

Reducing Pain and Inflammation Naturally - Part IV: Nutritional and Botanical Inhibition of NF-kappaB, the Major Intracellular Amplifier of the Inflammatory Cascade. *A Practical Clinical Strategy Exemplifying Anti-Inflammatory Nutrigenomics*

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Abstract: Modulation of genetic expression by the skillful use of dietary, nutritional, and botanical interventions is clearly the leading edge of modern nutritional practice. Thus, familiarity with the concepts and implementation of “nutrigenomics” must become incorporated into the clinical skill set of chiropractic and naturopathic physicians. This article focuses on the nutritional and botanical inhibition of the primary “amplifier of inflammation” known as nuclear transcription factor kappaB (NF-kappaB). From both clinical and pharmacological standpoints, the safe and effective inhibition of NF-kappaB is considered a major therapeutic goal for the prevention and treatment of conditions associated with an upregulated inflammatory response, namely diabetes, arthritis, cancer, autoimmunity, and the aging process in general. This article introduces concepts and terminology that will facilitate the effective clinical implementation of a nutritional protocol aimed at relieving excess inflammation by inhibiting NF-kappaB.

INTRODUCTION

New research is showing that many diseases are associated with inappropriate activation of nuclear transcription factor kappaB, generally referred to as NF-kappaB. Inhibition of NF-kappaB is now a major therapeutic goal in the treatment and prevention of a wide range of illnesses, including cancer, arthritis, autoimmune diseases, and neurologic illnesses such as Alzheimer’s and Parkinson’s disease.¹ While the development and use of drugs that inhibit NF-kappaB will take several years of additional research and will likely be associated with numerous adverse effects and exorbitant expense, the nutritional and botanical inhibition of NF-kappaB is available to us immediately with proven safety and near-universal affordability. This paper will take readers beyond the benefits which can be obtained with the health-promoting diet², combination fatty acid therapy³, and anti-inflammatory and analgesic nutrients and botanicals⁴ that were described in the first three articles in this series.

THE BIOCHEMISTRY OF INFLAMMATION: FROM NF-KAPPAB TO EICOSANOIDS

The process of inflammation may be said to begin with the translation of an environmental trigger into a biochemical signal that initiates the inflammatory pathway. Proinflammatory environmental triggers can include injury, radiation, infection, oxidative stress, and certain foods, particularly those high in fat and those with a high glycemic index (ie, “simple sugars”), as well as vitamin D deficiency. Regardless of the original locus or etiology, each of these stimuli may lead to activation of the NF-kappaB cascade, which is a major pathway for the amplification of inflammatory processes.⁵

As a ubiquitous nuclear transcription factor that promotes the activation of genes that encode for inflammatory

mediators and enzymes, NF-kappaB can be thought of as the major intracellular “amplifier” which ultimately increases the production of the direct mediators of inflammation such as cytokines, prostaglandins, leukotrienes, nitric oxide and other reactive oxygen species (“free radicals”). The process of inflammation begins when two subunit proteins—p50 and p65—merge in the cytoplasm to form NF-kappaB, which is kept in an inactive state by inhibitor kappaB (IκB). When triggered by any of the common stimuli listed above, IκB is phosphorylated and destroyed by inhibitor kappaB kinase (IKK). The destruction of IκB allows NF-kappaB to move into the nucleus of the cell where it binds with DNA and activates genes encoding for inflammatory responses. These genes then elaborate their inflammatory products such as interleukin-1 (IL-1), IL-6, tumor necrosis factor, and the proinflammatory destructive enzymes including inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), the lipoxygenases (LIPOX), and the matrix metalloproteinases (MMP) including collagenase and gelatinase, which destroy connective tissue. Nitric oxide synthase catalyses the formation of nitric oxide (NO-), which plays an important role in the development of peripheral osteoarthritis⁶ and spinal disc degeneration⁷ via oxidative destruction of articular tissues. Cyclooxygenase transforms arachidonic acid into prostaglandins and thromboxanes, which recruit leukocytes to the area of inflammation, exacerbate edema, sensitize peripheral neurons to increased pain perception, and ultimately facilitate the liberation of proteinases, such as matrix metalloproteinases, which destroy joint structures. Present in several isoforms, the lipoxygenase enzyme acts on arachidonic acid to produce leukotrienes that also increase inflammation, joint destruction, and production of MMP. Overall, this same inflammatory response contributes to the genesis and perpetuation of numerous inflammatory disorders, such as osteoarthritis, cancer, rheumatoid arthritis and other autoimmune diseases, and

Figure 1.
The creation and
activation of NF-
kappaB—a
crucial step in
the amplification
of proinflamma-
tory gene
expression.
*Adapted from
Vasquez A.
Integrative
Orthopedics.
(Optimal-
HealthResearch.c
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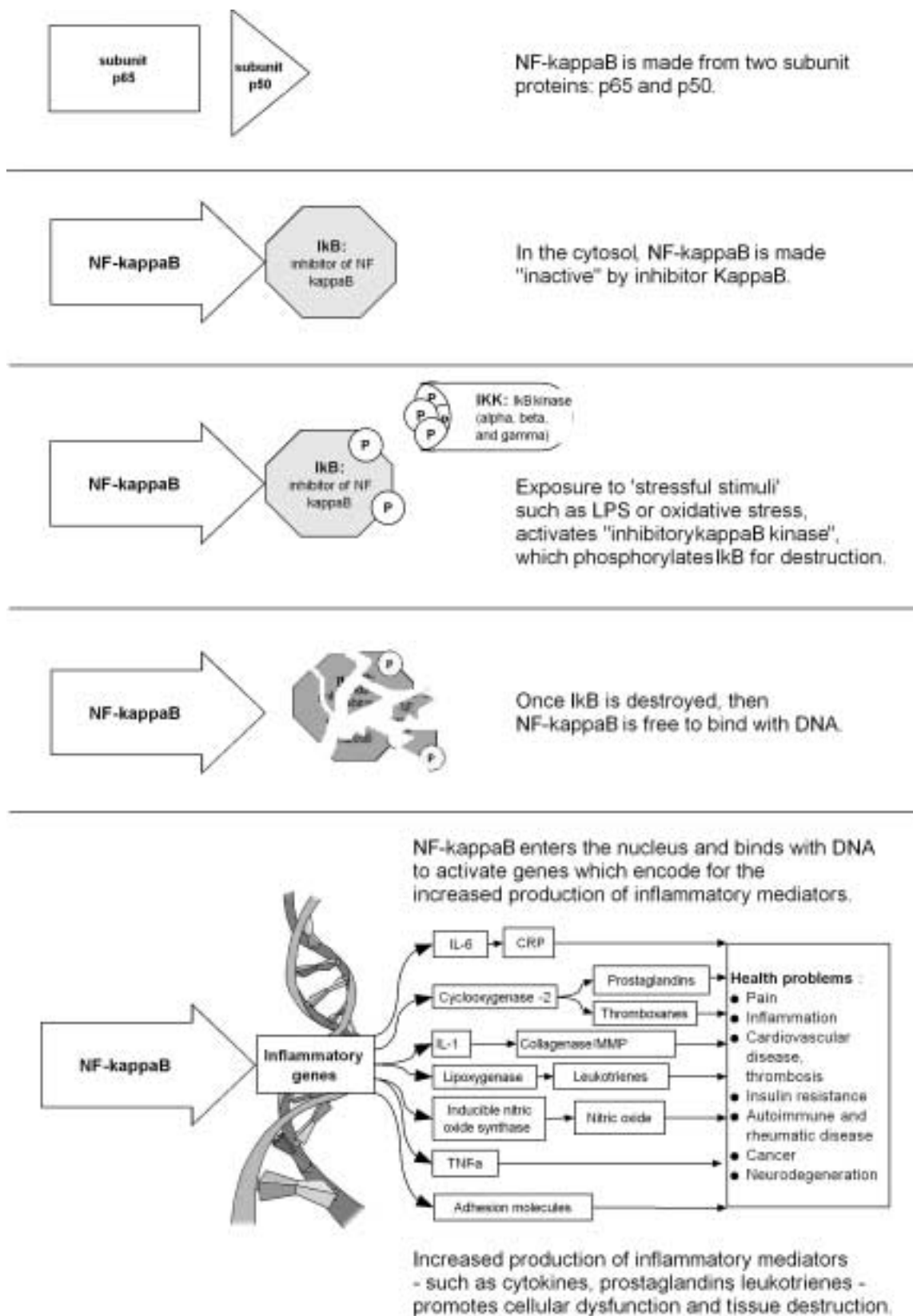
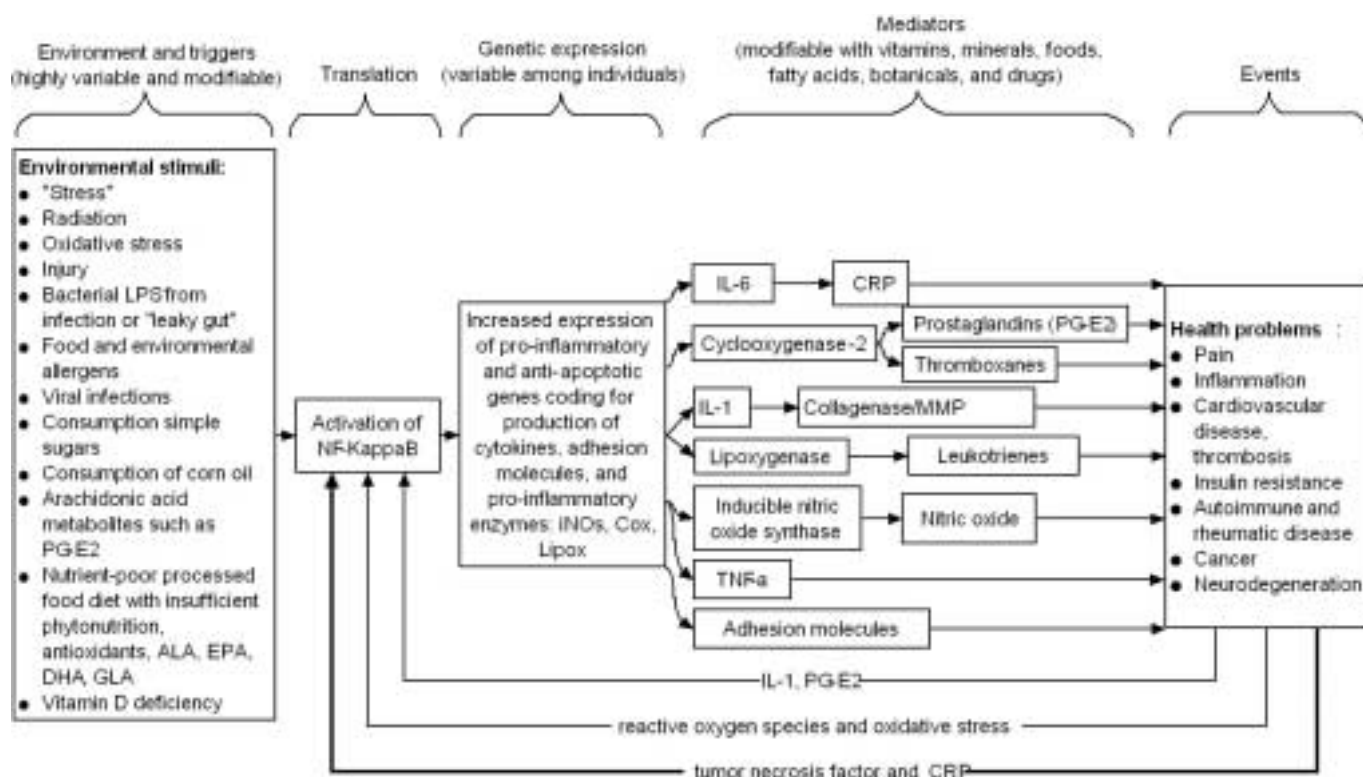


Figure 2. Translation of environmental traumas into biochemical inflammation. Note the self-perpetuating “vicious cycle” where inflammatory mediators promote additional inflammation via activation of NF-kappaB. Adapted from Vasquez A. *Integrative Orthopedics*. (OptimalHealthResearch.com): 2004



essentially all conditions associated with pain and inflammation. This process of NF-kappaB activation and modulation of genetic expression is illustrated in Figures 1 and 2.

FROM BIOCHEMICAL EFFECTS TO CLINICAL CONSEQUENCES

Activation of NF-kappaB leads to the elaboration of mediators that damage tissues and contribute to the clinical manifestations of poor health. IL-6 stimulates production of C-reactive protein (CRP), which is a sensitive serum marker of inflammation (such as in osteoarthritis and rheumatoid arthritis) and is associated with an increased risk of cardiovascular disease, progressively deteriorating health and "rapid biological aging" in men and women.^{8,9} iNOS increases production of the free radical nitric oxide which is elevated in degenerating joints⁶ and spinal discs⁷ and which contributes directly to joint destruction via oxidation of articular tissues.¹⁰ COX-2 is responsible for the conversion of arachidonic acid to prostaglandins, several of which increase the perception of pain by sensitizing peripheral nociceptors¹¹ and by a central hyperalgesic effect¹² and by promoting destruction of articular structures by increasing

elaboration of proteolytic enzymes, variously named collagenases, gelatinases, and matrix metalloproteinases.¹³ Similarly, LIPOX catalyzes the conversion of arachidonate to leukotrienes, which promote swelling, inflammation, chemotaxis, and tissue destruction via increased release of proteolytic enzymes. In their anti-inflammatory roles, LIPOX and COX act on GLA for the production of the anti-inflammatory 15-HETE and prostaglandin E-1, respectively, as well as on EPA and DHA for the production of anti-inflammatory prostaglandins, leukotrienes, docosatrienes, and resolvins as discussed previously.³ Our discussion of the mechanisms of anti-inflammatory nutritional interventions must also include the phytonutritional activation of peroxisome proliferator-activated receptors (PPARs), since fatty acids and selected botanical medicines exert their actions at least in part by activation of PPAR-alpha and PPAR-gamma, which then mediate health-promoting and clinically significant anti-inflammatory effects. As fatty acid receptors that influence genetic expression via suppression of NF-kappaB as well as via NF-kappaB-independent pathways, PPARs when moderately activated induce numerous beneficial physiologic responses, including direct and indirect anti-inflammatory, anti-cancer, and cardioprotective effects.¹⁴⁻¹⁶

NUTRIGENOMICS: MODULATION OF GENETIC EXPRESSION VIA INTERVENTIONAL NUTRITION

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.”¹⁷ 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 proinflammatory NF-kappaB and the anti-inflammatory peroxisome-proliferator activated receptors (PPARs). Indeed, 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 level.

Fatty acids and their end-products modulate genetic expression in several ways, as these examples will illustrate. 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 LA content, rapidly activates NF-kappaB and thus promotes tumor development, atherosclerosis, and elaboration of pro-inflammatory mediators such as TNF α .¹⁸⁻²⁰ Similarly, 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, inflammation manifested by an increase in PG-E2 leads to additive expression of cyclooxygenase, which further increases inflammation and elevates C-reactive protein.²¹ Some of the unique health-promoting effects of GLA are nutrigenomically mediated via activation of PPAR-gamma, resultant inhibition of NF-kappaB, and impairment of estrogen receptor function.^{22,23} Supplementation with ALA leads to a dramatic reduction of prostaglandin formation in humans²⁴, and this effect is probably mediated by downregulation of proinflammatory transcription, as evidenced by reductions in CRP, IL-6, and serum amyloid A.²⁵ EPA appears to exert much of its anti-inflammatory benefit by suppressing NF-kappaB activation and thus reducing elaboration of proinflammatory mediators.^{26,27} EPA also indirectly modifies gene expression and cell growth by reducing intracellular calcium levels, thereby providing an anti-cancer benefit.²⁸ DHA is the precursor to docosatrienes and resolvins which downregulate gene expression for proinflammatory IL-1, inhibit of TNF α ,

and reduce neutrophil entry to sites of inflammation.²⁹ Oxidized EPA activates PPAR-alpha and thereby suppresses NF-kappaB and the activation of proinflammatory genes.^{27,30} Therefore, we see that fatty acids (and other botanicals and nutrients, discussed below) directly affect gene expression by complex and multiple mechanisms, and the synergism and potency of these numerous anti-inflammatory nutraceuticals supports the rationale for the use of nutrition and select botanicals for the safe and effective treatment of inflammatory disorders.

NATURAL AND SYNERGISTIC INTERVENTIONS THAT INHIBIT NF-KAPPAB

This section efficiently reviews several of the more powerful nutritional and botanical treatments which have been shown to inhibit NF-kappaB. Using these treatments in combination provides additive and synergistic benefits compared to using one treatment at a time.

- **Vitamin D:** Vitamin D has potent anti-inflammatory and pain-relieving benefits in patients with musculoskeletal pain, as previously reviewed in this Journal¹⁴ and elsewhere.^{31,32} Impressively, vitamin D also modulates genetic transcription, as evidenced by its ability to reduce activation of NF-kappaB. Although 25-hydroxyvitamin D has limited biological activity, its more active metabolite, 1-alpha,25-dihydroxyvitamin D3 (1,25-(OH)2-D3) can inhibit NF-kappaB activity in human cells.^{33,34} Thus, it is not surprising that clinical studies in patients with critical illness and multiple sclerosis have shown an anti-inflammatory benefit from vitamin D. Vitamin D supplementation can reduce inflammation by 23% as objectively assessed with C-reactive protein levels.³⁵
- **Curcumin from *Curcuma longa* (“Turmeric”):** Turmeric is an ancient spice that has been used for thousands of years to add flavor and color to food. Although *in vitro* tests and animal studies have suggested that the active components related to curcumin may have potential as powerful agents against human diseases, most researchers and reporters have failed to realize that—in humans—curcumin is very poorly absorbed. Even when curcumin powder is administered in doses as high as 2,000 mg, there is no appreciable increase in serum levels in humans. However, when curcumin is coadministered with piperine, which increases intestinal absorption and reduces enterohepatic detoxification, serum levels of curcumin increase by 2,000% in humans.³⁶ Piperine is derived from *Piper nigrum*, also commonly known as black pepper, a spice found in nearly every kitchen in the

world. Piperine enhances absorption and reduces clearance of some drugs such as theophylline (detoxified by CYP3A4 and CYP1A2) and propranolol (detoxified by CYP2D6); this combination of effects (e.g., enhanced absorption and reduced clearance) may require dosage modification for numerous drugs. No adverse reactions have been reported with doses of piperine up to 15 milligrams per day.³⁷ Pregnant women and nursing mothers should generally avoid piperine supplementation.

- **Lipoic acid:** As a fat-soluble and water-soluble antioxidant with clear biologic activity, it is not surprising that lipoic acid is also noted to inhibit NF-kappaB activity in a dose-dependent manner.³⁸
- **Green tea extract:** Epigallocatechin gallate from green tea is an effective inhibitor of IKK activity. Thus, green tea extract inhibits activation of NF-kappaB. This may explain, at least in part, some of the reported anti-inflammatory and anticancer effects of green tea.³⁹
- **Rosemary:** Carnosol in rosemary inhibits NF-kappaB activation, and this is a likely mechanism of its anti-inflammatory and chemopreventive action.⁴⁰
- **Grape seed extract (GSE):** GSE is a potent antioxidant that has been shown to inhibit NF-kappaB.⁴¹
- **Propolis (a source of caffeic acid phenethyl ester):** Caffeic acid phenethyl ester (CAPE) is an anti-inflammatory component of propolis (honeybee resin) that is a specific inhibitor of NF-kappaB.⁴² CAPE has shown clinical benefit in the treatment of asthma, which is the prototype of chronic airway inflammation.⁴³ As with all bee products, allergy to propolis has been reported and may be more common in patients with a history of allergy to honey or other bee products.
- **Resveratrol:** Resveratrol shows anticarcinogenic, anti-inflammatory, and growth-modulatory effects which are due in part to the inhibition of NF-kappaB.⁴⁴ In fact, according to recent *in vitro* research, resveratrol and quercetin inhibit NF-kappaB more powerfully than the glucocorticosteroid, dexamethasone.⁴⁵ Further support for an anti-inflammatory benefit from resveratrol comes from research showing that resveratrol pretreatment reduces elaboration of COX-2 following administration of the proinflammatory agent, phorbol ester.⁴⁶ This effect is almost certainly a reflection of the ability of resveratrol to inhibit NF-kappaB and thereby reduce transcription of proinflammatory genes.

- **Phytolens (a patented extract from legumes):** Phytolens is a patented polyphenolic extract from lentils. Published experimental research has documented the *in vivo* antioxidant activity of Phytolens against superoxide and other reactive oxygen species.⁴⁷ Anecdotal reports have shown an anti-inflammatory benefit.

CONCLUSION AND CLINICAL IMPLEMENTATION

Inflammation is a destructive and self-perpetuating process wherein activation of NF-kappaB leads to the elaboration of proinflammatory mediators, several of which then lead to a cyclic, positive-feedback upregulation of NF-kappaB. In patients who require a rapid-onset anti-inflammatory benefit, or those who have not adequately responded to the dietary, fatty acid, and joint-supporting interventions described previously^{2-4,32}, intervention with the above-mentioned botanicals and nutrients can lead to efficient and objective reductions in inflammation. Using these natural treatments *in combination* helps to safely reduce activity of NF-kappaB and the resultant inflammation, thus promoting the restoration of homeostasis, the alleviation of pain, and a reduction in joint inflammation and degeneration.

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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>
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- Main archive: <https://vimeo.com/drvasquez>
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 - 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 media 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/IJHNFMM>
- International College of Human Nutrition and Functional Medicine (higher quality and academic news) <https://www.facebook.com/IntCollHumNutrFunctMed>
- Revista Latinoamericana de Nutrición Humana y Medicina Funcional <https://www.facebook.com/RevLatinoNutrHumMedFunc>
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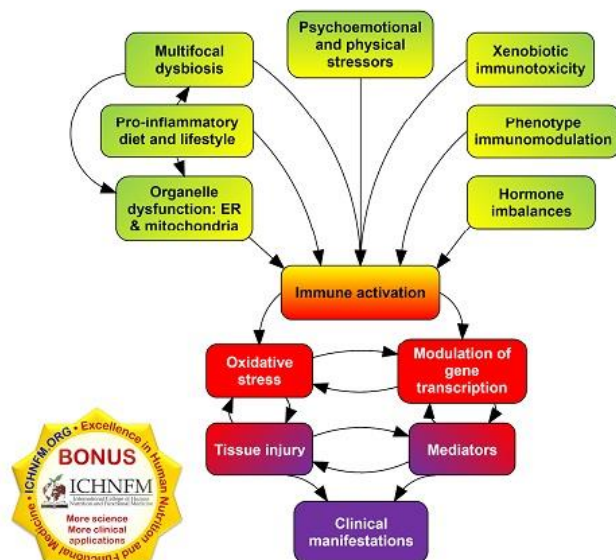
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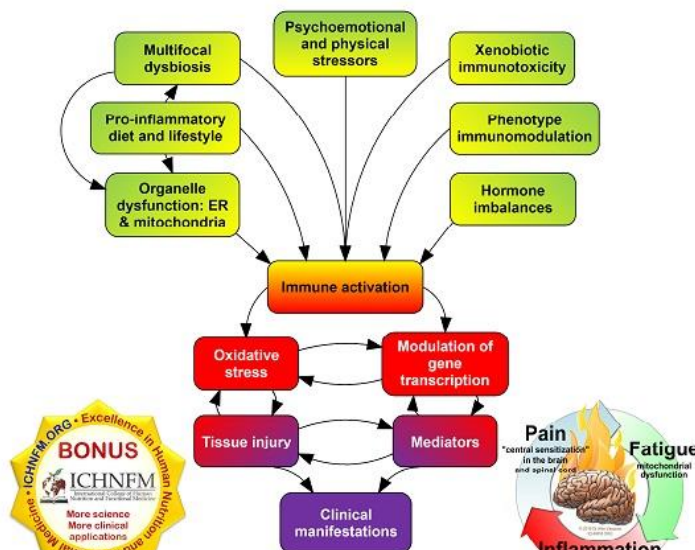
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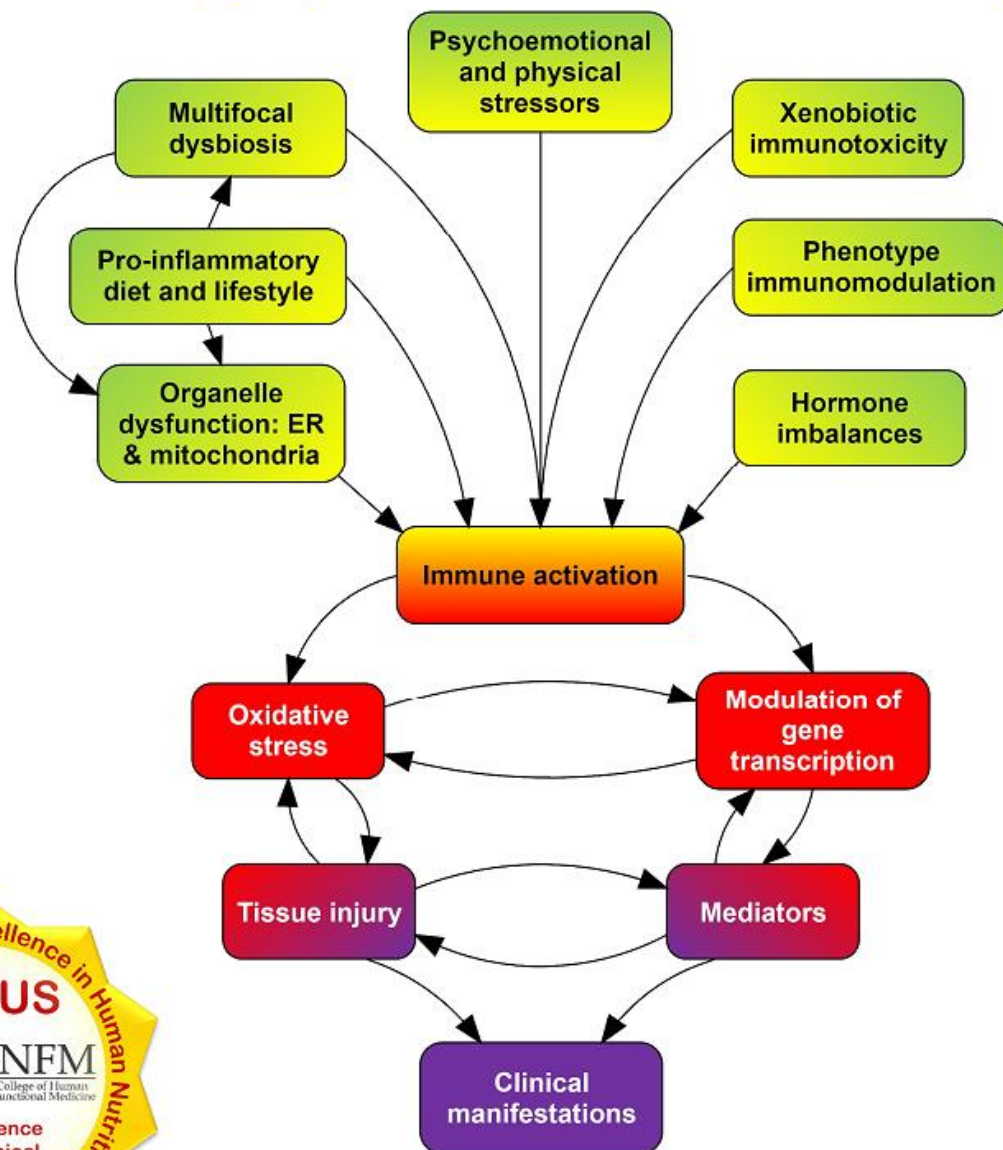
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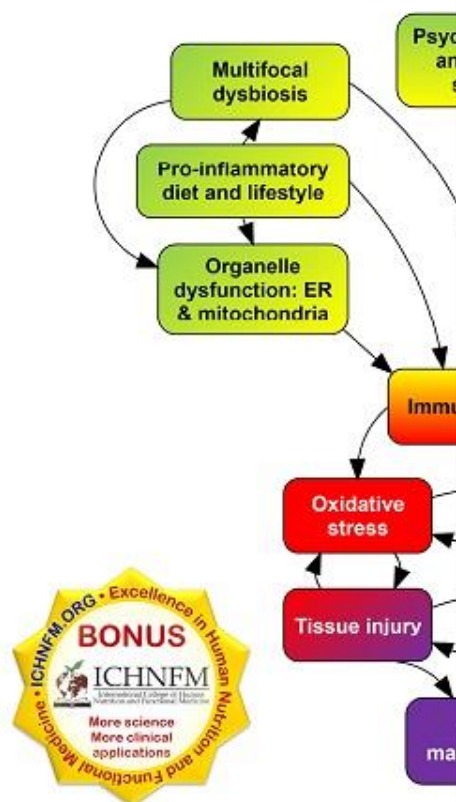
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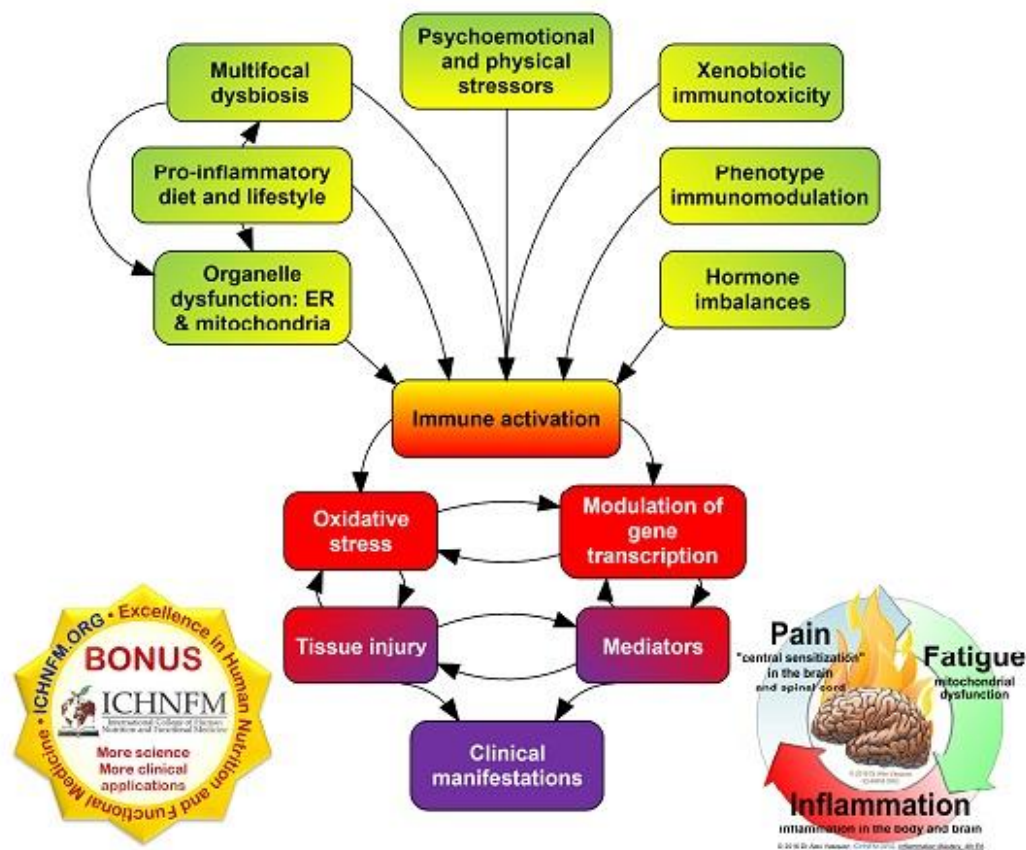
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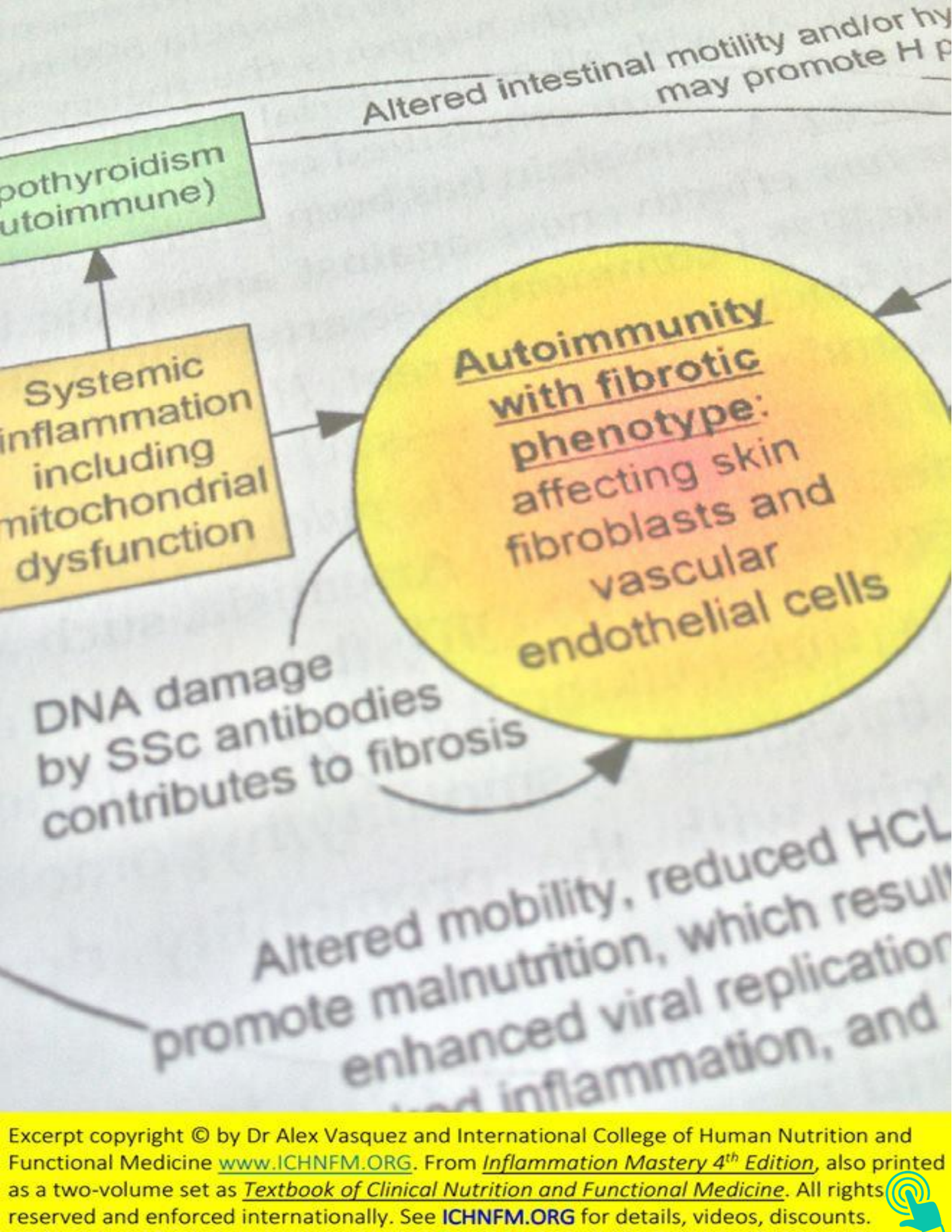
ALEX VASQUEZ D.C. N.D. D.O. F.A.C.N.

- Doctor of Osteopathic Medicine, graduate of University of North Texas Health Science Center, Texas College of Osteopathic Medicine (2010)
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- Doctor of Chiropractic, graduate of University of Western States (1996)
- Fellow of the American College of Nutrition (2013-present)
- Former Overseas Fellow of the Royal Society of Medicine
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- Private practice of integrative and functional medicine in Seattle, Washington (2000-2001), Houston, Texas (2001-2006), Portland, Oregon (2011-2013), consulting practice (present)
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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 at Maryland University of Integrative Health
 - Former Adjunct Professor (2009-2013) of Laboratory Medicine, Master of Science in Advanced Clinical Practice
 - Former Faculty (2004-2005, 2010-2013) and Forum Consultant (2003-2007), The Institute for Functional Medicine
 - Former Adjunct Professor (2011-2013) of Pharmacology, Evidence-Based Nutrition, Immune and Inflammatory Imbalances, Principles of Functional Medicine, Psychology of Wellness
 - Former Adjunct Professor of Orthopedics (2000), Radiographic Interpretation (2000), and Rheumatology (2001), Naturopathic Medicine Program, Bastyr University
- Author of more than 100 articles and letters published in *JAMA—Journal of the American Medical Association*, *BMJ—British Medical Journal*, TheLancet.com, *JAOA—Journal of the American Osteopathic Association*, *Annals of Pharmacotherapy*, *Journal of Clinical Endocrinology and Metabolism*, *Alternative Therapies in Health and Medicine*, *Nutritional Perspectives*, *Journal of Manipulative and Physiological Therapeutics*, *Integrative Medicine*, *Current Allergy and Asthma Reports*, *Nutritional Wellness*, *Evidence-based Complementary and Alternative Medicine*, and *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*

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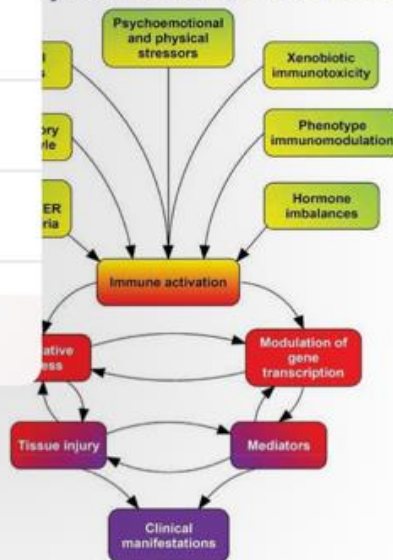


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practical clinical applications

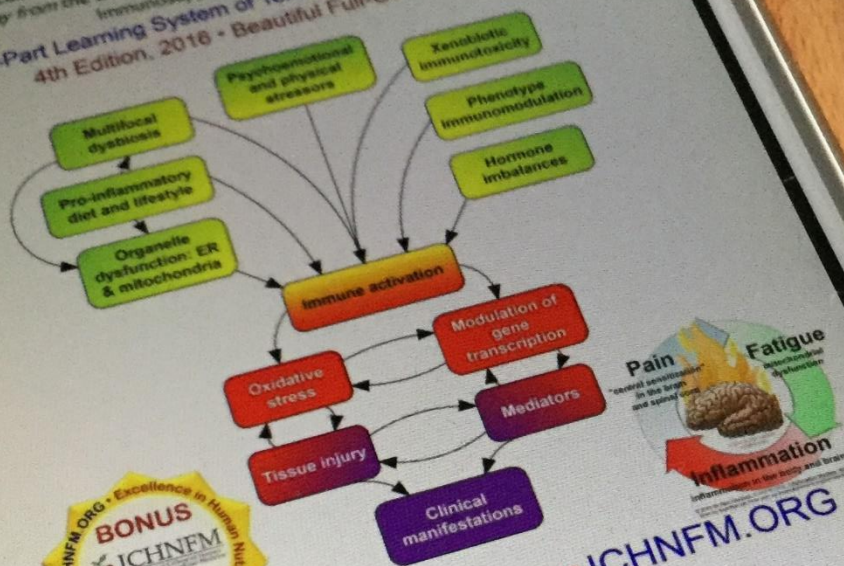
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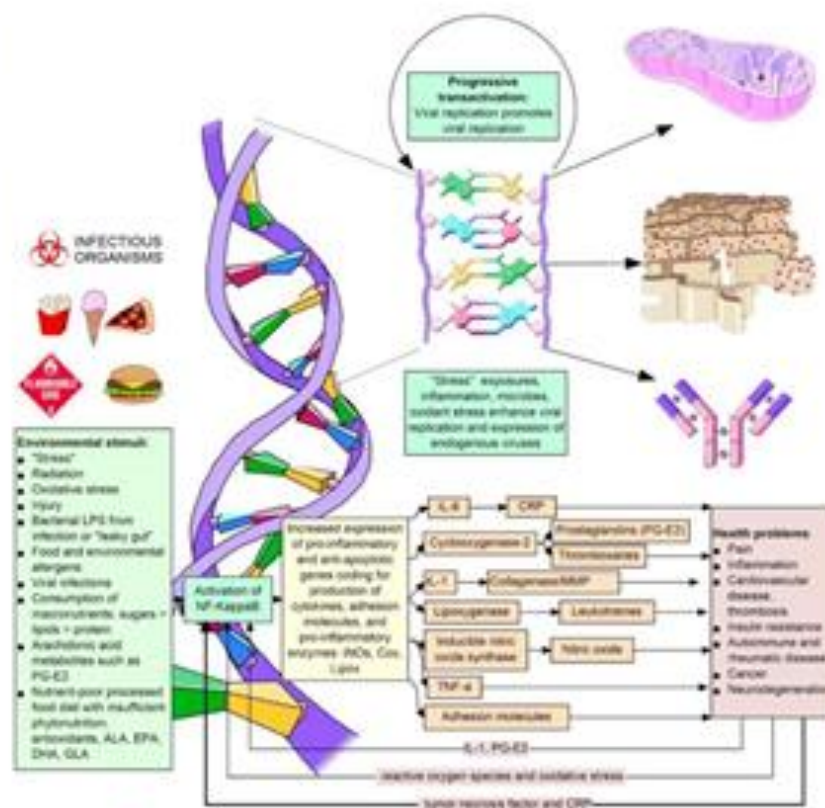
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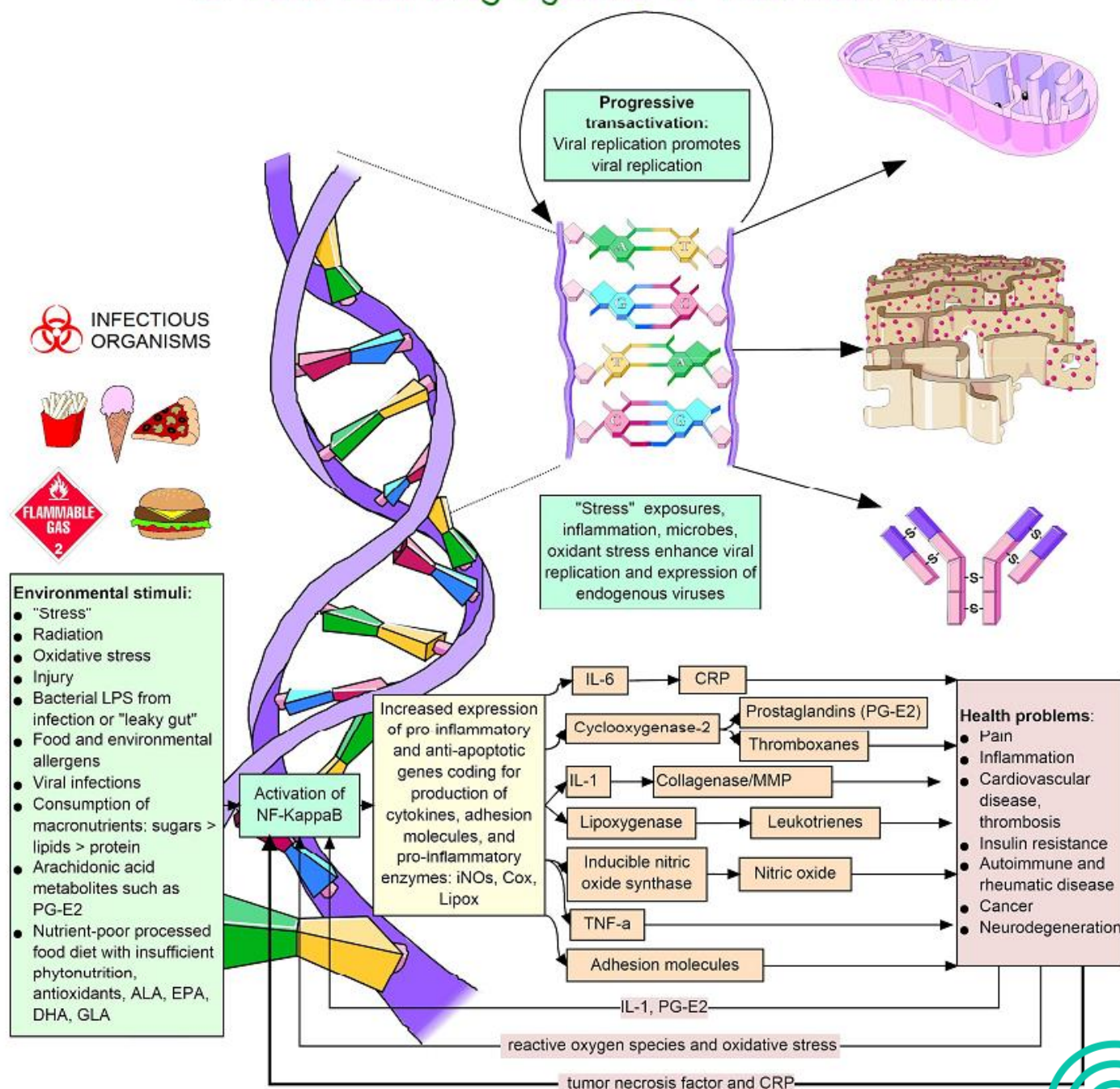


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THE PATH AHEAD

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 are worldwide.² While a specific disease human population nutrition research particularly concerning nutrition research healthcare professions nutrition. Clinical vast majority of medical training programs are obviously in gastroenterology⁷ training in clinical proclaims itself as including the entire and serious problem arises when unskilled and invalid research is published by authors (including nonphysician journalists¹¹) in major journals which mischaracterizes the validity of nutrition interventions (e.g., essentially always concluding that nutritional interventions are inefficacious

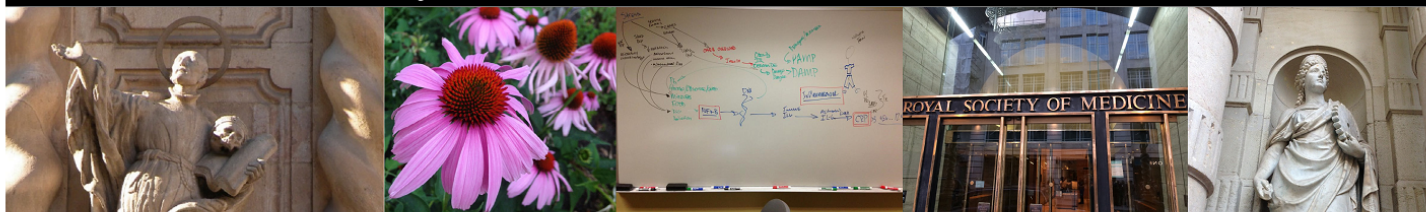
or potentially hazardous) and then such research is used politically and in the media to disparage, restrict and regulate practitioners and nutrition supplement industry¹² to the detriment of human health.

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 “headline news” in newspapers, magazines, and television via which they ent policy and ons of people. examples of ulations, lists sed solutions. pendent upon stigative and ts of clinical rovements are ignorance in

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- <https://ichnfm.academia.edu/AlexVasquez> (main archive/repository)
- <https://www.ichnfm.org/public>
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- **VIDEO:** Bad Science in Medical Nutrition: Politics of Fish Oil <https://vimeo.com/314997927>

tion review recent 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.



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 transfer 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 Academia, "nonprofits", and "Education"

I would be happiest to tell you that Administrators are vanguards of support for fellow Professors, and their commitment is to truth and reality, setting ablaze the passions of those they teach, lead, and supervise in flower fields like a professor.

singing a rhythmical rendition of *"The Hills are Alive...with the...Passions of Education and Intellectual Integrity."* But a Pollyannaic 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

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

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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 early on, in that kind of my entryway, I think, in that our assignment was to write a poem, and I remember writing this poem in class, on and on, and—compared with some of the other students—I just realized that writing for me was not a struggle.

Then again, when I was in a military school, I remember in our

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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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 some instances, radical departures from any attempt to provide descriptions that could be considered “reasonable” by the previous standard.¹ Especially related to the topic of nutrition, mainstream medical journals and the media, which parrots their conclusions have begun to make overt misrepresentations of Nutrition with regard for science, logic, biomedical history and

One has to be aware of a few key ironies that characterize mainstream medical discussions of nutrition: that 1) medical physicians receive essentially no training in clinical nutrition in their graduate school education and in their post-graduate residency training², 2) medical physicians and organizations publish “research” and commentaries (both of which commonly conclude that nutritional interventions are inefficacious or unsafe) despite their lack of formal education on the topic, and

stream 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 keep them ignorant on important topics; our educational sys-

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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>

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

Alex Vasquez, DC, ND, DO, FACN, is director of programs at the International College of Human Nutrition and Functional Medicine in Barcelona, Spain and online at ICHNFM.org. (*Altern Ther Health Med.* 2014;20(suppl 1):26-30.)

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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). In this time, contemporary clinicians

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 compartmentalized membrane that separates the matrix from the intermembrane space; (3) intermembrane space—the space between the inner and outer membranes; and (4) outer membrane—the outermost layer of the mitochondria, which is highly permeable and contains passive transport systems for select molecules that need to enter and exit the mitochondria. Clinicians need to appreciate that mitochondrial membrane integrity is of the highest importance; just as we have come to appreciate the

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stated during the recent International Conference on Human Nutrition and Functional Medicine¹ in Portland, Oregon, in September 2013, we have collectively arrived at a time when mitochondrial therapeutics and the contribution of mitochondrial dysfunction to clinical diseases must be

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 moved to a health school in the early 1990s. My "nutrition" book that I read as a teenager was *Your Nerves* (1975) by me. This was followed immediately by the lectures of Jonathan V Wright, MD, of whom would later be my mentor at the University. By the mid-1990s, I was studying Jeffrey Bland PhD had introduced me to integrative medicine, which I studied for personal and professional reasons. By 1994, I had contained several hundred articles on 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 for⁴ and published in⁵ 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 applications; we can reasonably assume that (and competent healthcare providers (adequate nutrition) are basic to submit a counterargument for all of my assertions, they are and more to the point, my assertions are regardless of personal position—we share some common ground including the following:

and deliver the best health solution, then we each want the best possible solution. Efficiency of time or money is not the top priority when we are seeking solutions

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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 articles³ 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 dysbiosis. In 2010, I found "dysbiosis" more than 1,200 times. The concept has become popular, but to do with it in *International Journal of Human Nutrition and Functional Medicine*, the complete microbiota project, the number of scientific papers linking the microbes that live in our gut to diseases ranging from diabetes and colitis to anxiety and depression has grown exponentially. Yet, these tantalizing connections have yielded few benefits from a therapeutics standpoint.⁴ To the extent that this information is being integrated into clinical practice at all, the current level of


"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 inexpensive test for only one culture of gastrointestinal popular to the clinical clues. Laboratory testing particular used methods to extract they only to suffering and


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International College of Human Nutrition and Functional Medicine

ICHNFM has many videos on the topics of dysbiosis, persistent infections, and dysbiotic clinical conditions such as fibromyalgia at www.Vimeo.com/ICHNFM



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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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tice for more than 35 years, he is Board Certified in Family Practice and is Associate Professor of Family Medicine at University of Texas Medical School in Houston. **John Cannell, MD**, is a medical physician practicing in Atascadero, California, and is president of the Vitamin D Council (Cholecalciferol-Council.com), a non-profit, tax-exempt organization working to promote awareness of the manifold adverse effects of vitamin D deficiency.

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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 at risk for vitamin D deficiency and hypersensitivity.
3. Know how to implement proper doses and with appropriate monitoring.

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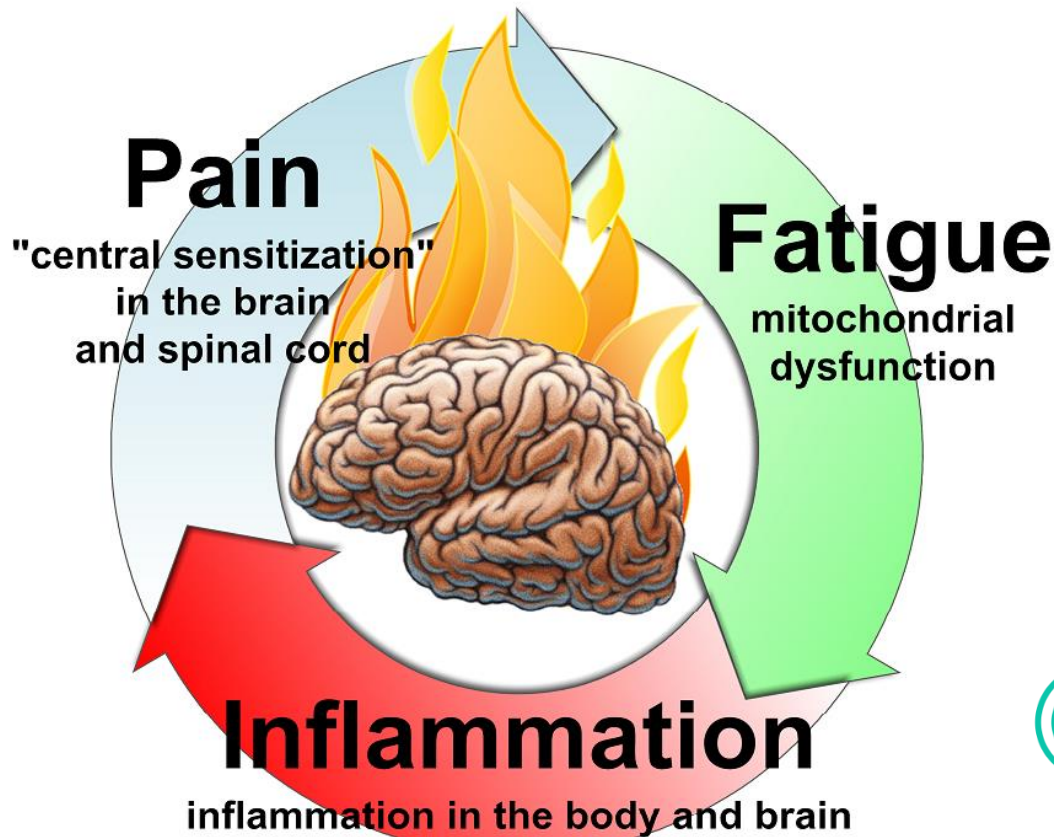
While we are all familiar with the important role of vitamin D in calcium absorption and bone metabolism, many doctors and patients are not aware of the recent research on vitamin D and the widening range of therapeutic applications available for cholecalciferol, which can be classified as both a vitamin 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 tis-

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BRAIN INFLAMMATION IN CHRONIC PAIN, MIGRAINE AND FIBROMYALGIA

THE PARADIGM-SHIFTING GUIDE FOR DOCTORS AND
PATIENTS DEALING WITH CHRONIC PAIN



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Biological plausibility of the gut–brain axis in autism

Alex Vasquez 

Organic abnormalities with neuroinflammation, purine metabolism, neurotransmitter metabolism, and many of these abnormalities are noted in autism, and many of these abnormalities are metabolites, and heightened serum levels of these metabolites.

Keywords: gut–brain axis; autism; metabolism

In their recent review, Sherwin *et al.*¹ among many other issues, the relationship between the gut microbiome–brain axis with autism. This section subtitled “Microbiota-based approaches to the treatment of autism: hype or reality?” *et al.*¹ largely discuss preclinical studies and the 2017 open-label study by Karpman *et al.*² used a sequence of oral vancomycin, polyethylene glycol laxative, and human fecal microbiota transplantation. Clinical benefit in subjects with autism was noted.

Readers will likely benefit from additional relevant clinical studies, including a study by Sandler *et al.*³ showing the effect of autistic manifestations following oral vancomycin, as well as case reports showing positive impact of various antibiotics (metronidazole, ketoconazole, ampicillin) in patients with autism.^{4,5} These studies have been shown to have gut dysregulation as well as *Clostridia* species,⁶ the group of bacteria noted for their production of neurotoxic substances. International studies have consistently demonstrated that Clostridia have heightened production of 3-(3-hydroxypropionic acid (HPHPA), a phenylalanine metabolite of Clostridia in the gastrointestinal tract.^{7,8} HPHPA reported to be involved with the conversion of dopamine to

Autism, Dysbiosis, and the Gut–Brain Axis



An Excerpt from "Deciphering
the Gut-Brain Axis in Clinical
Practice"

Alex Vasquez

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