapidly activates NFkB and thus promotes tumor development, atherosclerosis, and elaboration of proinflammatory mediators such as TNFa.[12,13,14] Similarly n-6 arachidonic acid increases production of the free radical *superoxide* approximately 4-fold when added to isolated Kupffer cells *in vitro*. Prostaglandin-E2 is produced from arachidonic acid by cyclooxygenase and increases genetic expression of cyclooxygenase and IL-6; thus, an increase in PG-E2 leads to additive expression of cyclooxygenase, which further increases inflammation and elevates C-reactive protein.[15] Some of the unique health-promoting effects of GLA are nutrigenomically mediated via activation of PPAR-gamma, resultant inhibition of NFkB, and impairment of estrogen receptor function.[16,17] Supplementation with ALA leads to a dramatic reduction of prostaglandin formation in humans[18], and this effect is probably mediated by downregulation of proinflammatory gene transcription, as evidenced by reductions in CRP, IL-6, and serum amyloid A.[19] EPA appears to exert much of its anti-inflammatory benefit by suppressing NFkB activation and thus reducing elaboration of proinflammatory mediators.[20,21] EPA also indirectly modifies gene expression and cell growth by reducing intracellular calcium levels and thus activating protein kinase R which impairs eukaryotic initiation factor-2alpha and inhibits protein synthesis at the level of translation initiation, thereby mediating an anti-cancer benefit.[22] DHA is the precursor to docosatrienes and resolvins which downregulate gene expression for IL-1, inhibit TNFa, and reduce neutrophil entry to sites of inflammation.[23] Oxidized EPA activates PPAR-alpha and thereby suppresses NFkB.[24,25] Other nutrients that inhibit the activation of NFkB include vitamin D[26,27], lipoic acid[28], green tea[29], rosemary[30], grape seed extract[31], resveratrol[32,33], caffeic acid phenethyl ester (CAPE) from bee propolis[34], indole-3-carbinol[35], N-acetyl-L-cysteine[36], selenium[37], and zinc.[38] Therefore, we see that fatty acids and nutrients

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[12] Rusyn I, et al. Corn oil rapidly activates nuclear factor-kappaB in hepatic Kupffer cells by oxidant-dependent mechanisms. *Carcinogenesis*. 1999 Nov;20(11):2095-100

[13] Rose DP, et al. Effect of diets containing different levels of linoleic acid on human breast cancer growth and lung metastasis in nude mice. *Cancer Res* 1993;53:4686-90

[14] Dichtl et al. Linoleic acid-stimulated vascular adhesion molecule-1 expression in endothelial cells depends on nuclear factor-kappaB. *Metabolism* 2002;51:327-33

[15] Bagga et al. Differential effects of prostaglandin from n-6 and n-3 polyunsaturated fatty acids on COX-2 expression and IL-6 secretion. *Proc Natl Acad Sci*. 2003 Feb:1751-6.

[16] Menendez JA, Colomer R, Lupu R. Omega-6 polyunsaturated fatty acid gamma-linolenic acid (18:3n-6) is a selective estrogen-response modulator in human breast cancer cells: gamma-linolenic acid antagonizes estrogen receptor-dependent transcriptional activity, transcriptionally represses estrogen receptor expression and synergistically enhances tamoxifen and ICI 182,780 (Faslodex) efficacy in human breast cancer cells. *Int J Cancer*. 2004 May 10;109(6):949-54

[17] Jiang WG, Redfern A, Bryce RP, Mansel RE. Peroxisome proliferator activated receptor-gamma (PPAR-gamma) mediates the action of gamma linolenic acid in breast cancer cells. *Prostaglandins Leukot Essent Fatty Acids*. 2000 Feb;62(2):119-27

[18] Adam O, et al. Effect of alpha-linolenic acid in the human diet on linoleic acid metabolism and prostaglandin biosynthesis. *J Lipid Res*. 1986 Apr;27(4):421-6

[19] Rallidis et al. Dietary alpha-linolenic acid decreases C-reactive protein, serum amyloid A and interleukin-6 in dyslipidaemic patients. *Atherosclerosis*. 2003;167:237-42

[20] Zhao et al. Eicosapentaenoic acid prevents LPS-induced TNF-alpha expression by preventing NFkB activation. *J Am Coll Nutr*. 2004 Feb;23(1):71-8

[21] Mishra et al. Oxidized omega-3 fatty acids inhibit NFkB activation via a PPARalpha-dependent pathway. *Arterioscler Thromb Vasc Biol*. 2004 Sep;24:1621-7

[22] Palakurthi et al. Inhibition of translation initiation mediates the anti-cancer effect of the n-3 polyunsaturated fatty acid EPA. *Cancer Res*. 2000 Jun 1;60(11):2919-25

[23] "These results indicate that DHA is the precursor to potent protective mediators generated via enzymatic oxygenations to novel docosatrienes and 17S series resolvins that each regulate events of interest in inflammation and resolution." Hong S, Gronert K, Devchand PR, Moussignac RL, Serhan CN. Novel docosatrienes and 17S-resolvins generated from docosahexaenoic acid in murine brain, human blood, and glial cells. Autacoids in anti-inflammation. *J Biol Chem*. 2003 Apr 25;278(17):14677-87

[24] Mishra et al. Oxidized omega-3 fatty acids inhibit NFkB activation via a PPARalpha-dependent pathway. *Arterioscler Thromb Vasc Biol*. 2004 Sep;24:1621-7

[25] Delerive P, Fruchart JC, Staels B. Peroxisome proliferator-activated receptors in inflammation control. *J Endocrinol*. 2001;169(3):453-9

[26] "1Alpha,25-dihydroxyvitamin D3 (1,25-(OH)2-D3), the active metabolite of vitamin D, can inhibit NFkB activity in human MRC-5 fibroblasts, targeting DNA binding of NFkB ..." Harant et al. 1Alpha,25-dihydroxyvitamin D3 decreases DNA binding of nuclear factor-kappaB in human fibroblasts. *FEBS Lett*. 1998 Oct 9;436(3):329-34

[27] "Thus, 1,25(OH)2D3 may negatively regulate IL-12 production by downregulation of NF-kB activation and binding to the p40-kB sequence." D'Ambrosio D, et al. Inhibition of IL-12 production by 1,25-dihydroxyvitamin D3. Involvement of NFkB downregulation. *J Clin Invest*. 1998 Jan 1;101(1):252-62

[28] "ALA reduced TNF-alpha-stimulated ICAM-1 expression in a dose-dependent manner, to levels observed in unstimulated cells. Alpha-lipoic acid also reduced NFkB activity in a dose-dependent manner." Lee et al. Alpha-lipoic acid modulates NFkB activity in human monocytic cells by direct interaction with DNA. *Exp Gerontol*. 2002 Jan:401-10

[29] "In conclusion, EGCG is an effective inhibitor of IKK activity. This may explain, at least in part, some of the reported anti-inflammatory and anti-cancer effects of green tea." Yang et al. The green tea polyphenol (-)-epigallocatechin-3-gallate blocks nuclear factor-kappa B activation by inhibiting I kappa B kinase activity in the intestinal epithelial cell line IEC-6. *Mol Pharmacol*. 2001 Sep;60(3):528-33

[30] "These results suggest that carnosol suppresses the NO production and iNOS gene expression by inhibiting NFkB activation, and provide possible mechanisms for its anti-inflammatory and chemopreventive action." Lo AH, Liang YC, Lin-Shiau SY, Ho CT, Lin JK. Carnosol, an antioxidant in rosemary, suppresses inducible nitric oxide synthase through down-regulating nuclear factor-kappaB in mouse macrophages. *Carcinogenesis*. 2002 Jun;23(6):983-91

[31] "Constitutive and TNFalpha-induced NFkB DNA binding activity was inhibited by GSE at doses > or =50 microg/ml and treatments for > or =12 h." Dhanalakshmi et al. Inhibition of NFkB pathway in grape seed extract-induced apoptotic death of human prostate carcinoma DU145 cells. *Int J Oncol*. 2003 Sep;23(3):721-7

[32] "Resveratrol's anticarcinogenic, anti-inflammatory, and growth-modulatory effects may thus be partially ascribed to the inhibition of activation of NFkB and AP-1 and the associated kinases." Manna SK, Mukhopadhyay A, Aggarwal BB. Resveratrol suppresses TNF-induced activation of nuclear transcription factors NF-kappa B, activator protein-1, and apoptosis: potential role of reactive oxygen intermediates and lipid peroxidation. *J Immunol*. 2000 Jun 15;164(12):6509-19

[33] "Both resveratrol and quercetin inhibited NFkB-, AP-1- and CREB-dependent transcription to a greater extent than the glucocorticosteroid, dexamethasone." Donnelly LE, et al. Anti-inflammatory Effects of Resveratrol in Lung Epithelial Cells. *Am J Physiol Lung Cell Mol Physiol*. 2004 Oct;287(4):L774-83

[34] "Caffeic acid phenethyl ester (CAPE) is an anti-inflammatory component of propolis (honeybee resin). CAPE is reportedly a specific inhibitor of nuclear factor-kappaB (NFkB)." Fitzpatrick LR, Wang J, Le T. Caffeic acid phenethyl ester, an inhibitor of nuclear factor-kappaB, attenuates bacterial peptidoglycan polysaccharide-induced colitis in rats. *J Pharmacol Exp Ther*. 2001 Dec;299(3):915-20

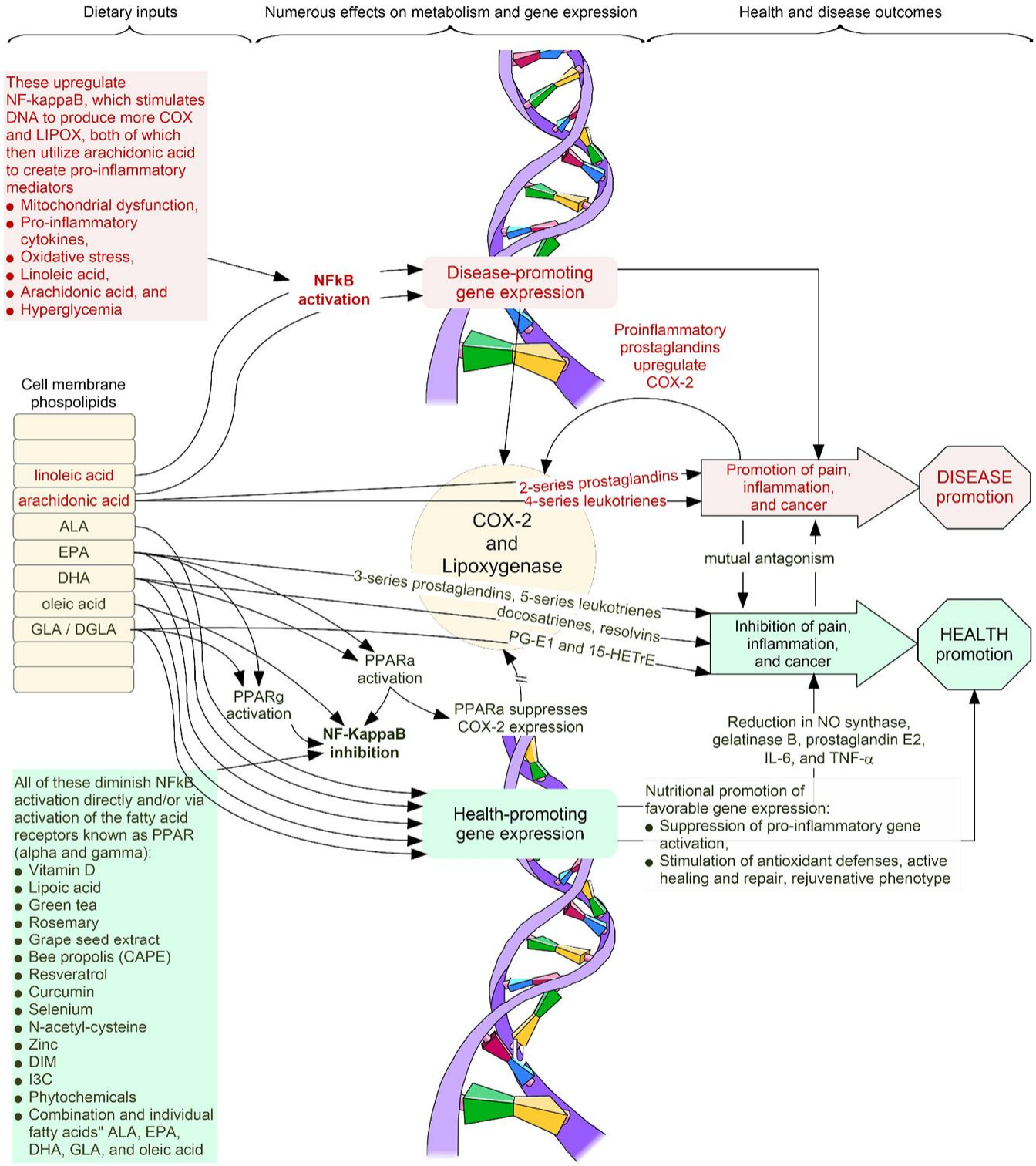
[35] Takada Y, Andreeff M, Aggarwal BB. Indole-3-carbinol suppresses NF-{kappa}B and I{kappa}B{alpha} kinase activation causing inhibition of expression of NF-{kappa}B-regulated antiapoptotic and metastatic gene products and enhancement of apoptosis in myeloid and leukemia cells. *Blood*. 2005 Apr 5; [Epub ahead of print]

[36] Paterson RL, Galley HF, Webster NR. The effect of N-acetylcysteine on nuclear factor-kappa B activation, interleukin-6, interleukin-8, and intercellular adhesion molecule-1 expression in patients with sepsis. *Crit Care Med*. 2003 Nov;31(11):2574-8

[37] Faure et al. Selenium supplementation decreases nuclear factor-kappa B activity in blood mononuclear cells from type 2 diabetic patients. *Eur J Clin Invest*. 2004;34(7):475-81

[38] Uzzo et al. Zinc inhibits nuclear factor-kappa B activation and sensitizes prostate cancer cells to cytotoxic agents. *Clin Cancer Res*. 2002;8(11):3579-83

directly affect gene expression by complex and multiple mechanisms, as graphically illustrated in the accompanying diagram, and the synergism and potency of these anti-inflammatory nutraceuticals supports the rationale for the use of nutrition and select botanicals for the safe and effective treatment of inflammatory disorders.




**Schematic Representation of Simultaneous Nutrigenomic and Metabolic Effects of Nutrients**: Although conceptually accurate, this diagram is highly simplified and not all-inclusive; rather, this diagram focuses exclusively on nutrients that affect the NFkB pathway. Updated from Vasquez 2005.[39]

[39] Vasquez A. New Insights into Fatty Acid Supplementation and Its Effect on Eicosanoid Production and Genetic Expression. *Nutritional Perspectives* 2005; Jan: 5-16

## A Five-Part Nutritional Wellness Protocol That Produces Consistently Positive Results: Brief Review of Scientific Rationale

This article was originally published in *Nutritional Wellness*
nutritionalwellness.com/archives/2005/sep/09_vasquez.php

**Introduction**: When I am lecturing here in the U.S., as well as in Europe, doctors often ask if I will share the details of my protocols with them. Thus, in 2004, I published a 486-page textbook for doctors that includes several protocols and important concepts for the promotion of wellness and treatment of musculoskeletal disorders.[40] In this article, I will share with you what I consider a basic protocol for wellness promotion. I've implemented this protocol as part of the treatment plan for a wide range of clinical problems. In my next column, I will provide several case reports of patients from my office to exemplify the effectiveness of this program and show how it can be the foundation upon which additional treatments can be added as necessary.

Nutrients are required in the proper amounts, forms, and approximate ratios for essential physiologic function; if nutrients are lacking, the body cannot function normally, let alone optimally. Impaired function results in subjective and objective manifestations of what is commonly labeled as "disease." Thus, a powerful and effective alternative to treating diseases with drugs is to re-establish normal/optimal physiologic function by replenishing the body with essential nutrients.

Of course, many diseases are multifactorial and therefore require multicomponent treatment plans, and some diseases actually require the use of drugs. However, while only a relatively small portion of patients actually need drugs for their problems, I am sure we all agree that everyone needs a foundational nutrition plan, as outlined and substantiated below.

1. Health-promoting diet: Following an extensive review of the research literature, I developed what I call the "supplemented Paleo-Mediterranean diet," which I have described in greater detail elsewhere.[41] In essence, this diet plan combines the best of the Mediterranean diet with the best of the Paleolithic diet, the latter of which has been detailed and popularized by Dr. Loren Cordain in his book, *The Paleo Diet*, and his numerous scientific articles.[42] This diet places emphasis on fruits, vegetables, nuts, seeds, and berries that meet the body's needs for fiber, carbohydrates, and most importantly, the 8,000+ phytonutrients that have additive and synergistic health benefits.[43] Preferred protein sources are lean meats such as fish and poultry. In contrast to Cordain's Paleo diet, I also advocate soy and whey for their high-quality protein and anticancer, cardioprotective, and mood-enhancing benefits. Rice and potatoes are discouraged due to their relatively high glycemic indexes and high glycemic loads, and their lack of fiber and phytonutrients (compared to other fruits and vegetables). Generally speaking, grains such as barley, rye, and wheat (e.g., the "toxic triad" of inflammatory gluten) are discouraged due to the high glycemic loads/indexes of most breads and pastries, as well as the allergenicity/immunogenicity of gluten, a protein that appears to help trigger disorders such as migraine, celiac disease, psoriasis, epilepsy, and autoimmunity. Sources of simple sugars such as high-fructose corn syrup (e.g., cola, soda) and processed foods (e.g., "TV dinners" and other manufactured snacks and convenience foods) are strictly forbidden. Chemical preservatives, colorants, sweeteners and carrageenan are likewise prohibited. In summary, this diet plan provides plenty of variety, as most dishes comprised of poultry, fish, soy, fruits, vegetables, nuts, berries, and seeds are allowed. The diet also provides plenty of fiber, phytonutrients, carbohydrates, potassium, and protein, while simultaneously being low in fat, sodium, arachidonic acid, and "simple sugars." The diet must be customized with regard to total protein and calorie intake, as determined by the size, status, and activity level of the patient, and individual food allergens should be avoided. Regular consumption of this diet has shown the ability to reduce hypertension, alleviate diabetes, ameliorate migraine headaches, and result in improvement of overall health and a lessening of the severity of many common "diseases." This diet is supplemented with vitamins, minerals, and fatty acids as described below.
2. Multivitamin and multimineral supplementation: Vitamin and mineral supplementation finally received endorsement from "mainstream" medicine when researchers from Harvard Medical School published a review

[40] Vasquez A. *Integrative Orthopedics: The Art of Creating Wellness While Managing Acute and Chronic Musculoskeletal Disorders*. 2004, 2007, 2012
[41] Vasquez A. The Importance of Integrative Chiropractic Health Care in Treating Musculoskeletal Pain and Reducing the Nationwide Burden of Medical Expenses and Iatrogenic Injury and Death: Concise Review of Current Research and Implications for Clinical Practice and Healthcare Policy. *The Original Internist* 2005; 12(4): 159-182
[42] Cordain L. *The Paleo Diet*. (John Wiley and Sons, 2002). Also: Cordain L. Cereal grains: humanity's double edged sword. *World Rev Nutr Diet* 1999;84:19-73 Access to most of Dr Cordain's articles is available at thepaleodiet.com/
[43] Liu RH. Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *Am J Clin Nutr* 2003;78(3 Suppl):517S-520S

article in *Journal of the American Medical Association* that concluded, "Most people do not consume an optimal amount of all vitamins by diet alone. ...It appears prudent for all adults to take vitamin supplements."[44] Long-term nutritional insufficiencies experienced by the majority of the population promote the development of "long-latency deficiency diseases" such as cancer, neuroemotional deterioration, and cardiovascular disease.[45] Impressively, the benefits of multivitamin/multimineral supplementation have been demonstrated in numerous clinical trials. Multivitamin/multimineral supplementation has been shown to improve nutritional status and reduce the risk for chronic diseases[46], improve mood[47], potentiate antidepressant drug treatment[48], alleviate migraine headaches (when used with diet improvement and fatty acids[49]), improve immune function and infectious disease outcomes in the elderly[50] (especially diabetics[51]), reduce morbidity and mortality in patients with HIV infection[52,53] alleviate premenstrual syndrome[54,55] and bipolar disorder[56], reduce violence and antisocial behavior in children[57] and incarcerated young adults (when used with essential fatty acids[58]), and improve scores of intelligence in children.[59] Vitamin supplementation has anti-inflammatory benefits, as evidenced by significant reduction in C-reactive protein, (CRP) in a double-blind, placebo-controlled trial.[60] The ability to safely and affordably deliver these benefits makes multimineral-multivitamin supplementation and essential component of any and all health-promoting and disease-prevention strategies. Vitamin A can result in liver damage with chronic consumption of 25,000 IU or more, and intake should generally not exceed 10,000 IU per day in women of childbearing age. Iron should not be supplemented except in patients diagnosed with iron deficiency by the blood test ferritin. Additional vitamin D should be used, as described in the next section.

3. Physiologic doses of vitamin D3: The prevalence of vitamin D deficiency varies from 40 percent (general population) to almost 100 percent (patients with musculoskeletal pain) in the American population. I described the many benefits of vitamin D3 supplementation in the previous issue of *Nutritional Wellness* and in the major monograph published in 2004.[61] In summary, vitamin D deficiency causes or contributes to depression, hypertension, seizures, migraine, polycystic ovary syndrome, inflammation, autoimmunity, and musculoskeletal pain such as low-back pain. Clinical trials using vitamin D supplementation have proven the cause-and-effect relationship between vitamin D deficiency and these conditions by showing that each of these could be cured or alleviated with vitamin D supplementation. In our review of the literature, we concluded that daily vitamin D doses should be 1,000 IU for infants, 2,000 IU for children, and 4,000 IU for adults. Cautions and contraindications include the use of thiazide diuretics (e.g., hydrochlorothiazide) or any other medications that can promote hypercalcemia, as well as granulomatous diseases such as sarcoidosis, tuberculosis, and certain types of cancer, especially lymphoma. Effectiveness is monitored by measuring serum 25-OH-vitamin D, and safety is monitored by measuring serum calcium.
4. Balanced and complete fatty acid supplementation: A detailed survey of the literature reveals five major health-promoting anti-inflammatory fatty acids found in the human diet.[62] These are alpha-linolenic acid (ALA; omega-3, from flaxseed oil), eicosapentaenoic acid (EPA; omega-3, from fish oil), docosahexaenoic acid (DHA; omega-3, from fish oil and algae), gamma-linolenic acid (GLA; omega-6, most concentrated in borage oil), and oleic acid (omega-9, mainly from olive oil, also found in flaxseed and borage oils). Each of these fatty acids has health benefits that cannot be fully attained from supplementing a different fatty acid. The benefits of GLA

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(borage oil) are not attained by consumption of EPA and DHA (fish oil); in fact, consumption of fish oil can actually promote a deficiency of GLA.[63] Likewise, consumption of GLA alone can reduce EPA levels while increasing levels of proinflammatory arachidonic acid; both of these problems are avoided with co-administration of fish oil any time borage oil is used. Using ALA (flaxseed oil) alone only slightly increases EPA but generally leads to no improvement in DHA status and can lead to a reduction of oleic acid; thus, fish oil, olive oil (and borage oil) should be supplemented when flaxseed oil is used.[64] Obviously, the goal here is a balanced intake of all of the health-promoting fatty acids; using only one or two sources of fatty acids is not balanced and results in suboptimal improvement, at best. In clinical practice, I routinely use combination fatty acid therapy comprised of ALA, EPA, DHA, and GLA for essentially all patients. The product also contains a modest amount of oleic acid, and I encourage use of olive oil for salads and cooking. This approach results in complete and balanced fatty acid intake, and the clinical benefits are impressive.

5. Probiotics /gut flora modification: Proper levels of good bacteria promote intestinal health, proper immune function, and support overall health. Excess bacteria or yeast, or the presence of harmful bacteria, yeast, or "parasites" such as amoebas and protozoans, can cause "leaky gut," systemic inflammation, and a wide range of clinical problems. Intestinal flora can become imbalanced by poor diets, excess stress, immunosuppressive drugs, antibiotics, or exposure to contaminated food or water, all of which are common among American patients. Thus, as a rule, I reinstate the good bacteria by the use of probiotics (good bacteria and yeast), prebiotics (fiber, arabinogalactan, and inulin), and the use of fermented foods such as kefir (in patients not allergic to milk). Harmful yeast, bacteria, and other "parasites" can be eradicated with the combination of dietary change, drugs, and/or herbal extracts. For example, oregano oil in an emulsified, time-released form has proven safe and effective for the elimination of various parasites encountered in clinical practice.[65] Likewise, the herb *Artemisia annua* (sweet wormwood) commonly is used to eradicate specific bacteria and has been used for thousands of years in Asia for the treatment and prevention of infectious diseases, including malaria.[66]

**Conclusion**: In this brief review, I have outlined and scientifically substantiated a fundamental protocol that can serve as effective therapy for patients with a wide range of "diseases." Customizing the Paleo-Mediterranean diet to avoid food allergens, using vitamin-mineral supplements along with physiologic doses of vitamin D and broad-spectrum balanced fatty acid supplementation, and ensuring gastrointestinal health with the skillful use of probiotics, prebiotics, and antimicrobial treatments provides an excellent health-promoting and disease-eliminating foundation and lifestyle for many patients. Often, this simple protocol is all that is needed for the effective treatment of a wide range of clinical problems. For other patients with more complex illnesses, of course, additional interventions and laboratory assessments can be used to customize the treatment plan. However, we must always remember that the attainment and preservation of health requires that we meet the body's basic nutritional needs. This five-step protocol begins the process of meeting those needs. In my next article, I'll give you some examples from my clinical practice and additional references to show this protocol's safety and effectiveness.

**Ayurvedic proverb**

"When the diet is wrong,
medicine is of no use.
When the diet is correct,
medicine is of no need."

## Implementing the Five-Part Nutritional Wellness Protocol for the Treatment of Various Health Problems

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nutritionalwellness.com/archives/2005/nov/11_vasquez.php

**Introduction**: In my last article in *Nutritional Wellness* I described a 5-part nutritional protocol that can be used in the vast majority of patients without adverse effects and with major benefits. For many patients, the basic protocol consisting of 1) the Paleo-Mediterranean diet, 2) multivitamin/multimineral supplementation, 3) additional vitamin D3, 4) combination fatty acid therapy with an optimal balance of ALA, GLA, EPA, DHA, and oleic acid, and 5) probiotics (including the identification and eradication of harmful yeast, bacteria, and other "parasites") is all the

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treatment that they need. For patients who need additional treatment, this foundational plan still serves as the core of the biochemical aspect of their intervention. Of course, in some cases, we have to use other lifestyle modifications (such as exercise), additional supplements (such as policosanol or antimicrobial herbs), manual treatments (including spinal manipulation) and occasionally select medications (such has hormone modulators) to obtain our goal of maximum improvement.

The following examples show how the 5-part protocol serves to benefit patients with a wide range of conditions. For the sake of saving space, I will use only highly specific citations to the research literature, since I have provided the other references in the previous issue of *Nutritional Wellness* and elsewhere.[67]

- A Man with High Cholesterol: This patient is a 41-year-old slightly overweight man with very high cholesterol. His total cholesterol was 290 (normal < 200), LDL cholesterol was 212 (normal <130), and his triglycerides were 148 (optimal <100). I am quite certain that nearly every medical doctor would have put this man on cholesterol-lowering statin drugs for life. ***Treatment***: In contrast, I advised a low-carb Paleo-Mediterranean diet because such diets have been shown to reduce cardiovascular mortality more powerfully that "statin" cholesterol-lowing drugs in older patients.[68] Likewise, fatty acid supplementation is more effective than statin drugs for reducing cardiac and all-cause mortality.[69] We added probiotics, because supplementation with *Lactobacillus* and *Bifidobacterium* has been shown to lower cholesterol levels in humans with high cholesterol.[70] Finally, I also prescribed 20 mg of policosanol for its well-known ability to favorably modify cholesterol levels.[71] ***Results***: Within ***one month*** the patient had lost weight, felt better, and his total cholesterol had dropped to normal at 196 (from 290!), LDL was reduced to 141, and triglycerides were reduced to 80. Basically, this treatment plan was "the protocol + policosanol." Drug treatment of this patient would have been more expensive, more risky, and would not have resulted in global health improvements.
- A Child with Intractable Seizures: This is a 4-year-old nonverbal boy with 3-5 seizures per day despite being on two anti-seizure medications and having previously had several other "last resort" medical and surgical procedures. He also had a history of food allergies. ***Treatment***: Obviously, there was no room for error in this case. We implemented a moderately low-carb hypoallergenic diet since both carbohydrate restriction[72] and allergy avoidance[73] can reduce the frequency and severity of seizures. Since many "anti-seizure" medications actually cause seizures by causing vitamin D deficiency[74], I added 800 IU per day of emulsified vitamin D3 for its antiseizure benefit.[75] We used 1 tsp per day of a combination fatty acid supplement that provides balanced amounts of ALA, GLA, EPA, and DHA, since fatty acids appear to have potential antiseizure benefits.[76] Vitamin B-6 (250 mg of P5P) and magnesium (bowel tolerance) were also added to reduce brain hyperexcitability.[77] Stool testing showed an absence of *Bifidobacteria* and *Lactobacillus*; probiotics were added for their anti-allergy benefits.[78] ***Results***: Within about 2 months seizure frequency reduced from 3-5 per day to one seizure every other day: ***an 87% reduction in seizure frequency***. Patient was able to discontinue one of the anti-seizure medications. His parents also noted several global improvements: the boy started making eye contact with people, he was learning again, and intellectually he was "making gains every day." His parents considered this an "amazing difference." Going from 30 seizures per week to 4 seizures per week while reducing medication use by 50% is a major achievement. Notice that we simply used the basic wellness protocol with some additional B6 and magnesium. It is highly unlikely that B6 and magnesium alone would have produced such a favorable response.
- A Young Woman with Full-Body Psoriasis Unresponsive to Drug Treatment: This is a 17-year-old woman with head-to-toe psoriasis since childhood. She wears long pants and long-sleeved shirts year-round, and the

[67] Vasquez A. *Integrative Orthopedics*. By now of course, this book has been surpassed in content of nutritional information, particularly in books printed past 2009.
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psoriasis is a major interference to her social life. Medications have ceased to help. ***Treatment***: The Paleo-Mediterranean diet was implemented with an emphasis on food allergy identification.[1] We used a multivitamin-mineral supplement with 200 mcg selenium to compensate for the nutritional insufficiencies and selenium deficiency that are common in patients with psoriasis; likewise 10 mg of folic acid was added to address the relative vitamin deficiencies and elevated homocysteine that are common in these patients.[79] Combination fatty acid therapy with EPA and DHA from fish oil and GLA from borage oil was used for the anti-inflammatory and skin-healing benefits.[80] Vitamin E (1200 IU of mixed tocopherols) and lipoic acid (1,000 mg per day) were added for their anti-inflammatory benefits and to combat the oxidative stress that is characteristic of psoriasis.[81] Of course, probiotics were used to modify gut flora, which is commonly deranged in patients with psoriasis.[82] ***Results***: Within a few weeks, this patient's "lifelong psoriasis" was essentially gone. Food allergy identification and avoidance played a major role in the success of this case. When I saw the patient again 9 months later for her second visit, she had no visible evidence of psoriasis. Her "medically untreatable" condition was essentially cured by the use of my basic protocol, with the addition of a few extra nutrients.

- A Man with Fatigue and Recurrent Numbness in Hands and Feet. This 40-year-old man had seen numerous neurologists and had spent tens of thousands of dollars on MRIs, CT scans, lumbar punctures, and other diagnostic procedures. No diagnosis had been found, and no effective treatment had been rendered by medical specialists. ***Assessments***: We performed a modest battery of lab tests which revealed elevations of fibrinogen and C-reactive protein (CRP), two markers of acute inflammation. Assessment of intestinal permeability with the lactulose-mannitol assay showed major intestinal damage ("leaky gut"). Follow-up parasite testing on different occasions showed dysbiosis caused by *Proteus*, *Enterobacter*, *Klebsiella*, *Citrobacter*, and *Pseudomonas aeruginosa*—of course, these are gram-negative bacteria that can induce immune dysfunction and autoimmunity, as described elsewhere.[1] Specifically, *Pseudomonas aeruginosa* has been linked to the development of nervous system autoimmunity, such as multiple sclerosis.[83] ***Treatment***: We implemented a plan of diet modification, vitamins, minerals, fatty acids, and probiotics. The dysbiosis was further addressed with specific antimicrobial herbs (including caprylic acid and emulsified oregano oil[84]) and drugs (such as tetracycline, Bactrim, and Augmentin). The antibiotic drugs proved to be ineffective based on repeat stool testing. ***Results***: Within one month we witnessed impressive improvements, both subjectively and objectively. Subjectively, the patient reported that the numbness and tingling almost completely resolved. Fatigue was reduced, and energy was improved. Objectively, the patient's elevated CRP plummeted from abnormally high at 11 down to completely normal at 1. Eighteen months later, the patient's CRP had dropped to less than 1 and fatigue and numbness were no longer problematic. Notice that this treatment plan was basically "the protocol" with additional attention to eradicating the dysbiosis we found with specialized stool testing.
- A 50-year-old Man with Rheumatoid Arthritis. This patient presented with a 3-year history of rheumatoid arthritis that had been treated unsuccessfully with drugs (methotrexate and intravenous Remicade). The first time I tested his hsCRP level, it was astronomically high at 124 mg/L (normal is <3). Because of the severe inflammation and other risk factors for sudden cardiac death, I referred this patient to an osteopathic internist for immune-suppressing drugs; the patient refused, stating that he was no longer willing to rely on immune-suppressing chemical medications. His treatment was entirely up to me. ***Assessments and Treatments***: We implemented the Paleo-Mediterranean diet and a program of vitamins, minerals, optimal combination fatty acid therapy (providing ALA, GLA, EPA, DHA, and oleic acid), and 4000 IU of vitamin D in emulsified form to overcome defects in absorption that are seen in older patients and those with gastrointestinal problems.[85] Hormone testing showed abnormally low DHEA, low testosterone, and slightly elevated estrogen; these problems were corrected with DHEA supplementation and the use of a hormone-modulating drug (Arimidex) that lowers estrogen and raises testosterone. Specialized stool testing showed absence of *Lactobacillus* and *Bifidobacteria* and intestinal overgrowth of *Citrobacter* and *Enterobacter* which was corrected with probiotics and antimicrobial treatments including undecylenic acid and emulsified oregano oil. Importantly, I also decided to

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[80] Vasquez A. New Insights into Fatty Acid Supplementation and Its Effect on Eicosanoid Production and Genetic Expression. *Nutritional Perspectives* 2005; January: 5-16
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[85] Vasquez A. Subphysiologic Doses of Vitamin D are Subtherapeutic: Comment on the Study by The Record Trial Group. *TheLancet.com* Accessed June 16, 2005

inhibit NFkB (the primary transcription factor that upregulates the pro-inflammatory response[86]) by using a combination botanical formula that contains curcumin, piperine, lipoic acid, green tea extract, propolis, rosemary, resveratrol, ginger, and Phytolens™ (an antioxidant extract from lentils that may inhibit autoimmunity[87])—all of these herbs and nutrients have been shown to inhibit NFkB and to thus downregulate inflammatory responses.[88] ***Results***: Within 6 weeks, this patient had happily lost 10 lbs of excess weight and was able to work without pain for the first time in years. **Follow-up testing showed that his hsCRP had dropped from 124 to 7 mg/L—a drop of 114 points—95%!—in less than one month: better than had ever been achieved even with the use of intravenous immune-suppressing drugs!** This patient continues to make significant progress. Obviously this case was complex, and we needed to do more than the basic protocol. Nonetheless, the basic protocol still served as the foundation for the treatment plan. Note that vitamin D has significant anti-inflammatory benefits and can cause major reductions in inflammation measured by CRP.[89] The correction of the hormonal abnormalities and the dysbiosis, and downregulating NFkB with several botanical extracts were also critical components of this successful treatment plan.

**Summary and Conclusions**: These examples show how the nutritional wellness protocol that I described in the September issue of *Nutritional Wellness* can be used as the foundational treatment for a wide range of health problems. In many cases, implementation of the basic protocol is all that is needed. In more complex situations, we use the basic protocol and then add more specific treatments to address dysbiosis and hormonal problems, and we can add additional nutrients as needed. However, nothing will ever replace a healthy diet, sufficiencies of vitamin D and all five of the health-promoting fatty acids (i.e., ALA, GLA, EPA, DHA, and oleic acid), and normalization of gastrointestinal flora. Without these basics, survival and the appearance of health are possible, but true health and recovery from "untreatable" illnesses is not possible. In order to attain optimal health, we have to create the conditions that allow for health to be attained, and we start this process by supplying the body with the nutrients that it needs to function optimally. In the words of naturopathic physician Jared Zeff from the *Journal of Naturopathic Medicine*, "The work of the naturopathic physician is to elicit healing by helping patients to create or recreate the conditions for health to exist within them. Health will occur where the conditions for health exist. Disease is the product of the conditions which allow for it."[90]

## Common Oversights and Shortcomings in the Study and Implementation of Nutritional Supplementation

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**Introduction**: An impressive discrepancy often exists between the low efficacy of nutritional interventions reported in the research literature and the higher efficacy achieved in the clinical practices of clinicians trained in the use of interventional nutrition (i.e., naturopathic physicians). This discrepancy is dangerous for at least two reasons. First, it results in an undervaluation of the efficacy of nutritional supplementation, which ultimately leaves otherwise treatable patients untreated. Second, such untreated and undertreated patients are often then forced to use dangerous and expensive pharmaceutical drugs and surgical interventions to treat conditions that could have otherwise been easily and safely treated with nutritional supplementation and diet modification. Consequently, the burden of suffering, disease, and healthcare expense in the US is higher than it would be if nutritionally-trained clinicians were more fully integrated into the healthcare system.

**Obstacles to Efficacy in the Use of Nutritional Supplementation**: Below are listed some of the most common causes for the underachievement of nutritional supplementation in practice and in published research. While this list is not all-inclusive, it will serve as a review for clinicians and an introduction for chiropractic/naturopathic

[86] Tak PP, Firestein GS. NFkB: a key role in inflammatory diseases. *J Clin Invest*. 2001 Jan;107(1):7-11
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[90] Zeff JL. The process of healing: a unifying theory of naturopathic medicine. *Journal of Naturopathic Medicine* 1997; 7: 122-5

students. In both practice and research, the problems listed below often overlap and function synergistically to reduce the efficacy of nutritional supplementation.

1. Inadequate dosing (quantity): Many clinical trials published in major journals and many doctors in clinical practice have used inadequate doses of vitamins (and other natural therapeutics) and have thus failed to achieve the results that would have easily been obtained had they implemented their protocol with the proper physiologic or supraphysiologic dose of intervention. The best example in my experience centers on vitamin D, where so many of the studies are performed with doses of 400-800 IU per day only to conclude that vitamin supplementation is ineffective for the condition being treated. The problem here is that the researchers failed to appreciate that the physiologic requirement for vitamin D3 in adults is approximately 3,000-5,000 IU per day[91] and that therefore their supplemental dose of 400-800 IU is only 10-20% of what is required. Subphysiologic doses are generally subtherapeutic. In this regard, I have had to correct journals such as *The Lancet*[92], *JAMA*[93], and *British Medical Journal*[94] from misleading their readers (many of whom are major policymakers) from concluding that nutritional supplementation is impotent; rather, their researchers and editors were not sufficiently educated in the design and review of studies using nutritional interventions. These journals should hire chiropractic and naturopathic physicians so that they have staff trained in natural treatments and who can thus provide an educated review of studies on these topics.[95]
2. Inadequate dosing (duration): Often the effects of long-term nutritional deficiency are not fully reversible and/or may require a treatment period of months or years to achieve maximal clinical response. For example, full replacement of fatty acids in human brain phospholipids is an ongoing process that occurs over a period of several years; thus studies using fatty acid supplements for a period of weeks or 2-3 months generally underestimate the enhanced effectiveness that can be obtained with administration over many months or several years of treatment. Relatedly, recovery from vitamin D deficiency takes several weeks of high-dose supplementation in order to achieve tissue saturation and subsequent cellular replenishment; studies of short duration are destined to underestimate the results that could have been achieved with supplementation carried out over several months.[96]
3. Failure to use proper forms of nutrients (quality): Nutrients are often available in different forms, not the least of which are "active" versus "inactive" and "natural" versus "unnatural." Most vitamin supplements, particularly high-potency B vitamins, are manufactured synthetically and are not from "natural sources" despite the marketing hype promulgated by companies that, for example, mix their synthetic vitamins with a vegetable powder and then call their vitamin supplements "natural." The simple fact is that production of high-potency supplements from purely natural sources would be prohibitively wasteful, inefficient, and expensive. Thus, while it is not necessary for vitamins to be "natural" in order to be useful, it is necessary that the vitamins are useable and preferably not "unnatural." The best example of the use of unnatural supplements is the use of synthetic DL-tocopherol in the so-called "vitamin E" studies; DL-tocopherol is 50% comprised of the L-isomer of tocopherol which is not only unusable by the human body but is actually harmful in that it interferes with normal metabolism and can exacerbate hypertension and cause symptomatic complications (e.g., headaches). Further, tocopherols exist within the body in relationship with the individual forms of the vitamin, such that supplementation with one form (e.g., alpha-tocopherol) can result in a relative deficiency of another form (e.g., gamma-tocopherol). One final example of the failure to use proper forms of nutrients is in the use of pyridoxine HCl as a form of vitamin B6; while this practice itself is not harmful, clinicians need to remember that pyridoxine HCl is ineffective until converted to the more active forms of the vitamin including pyridoxal-5-phosphate. Since this conversion requires co-nutrients such as magnesium and zinc, we can easily see that the reputed failure of B6 supplementation when administered in the form of pyridoxine HCl might actually be due to untreated insufficiencies of required co-nutrients, as discussed in the following section.
4. Failure to ensure adequacy of co-nutrients: Vitamins, minerals, amino acids, and fatty acids work together in an intricately choreographed and delicately orchestrated dance that culminates in the successful completion of

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[96] Vasquez A, Manso G, Cannell J. The clinical importance of vitamin D (cholecalciferol): a paradigm shift. *Altern Ther Health Med*. 2004 Sep-Oct;10(5):28-36

interconnected physiologic functions. If any of the performers in this event are missing (i.e., nutritional deficiency) or if successive interconversions are impaired due to lack of enzyme function, then the show cannot go on, or—if it does go on—impaired metabolism and defective function will result. So, if we take a patient with "vitamin B6 deficiency" and give him vitamin B6 in the absence of other co-nutrients needed for the proper activation and metabolic utilization of vitamin B6, we cannot honestly expect the "nutritional supplementation" to work in this case; rather, we might see a marginal benefit or perhaps even a negative outcome as an imbalanced system is pushed into a different state of imbalance despite supplementation with the "correct" vitamin. In the case of vitamin B6, necessary co-nutrients include zinc, magnesium, and riboflavin; deficiency of any of these will result in a relative "failure" of B6 supplementation even if a patient has a B6-responsive condition. Notably, overt magnesium deficiency is alarmingly common among patients and citizens in industrialized nations[97,98,99], and this epidemic of magnesium deficiency is due not only to insufficient intake but also to excessive excretion caused by consumption of high-glycemic foods, caffeine, and a diet that promotes chronic metabolic acidosis with resultant urinary acidification.

5. Failure to achieve urinary alkalinization: Western/American-style diets typified by overconsumption of grains, dairy, sugar, and salt result in a state of subclinical chronic metabolic acidosis which results in urinary acidification, relative hypercortisolemia, and consequent hyperexcretion of minerals such as calcium and magnesium.[100] [101] Thus, the common conundrum of magnesium replenishment requires not only magnesium supplementation but also dietary interventions to change the internal climate to one that is conducive to bodily retention and cellular uptake of magnesium.[102]
6. Use of mislabeled supplements: Even in the professional arena of nutritional supplement manufacturers, some companies habitually underdose their products either in an attempt to spend less in the manufacture of their products or as a consequence of poor quality control. If a product is labeled to contain 1,000 IU of vitamin D but only contains 836 IU of the nutrient, then obviously full clinical efficacy will not be achieved; this was a problem in a recent clinical trial involving vitamin D.[103] The problem for clinicians is in trusting the companies that supply nutritional supplements; some companies do "in house" testing which lacks independent review, while other companies use questionable "independent testing" which is not infrequently performed by a laboratory that is a wholly owned subsidiary of the parent nutritional company. Manufacturing regulations that are sweeping through the industry will cleanse the nutritional supplement world of poorly made products, and these same regulations will sweep some unprepared companies right out the door when they are unable to meet the regulatory requirements.
7. Failure to ensure/assess bioavailability and optimal serum/cellular levels: Clinical trials with nutritional therapies need to monitor serum or cellular levels to ensure absorption, product bioavailability, and the attainment of optimal serum levels. This is particularly relevant in the treatment of chronic disorders such as the autoimmune diseases, wherein so many of these patients have gastrointestinal dysbiosis and often have concomitant nutrient malabsorption.[104] Simply dosing these patients with supplements is not always efficacious; often the gut must be cleared of dysbiosis so that the mucosal lining can be repaired and optimal nutrient absorption can be reestablished.
8. Coadministration of food with nutritional supplements (sometimes right, sometimes wrong): Food can help or hinder the absorption of nutritional supplements. Phytate and tannins in grains and teas, respectively, are notorious for inhibiting mineral absorption. Some supplements, like coenzyme Q10, should be administered with fatty food to enhance absorption. Other supplements, like amino acids, should be administered away from

[97] "Altogether 43% of 113 trauma patients had low magnesium levels compared to 30% of noninjured cohorts." Frankel H, Haskell R, Lee SY, Miller D, Rotondo M, Schwab CW. Hypomagnesemia in trauma patients. *World J Surg*. 1999 Sep;23(9):966-9
[98] "There was a 20% overall prevalence of hypomagnesemia among this predominantly female, African American population." Fox CH, Ramsoomair D, Mahoney MC, Carter C, Young B, Graham R. An investigation of hypomagnesemia among ambulatory urban African Americans. *J Fam Pract*. 1999 Aug;48(8):636-9
[99] "Suboptimal levels were detected in 33.7 per cent of the population under study. These data clearly demonstrate that the Mg supply of the German population needs increased attention." Schimatschek et al. Prevalence of hypomagnesemia in an unselected German population of 16,000 individuals. *Magnes Res*. 2001 Dec;14(4):283-90
[100] Cordain L, et al. Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr*. 2005 Feb;81(2):341-54
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[104] Vasquez A. Nutritional and Botanical Treatments Against "Silent Infections" and Gastrointestinal Dysbiosis. *Nutritional Perspectives* 2006; January

protein-rich foods and are often better administered with simple carbohydrate to enhance cellular uptake; this is especially true with tryptophan.

9. Correction of gross dietary imbalances enhances supplement effectiveness: If the diet is grossly imbalanced, then nutritional supplementation is less likely to be effective. The best example of this is in the use of fatty acid supplements, particularly in the treatment of inflammatory disorders. If the diet is laden with dairy, beef, and other sources of arachidonate, then fatty acid supplementation with EPA, DHA, and GLA is much less likely to be effective, or much higher doses of the supplements will need to be used in order to help restore fatty acid balance. Generally speaking, the diet needs to be optimized to enhance the efficacy of nutritional supplementation.

**Conclusion**: In this brief review, I have listed and discussed some of the most common impediments to the success of nutritional supplementation. I hope that naturopathic students, clinicians, and researchers will find these points helpful in their design of clinical treatment protocols.

## Revisiting the Five-Part Nutritional Wellness Protocol: Supplemented Paleo-Mediterranean Diet

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**Abstract: This article reviews the five-part nutritional protocol that incorporates a health-promoting nutrient-dense diet and essential supplementation with vitamins/minerals, specific fatty acids, probiotics, and physiologic doses of vitamin D3. This foundational nutritional protocol has proven benefits for disease treatment, disease prevention, and health maintenance and restoration. Additional treatments such as botanical medicines, additional nutritional supplements, and pharmaceutical drugs can be used atop this foundational protocol to further optimize clinical effectiveness. The rationale for this five-part protocol is presented, and consideration is given to adding iodine-iodide as the sixth component of the protocol.**

**Introduction**: In 2004 and 2005 I first published a "five-part nutrition protocol"[105,106] that provides the foundational treatment plan for a wide range of health disorders. This protocol served and continues to serve as the foundation upon which other treatments are commonly added, and without which those other treatments are likely to fail, or attain suboptimal results at best.[107] Now as then, I will share with you what I consider a basic foundational protocol for wellness promotion and disease treatment. I have used this protocol in my own self-care for many years and have used it in the treatment of a wide range of health-disease conditions in clinical practice.

This nutritional protocol is validated by biochemistry, physiology, experimental research, peer-reviewed human trials, and the clinical application of common sense. It is the most nutrient-dense diet available, satisfying nutritional needs and thereby optimizing metabolic processes while promoting satiety and weight loss/optimization. Nutrients are required in the proper amounts, forms, and approximate ratios for critical and innumerable physiologic functions; if nutrients are lacking, the body cannot function *normally*, let alone *optimally*. Impaired function results in subjective and objective manifestations of what is eventually labeled as "disease." Thus, a powerful and effective alternative to treating diseases with drugs is to re-establish normal/optimal physiologic function by replenishing the body with essential nutrients, reestablishing hormonal balance ("orthoendocrinology"), promoting detoxification of environmental toxins, and by reestablishing the optimal microbial milieu, especially the eradication of (multifocal) dysbiosis; this multifaceted approach can be applied to several diseases, especially those of the inflammatory and autoimmune varieties.[108]

Of course, most diseases are multifactorial and therefore require multicomponent treatment plans, and some diseases actually require the use of drugs in conjunction with assertive interventional nutrition. However, while only a smaller portion of patients actually need drugs for the long-term management their problems, all clinicians should agree that everyone needs a foundational nutrition plan because nutrients—not drugs—are universally required for life and health. This five-part nutrition protocol is briefly outlined below; a much more detailed substantiation of the underlying science and clinical application of this protocol was recently published in a review of more than 650 pages and approximately 3,500 citations.[109]

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[106] Vasquez A.Five-Part Nutritional Protocol that Produces Consistently Positive Results.*NutrWellness*2005Sep nutritionalwellness.com/archives/2005/sep/09_vasquez.php
[107] Vasquez A. Common Oversights and Shortcomings in the Study and Implementation of Nutritional Supplementation. *Naturopathy Digest* 2007 June.
[108] Vasquez A. Integrative Rheumatology. IBMRC: 2006, 2009.
[109] Vasquez A. *Chiropractic and Naturopathic Mastery of Common Clinical Disorders*. IBMRC: 2009

1. Health-promoting Paleo-Mediterranean diet: Following an extensive review of the research literature, I developed what I call the "supplemented Paleo-Mediterranean diet." In essence, this diet plan combines the best of the Mediterranean diet with the best of the Paleolithic diet, the latter of which has been best distilled by Dr. Loren Cordain in his book "The Paleo Diet"[110] and his numerous scientific articles.[111,112,113] The Paleolithic diet is superior to the Mediterranean diet in nutrient density for promoting satiety, weight loss, and improvements/normalization in overall metabolic function.[114,115] This diet places emphasis on fruits, vegetables, nuts, seeds, and berries that meet the body's needs for fiber, carbohydrates, and most importantly, the 8,000+ phytonutrients that have additive and synergistic health effects[116]—including immunomodulating, antioxidant, anti-inflammatory, and anti-cancer benefits. High-quality protein sources such as fish, poultry, eggs, and grass-fed meats are emphasized. Slightly modifying Cordain's Paleo diet, I also advocate soy and whey protein isolates for their high-quality protein and their anticancer, cardioprotective, and mood-enhancing (due to the high tryptophan content) benefits. Potatoes and other starchy vegetables, wheat and other grains including rice are discouraged due to their high glycemic indexes and high glycemic loads, and their relative insufficiency of fiber and phytonutrients compared to fruits and vegetables. Grains such as wheat, barley, and rye are discouraged due to the high glycemic loads/indexes of most breads, pastries, and other grain-derived products, as well as due to the immunogenicity of constituents such as gluten, a protein composite (consisting of a prolamin and a glutelin) that can contribute to disorders such as migraine, epilepsy, eczema, arthritis, celiac disease, psoriasis and other types of autoimmunity. Sources of simple sugars and foreign chemicals such as colas/sodas (which contain artificial colors, flavors, and high-fructose corn syrup, which contains mercury[117] and which can cause the hypertensive-diabetic metabolic syndrome[118]) and processed foods (e.g., "TV dinners" and other manufactured snacks and convenience foods) are strictly forbidden. Chemical preservatives, colorants, sweeteners, flavor-enhancers such as monosodium glutamate and carrageenan are likewise avoided. In summary, this diet plan provides plenty of variety, as most dishes comprised of poultry, fish, lean meats, soy, eggs, fruits, vegetables, nuts, berries, and seeds are allowed. The diet provides an abundance of fiber, phytonutrients, carbohydrates, potassium, and protein, while simultaneously being low in fat, sodium, arachidonic acid, and "simple sugars." The diet must be customized with regard to total protein and calorie intake, as determined by the size, status, and activity level of the patient; individual per-patient food allergens should be avoided. Regular consumption of this diet has shown the ability to reduce hypertension, alleviate diabetes, ameliorate migraine headaches, and result in improvement of overall health and a lessening of the severity of many common "diseases", particularly those with an autoimmune or inflammatory component. This Paleo-Mediterranean diet is supplemented with vitamins, minerals, fatty acids, and probiotics—making it the "supplemented Paleo-Mediterranean diet" as described below. The main considerations/contraindications to recommending increased intake of fruits and vegetables are 1) increased intake of vitamin K in the few patients taking warfarin for anticoagulation, and 2) increased intake of potassium in patients with pre-existing renal insufficiency as discussed in this video tutorial: vimeo.com/152296851 also at vimeo.com/152293616.
2. Multivitamin and multimineral supplementation: Vitamin and mineral supplementation has been advocated for decades by the chiropractic/naturopathic professions while being scorned by so-called "mainstream

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[113] Cordain L, et al. Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr*. 2005 Feb;81(2):341-54
[114] "A high micronutrient density diet mitigates the unpleasant aspects of the experience of hunger even though it is lower in calories. Hunger is one of the major impediments to successful weight loss. Our findings suggest that it is not simply the caloric content, but more importantly, the micronutrient density of a diet that influences the experience of hunger. It appears that a high nutrient density diet, after an initial phase of adjustment during which a person experiences "toxic hunger" due to withdrawal from pro-inflammatory foods, can result in a sustainable eating pattern that leads to weight loss and improved health." Fuhrman J, Sarter B, Glaser D, Acocella S. Changing perceptions of hunger on a high nutrient density diet. *Nutr J*. 2010 Nov 7;9:51 nutritionj.com/content/9/1/51
[115] "The Paleolithic group were as satiated as the Mediterranean group but consumed less energy per day (5.8 MJ/day vs. 7.6 MJ/day, Paleolithic vs. Mediterranean, p=0.04). Consequently, the quotients of mean change in satiety during meal and mean consumed energy from food and drink were higher in the Paleolithic group (p=0.03). Also, there was a strong trend for greater Satiety Quotient for energy in the Paleolithic group (p=0.057). Leptin decreased by 31% in the Paleolithic group and by 18% in the Mediterranean group with a trend for greater relative decrease of leptin in the Paleolithic group." Jonsson T, Granfeldt Y, Erlanson-Albertsson C, Ahren B, Lindeberg S. A Paleolithic diet is more satiating per calorie than a Mediterranean-like diet in individuals with ischemic heart disease. *Nutr Metab* (Lond). 2010 Nov 30;7(1):85.
[116] Liu RH. Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *Am J Clin Nutr* 2003;78(3 Suppl):517S-520S
[117] "With daily per capita consumption of HFCS in the US averaging about 50 grams and daily mercury intakes from HFCS ranging up to 28 µg, this potential source of mercury may exceed other major sources of mercury especially in high-end consumers of beverages sweetened with HFCS." Dufault R, et al. Mercury from chlor-alkali plants: measured concentrations in food product sugar. *Environ Health*. 2009 Jan 26;8:2 ehjournal.net/content/8/1/2
[118] Vasquez A. *Integrative Medicine and Functional Medicine for Chronic Hypertension: An Evidence-based Patient-Centered Monograph for Advanced Clinicians*. IBMRC; 2011. See also: Reungjui S, et al. Thiazide diuretics exacerbate fructose-induced metabolic syndrome. *J Am Soc Nephrol*. 2007 Oct;18(10):2724-31

medicine." Vitamin and mineral supplementation finally received bipartisan endorsement when researchers from Harvard Medical School published a review article in *Journal of the American Medical Association* that concluded, "Most people do not consume an optimal amount of all vitamins by diet alone. ...it appears prudent for all adults to take vitamin supplements."[119] Long-term nutritional insufficiencies experienced by "most people" promote the development of "long-latency deficiency diseases"[120] such as cancer, neuroemotional deterioration, and cardiovascular disease. Impressively, the benefits of multivitamin/multimineral supplementation have been demonstrated in numerous clinical trials. Multivitamin/multimineral supplementation has been shown to improve nutritional status and reduce the risk for chronic diseases[121], improve mood[122], potentiate antidepressant drug treatment[123], alleviate migraine headaches (when used with diet improvement and fatty acids[124]), improve immune function and infectious disease outcomes in the elderly[125] (especially diabetics[126]), reduce morbidity and mortality in patients with HIV infection[127,128], alleviate premenstrual syndrome[129,130] and bipolar disorder[131], reduce violence and antisocial behavior in children[132] and incarcerated young adults (when used with essential fatty acids[133]), and improve scores of intelligence in children.[134] Multivitamin and multimineral supplementation provides anti-inflammatory benefits, as evidenced by significant reduction in C-reactive protein (CRP) in a double-blind, placebo-controlled trial.[135] The ability to safely and affordably deliver these benefits makes multimineral-multivitamin supplementation an essential component of any and all health-promoting and disease-prevention strategies. A few cautions need to be observed; for example, vitamin A can (rarely) result in liver damage with chronic consumption of 25,000 IU or more, and intake should generally not exceed 10,000 IU per day in women of childbearing age. Also, iron should not be supplemented except in patients diagnosed with iron deficiency by a blood test (serum ferritin).

3. Physiologic doses of vitamin D3: The prevalence of vitamin D deficiency varies from 40-80 percent (general population) to almost 100 percent (patients with musculoskeletal pain) among Americans and Europeans. Vasquez, Manso, and Cannell described the many benefits of vitamin D3 supplementation in a "paradigm-shifting" review published in 2004.[136]

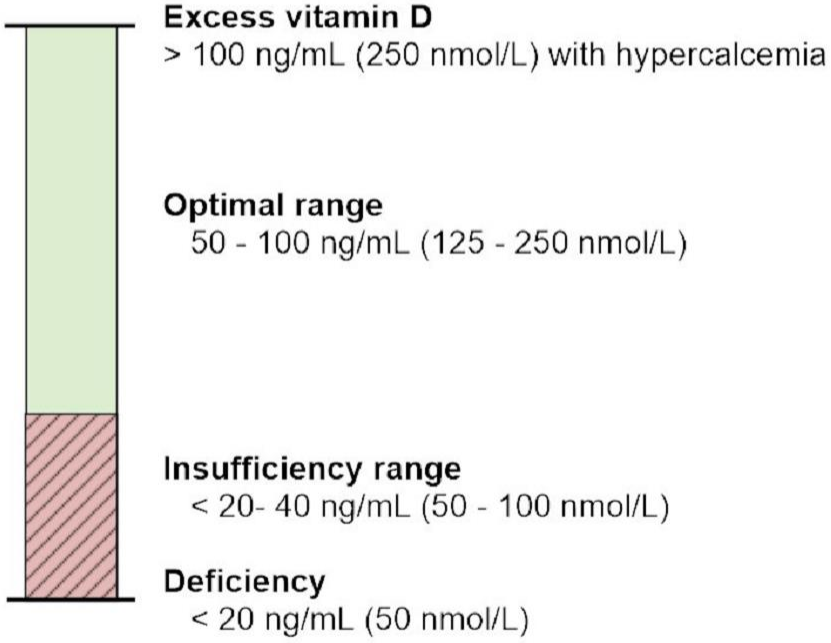


**Image right: Interpretation of serum 25(OH) vitamin D levels:** Updated from Vasquez et al, *Alternative Therapies in Health and Medicine* 2004 Sep

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Our review showed that vitamin D deficiency causes or contributes to depression, hypertension, seizures, migraine, polycystic ovary syndrome, inflammation, autoimmunity, and musculoskeletal pain, particularly low-back pain. Clinical trials using vitamin D supplementation have proven the cause-and-effect relationship between vitamin D deficiency and most of these conditions by showing that each could be cured or alleviated with vitamin D supplementation. Per our review, daily vitamin D doses should be 1,000 IU for infants, 2,000 IU for children, and 4,000 IU for adults, although some adults respond better to higher doses of 10,000 IU per day. Cautions/contraindications include the use of thiazide diuretics (e.g., hydrochlorothiazide) or any other medications that promote hypercalcemia, as well as granulomatous diseases such as sarcoidosis, tuberculosis, and certain types of cancer, especially lymphoma. Effectiveness is monitored by measuring serum 25-OH-vitamin D, and safety is monitored by measuring serum calcium. Dosing should be tailored for the attainment of optimal serum levels of 25-hydroxy-vitamin D3, generally 50-100 ng/ml (125-250 nmol/l) as illustrated.

4. Balanced and complete fatty acid supplementation: A detailed survey of the literature shows that five fatty acids have major health-promoting disease-preventing benefits and should therefore be incorporated into the daily diet and/or regularly consumed as dietary supplements.[137] These are alpha-linolenic acid (ALA; omega-3, from flaxseed oil), eicosapentaenoic acid (EPA; omega-3, from fish oil), docosahexaenoic acid (DHA; omega-3, from fish oil and algae), gamma-linolenic acid (GLA; omega-6, most concentrated in borage oil but also present in evening primrose oil, hemp seed oil, black currant seed oil), and oleic acid (omega-9, most concentrated in olive oil, which contains in addition to oleic acid many anti-inflammatory, antioxidant, and anticancer phytonutrients). Supplementing with one fatty acid can exacerbate an insufficiency of other fatty acids; hence the importance of balanced combination supplementation. Each of these fatty acids has health benefits that cannot be fully attained from supplementing a different fatty acid; hence, again, the importance of balanced combination supplementation. The benefits of GLA are not attained by consumption of EPA and DHA; in fact, consumption of fish oil can actually promote a deficiency of GLA.[138] Likewise, consumption of GLA alone can reduce EPA levels while increasing levels of proinflammatory arachidonic acid; both of these problems are avoided with co-administration of EPA any time GLA is used because EPA inhibits delta-5-desaturase, which converts dihomo-GLA into arachidonic acid. Using ALA alone only slightly increases EPA but generally leads to no improvement in DHA status and can lead to a reduction of oleic acid; thus, DHA and oleic acid should be supplemented when flaxseed oil is used.[139] Obviously, the goal here is physiologically-optimal (i.e., "balanced") intake of all of the health-promoting fatty acids; using only one or two sources of fatty acids is not balanced and results in suboptimal improvement. In clinical practice, I routinely use combination fatty acid therapy comprised of ALA, EPA, DHA, and GLA for essentially all patients; when one appreciates that the average daily Paleolithic intake of n-3 fatty acids was 7 grams per day contrasted to the average daily American intake of 1 gram per day, we can see that—by using combination fatty acid therapy emphasizing n-3 fatty acids—we are simply meeting physiologic expectations via supplementation, rather than performing an act of recklessness or heroism. The product I use also contains a modest amount of oleic acid that occurs naturally in flax and borage seed oils, and I encourage use of olive oil for salads and cooking. This approach results in complete and balanced fatty acid intake, and the clinical benefits are impressive. Benefits are to be expected in the treatment of premenstrual syndrome, diabetic neuropathy, respiratory distress syndrome, Crohn's disease, lupus, rheumatoid arthritis, cardiovascular disease, hypertension, psoriasis, eczema, migraine headaches, bipolar disorder, borderline personality disorder, mental depression, schizophrenia, osteoporosis, polycystic ovary syndrome, multiple sclerosis, and musculoskeletal pain. The discovery in September 2010 that the G protein-coupled receptor 120 (GPR120) functions as an n-3 fatty acid receptor that, when stimulated with EPA or DHA, exerts broad anti-inflammatory effects (in cell experiments) and enhances systemic insulin sensitivity (in animal study) confirms a new mechanism of action of fatty acid supplementation and shows that we as clinician-researchers are still learning the details of the beneficial effects of commonly used treatments.[140]

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5. Probiotics /gut flora modification: Proper levels of good bacteria promote intestinal health, support proper immune function, and encourage overall health. Excess bacteria or yeast, or the presence of harmful bacteria, yeast, or "parasites" such as amoebas and protozoans, can cause "leaky gut," systemic inflammation, and a wide range of clinical problems, especially autoimmunity. Intestinal flora can become imbalanced by poor diets, excess stress, immunosuppressive drugs, and antibiotics, and all of these factors are common among American patients. Thus, as a rule, I reinstate the good bacteria by the use of probiotics (good bacteria and yeast), prebiotics (fiber, arabinogalactan, and inulin), and the use of fermented foods such as kefir and yogurt for patients not allergic to milk. Harmful yeast, bacteria, and other "parasites" can be eradicated with the combination of dietary change, antimicrobial drugs, and/or herbal extracts. For example, oregano oil in an emulsified, time-released form has proven safe and effective for the elimination of various parasites encountered in clinical practice.[141] Likewise, the herb *Artemisia annua* (sweet wormwood) commonly is used to eradicate specific bacteria and has been used for thousands of years in Asia for the treatment and prevention of infectious diseases, including drug-resistant malaria.[142] Restoring microbial balance by providing probiotics, restoring immune function (immunorestoration) and eliminating sources of dysbiosis, especially in the gastrointestinal tract, genitourinary tract, and oropharynx, is a very important component in the treatment plan of autoimmunity and systemic inflammation.[143]

**Should combinations of iodine and iodide be the sixth component of the Protocol?***: Both iodine and iodide have biological activity in humans. An increasing number of clinicians are using combination iodine-iodide products to provide approximately 3-6 mg/d [changed/corrected*]. Collectively, iodine and iodide provide antioxidant, antimicrobial, mucolytic, immunosupportive, antiestrogen, and anticancer benefits that extend far beyond the mere incorporation of iodine into thyroid hormones.[5] Benefits of iodine/iodide in the treatment of asthma[144,145] and systemic fungal infections[146,147] have been documented, and many clinicians use combination iodine/iodide supplementation for the treatment of estrogen-driven conditions such as fibrocystic breast disease.[148] While additional research is needed and already underway to further establish the role of iodine-iodide as a routine component of clinical care, clinicians can reasonably begin incorporating this nutrient into their protocols based on the above-mentioned physiologic roles and clinical benefits. *See update/addendum following this reprint.*

**Summary and Conclusions**: In this brief review, I have described and substantiated a fundamental protocol that can serve as effective therapy for patients with a wide range of diseases and health disorders. Customizing the Paleo-Mediterranean diet to avoid patient-specific food allergens, using vitamin-mineral supplements along with physiologic doses of vitamin D and broad-spectrum balanced fatty acid supplementation, and ensuring "immunomicrobial" health with the skillful use of probiotics, prebiotics, immunorestoration, and antimicrobial treatments provides an excellent health-promoting and disease-eliminating foundation and lifestyle for many patients. Often, this simple protocol is all that is needed for the effective treatment of a wide range of clinical problems, even those that have been "medical failures" for many years. For other patients with more complex illnesses, of course, additional interventions and laboratory assessments can be used to optimize and further customize the treatment plan. Clinicians should avoid seeking "silver bullet" treatments that ignore overall metabolism, immune function, and inflammatory balance, and we must always remember that the attainment and preservation of health requires that we first meet the body's basic nutritional and physiologic needs. This five-step protocol begins the process of meeting those needs. With it, health can be restored and the need for disease-specific treatment is obviated or reduced; without it, fundamental physiologic needs are not met, and health cannot be obtained and maintained. Addressing core physiologic needs empowers doctors to deliver the most effective healthcare possible, and it allows patients to benefit from such treatment.

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[147] Bonifaz A, et al. Sporotrichosis in childhood: clinical and therapeutic experience in 25 patients. *Pediatr Dermatol*. 2007 Jul-Aug;24(4):369-72
[148] Ghent WR, Eskin BA, Low DA, Hill LP. Iodine replacement in fibrocystic disease of the breast. *Can J Surg*. 1993 Oct;36(5):453-60

***Update and addendum to information on iodine and iodide**:

- Authoritative enthusiasm for high-dose iodine-iodide: Several authoritative articles/authors stated that an advisable level of intake for iodine-iodide for the prevention and treatment of various conditions is approximately 12 mg/d. Because of these well-referenced and apparently authoritative publications, many clinicians and nutrition professionals began using higher doses iodine-iodide with patients and clients, quite often with benefit and nearly always with the absence of serious adverse effects. Several popular nutritional supplements used by clinicians and nutritionists contain both iodi*n*e (the *n*atural, diatomic form) and iodi*d*e (the *d*ivided/ionic form most commonly consumed in *d*ietary supplements, such as potassium iodi*d*e); both forms of this volatile metal have biologic properties in humans. Benefits of iodine-iodide supplementation focus mostly on the mucolytic, antimicrobial, and anti-estrogen effects.
    - Dr Jonathan V Wright (*Nutrition and Healing* 2002 Nov and 2005 May): In *Nutrition and Healing* (2002 Nov), well-respected nutrition expert, pioneer, and clinician Jonathan V. Wright MD advocated high-dose iodine-iodide for a wide range of conditions, particularly those related to inflammation, excess estrogen, and microbial infections. In another issue of *Nutrition and Healing* (2005 May) Dr Wright wrote "12.5 milligrams (that's 12,500 micrograms) is the optimal daily amount of iodine, not only for your thyroid but for the rest of your body, too." In that same article, Dr Wright stated, "The Japanese have traditionally consumed more iodine, mostly from seaweed, than any other population. The average daily intake of iodine in Japan [is] 13.8 milligrams…", and throughout the article Dr Wright advocates that 12.5 mg/d is "the optimal daily dose" of combined iodine-iodine.
    - Extrathyroidal benefits of iodine (*Journal of American Physicians and Surgeons* 2006 Winter): Independently and in a peer-reviewed publication, Donald Miller MD (Professor of Surgery, Division of Cardiothoracic Surgery, University of Washington School of Medicine) supported the daily intake of 12.5 mg/d in *Journal of American Physicians and Surgeons* and even supported higher doses with the statement "More than 4,000 patients in this project [Iodine Project] take iodine in daily doses ranging from 12.5 to 50 mg, and those with diabetes can take up to 100 mg /day." Miller also noted that dermatologists "treat inflammatory dermatoses, like nodular vasculitis and pyoderma gangrenosum, with SSKI (supersaturated potassium iodide), beginning with an iodine dose of 900 mg/day, followed by weekly increases of up to 6 g/day as tolerated. Fungal eruptions, like sporotrichosis, are treated initially in gram amounts with great effect."
    - Iodine deficiency and therapeutic considerations (*Alternative Medicine Review* 2008 Jun): In 2008, Patrick wrote "Estimates of the average daily Japanese iodine consumption vary from 5,280 mcg to 13,800 mcg…" and this again supported and reinforced enthusiasm for doses of approximately 12 mg/d of iodine-iodine. However, in this article, Patrick did not advocate any specific daily dosage, citing 3-6 mg/d as beneficial and without adverse effect.
- Review, reanalysis, and caution: Soon after these enthusiastic publications, Alan Gaby MD published in several magazines, presented in post-graduate educational events, and discussed in his book *Nutritional Medicine* a review and reanalysis of the original data and concluded that the estimated average daily intake of iodine-iodine in Japan had been *overestimated* by a mathematical error (mistakenly interchanging wet and dry weights of seaweed and thus overestimating the daily Japanese intake of iodine-iodine). Per Gaby (*Nutritional Medicine*, page 175), the true intake of iodine-iodide in Japan averages 330-500 mcg/d, which is 25-fold lower than the estimate of 13.8 mg/d, upon which rested much of the rationale for implementing high-dose iodine-iodide supplementation empirically and routinely.
- Benefits, perspectives, and additional research: Many clinicians including the current author have used high-dose iodine-iodide ranging from approximately 12-48 mg/d for variable periods of time without personally experiencing or clinically observing apparent adverse effects; that statement does not imply endorsement of routine universal high-dose iodine-iodide supplementation. Some degree of caution is advised in consideration of the risks of inducing thyroid dysfunction (hyperthyroidism, hypothyroidism), intestinal hemorrhage[149], and

[149] Kinoshita et al. Severe duodenal hemorrhage induced by Lugol's solution administered for thyroid crisis treatment. *Intern Med.* 2010;49(8):759-61

anaphylaxis-like reactions.[150] Topical and systemic antimicrobial benefits of iodine-iodide are well known and well documented; oral high-dose iodine-iodide has been used to treat drug-resistant fungal infections (cited below). When applied for sufficient concentrations and durations, both diatomic iodine and ionic iodide possess potent broad-spectrum antimicrobial properties; essentially no "drug resistance" against iodine-iodide exists for bacteria, fungi, viruses, and protozoans. Iodine also has documented molecular and clinical anti-estrogen effects, thus providing scientific explanation for its ability to treat and prevent estrogen-related disorders ranging from fibrocystic breast disease to cancer. Indeed, iodine treatment of breast cancer cells has been shown to increase the mRNA levels of several genes involved in estrogen metabolism and "detoxification" such as cytochrome p450-1A1 while also decreasing the levels of estrogen responsive genes such as TFF1 and WISP2; also noted following iodine treatment is upregulation of gene expression for the enzyme glutathione peroxidase, an important selenium-dependent component of antioxidant defense mechanisms.[151]

- Ultra-high dose iodide for sporotrichosis in childhood (*Pediatric Dermatology* 2007 Jul-Aug): Nineteen pediatric patients with proven sporotrichosis were successfully treated with potassium iodide per the following quoted protocol: "All patients were initially treated with potassium iodide (KI), and only those who were unresponsive or who developed side effects were given itraconazole. The dose of KI used was 1–3 g/day, starting at 1 g/day and increasing until the dose of 3 g/day was reached. … Treatments were sustained until remission was reached, which ranged from 3 to 6 months."[152] Per the review by Miller[153] cited previously, KI 1g (1,000 mg) contains 770 mg of iodide. Thus, the pediatric patients in this case series were treated with 770-2,310 mg/d of iodide for successful antimycotic treatment. Two patients from the original group of 23 patients experienced nausea and vomiting from the KI and were switched to itraconazole; two other patients were lost to follow-up. The authors note that, "Side effects occur in 5% to 10% of patients, mainly presenting as gastrointestinal symptoms as well as headache and rhinorrhea to a lesser extent."
- Ultra-high dose iodide for rhinofacial zygomycosis—case report (*Journal of European Academy of Dermatology and Venereology* 2007 Jan): A 19-year-old male "was put on oral SSKI at an initial dose of 0.5 mL three times daily. This was gradually increased by 0.1 mL/dose/day until a dose of 5 mL three times daily was reached."[154] Generic formulation of "saturated solution of potassium iodide" (SSKI) contains 1000 mg of KI per mL of solution, which provides roughly 750 mg iodide; thus, SSKI dosed at 5 mL thrice daily = 15 mL/d = 11,250 mg/d (slightly more than 11 grams per day) of iodide for this adult patient with rhinofacial zygomycosis. Treatment was continued for at least 12 months without report of adverse effect.
- Modest dose iodine replacement in fibrocystic disease of the breast (*Canadian Journal of Surgery* 1993 Oct): Ghent and colleagues[155] sought to determine the response of patients with fibrocystic breast disease to "iodine replacement therapy" and reviewed three clinical studies of different design containing 233, 145 (later up to 1365), and 23 subjects; overall, subjective alleviation of pain and objective alleviation of breast fibrosis was seen in approximately 70% of patients. Consistent with other reports and impressions, the authors noted that, "Molecular iodine is nonthyrotropic and was the most beneficial." The dose of molecular iodine averaged 0.08 mg/kg body weight, which for an average 140-lb (63-kg) patient equates to approximately 5 mg/d.
- Modest dose iodine in patients with cyclic mastalgia (*Breast Journal* 2004 Jul-Aug): Kessler[156] reports a randomized, double-blind, placebo-controlled, multicenter clinical trial was conducted with 111 otherwise healthy euthyroid women with a history of breast pain and fibrosis; subjects received molecular iodine for 6 months. Physicians assessed breast pain, tenderness, and nodularity each cycle; patients assessed breast pain and tenderness with the Lewin breast pain scale at 3-month intervals and with a VAS at each cycle. All iodine-treated subjects improved compared to no improvement seen in

[150] Indraccolo et al. Anaphylactic-like reaction to Lugol solution during colposcopy. *South Med J* 2009 Jan;102(1):96-7
[151] "Quantitative RT-PCR confirmed the array data demonstrating that iodine/iodide treatment increased the mRNA levels of several genes involved in estrogen metabolism (CYP1A1, CYP1B1, and AKR1C1) while decreasing the levels of the estrogen responsive genes TFF1 and WISP2." Stoddard FR 2nd, et al. Iodine alters gene expression in the MCF7 breast cancer cell line: evidence for an anti-estrogen effect of iodine. *Int J Med Sci*. 2008 Jul 8;5(4):189-96
[152] Bonifaz A, et al. Sporotrichosis in childhood: clinical and therapeutic experience in 25 patients. *Pediatr Dermatol*. 2007 Jul-Aug;24(4):369-72
[153] Said of KI, "The standard dose was 1g, which contains 770 mg of iodine." Miller DW. Extrathyroidal benefits of iodine. *J Am Physicians Surgeons* 2006;Winter,106-10
[154] Tripathy et al. Rhinofacial zygomycosis successfully treated with oral saturated solution of potassium iodide. *J Eur Acad Dermatol Venereol*. 2007;21:117-9
[155] Ghent et al. Iodine replacement in fibrocystic disease of the breast. *Can J Surg*. 1993 Oct;36(5):453-60
[156] Kessler JH. The effect of supraphysiologic levels of iodine on patients with cyclic mastalgia. *Breast J*. 2004 Jul-Aug;10(4):328-36

the placebo group. "Reductions in all three physician assessments were observed in patients after 5 months of therapy in the 3.0 mg/day (7/28; 25%) and 6.0 mg/day (15/27; 18.5%) treatment groups, but not the 1.5 mg/day or placebo group. Patients recorded statistically significant decreases in pain by month 3 in the 3.0 and 6.0 mg/day treatment groups, but not the 1.5 mg/day or placebo group; more than 50% of the 6.0 mg/day treatment group recorded a clinically significant reduction in overall pain. All doses were associated with an acceptable safety profile. No dose-related increase in any adverse event was observed." Notably, the failure of the 1.5 mg/day dose implies that this dose is inadequate and thereby justifies higher routine dosing.

- Clinical implementation and the author's perspective: Iodide has a stronger effect on thyroid function and provides tissue-penetrating antimicrobial benefits from oral administration. Molecular iodine has anti-estrogen effects that correlate with the clinical alleviation of cyclic breast pain and fibrocystic breast disease; other anti-estrogen benefits such as an anti-cancer benefit are reasonably anticipated from supplemental iodine. Products with combined iodine and iodide are available and reasonable for clinical use, and a daily dose range of 3-6 mg does not appear unreasonable and has been shown to be beneficial in human studies. Iodine and iodide are impressively well tolerated. Nicely summarized in a personal email from Michael Gonzalez DSc PhD in November 2012, an overview of iodine-iodine's clinical applications may be stated as follows:

  "Different tissues of the body respond to different forms of iodine. The Iodide form is believed to be particularly useful for the thyroid. But the supplement of choice for the breast is "iodine" not "iodide." Lugol's formula is Iodine 5% + Potassium iodide (KI) 10% in distilled water. Because different tissues concentrate different forms of iodine, using a supplement that contains both iodine and iodide is preferable to using a supplement that contains only one form. With different tissues responding to different forms of iodine, it would make common sense that a greater therapeutic benefit from iodine will be achieved by using a combination of iodide and iodine. … The most frequent adverse reactions to potassium iodide are stomach upset, diarrhea, nausea, vomiting, stomach pain, salivary gland swelling/tenderness, acne and skin rash."

  Antioxidant support in general and supplementation with selenium in particular are recommended always, and particularly when iodine-iodide doses greater than 1-3 mg/d are used. Selenium 200 mcg/d has been shown in several studies to have an ameliorating effect on thyroid autoimmunity and a supportive effect on peripheral thyroid hormone metabolism. Although iodine is generally considered nonthyrotropic, periodic assessment of thyroid function and for thyroid autoimmunity is reasonable for patients taking long-term high-dose treatment. Clinicians should take advantage of iodine-iodide's safe and effective mucolytic, antimicrobial, and anti-estrogen benefits.

**Distinguishing iodiNe from iodiDe**

**iodiNe**

- **Natural** elemental form—diatomic.
- **Nonthyrotropic**—no immediate adverse effects on thyroid function.
- **Nuclear**—affects gene expression, for example by promoting estrogen detoxification and reducing estrogen responsiveness.
- **Nixes microbes**, antimicrobial—very broad spectrum; povidone iodine is one of the most widely used topical antimicrobials in the history of microbiology and medicine.

**iodiDe**

- **Divided**—ionic, nondiatomic.
- **Dietary** form, such as in iodized salt which typically contains potassium iodate, potassium iodide, sodium iodate, or sodium iodide.
- **Dissolves mucus**—mucolytic benefits advantageous in the treatment of asthma, bronchitis and respiratory tract infections. Potassium iodide is thought to act as an expectorant by increasing respiratory tract secretions and thereby decreasing the viscosity of mucus; iodide levels increase in respiratory secretions within approximately 15 minutes after oral administration.
- **Directly thyrotropic**—necessary for thyroid hormone production; high doses can cause thyroid dysfunction, which may be problematic (exacerbation of thyroid autoimmunity, hypothyroidism, or hyperthyroidism) or therapeutic (inhibition of thyroid hormone production during hyperthyroidism).
- **Deals death to microbes**, antimicrobial—very broad spectrum, used in the form of potassium iodide (KI, SSKI) for the treatment of microbial infections such as zygomycosis and sporotrichosis.

**Purple coneflower (*Echinacea purpurea*) with honey bee (*Apis* genus)**: Portland Oregon 2011, photo by DrV

**Progressive awakening**

"**Only that day dawns to which we are awake.**"

Henry David Thoreau, *Walden*[412]

"In virtually all of the great spiritual and philosophical traditions of the world there appears some form of the idea that most human beings are sleepwalking through their own existence. **Enlightenment is identified with waking up.** Evolution and progress are identified with an expansion of consciousness."

Nathaniel Branden, *Six Pillars of Self-Esteem*[413]

"**And once you are awake, then shall you ever remain awake.**"

Friedrich Nietzsche, *Thus Spoke Zarathustra*[414]

[412] Thoreau HD. (Owen Thomas, Ed). *Walden and Civil Disobedience*. New York; WW Norton and Company: 1966, page 221
[413] Nathaniel Branden *The Six Pillars of Self-Esteem*, p. 67
[414] Nietzsche FW. *Thus Spoke Zarathustra*.

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AUTOIMMUNITY (TK TARRANT, SECTION EDITOR)

# Reply to "Role of Western Diet in Inflammatory Autoimmune Diseases" by Manzel et al. in *Current Allergy and Asthma Reports* (Volume 14, Issue 1, January 2014)

**Alex Vasquez**

Published online: 20 June 2014


To the Editor,

Regarding the recent review "Role of Western Diet in Inflammatory Autoimmune Diseases" [1], while I appreciate the importance of this topic and the authors' review, I noted several shortcomings in this review and have questions about the omission of certain information. The authors failed to include relevant and important human data while instead relying on animal studies (their Table 1). The authors also include erroneous information, without appropriate citation.

The authors state that "a high-fat diet is a prominent factor in promoting obesity" but failed to provide citation for this. Importantly, other researchers have shown that high-fat ketogenic diets promote weight loss rather than obesity.

I found the reliance on animal data (especially their Table 1) and the exclusion of human data inappropriate for a review article of this nature and at this time in biomedical history. Several clinical trials have already documented the effectiveness of dietary intervention in human autoimmune diseases. For example, diets which emphasize increased consumption of plant foods (excluding gluten-containing grains) and dietary alteration of gastrointestinal flora have already shown clinical benefits [2]. Exclusion of gluten is of critical importance for some patients, and well established is gluten's role in inflammation, alteration of gastrointestinal flora, increasing intestinal permeability, and direct stimulation of inflammatory pathways. The authors mentioned hypertension four times in their review but failed to mention the remarkable efficacy of therapeutic fasting for this condition [3]. Clinical trials showing the safety and efficacy of dietary fatty acid supplementation were also excluded from the review, despite showing remarkable clinical safety and antirheumatic efficacy [4]. Antiinflammatory mechanisms of dietary intervention not mentioned in their review include alleviation of oxidative stress, alleviation of dysbiosis, reduced reactivity to dietary antigens, normalization of intestinal hyperpermeability, and alleviation of proinflammatory mitochondrial dysfunction [5].

This article is part of the Topical Collection on *Autoimmunity*

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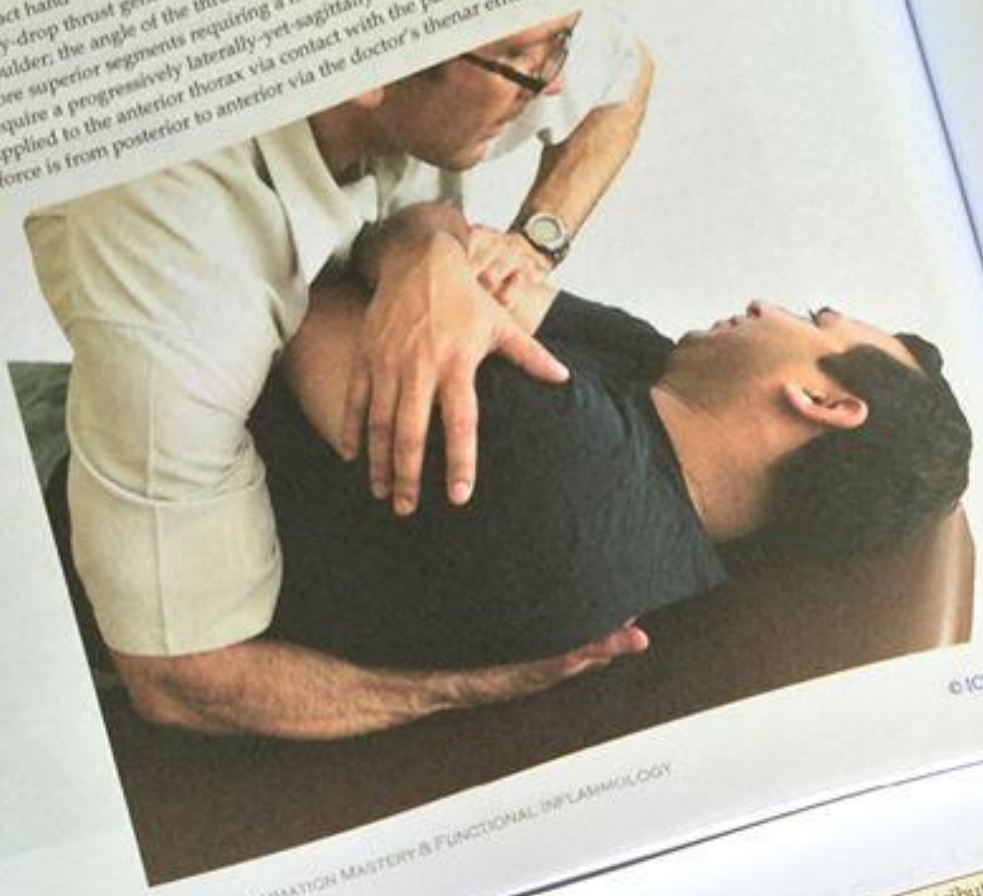
2. Peltonen R, Nenonen M, Helve T, et al. Faecal microbial flora and disease activity in rheumatoid arthritis during a vegan diet. Br J Rheumatol. 1997;36(1):64–8.
3. Goldhamer A, Lisle D, Parpia B, Anderson SV, Campbell TC. Medically supervised water-only fasting in the treatment of hypertension. J Manip Physiol Ther. 2001;24(5):335–9.
4. Belch JJ, Ansell D, Madhok R, O'Dowd A, Sturrock RD. Effects of altering dietary essential fatty acids on requirements for non-steroidal anti-inflammatory drugs in patients with rheumatoid arthritis: a double blind placebo controlled study. Ann Rheum Dis. 1988;47(2):96–104.
5. Vasquez A. Integrative rheumatology and inflammation mastery, Third Edition. Create Space Publishers; 2014.

- manipulative th
- Patient is supine; after p
upper arm, then pulls downward
not muscular force) while raising the
contact hand
- Body-drop thrust generally superiorly and laterally
shoulder; the angle of the thrust changes depending on the
more superior segments requiring a more superiorly directed thrust,
require a progressively laterally-yet-sagittally directed thrust. Notably, the manipulative
applied to the anterior thorax via contact with the patient's upper arm, yet the true manipulative
force is from posterior to anterior via the doctor's thenar eminence positioned posteriorly.







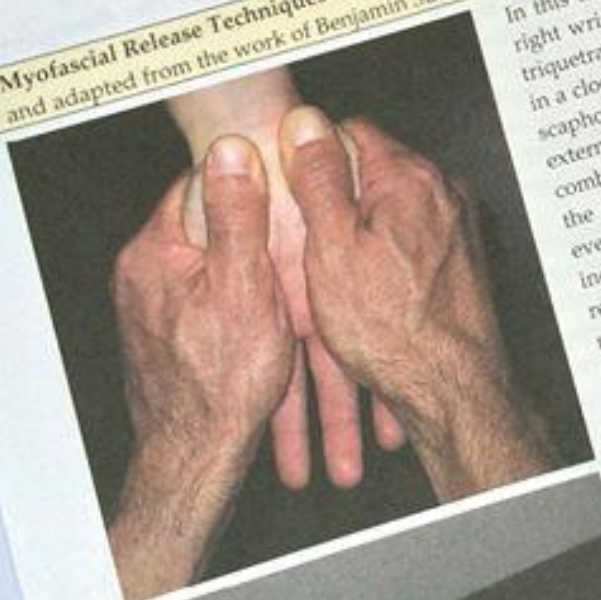




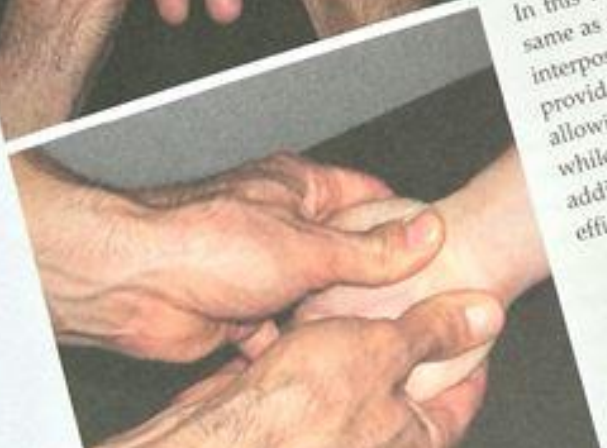
## Proprioceptive Rehabilita

The central nervous system pla
the prevention of joint injuri
essential for proper musculo
either by injury or more co
chronic pain. **Muscle spasm**
**a context that appreciate**
**painful musculoskeletal**

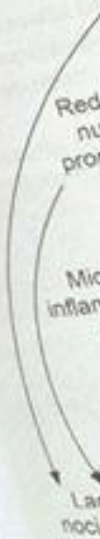
**Myofascial Release Techniques for the Treatment of Carpal Tunnel Syndrome:** Respectfully attributed to and adapted from the work of Benjamin Sucher, D.O.[368,369,370]



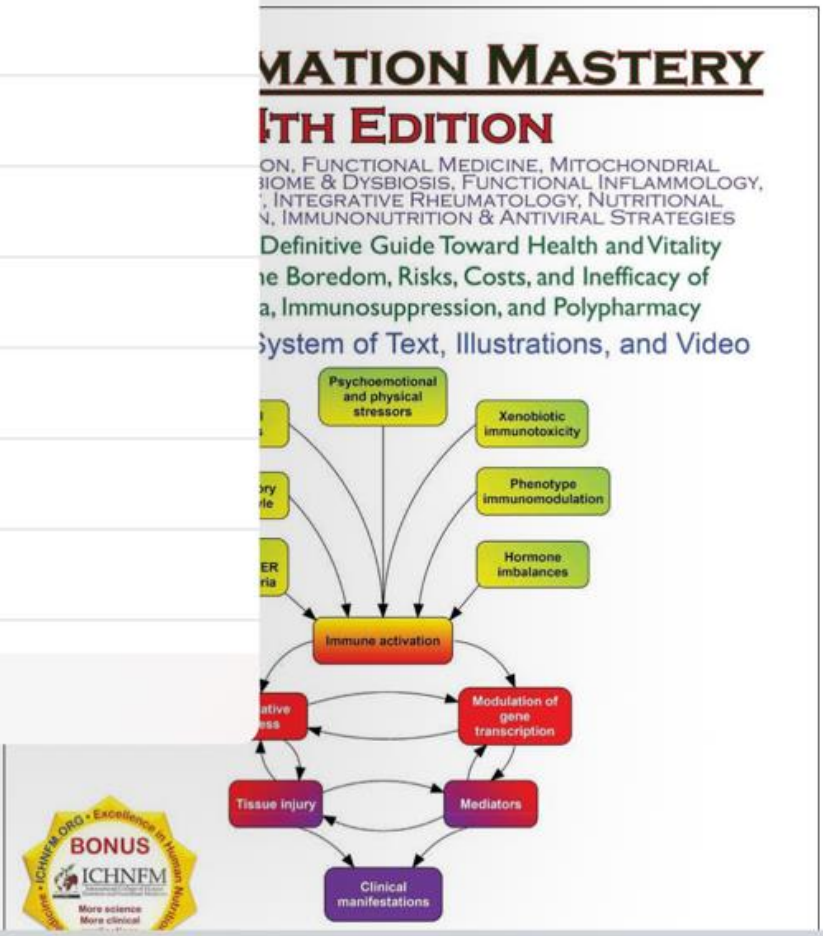
In this demonstration, the doctor is working on the patient's right wrist. In the doctor's right hand, the patient's triquetral, and hamate bones are grasped and rolled externally, in a clockwise direction. In the doctor's left hand, the patient's scaphoid and trapezium bones are grasped and rolled externally from midline, in a counterclockwise direction. The combination of these two motions generates strong tension in the transverse carpal ligament (flexor retinaculum) that eventually leads to relaxation of the ligament and allows for increased cross-sectional area within the carpal tunnel, thus relieving pressure on its contents, particularly the median nerve. This maneuver is generally referred to as the *opponens roll*, and the following techniques are variations of same.



In this maneuver, the doctor's contacts and motions are the same as above, except that in this case the doctor's fingers are interposed between those of the patient. This positioning provides for greater control of the patient's distal palm, allowing the doctor to force the patient's wrist into extension while applying tension to the transverse carpal ligament. The addition of wrist extension appears to increase the clinical efficacy of the maneuver.



ions are the same as above, *but the*
n thumbs to apply *the*
the patient's
rolled



potassium:chloride ratio (chloride reduces effectiveness and retention of potassium), and the overall pH/acid-base balance of the human host (i.e., metabolic acidosis reduces effectiveness and retention of potassium, while an alkaline state improves retention and effectiveness of potassium). Importantly, magnesium status is an important positive-direct determinant of potassium status, particularly in patients with recalcitrant hypokalemia and/or hyperaldosteronism.[122] Respective amounts of potassium per serving of food or juice (1 cup = 8 fluid ounces =240 milliliters) are provided in the table below; renal insufficiency and potassium-sparing drugs/diuretics promote hyperkalemia, generally contraindicate high intake of potassium, and mandate periodic assessment of serum potassium.

**Potassium content of common foods**

| Food serving | Potassium in mg (Na as available) |
|---|---|
| One papaya | 780 |
| One cup of mixed vegetable juice | 740 (35-630 mg Na) |
| One cup of prune juice | 700 |
| One cup of carrot juice | 520 (160 mg Na) |
| One cup plain low-fat yogurt | 510 (150 mg Na) |
| One cup of cantaloupe | 490 |
| One cup of orange juice | 470 |
| One small banana | 465 |
| One cup of honeydew melon | 460 |
| One-third cup of raisins | 365 |
| One cup of carrot-orange juice | 360 (35 mg Na) |
| One medium mango | 320 |
| One medium kiwi | 250 |
| One small orange | 240 |
| One medium pear | 210 |

**The importance of potassium**

"**Adults should consume at least 4.7 grams of potassium per day to lower blood pressure**, blunt the effects of salt, and reduce the risk of kidney stones and bone loss. However, most American women 31 to 50 years old consume no more than half of the recommended amount of potassium, and men's intake is only moderately higher."

Food and Nutrition Board of the Institute of Medicine of the National Academies. "Dietary Reference Intakes: Water, Potassium, Sodium, Chloride, and Sulfate." Released: February 11, 2004 iom.edu/Reports/2004/Dietary-Reference-Intakes-Water-Potassium-Sodium-Chloride-and-Sulfate.aspx

Antihypertensive mechanisms of potassium include vasodilator activity, diuretic and naturietic effects, and suppression of renin, angiotensin, and adrenergic tone.[123] In February 2004, the Institute of Medicine (IOM) set the Adequate Intake of potassium for adults at 4.7 grams a day—more than double previous recommendations; more than 90% of American adults do not meet these recommendations. If 90% of the population is not meeting recommended intakes of potassium, and these recommendations from the IOM come after an extensive review of the scientific literature, then potassium assessment and supplementation should be routine components of patient care; furthermore, this shows to the inadequacy of current laboratory assessments for evaluating potassium status and potassium balance.

- Randomized trial with 1-year follow-up and a title that says it all: Increasing the dietary potassium intake reduces the need for antihypertensive medication (*Annals of Internal Med* 1991 Nov): Forty-seven patients with medication-controlled hypertension completed one year of dietary treatment (or control nonintervention); dietary intervention focused on potassium-rich foods, with compliance monitored by 3-day food records and 24-hour urinary potassium excretion. Results showed: "After 1 year, the average drug consumption (number of pills per day) relative to that at baseline was 24% in group 1 (potassium-rich diet) and 60% in group 2 (control diet). By the end of the study, blood pressure could be controlled using less than 50% of the initial [drug] therapy in 81% of the patients in group 1 compared with 29% of the patients in group 2. … CONCLUSION: Increasing the dietary potassium intake from natural foods is a feasible and effective measure to reduce antihypertensive drug treatment."

[122] "Magnesium deficiency is frequently associated with hypokalemia. Concomitant magnesium deficiency aggravates hypokalemia and renders it refractory to treatment by potassium. Herein is reviewed literature suggesting that magnesium deficiency exacerbates potassium wasting by increasing distal potassium secretion. A decrease in intracellular magnesium, caused by magnesium deficiency, releases the magnesium-mediated inhibition of ROMK channels and increases potassium secretion. Magnesium deficiency alone, however, does not necessarily cause hypokalemia. An increase in distal sodium delivery or elevated aldosterone levels may be required for exacerbating potassium wasting in magnesium deficiency." Huang CL, Kuo E. Mechanism of hypokalemia in magnesium deficiency. *J Am Soc Nephrol*. 2007 Oct;18(10):2649-52

[123] Patki et al. Efficacy of potassium and magnesium in essential hypertension: a double-blind, placebo controlled, crossover study. *BMJ*. 1990 Sep 15;301(6751):521-3

**Practical overview of common abnormalities on the chemistry/metabolic panel**—*continued*

| Low values—considerations | Analyte | High values—considerations |
|---|---|---|
| **Hypokalemia can cause fatal cardiac arrhythmias and needs to be taken seriously.** Replacement is generally via oral administration of potassium-rich foods, juices, or supplements such as potassium citrate (best option) or potassium chloride (KCl, inexpensive and therefore commonly used in medical settings even though KCl is clearly not optimal therapy due to the acidifying effect of the chloride anion). Recalcitrant hypokalemia is often a sign of magnesium depletion.[95] Causes of hypokalemia include diarrhea, vomiting, diuretics, Cushing disease/syndrome, dietary insufficiency, overhydration with mineral-free fluids, hyperaldosteronism and renal artery stenosis. Acute metabolic acidosis should cause relative or absolute elevations in serum K; the finding of normal or low serum K in a patient with acidosis (e.g., diabetic ketoacidosis) indicates (severe) potassium depletion. | **Potassium**: 3.6 - 5.2 mEq/L (mmol/L) | **Hyperkalemia is defined as a potassium level greater than 5.5 mmol/L. Severe hyperkalemia (>7 mmol/L) can be fatal and needs to be taken seriously.** In severe hyperkalemia, treatment and emergency management should be implemented before a complete evaluation and differential diagnosis are performed.[96] ❶ Ensure that blood sample was not hemolyzed. Repeat test if patient is stable and time allows. ❷ If hyperkalemia is severe or patient is symptomatic or has electrocardiographic changes, treat hyperkalemia with intravenous calcium, beta-adrenergic agonists (e.g., albuterol), bicarbonate, insulin and glucose; magnesium sulfate may also help alleviate arrhythmias; oral sodium polystyrene sulfonate (SPS, also known as Kayexalate) is a frequently used potassium-binding agent. ❸ DDX includes adrenal insufficiency, potassium-sparing diuretics, ACE-inhibitors and ARBs, NSAIDs, rhabdomyolysis, renal failure, and massive cell necrosis such as with tumor lysis syndrome. |
| Evaluate hypocalcemia clinically with Chvostek's sign (~30% sensitive) and Trousseau sign (~90% sensitive) which may also be present in hypomagnesemia; evaluate clinically for arrhythmia, muscle spasm/hypertonicity, and hyperreflexia. Measure serum albumin and perform equation for "corrected calcium" if albumin is low. DDX includes renal failure, hypoparathyroidism, malabsorption, and drug effect (e.g., rarely a loop diuretic such as furosemide). Chronic mild hypocalcemia is treated with oral vitamin D and calcium supplementation; subacute symptomatic hypocalcemia can be treated with intravenous calcium gluconate especially if cardiac arrhythmias are present. | **Calcium**: 8.6 - 10.2 mg/dL | Outpatient hypercalcemia is potentially serious and needs to be evaluated in a stepwise manner: ❶ repeat the test to rule out lab error unless you are confident in the performance of the laboratory and stability of the submitted sample,❷ review drug list for adverse effect, such as from hydrochlorothiazide (HCTZ) or rarely from excess cholecalciferol intake, ❸ test intact parathyroid hormone (iPTH) to evaluate for hyperparathyroidism, ❹ evaluate for possible granulomatous disease such as sarcoidosis, tuberculosis, Crohn's disease, and possible leukemia or lymphoma, ❺ consider metabolic bone disease such as Paget disease of bone or metastatic bone disease, ❻ evaluate for cancer, ❼ test urine calcium for familial hypocalciuric hypercalcemia, ❽ refer to specialist such as internist or endocrinologist if hypercalcemia persists and answer is not forthcoming. |

| **Corrected calcium (cCa) equations: Used when both serum calcium and albumin are low** |
|---|
| American units: cCa (mg/dL) = serum Ca (mg/dL) + 0.8 (4.0 - serum albumin [g/dL]) |
| International units: cCa (mmol/L) = measured total Ca (mmol/L) + 0.02 (40 - serum albumin [g/L]) |

[95] "Herein is reviewed literature suggesting that magnesium deficiency exacerbates potassium wasting by increasing distal potassium secretion." Huang CL, Kuo E. Mechanism of hypokalemia in magnesium deficiency. *J Am Soc Nephrol*. 2007;18:2649-52 jasn.asnjournals.org/content/18/10/2649

[96] "If the hyperkalemia is severe (potassium >7.0 mEq/L) or if the patient is symptomatic, begin treatment before diagnostic investigation of the underlying cause." Garth D. Hyperkalemia in emergency medicine treatment and management. *Medscape Reference* emedicine.medscape.com/article/766479-treatment#a1126 Accessed June 2011

# Inflammation Mastery

## 4th Edition: The Colorful and Definitive Guide toward Health and Vitality and away from the Boredom, Risks, Costs, and Inefficacy of Endless Analgesia, Immunosuppression, and Polypharmacy

### A Three-Part Learning System of Text, Images, and Video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- Consultant Researcher and Lecturer (2004-present), Biotics Research Corporation
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    - Founder and Former Program Director of the world's first accredited university-affiliated graduate-level program in Functional Medicine
    - Adjunct Professor, Integrative and Functional Nutrition in Immune Health, Doctor of Clinical Nutrition program
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International College of Human Nutrition & Functional Medicine

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**Notices**: The intended audiences for this book are health science students and doctorate-level licensed medical clinicians. This book has been written with every intention to make it as accurate as possible, and each section has undergone peer-review by an interdisciplinary group of clinicians. In view of the possibility of human error and as well as ongoing discoveries in the biomedical sciences, neither the author nor any party associated in any way with this text warrants that this text is perfect, accurate, or complete in every way, and all disclaim responsibility for harm or loss associated with the application of the material herein. Information and treatments applicable to a specific *condition* may not be appropriate for or applicable to a specific patient; this is especially true for patients with multiple comorbidities and those taking pharmaceutical medications, which are generally associated with multiple adverse effects and drug/nutrient/herb interactions. Given that this book is available on an open market, lay persons who read this material should discuss the information with a licensed medical provider before implementing any treatments and interventions described herein.

associated with complications such as pancytopenia, organ failure, and death[408], it is not a treatment to be taken lightly nor should inexperienced physicians administer it. Colchicine can be administered orally, but its low therapeutic efficacy in relation to its moderate gastrointestinal toxicity limits its applicability. In a poorly designed study by Schnebel and Simmons[409], orally administered colchicine was no better yet was more toxic than placebo; this study appears to have been designed specifically to show inefficacy and toxicity of colchicine since the patients were either given *no treatment* alternating with a *gastroirritative toxic dose* of colchicine.

**Statue of Silvius Brabo**, a mythical Roman soldier who is said to have killed a giant and thrown his hand into the river, hence the name of the city Antwerp, which translates to "hand throwing." Photo at Antwerp City Hall, Belgium 2012 by DrV.

[408] "Bone marrow depression has been reported, primarily in cases of acute colchicine intoxication, and intravenous administration of the drug has been associated with severe pancytopenia and death." Levy M, Spino M, Read SE. Colchicine: a state-of-the-art review. *Pharmacotherapy*. 1991;11(3):196-211

[409] Schnebel BE, Simmons JW. The use of oral colchicine for low back pain. A double-blind study. *Spine*. 1988 Mar;13(3):354-7 Use of colchicine in this study varied from abstinence for 3 days followed by a toxic dose on day 4; therefore patients in the treatment group were subjected to no treatment for 75% of the time, followed by a dose that caused gastrointestinal toxicity—vomiting and diarrhea—the other 25% of the time. At neither phase of the study were patients exposed to a treatment that had any possibility of being effective in relation to the potential toxicity. This study was so poorly designed that its publication brings into question the editorial quality of *Spine* during this era.

**Index**:

As of 2019 and for the foreseeable future, the most current versions of all major patient management and clinical treatment protocols is published in ***Inflammation Mastery, 4th Edition*** as a single volume of 1,182 pages available in full-color print at discounted pricing directly from ICHNFM from https://www.ichnfm.org/im4, while the digital formats are available via several different platforms, including Amazon's Kindle (free) software, Barnes and Noble's Nook, Apple iBook, etc as hyperlinked below. Per popular request by students who were studying (as a required textbook) only one section at a time, "IM4" was also published in two easier-to-carry separate volumes under the name ***Textbook of Clinical Nutrition and Functional Medicine***, which contain chapters 1-4 (pages 1-712+index) and 5 (713-1154+index), respectively. Video access is included with ***IM4*** and ***TCNFM,1+2***. Availability in print and digital formats (examples): https://www.**ichnfm**.org/im4 , https://books.**apple**.com/us/author/alex-vasquez/id1139497284
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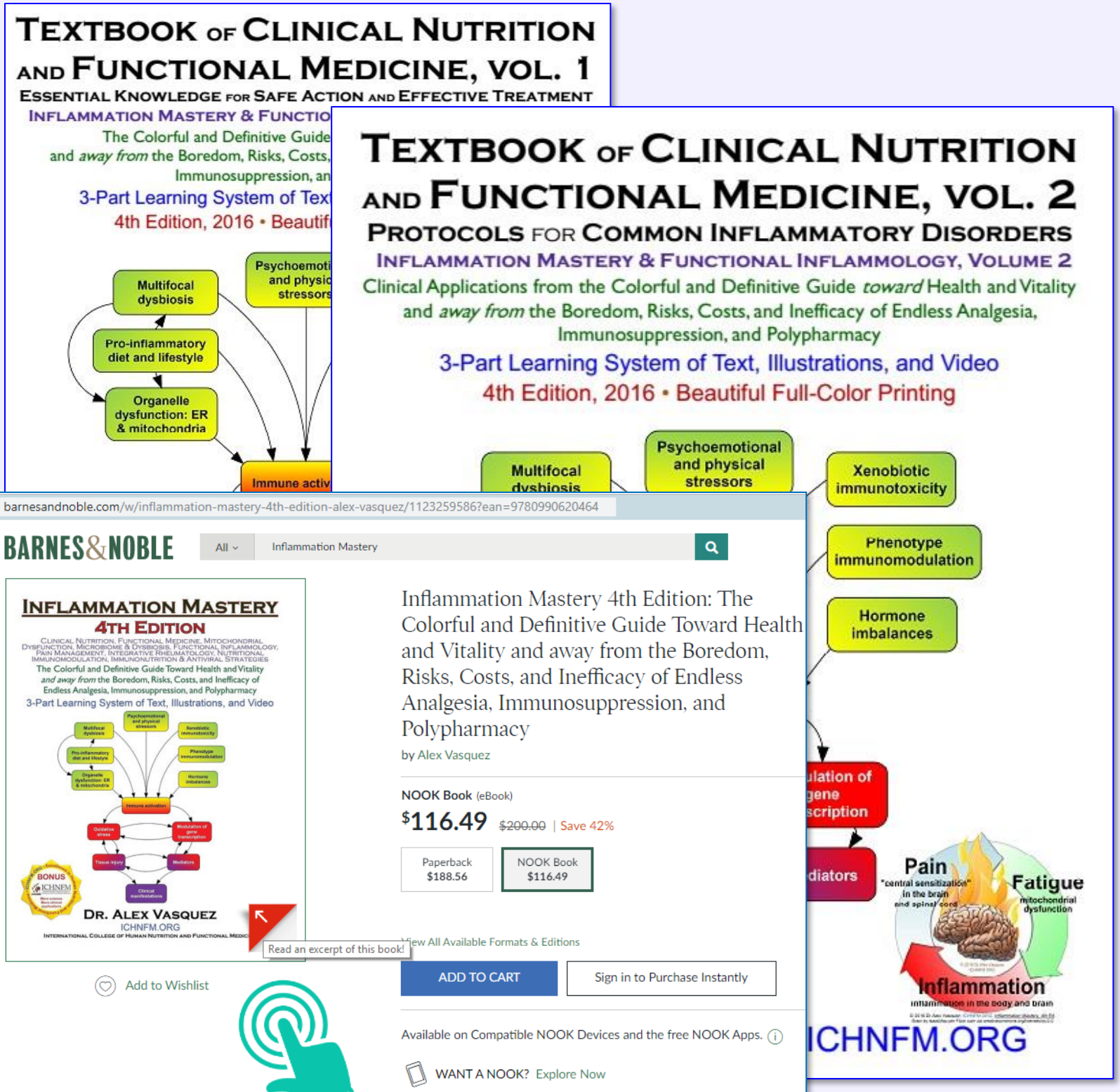

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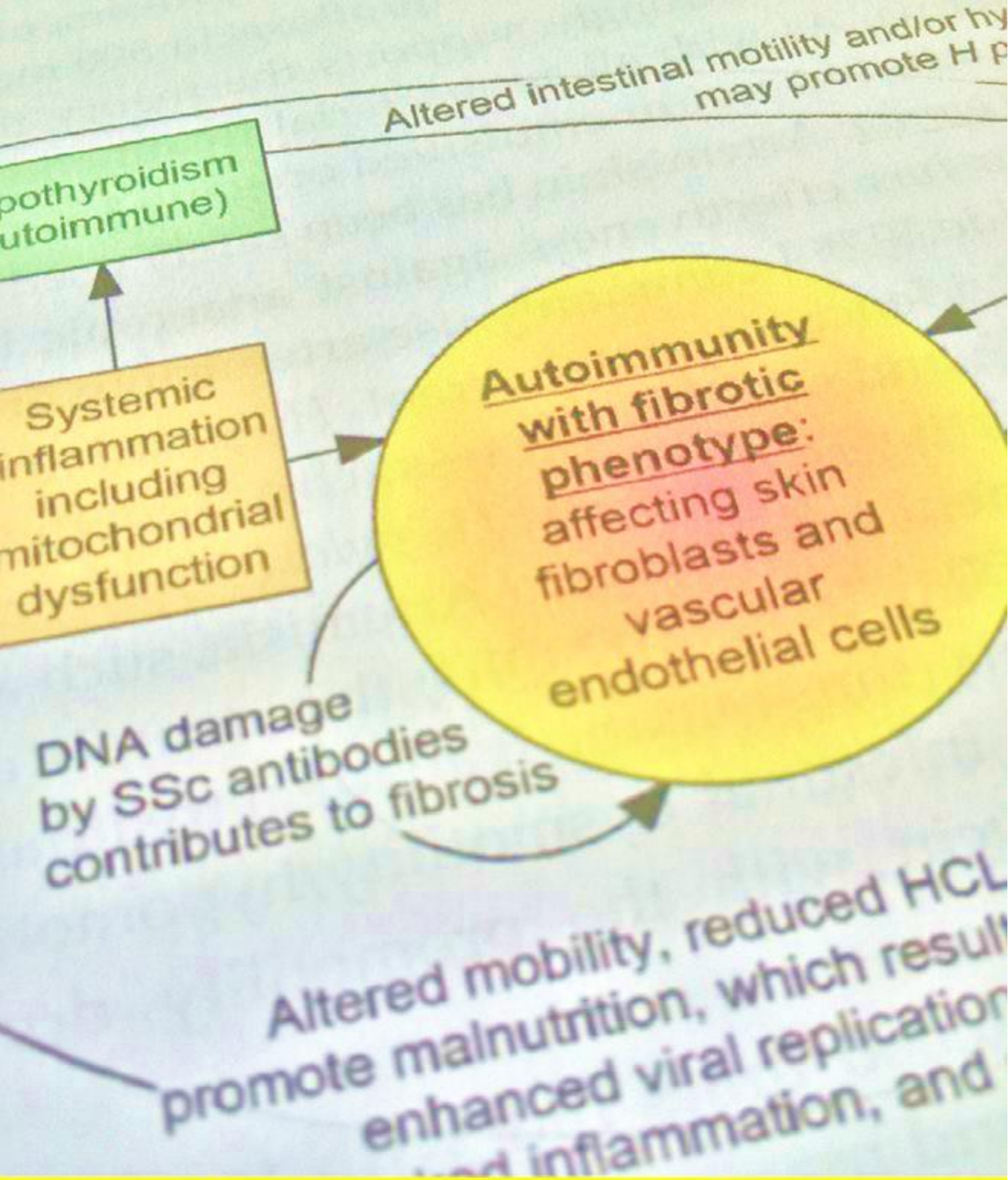

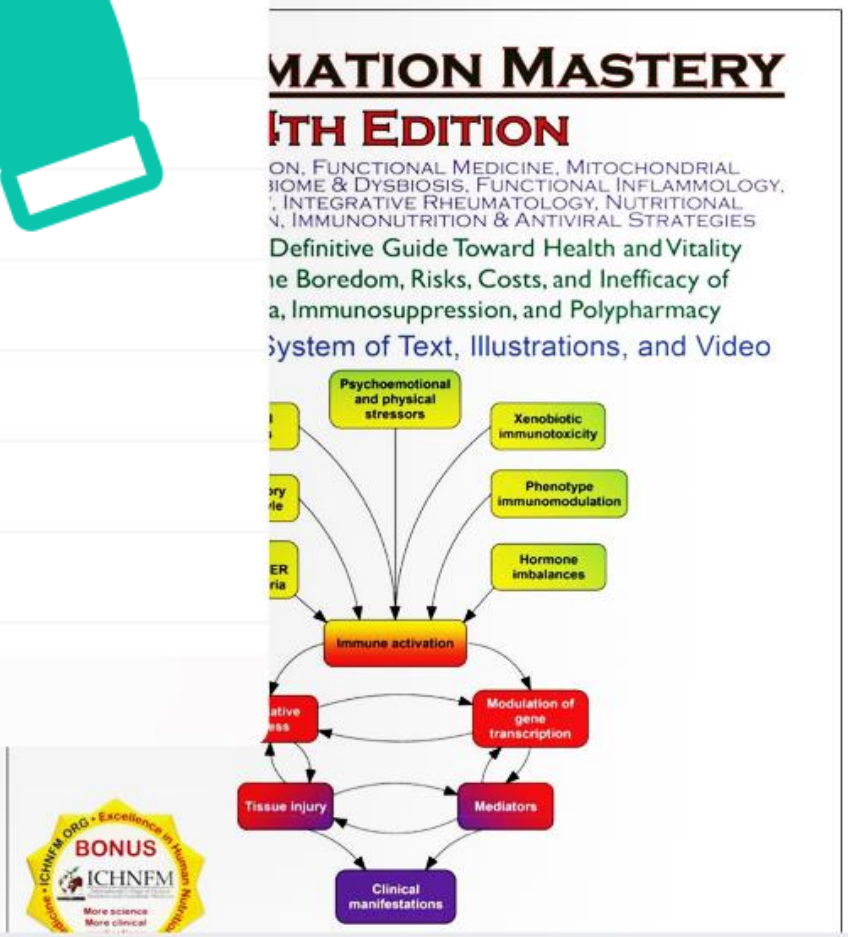




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**Chapter and Introduction**

Preamble

Volume 1

1. Patient Assessments, Laboratory Interpretation, Clinical Concepts, Patient Management, Practice Management and Risk Reduction: *This chapter introduces/reviews/updates patient assessments, laboratory interpretation, musculoskeletal emergencies, healthcare paradigms; the common and important conditions hemochromatosis and hypothyroidism are also included in this chapter since these need to be considered on a frequent basis in clinical practice*
2. Wellness Promotion & Re-Establishing the Foundation for Health: *Reviewed here are diet, lifestyle, psychosocial health, and—given the pervasiveness of persistent organic pollutants and their increasingly recognized clinical importance—an introduction to environmental medicine*
3. Basic Concepts and Therapeutics in (Nondrug) Musculoskeletal Care and Integrative Pain Management: *Nonpharmacologic management of musculoskeletal problems is preferred over pharmacologic (e.g., NSAID, Coxib, steroid, opioid) management because of the collateral benefits, safety, and cost-effectiveness associated with manual, dietary, botanical, and nutritional treatments. A brief discussion of the current crisis in musculoskeletal medicine is provided for contextualization and emphasis of the importance of expanding clinicians' knowledge of effective nondrug treatments*
4. The Major Modifiable Factors in Sustained Inflammation: *Major components of the "Functional Inflammology Protocol" are reviewed here, from concepts and molecular biology to an emphasis on practical clinical applications*

1) Food & Basic Nutrition

2) Infections: Dysbiosis / Viral

3) Nutritional Immunomodulation

4) Dysmetabolism, Mitochondrial Dysfunction, ERS/UPR, mTOR

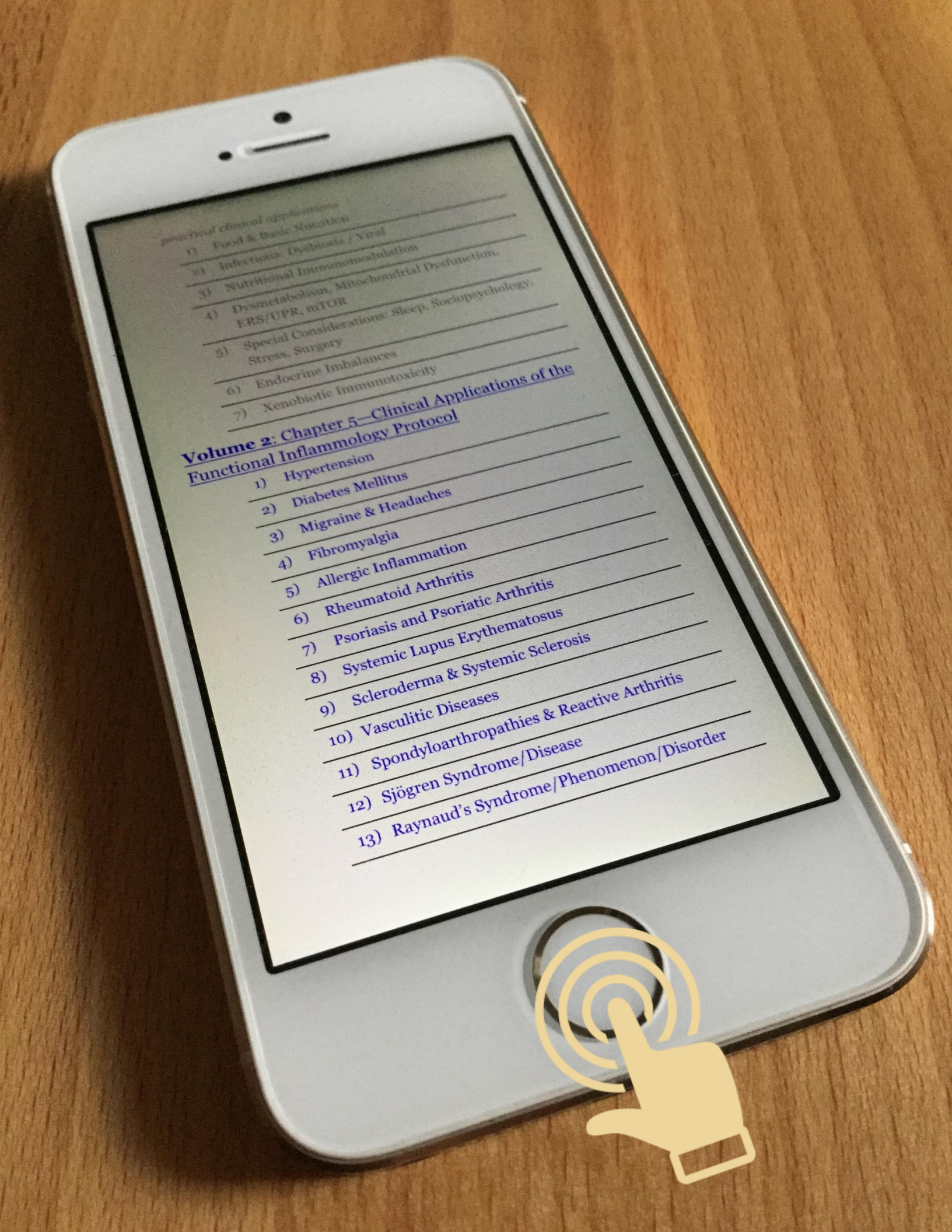
5) Special Considerations: Sleep, Sociopsychology, Stress, Surgery

6) Endocrine Imbalances

7) Xenobiotic Immunotoxicity



Volume 2: Chapter 5—Clinical Applications of the Functional Inflammology Protocol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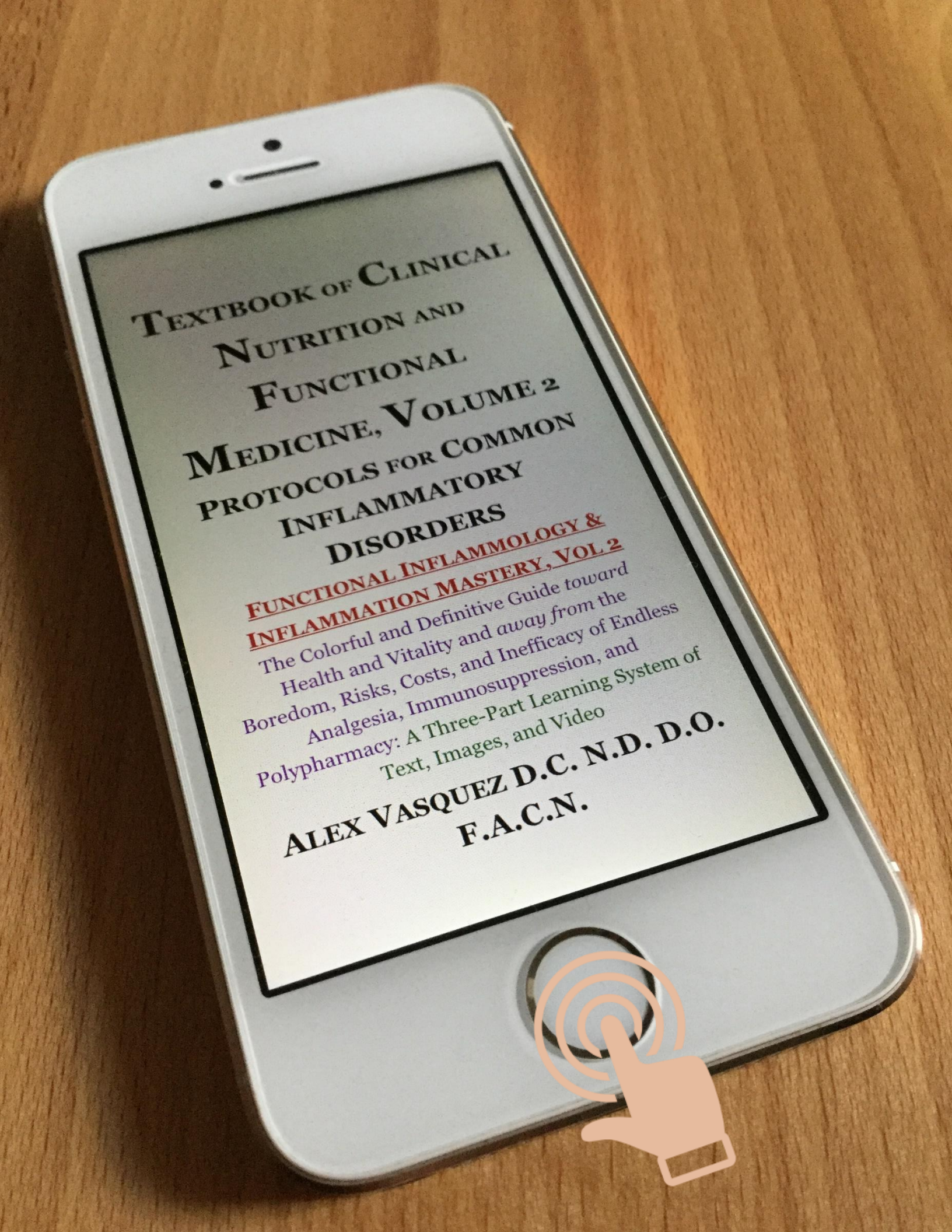
Volume 2: Chapter 5—Clinical Applications of the Functional Inflammology Protocol
1) Hypertension
2) Diabetes Mellitus
3) Migraine & Headaches
4) Fibromyalgia
5) Allergic Inflammation
6) Rheumatoid Arthritis
7) Psoriasis and Psoriatic Arthritis
8) Systemic Lupus Erythematosus
9) Scleroderma & Systemic Sclerosis
10) Vasculitic Diseases
11) Spondyloarthropathies & Reactive Arthritis
12) Sjögren Syndrome/Disease
13) Raynaud's Syndrome/Phenomenon/Disorder


Textbook of Clinical Nutrition and Functional Medicine, Volume 2
Protocols for Common Inflammatory Disorders
Functional Inflammology & Inflammation Mastery, Vol 2
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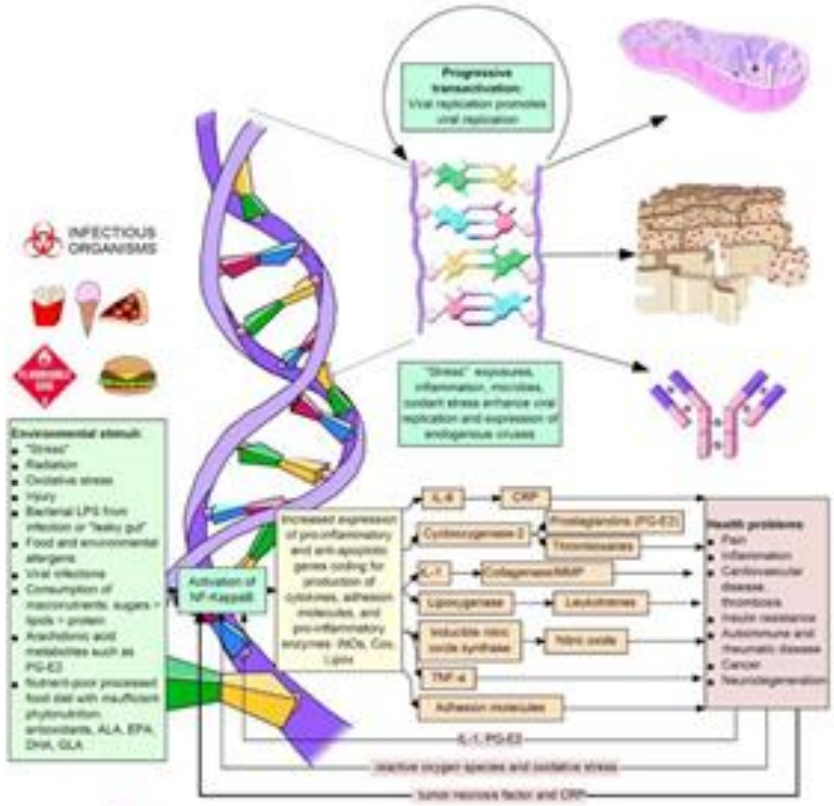



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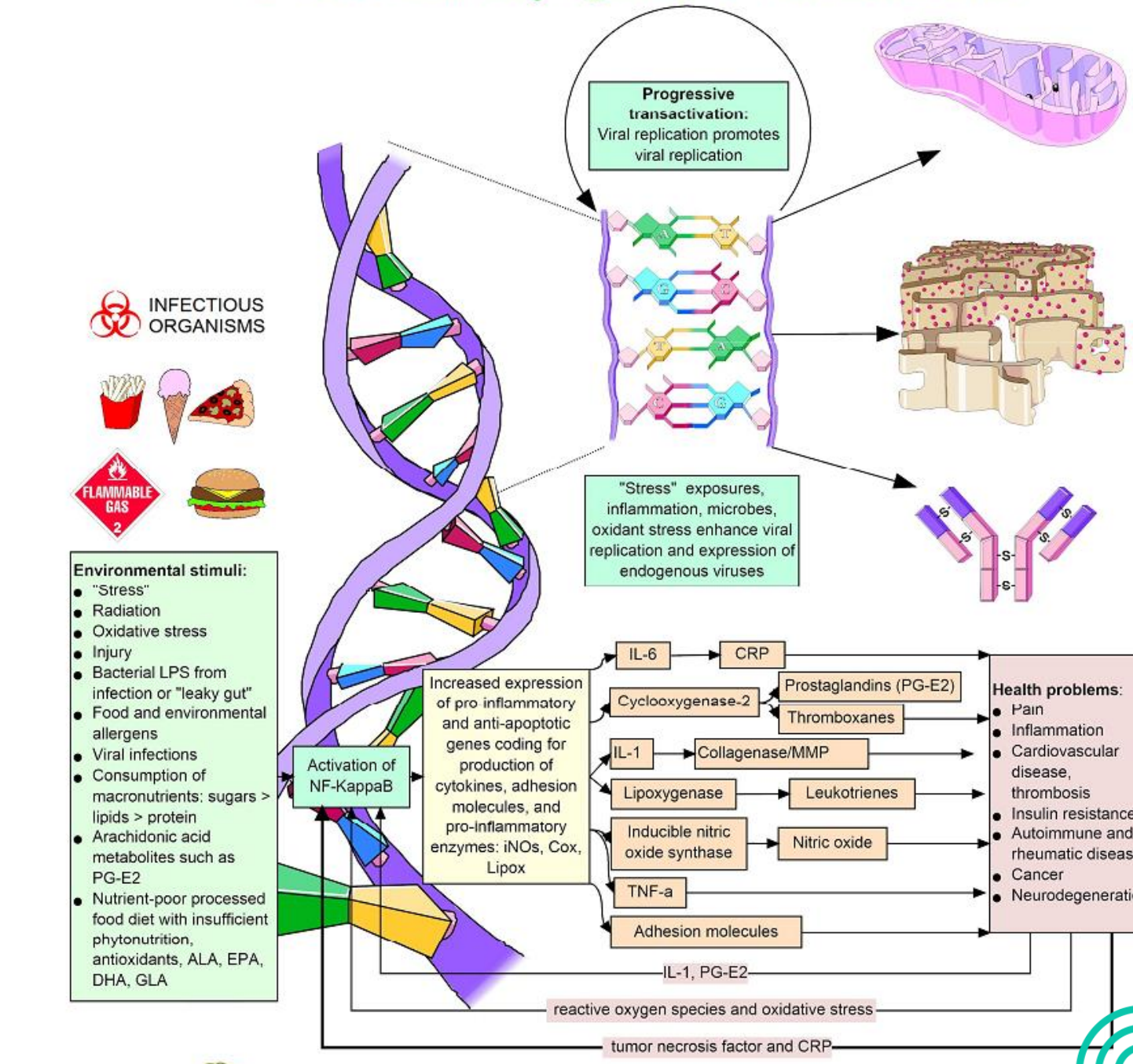



**Dr. Alex Vasquez**

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# Concerns About The Integrity of The Scientific Research Process—Focus On Recent Negative Publications Regarding Nutrition, Multivitamins, Fish Oil And Cardiovascular Disease

*Alex Vasquez, DC, ND, DO; Joseph Pizzorno, ND, Editor in Chief*

**Abstract**

The next step in reestablishing credibility seems to us honesty and recognizing we all share a common goal of the health and wellness of the human community and the planet. Everyone agrees that the current healthcare system, despite its many incredible successes, is also showing its limitations and is no longer sustainable. We believe the solution starts with us the researchers and editors. A good first step might be formally recognizing the errors and showing how we can and *intend* to get better.

Evidence-based medicine—by definition—requires objective, reliable and accurate research and reviews from which to make the best decisions in patient care and public policy. The causes of inaccurate information, ranging from presumably innocent mistakes all the way to apparently intentional fraud, affect all scientific and biomedical disciplines.[1] While these accidental and intentional errors can derail our understanding of diseases and impact tens of thousands of affected patients such inaccuracies in the field of nutrition c ent policy and worldwide.[2] While ons of people. a specific disease examples of human populatio lications, lists nutrition researcl sed solutions. particularly conte pendent upon nutrition researcl stigative and healthcare profess s of clinical nutrition. Clinical rovements are vast majority of ignorance in medical training p are obviously i gastroenterology[7] tion training in clini proclaims itself a eview recent including the entire territory of clinical nutrition.[10] A major and serious problem arises when unskilled and invalid research is published by authors (including nonphysician journalists[11]) in major journals which mischaracterizes the validity of nutrition interventions (e.g., essentially always concluding that nutritional interventions are inefficacious or potentially hazardous) and then such research is used politically and in the media to disparage, restrict and regulate practitoners and nutrition supplement industry[12] to the detriment of human health.

Several factors disrupting the integrity of nutrition research are commonly found in studies published by "elite" universities in "top-tier" journals, which are then republished and distributed as "headlining news" in newspapers, magazines, and television via which they

**PDF articles**: Full-text archives of the author's articles are available per the following:

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- **VIDEO**: BRIEF Critique of "Effects of n−3 Fatty Acid Supplements in Diabetes Mellitus: ASCEND Study" https://vimeo.com/287650812
- **VIDEO:** Bad Science in Medical Nutrition: Politics of Fish Oil https://vimeo.com/314997927

examples of questionable or inaccurate publications related to nutrition. Perceived shortcomings are documented with both citations here and links to more detailed and authoritative reviews and video presentations. In some instances, speculations regarding the cause and consequences of identified errors are provided.

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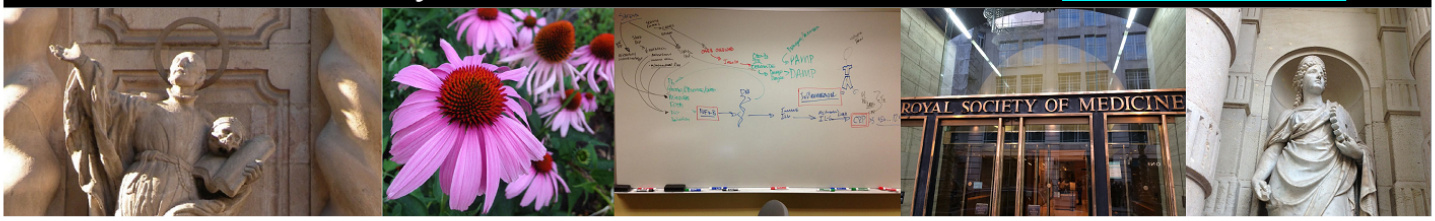


**Perspective, Opinion, Editorial** • Education • Academia • Wage Theft • Corruption

# Ending the Exploitation of Experts Begins with Educating Them about Employment, Curbing Enthusiasm to Preserve Enthusiasm

Alex Vasquez DC ND DO FACN

***My own paths toward and perspectives on Education***

My passion for teaching and education began "formally" when I was about 9 years of age, sitting on the floor of Ms Hall's 4th grade classroom; from that vantage as I sat somewhat near my best friend Robert, I saw the destructive power of bad teaching and discrimination, and from that day I started analyzing teachers, teaching methods, educational and social structures, and ways to convey knowledge and inspire students. Additionally inspired by my teacher of English and Literature in my final years at Riverside Military Academy, I began college with the plan of eventually teaching "something—most likely English and Literature" because I appreciated and valued teaching, proper grammatical structure, and nuanced use of language; I later developed and interconnected my interests in teaching, writing, language, physiology, medicine, and nutrition to complete three doctorate degrees in the health sciences and publish more than 120 articles, letters, rebuttals, monographs, and books on a wide range of topics, with those publications ranging from dense 1-page Letters and Responses to published research up to single-author textbooks of more than 1,180 pages. I have taught at various colleges and universities at the undergraduate, graduate/Masters, and Doctorate levels and have lectured internationally for post-graduate medical education. I see teaching not simply as effective transferal of information, but also as a means to interconnect and inspire generations of people, notably in a reciprocal manner. At its best, teaching and learning are activities that reflect and support love for life itself.

***Oh, the stories I could tell you about the innards of Academia, "nonprofits", and "accredited" schools***

I would be happiest to tell you that Academics and Administrators are vanguards
support for fellow Professors, and
commitment is to truth and realit
setting ablaze the passions of the
they teach, lead, and supervise; I'
in flower fields like a professoria
singing a rhythmical rendition of "*The Hills are Alive…with the…Passions of Education and Intellectual Integrity*." But a pollyannic representation of my observations would be a misrepresentation of the realities I have seen and experienced. I have seen university presidents lie to their students, expel experts for the sake of maintaining their own petty powers and preferences, and I have seen entire academic administrations lie (misrepresent) in unison to their boards of trustees and their accreditation commissions. I have seen stand-alone academic programs make millions of dollars in profit, while its administrators refuse to pay a living wage to doctorate-level infrastructure and while allowing themselves 6-week European vacations during major institutional initiatives. I have seen administrators lie to accreditors and allow students to cheat their way through graduate programs (by bypassing faulty examination software in online programs), and I have seen accreditors turn a blind eye to obvious university corruption, made worse when the accreditation commission is infiltrated by university administrators—thus did "accreditation" come to lose its value. I have seen "nonprofit educational institutions" underpay their faculty, plagiarize from their faculty, resell the work of other professionals without notice or compensation, and then pay their upper administrators in excess of US$160,000 for less than part-time work—thus did "nonprofit organization" come to lose its value. I have seen schools blackmail excellent professors and leaders in education with gag orders, legal threats, and financial bribery (range US$25,000 up to $250,000) to buy their silence about institutional corruption. I have corresponded with employment attorneys, State Attorneys General, and US Department of Education, most of whom shrugged their shoulders and said, "That's the way it is in academia." Sorry

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Barceloneta sunset © 2019 by Dr Vasquez

**Tutorial & Editorial** • Scientific Writing • Journal Editing • Professional Experience • Video

# How to Improve Scientific Writing and Journal Editing: A Short Narrative-Video Guide, Part I

Alex Vasquez DO ND DC FACN

## *Introduction*

"Hello everyone, Dr. Alex Vasquez here, and today I'm going to start a different series of videos, and this time the conversation is going to focus around journal editing and writing. I'm calling this "*Editing and Writing Tips #1*", and I'm going to start with a few of my own perspectives and experiences, then I'll talk about a few basics, and a few influential ideas. In later videos, I will talk about some more specific examples, and then perhaps at some point we will have a review and conclusion.

## *Early Experiences and Influences*

Very briefly I'll talk about some of my own experiences, and the reason for my doing this is to share with you and segue into some examples that I think are very important. Basic though they might be, a lot of our success in various fields of life actually comes from respecting and appreciating and utilizing those basic concepts.

Let us start here with some of my initial experiences. I started becoming aware of language and the fact that I had some facility for it, first, when I was about 12 years old. I remember writing a poem in class, and again this is somewhat peripheral to the main topic of today, but I do remember that e
kind of my entryway, I think, i
that our assignment was to wr
remember writing this poem in cl
on and on, and—compared with s
I just realized that writing for me

Then again, when I wa
military school, I remember in ou

being asked questions, and I remember just how the answers to understanding grammar and language just came very easy to me, and I do remember feeling like I had some facility for the structure of language.

Another influential experience I had when I was about 11 years old, totally unrelated to language, is that we took, in the late 1970s or early '80s, a Computer Science class in our elementary school, and I remember that class also specifically having some influence on me, in terms of structuring logic. We basically had to write our own computer programs and this was back when computers were very new. Obviously today everybody has computers; back in the late '70s, computers were a novelty. I consider myself lucky to have taken this Computer Science class; it was obviously extremely basic, but we did have to write some code and what I remember from that is just the sequential manner in which communication has to take place in order to be successful. In this case, we were writing programs for computers and doing basic

> "Writing comes from the entirety of one's experience."
> Dr Alex Vasquez

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- See original video here: https://vimeo.com/318326979


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JOURNAL OF ORTHOMOLECULAR MEDICINE

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Editorial

# Misrepresentations of Clinical Nutrition in Mainstream Medical Media: Growing Importance of Legitimate Expertise in Independent Peer-Reviewed Publications - Part 1

## 2018 As a Milestone in the Post-Truth Era

Among the various topics that have either interested or fascinated me throughout my youth and well into my adult years, Nutrition has certainly reigned supreme. My personal routine has been to read as much as reasonably and practically possible on the topic, while not doing so to the exclusion of other topics in biomedicine, psychosociology and philosophy. Thus, with roughly 30 years of experience in reading books and primary research in the field of Nutrition, I could not help but notice the radical departures that occurred in 2018 from the previous norms to which I had grown accustomed.

Of course, 2018 was not the first year during which "bad research" was published in mainstream medical journals and then replicated throughout the echo chamber of mass media; one could observe this periodically occurring throughout the past 50 years, starting not at least with the demonization of dietary cholesterol and the glorification of processed foods, especially refined grains and so-called vegetable oils. But in 2018 what many of us observed was not simply poorly performed research but, in s
es, radical departures from any attempt to pre
descriptions that could be considered "reason
previous standard.[1] Especially related to the
trition, mainstream medical journals and the
which parrots their conclusions have begun
overt misrepresentations of Nutrition with re
gard for science, logic, biomedical history and

One has to be aware of a few key ironies
terize mainstream medical discussions of nutri
that 1) medical physicians receive essentially
in clinical nutrition in their graduate school e
in their post-graduate residency training[2], 2)
sicians and organizations publish "research"
commentaries (both of which commonly conc
tritional interventions are inefficacious or unsafe), despite their lack of formal education on the topic, and then 3) mainstream medical voices consistently call for "regulating the nutrition supplement industry" despite their lack of training on the topic and because of negative conclusions based on their own poorly conducted research and self-serving conclusions. As such, not only are the map-makers blind, but they mislead their blind followers, and then both groups promote themselves as expert cartographers and guides when advising the public on an area that none of them have studied or understood. We should have no surprise whatsoever when the "medical community" publishes poorly conducted and self-serving "research" on the topic of nutrition, to reach their desired conclusion that nutrition is unsafe and inefficacious, and that the profitable market needs to be managed of course by the selfsame "medical community" that is never received a decent 15 minutes on the topic of therapeutic nutrition. Pervasive and persistent ignorance on the topic of nutrition among medical physicians must be understood as intentional and strategic, because otherwise this problem would have been solved 30 years ago when it was first discussed during what was called at the time the "golden age of nutrition."[3] The easiest way to manipulate people and to keep them in a perpetual state of confusion, ineffectiveness, and dependency is to

**PDF articles**: Full-text archives of the author's articles are available per the following:

- https://ichnfm.academia.edu/AlexVasquez
- https://www.ichnfm.org/public
- VIDEO: BRIEF Critique of "Effects of n−3 Fatty Acid Supplements in Diabetes Mellitus: ASCEND Study" https://vimeo.com/287650812
- VIDEO: Bad Science in Medical Nutrition: Politics of Fish Oil https://vimeo.com/314997927

when pondering the probable future of intellectual integrity and the products of education.

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# Mitochondrial Medicine Arrives to Prime Time in Clinical Care: Nutritional Biochemistry and Mitochondrial Hyperpermeability ("Leaky Mitochondria") Meet Disease Pathogenesis and Clinical Interventions

Alex Vasquez, DC, ND, DO, FACN

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## MITOCHONDRIAL MEDICINE ARRIVES TO GENERAL PRACTICE AND ROUTINE PATIENT CARE

Mitochondrial disorders were once relegated to "orphan" status as topics for small paragraphs in pathology textbooks and the hospital-based practices of subspecialists. With the increasing appreciation of the high frequency and ease of treatment of mitochondrial dysfunction, this common cause and consequence of many conditions seen in both primary and specialty care deserves the attention of all practicing clinicians.

We all know that mitochondria are the intracellular organelles responsible for the production of the currency of cellular energy in the form of the molecule adenosine triphosphate (ATP); by this time, contemporary clinicians should be developing an awareness of the other roles that mitochondria play in (patho)physiology and clinical practice. Beyond being simple organelles that make ATP, mitochondria play clini… ce—contains inflammati… kinase and disease such… omparatively disorders su… n) and—like stated durin… h active and Nutrition a… that need to September … to appreciate mitochond… the highest mitochondrial dysfunction to clinical diseases must be considered on a routine basis in clinical practice. *Mitochondrial medicine* is no longer an orphan topic, nor is it a superfluous consideration relegated to boutique practices. Mitochondrial medicine is ready for prime time—now—both in the general practice of primary care as well as in specialty and subspecialty medicine. What I describe here as the "new" mitochondrial medicine is the application of assessments and treatments to routine clinical practice primarily for the treatment of secondary/acquired forms of mitochondrial impairment that contribute to common conditions such as fatigue, depression, fibromyalgia, diabetes mellitus, hypertension, neuropsychiatric and neurodegenerative conditions, and other inflammatory and dysmetabolic conditions such as allergy and autoimmunity.



## BEYOND BIOCHEMISTRY

Structure and function are of course intimately related and must be appreciated before clinical implications can be understood and interventions thereafter applied with practical precision. The 4 main structures and spaces of the mitochondria are (1) intramitochondrial matrix—the innermost/interior aspect of the mitochondria containing various proteins, enzymes of the Krebs cycle, and mitochondrial DNA; (2) inner membrane—the largely impermeable lipid-rich convoluted/invaginated membrane that envelopes and defines the matrix and which is the structural home of many enzymes, transport systems, and important structures such as cardiolipin and the electron

importance; just as we have come to appreciate the

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Editorial

# Orthomolecular Medicine, Catalytic Creativity, and the Psychosocial Ecosystem

## Transitioning From One Year to the Next

Various cultures since time immemorial have marked and celebrated the winter solstice with celebrations, meals with friends and family, and time away from work; transitioning from one calendar year to the next has given people pause and a moment to reflect on the events that happened in the past year and what might be anticipated in the next. Reflection with anticipation along with the realization that the future is somewhat malleable inclines people to imagine how the future might be shaped by the exertion of some modicum of creativity and effort. Any realistic conception of how we might improve the near future must segue from our recent past; we must have an awareness of what is going on around us as we look toward the future to visualize ourselves living within it and also acting upon it. What is going on in the world and how might I act upon that trend and flow in order to improve both its transition and its destination? What should each of us do on a personal level to (in the words of Mahatma Gandhi) be, embody, and materialize the change(s) that we want to see in the world?

## Salutation and Introduction From the Journal's New Editor

Over the past few years I have reflected on several occasions how much I enjoy editing, and so I was correspondingly surprised and pleased when I was offered the opportunity to be the next Editor for the *Journal of Orthomolecular Medicine.* I began studying nutrition and orthomolecular concepts in my teen years and more diligently as I entered graduate school in the early 199 trition" book that I read *Your Nerves* (1975) by this was followed imm tures of Jonathan V Wr of whom would later b University. By the mid- Jeffrey Bland PhD had tional medicine, which and personal[3] reasons. By this time my own personal library contained several hundred books, mostly dedicated to nutrition and health with another large section on philosophy and psychology. In 1994, I joined the Review Staff of the *Journal of Naturopathic Medicine,* and I started publishing nutrition articles, perhaps most of which might be seen as practice in preparation of an important letter published in 1996 by the American College of Rheumatology in their journal *Arthritis and Rheumatism.* Since those early years and during the course of three doctorate degrees and teaching thousands of students/attendees internationally, I have reviewed for[4] and published in[5] a wide range of refereed journals in addition to publishing commissioned books, chapters, and independent publications and videos. Being an author and reviewer for many different publications—along with my experiences teaching internationally, treating patients in various settings, designing and directing academic programs, and producing educational videos—has given me a wide range of experiences and insights that I hope to bring to the benefit of the *Journal of Orthomolecular Medicine.*

## We Must Work Together if We Are Going to Succeed

I have to start this conversation with a few hopes, assumptions, and beliefs, namely that you (the reader) and I (the author and new Editor) have a few things in common. On a professional level, by virtue of the fact that you are reading this essay, I will assume that you are interested or actively engaged in healthcare, medicine, nutrition, research and/or public health. I might also imagine that some smaller percentage of our new and established readers are perhaps less inclined toward the mechanisms and more drawn to the *Journal of Orthomolecular Medicine* for its potential humanistic insights and social contributions; we can reasonably competent healthcare ate nutrition) are basic mit a counterargument of my assertions, they more to the point, my rdless of personal po- share some common the following:

- We each want to receive and deliver the best healthcare possible: If we have a problem, then we each want the best possible solution. Efficiency of time or money is not the top priority when we are seeking solutions

International Journal of Human Nutrition and Functional Medicine www.ICHNFM.org



Mini-Review • Continuing Education • Microbiome • Dysbiosis • Infectious Disease

# Translating Microbiome (Microbiota) and Dysbiosis Research into Clinical Practice: The 20-Year Development of a Structured Approach that Gives Actionable Form to Intellectual Concepts

Alex Vasquez DC ND DO FACN

***Experience and Perspectives***

Many years ago when I published my first books[1,2] and articles[3] detailing "dysbiosis", the word could hardly be found in the Medline index, the topic was controversial at best and ethereal at worst, the term "microbiome" (first published in French in 1949 and in English in 1988) was virtually unknown, and I spent most of the time and space in my lectures and articles substantiating and defending the condition's existence. These days, everyone is talking about microbiome, dysbiosis, "leaky gut" (thanks largely to Leo Galland MD), and my 1996 article on "Silent Infections and Gastrointestinal Dysbiosis" has been downloaded at least 4,000 times and is one of the top 1% most popular articles on Academia.edu.[4] In the preparation of my dysbiosis lecture at a major functional medicine conference in 2010, I found that only 180 Medline articles indexed the term "dysbiosis", and now—slightly less than five years later—more than 1,200 articles index that term. Obviously, the dysbiosis concept has

**"Dysbiosis" is an important concept, but doctors cannot treat concepts.**

We have to define, describe, and deconstruct the microbes, molecules, and mechanisms into their components, then rebuild a conceptual scaffold and intellectual structure that becomes a useful tool that, with study and experience, can be used in a clinical setting to effective benefit.

practical application is a bit indelicate and cumbersome beyond the most commonly repeated advice of advocating probiotics, avoiding antibiotics, perhaps delving into using botanical antimicrobials and laboratory testing. Breath testing (an insensitive test for only one subtype of gastrointestinal dysbiosis) and microbiologic testing have become popular to the point of overuse as doctors grapple for clinical clues. (Noteworthy in the conversation on functional laboratory testing is that one functional medicine laboratory in particular used inaccurate proprietary microbe-identification methods to extract

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CME
CONTINUING MEDICAL EDUCATION

# THE CLINICAL IMPORTANCE OF VITAMIN D (CHOLECALCIFEROL): A PARADIGM SHIFT WITH IMPLICATIONS FOR ALL HEALTHCARE PROVIDERS

Alex Vasquez, DC, ND, Gilbert Manso, MD, John Cannell, MD

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InnoVision Communications is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The learner should study the article and its figures or tables, if any, then complete the self-evaluation at the end of the activity. The activity and self-evaluation are expected to take a maximum of 2 hours.

**OBJECTIVES**

Upon completion of this article, participants should be able to do the following:

1. Appreciate and identify the manifold clinical presentations and consequences of vitamin D deficiency
2. Identify patient groups that are predisposed to vitamin D hypersensitivity
3. Know how to imple
proper doses and wi

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While we are all familiar with the important role of vitamin D in calcium absorption and bone metabolism, many doctors and patients are not aware of the recent research on vitamin D and the widening range of therapeutic applications available for cholecalciferol, which can be classified as both a vitamin and a pro-hormone. Additionally, we also now realize that the Food and Nutrition Board's previously defined Upper Limit (UL) for safe intake at 2,000 IU/day was set far too low and that the physiologic requirement for vitamin D in adults may be as high as 5,000 IU/day, which is less than half of the >10,000 IU that can be produced endogenously with full-body sun exposure.[1,2] With the discovery of vitamin D receptors in tissues other than the gut and bone—especially the brain, breast, prostate, and lymphocytes—and the recent research suggesting

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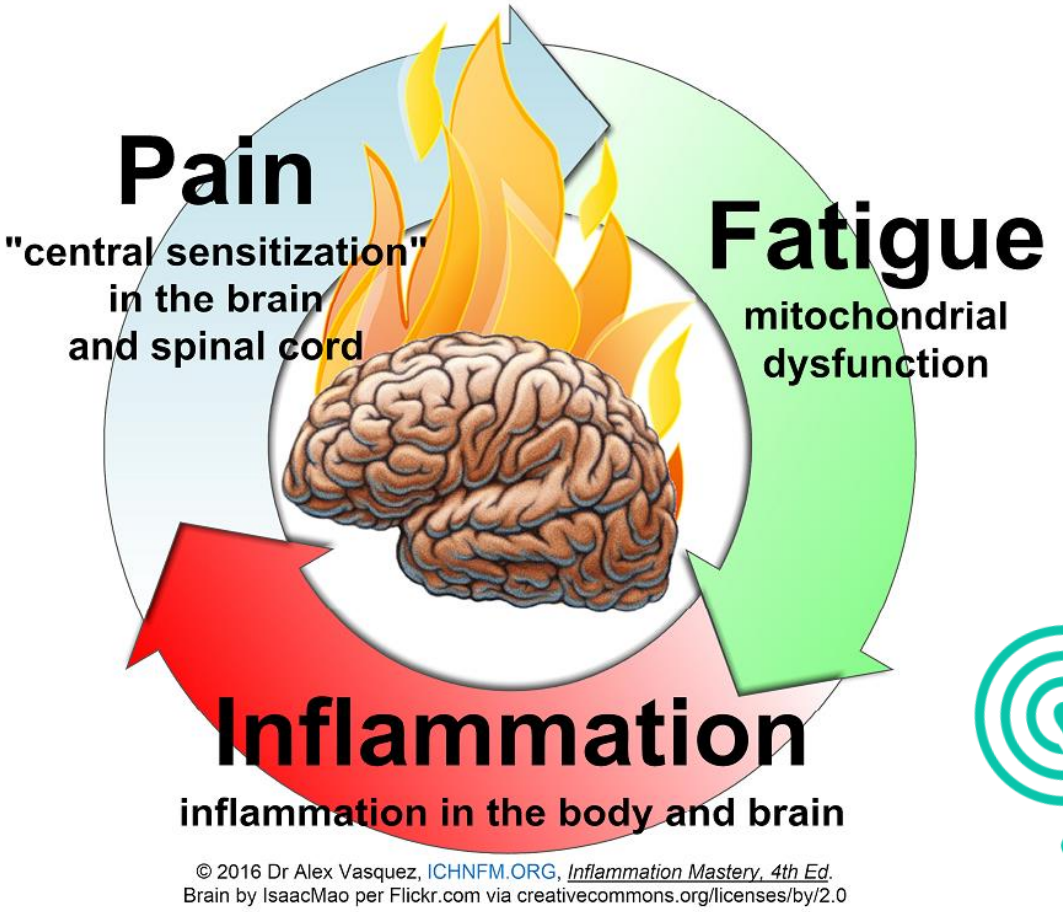




Alex Vasquez, D.C., N.D., D.O., F.A.C.N.
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- From ***Inflammation Mastery, chapter 5***, the two sections specific to migraine and fibromyalgia were also published separately as ***Pain Revolution*** (full-color printing; https://www.amazon.com/dp/B01AR3NX0S) and ***Brain Inflammation in Chronic Pain, Migraine and Fibromyalgia: The Paradigm-Shifting Guide for Doctors and Patients Dealing with Chronic Pain*** (black-and-white printing; https://www.amazon.com/dp/B01EQ9KMH6/); both versions are also available in digital ebook format for phone, computer, iPad via the free Kindle software

The New York Academy of Sciences 200 Years

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: Annals *Reports*
COMMENTARY

# Biological plausibility of the gut–brain axis in autism

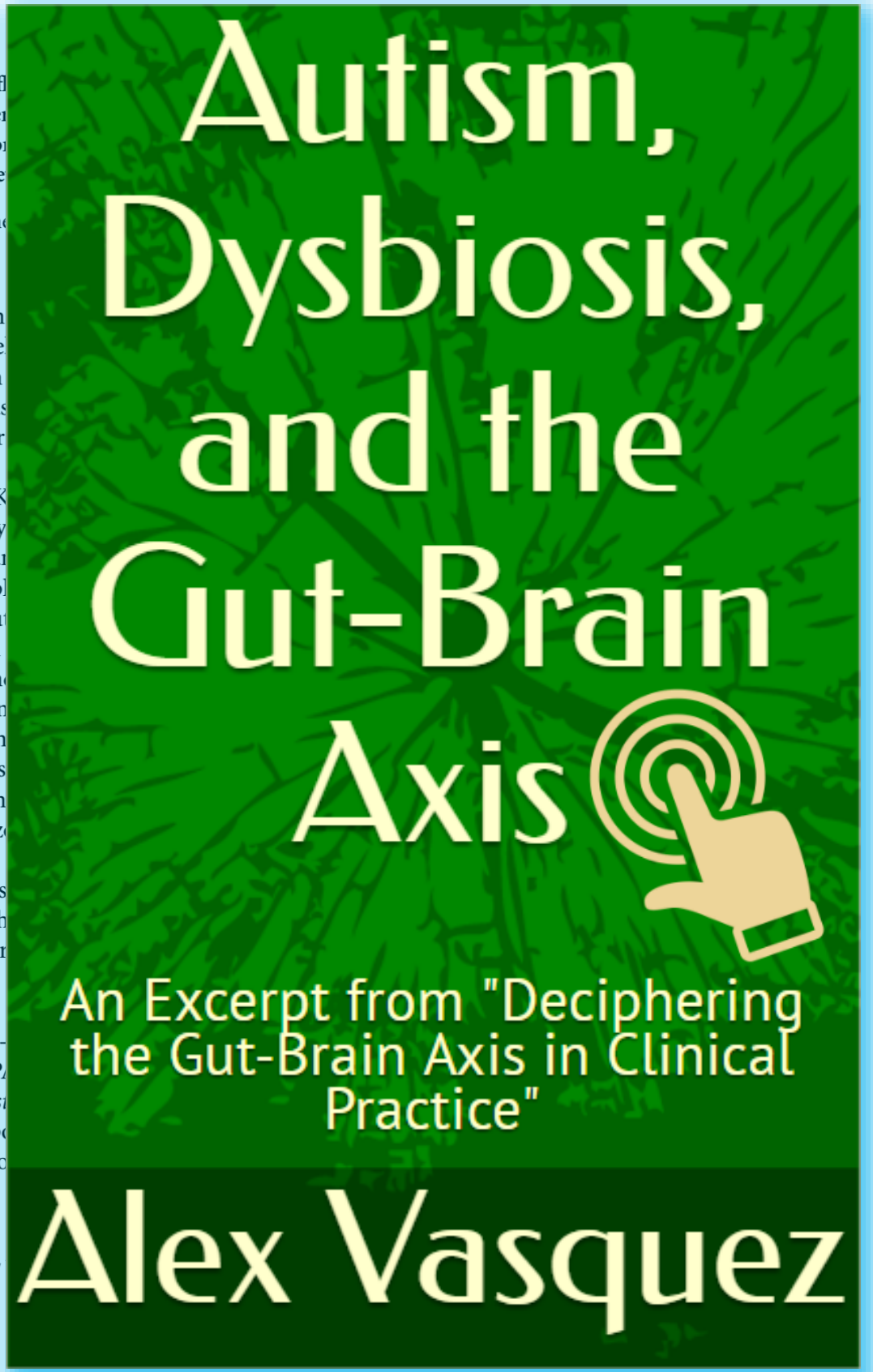
Alex Vasquez

**Organic abnormalities with neuroinfl
purine metabolism, neurotransmitte
noted in autism, and many of these ab
metabolites, and heightened serum le**

**Keywords:** gut–brain axis; autism; m

In their recent review, Sherwin
among many other issues, the re
gut microbiome–brain axis with
section subtitled "Microbiota-bas
the treatment of autism: hype or
*et al.*[1] largely discuss preclinical
the 2017 open-label study by K
used a sequence of oral vancomy
polyethylene glycol laxative, a
human fecal microbiota transpl
clinical benefit in subjects with au

Readers will likely benefit from
tional relevant clinical studies, in
lication by Sandler *et al.*[3] showin
of autistic manifestations followin
oral vancomycin, as well as cas
ing positive impact of various an
apies (metronidazole, ketoconaz
cillin) in patients with autism.[4,5]
have been shown to have gut dys
as well as *Clostridia* species,[6] th
group of bacteria noted for their pr
rotoxic substances. International
consistently demonstrated that
have heighted production of 3-(3-
3-hydroxypropionic acid (HPHP
phenylalanine metabolite of *Clos*
trointestinal tract.[7,8] HPHPA rep
with the conversion of dopamine to

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As of 2019 and for the foreseeable future, the most current versions of all major patient management and clinical treatment protocols are published in ***Inflammation Mastery, 4th Edition*** as a single volume of 1,182 pages available in full-color print at discounted pricing directly from ICHNFM from https://www.ichnfm.org/im4, while the digital formats are available via several different platforms, including Amazon's Kindle (free) software, Barnes and Noble's Nook, Apple iBook, etc as hyperlinked below. Per popular request by students who were studying (as a required textbook) only one section at a time, "IM4" was also published in two easier-to-carry separate volumes under the name ***Textbook of Clinical Nutrition and Functional Medicine***, which contain chapters 1-4 (pages 1-712+index) and 5 (713-1154+index), respectively. Video access is included with ***IM4*** and ***TCNFM,1+2***.

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