

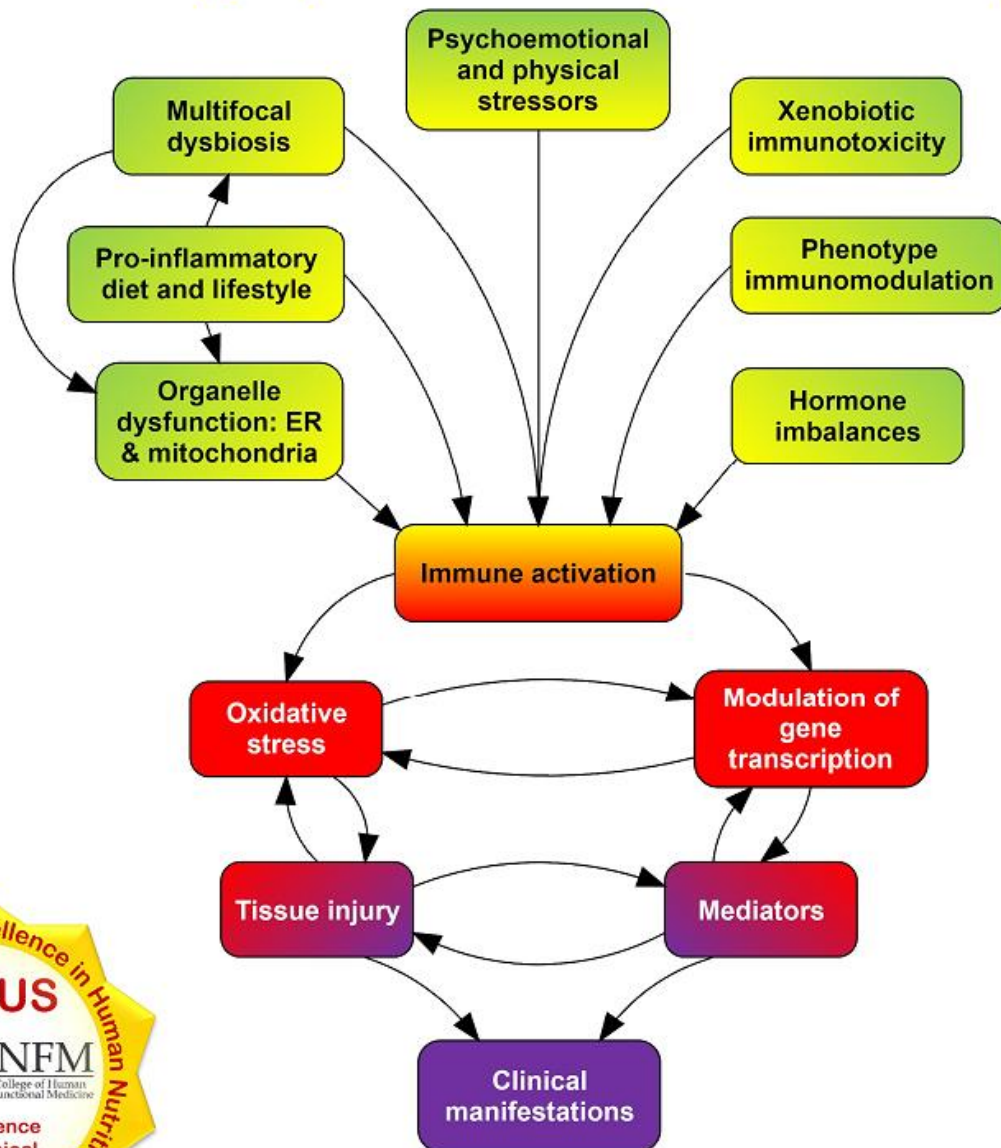
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**DR. ALEX VASQUEZ**  
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## Intracellular Hypercalcinosis: A Functional Nutritional Disorder with Implications Ranging from Myofascial Trigger Points to Affective Disorders, Hypertension, and Cancer

This article was originally published in *Naturopathy Digest* in 2006  
[naturopathydigest.com/archives/2006/sep/vasquez.php](http://naturopathydigest.com/archives/2006/sep/vasquez.php)

**Introduction:** Let us explore the possibility that elevated levels of calcium *within the cell* (intracellular hypercalcinosis) might predispose toward a wide range of clinical problems including migraine, hypertension, myofascial trigger points, inflammation, and cancer. Further, let's review the data showing that several commonly employed nutritional interventions can be used synergistically to counteract and correct this problem. By the time readers complete this article, they will have 1) an understanding of this problem, 2) a protocol for how to correct this problem, and 3) be able to explain the biochemical rationale for using these nutritional protocols in patients who might otherwise be treated with drugs in general and calcium-channel-blocking drugs in particular.

Although prescription drugs are often used by medical doctors in a "willy-nilly manner" (according to Harvard Medical School Professor Dr. Jerry Avorn<sup>581</sup>), let's assume for a moment that legitimate reasons exist for the widespread use of drugs that block calcium channels in cell membranes—the "calcium-channel-blocking drugs." Although it is counterintuitive to promote health by interfering with the body's natural function, calcium-channel-blocking drugs are routinely used in pharmaceutical medicine for a broad range of problems including hypertension, heart rhythm disturbances, bipolar disorder, and anxiety/panic disorders. Widespread medical use of calcium-channel-blocking drugs appears to validate the supposition that excess intracellular calcium is an important contributor to these and perhaps other problems. Therefore, if intracellular hypercalcinosis is the problem, then any safe and cost-effective treatment that can correct this problem should be met with the same widespread acceptance given to calcium-channel-blocking drugs, which are universally accepted and utilized in the allopathic "conventional medicine" society. At the very least, we can generally state that all phenomena that contribute to calcium deficiency result in an increase in intracellular calcium levels (the "calcium paradox") due to the effect of parathyroid hormone, which specifically promotes calcium uptake in cells while mobilizing calcium from bone. Additionally, a few other nutritional influences (such as fatty acid imbalances) modulate cellular calcium balance, and these will be discussed in the section on clinical interventions.

**The Problem of Excess Intracellular Calcium:** Although the current author is the first to coin the phrase "intracellular hypercalcinosis", several other authors have pointed to the problem of the "calcium paradox" and the means by which *body-wide calcium deficiency* can result in *intracellular calcium overload*, which triggers a cascade of events leading to adverse health effects. Most notably, the work of Takuo Fujita<sup>582,583</sup> stands out in its clarity and specificity in linking intracellular hypercalcinosis with disorders such as hypertension, arteriosclerosis, diabetes mellitus, neurodegenerative diseases, malignancy, and degenerative joint disease.

Mechanisms by which intracellular hypercalcinosis contributes to disease have been defined, at least partially. However, we must remember that nutritional disorders never occur in isolation, and that the effects of intracellular hypercalcinosis observed clinically are overlaid with manifestations of the primary nutritional/metabolic disorder. Stated differently, contrary to what the pharmaceutical paradigm's monotherapeutic use of calcium-channel-blocking drugs would imply, intracellular hypercalcinosis never occurs by itself. For example, if intracellular hypercalcinosis is contributed to by vitamin D3 deficiency, then some of the observed clinical complications of that condition are due to and yet independent from the excess intracellular calcium since the primary problem (vitamin D3 deficiency) causes adverse effects and deficiency symptoms that are independent of its effect on intracellular calcium levels. To better understand the specific effects of excess intracellular calcium, a brief review of a few specific biochemical/physiologic mechanisms by which intracellular hypercalcinosis can contribute to disease is warranted. We must start by realizing that calcium is much more than a "bone nutrient" and that it functions as an electrolyte, intracellular messenger, and regulator of cell replication and metabolism. Let's talk about five pathways by which increased intracellular calcium promotes disease:

<sup>581</sup> America the Medicated. [cbsnews.com/stories/2005/04/21/health/main689997.shtml](http://cbsnews.com/stories/2005/04/21/health/main689997.shtml)

<sup>582</sup> Fujita T. Calcium paradox: consequences of calcium deficiency manifested by a wide variety of diseases. *J Bone Miner Metab.* 2000;18(4):234-6

<sup>583</sup> Fujita et al. Calcium paradox disease: calcium deficiency prompting secondary hyperparathyroidism and cellular calcium overload. *J Bone Miner Metab.* 2000;18(3):109-25

1. Adverse effects on membrane receptors and intracellular transduction: The concentration of extracellular calcium exceeds the concentration of intracellular calcium by a ratio of 10,000 to one. When intracellular calcium levels rise even slightly, receptors and messaging systems in the cell membrane fail to function optimally. Thereby, increased intracellular calcium can predispose to insulin resistance (via interference with insulin receptors) and can promote neurodegeneration by amplifying the intracellular cascade of effects that follows activation of the brain's NMDA-receptors (excitotoxicity). More specifically, we must note that the recently discovered "calcium-sensing receptor" (CaR, a G protein-coupled plasma membrane receptor) senses minute alterations in serum calcium levels and then ultimately translates these variations into changes in cellular function, notably alterations in cell replication (think cancer) and eicosanoid production (think inflammation).<sup>584,585</sup> Given that CaR are found in a wide range of cell types, including those found in bone, the kidneys, and immune system, we can see a pathway by which alterations in calcium balance could be implicated in a wide range of diseases. CaR-mediated alterations in cell function are likely to be complicated by disorders of vitamin D3 nutrition and metabolism (that commonly complicate disorders of calcium homeostasis), which affect an even wider range of cell types including those of the breast, prostate, ovary, lung, skin, lymph nodes, colon, pancreas, adrenal medulla, brain (pituitary, cerebellum, and cerebral cortex), aortic endothelium, and immune system, including monocytes, transformed B-cells, and activated T-cells. This is an example of the complexity involved in understanding nutrition in general and the effects of nutritional deficiency (always multifaceted) in particular.
2. Mitochondrial failure and cell death: According to the most recent edition of the classic text *Robbins Pathologic Basis of Disease* (pages 15-16), increased intracellular calcium is a major cause of cell death. When calcium levels are increased within the cell, one adverse effect is the inhibition of mitochondrial function. Since calcium is pumped out of the cell in an energy-dependent process, and because dysfunctional mitochondria pour calcium into the intracellular space, calcium-induced mitochondrial failure results in an additional increase in intracellular calcium. Further complicating this problem is the fact that the cell membrane becomes increasingly permeable to calcium as calcium levels increase. Elevated intracellular calcium levels activate enzymes such as ATPase, phospholipase, proteases, and endonucleases that promote cell death.
3. Pro-inflammatory effects of intracellular calcium: The recent finding that intracellular calcium activates NF-kappaB<sup>586</sup> has obvious implications given the pivotal role of NF-kappaB in the promotion of systemic inflammation and diseases such as rheumatoid arthritis.<sup>587</sup> Thus, increased intracellular calcium appears to promote inflammation. This may explain in part how vitamin D3 supplementation (which lowers intracellular calcium levels) exerts its clinically impressive anti-inflammatory and immunomodulatory benefits.<sup>588</sup>
4. Enhanced production of lipid peroxides: Fujita notes that lipid peroxides lead to an increase in cell membrane permeability to calcium, which results in increased intracellular calcium; this activates metabolic pathways that increase oxidative stress, thus leading to a vicious cycle stimulated by the production of additional lipid peroxides. Thus, intracellular hypercalcinosis promotes oxidative stress, which becomes self-perpetuating by this and other mechanisms. Of course, we all know by now that increased production of free radicals contributes to the development of many health problems, such as cancer, cardiovascular disease, arthritis, autoimmunity, diabetes, and other forms of rapid biological aging.
5. Myofascial trigger points, chronic muscle spasm, and increased vascular tone (hypertension): The release of calcium from the sarcoplasmic reticulum triggers muscle contraction and plays a role in hypertension (hence the use of calcium-channel-blocking drugs in the treatment of hypertension), chronic muscle spasm (especially when complicated by magnesium deficiency), and the perpetuation of myofascial trigger points.<sup>589</sup> Reducing the levels of cytosolic and sarcoplasmic calcium promotes muscle relaxation.

<sup>584</sup> Peterlik M, Cross HS. Vitamin D and calcium deficits predispose for multiple chronic diseases. *Eur J Clin Invest.* 2005 May;35(5):290-304

<sup>585</sup> Heaney RP. Long-latency deficiency disease: insights from calcium and vitamin D. *Am J Clin Nutr.* 2003 Nov;78(5):912-9

<sup>586</sup> "Furthermore, a calcium chelator, BAPTA-AM, attenuated the NF-kappaB activation... CONCLUSIONS: Induction of NF-kappaB within 30 min by TNF-alpha- and IL-1beta was mediated through intracellular calcium but not ROS." Chang JW, Kim CS, Kim SB, Park SK, Park JS, Lee SK. Proinflammatory cytokine-induced NF-kappaB activation in human mesangial cells is mediated through intracellular calcium but not ROS: effects of silymarin. *Nephron Exp Nephrol.* 2006;103:e156-65

<sup>587</sup> Tak PP, Firestein GS. NF-kappaB: a key role in inflammatory diseases. *J Clin Invest.* 2001 Jan;107(1):7-11

<sup>588</sup> Timms et al. Circulating MMP9, vitamin D and variation in the TIMP-1 response with VDR genotype: mechanisms for inflammatory damage in chronic disorders? *QJM.* 2002 Dec;95(12):787-96. See also: Vasquez A, Manso G, Cannell J. The clinical importance of vitamin D. *Altern Ther Health Med.* 2004 Sep-Oct;10(5):28-36

<sup>589</sup> Simons DG. Cardiology and myofascial trigger points: Janet G. Travell's contribution. *Tex Heart Inst J.* 2003;30(1):3-7

**Nutritional Interventions to Ameliorate Intracellular Hypercalcinosis:** Now that we've reviewed the data implicating intracellular hypercalcinosis as a legitimate contributor to a wide range of clinical disorders and diseases, let's explore some nutritional solutions.

1. **Correction of vitamin D deficiency:** Vitamin D deficiency causes calcium deficiency which increases parathyroid hormone production resulting in increased intracellular calcium levels. Vitamin D deficiency is common (40-80% of most populations) and can be established via history and more objectively by measurement of serum 25-hydroxyl-vitamin D. Replacement doses are in the range of 1,000 IU per day for infants, 2,000 IU per day for children, and 4,000 IU per day for adults.<sup>590</sup> Vitamin D2 (ergocalciferol) should be avoided, and vitamin D3 (cholecalciferol) should be used, preferably in emulsified form to facilitate absorption, especially in older patients and those with impaired digestion and absorption.<sup>591</sup>
2. **Reduction in dietary arachidonic acid intake:** Arachidonic acid promotes intracellular calcium uptake, as demonstrated in a recent study using human erythrocytes.<sup>592</sup> Rich sources of arachidonic acid include beef, liver, pork, lamb, and cow's milk.
3. **Increase intake of eicosapentaenoic acid (EPA):** EPA reduces intracellular calcium levels in experimental models<sup>593</sup> and anticancer, antihypertensive, and anti-inflammatory effects of EPA are seen clinically. One to three grams per day is reasonable for adults.
4. **Urinary alkalization:** Diet-induced chronic metabolic acidosis<sup>594</sup> promotes loss of calcium in urine<sup>595</sup> and thus indirectly contributes to calcium deficiency and the resultant rise in parathyroid hormone and intracellular calcium levels. An alkalizing plant-based Paleo-Mediterranean diet should be the foundational treatment for numerous reasons<sup>596</sup>; however some patients may need to supplement with vegetable culture, potassium citrate, potassium bicarbonate, and/or sodium bicarbonate either regularly or "as needed"/PRN.
5. **Ensuring adequate intake of calcium:** A healthy diet can supply upwards toward 1,000 mg of calcium per day, and some people may choose to supplement with an additional 500 to 1,500 mg daily. Calcium supplementation should be used with magnesium, vitamin D and other components of the supplemented Paleo-Mediterranean diet.
6. **Avoiding other dietary and lifestyle factors that promote calcium loss in urine:** Caffeine, sugar, alcohol/ethanol, and psychoemotional stress all increase calcium loss in urine and thus contribute to secondary hyperparathyroidism and intracellular hypercalcinosis.

**Conclusions:** In this brief article, I have introduced and reviewed important concepts related to diet-induced alterations in cellular calcium balance. Notice that this discussion of calcium has transcended the usual conversation of simple "deficiency" and "excess." What I've done here is review data showing that we can indirectly modulate certain aspects of intracellular nutrition to promote optimal biochemical balance within the cell in order to optimize health and prevent and correct disease and dysfunction. Next time someone tells you that there is no scientific basis for interventional nutrition, sit them down and give them a lecture on causes and treatments for intracellular hypercalcinosis. Tell them it is only the tip of the iceberg, and that they'd be wise to take interventional nutrition seriously. Just because we buy groceries and nutritional supplements without a prescription (for now), this does not mean that these choices are not powerful or lacking in scientific merit. Amazing results can be achieved with diet modification and nutritional/botanical supplementation.

<sup>590</sup> Vasquez A, Manso G, Cannell J. The clinical importance of vitamin D (cholecalciferol). *Altern Ther Health Med.* 2004 Sep-Oct;10(5):28-36

<sup>591</sup> Vasquez A. Subphysiologic Doses of Vitamin D are Subtherapeutic: Comment on the Study by The Record Trial Group. *The Lancet* 2005 Published on-line May 6

<sup>592</sup> "The Ca(2+) influx rate varied from 0.5 to 3 nM Ca(2+)/s in the presence of AA and from 0.9 to 1.7 nM Ca(2+)/s with EPA." Soldati L, Lombardi C, Adamo D, Terranegra A, Bianchin C, Bianchi G, Vezzoli G. Arachidonic acid increases intracellular calcium in erythrocytes. *Biochem Biophys Res Commun.* 2002 May 10;293(3):974-8

<sup>593</sup> "This is a consequence of the ability of EPA to release Ca2+ from intracellular stores while inhibiting their refilling via capacitative Ca2+ influx that results in partial emptying of intracellular Ca2+ stores and thereby activation of protein kinase R." Palakurthi SS, Fluckiger R, Aktas H, Changolkar AK, Shahsafaei A, Harnett S, Kilic E, Halperin JA. Inhibition of translation initiation mediates the anticancer effect of the n-3 polyunsaturated fatty acid eicosapentaenoic acid. *Cancer Res.* 2000 Jun 1;60(11):2919-25

<sup>594</sup> Maurer M, Riesen W, Muser J, Hulter HN, Krapf R. Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans. *Am J Physiol Renal Physiol.* 2003 Jan;284(1):F32-40

<sup>595</sup> Sellmeyer et al. Potassium citrate prevents increased urine calcium excretion and bone resorption induced by a high sodium chloride diet. *J Clin Endocrinol Metab.* 2002

May;87(5):2008-12

<sup>596</sup> Vasquez A. A Five-Part Nutritional Protocol that Produces Consistently Positive Results. *Nutritional Wellness* 2005 September [inflammationmastery.com/reprints](http://inflammationmastery.com/reprints)

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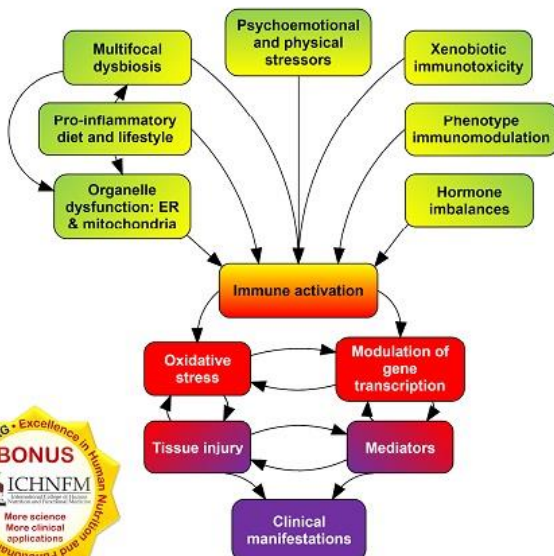
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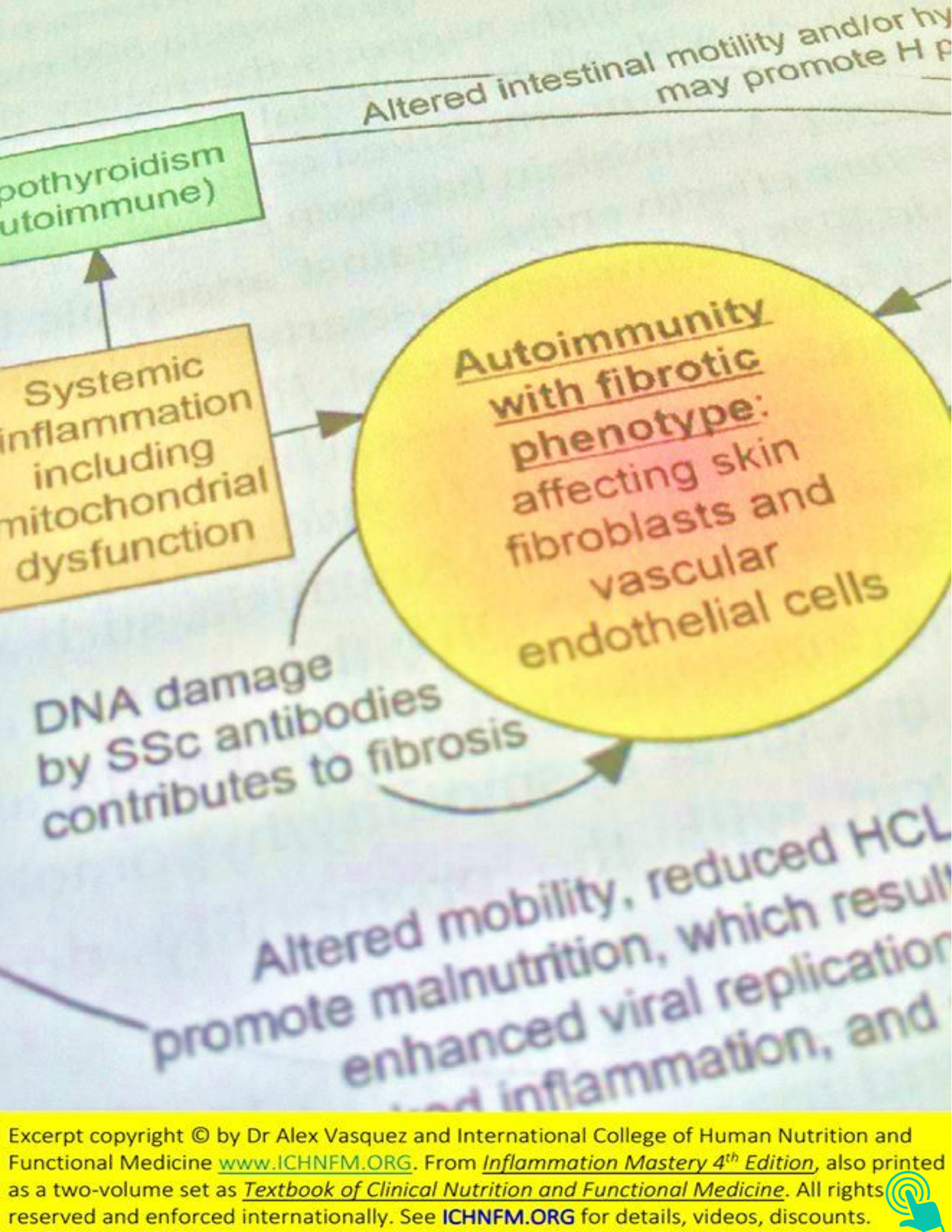
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- "The time is now past when accidents could befall me; and what **could** now fall to my lot which has not already be my own!? It returns only, it comes home to me at last—mine own Self. And such of it as has been long abroad, and scattered among things and accidents. And one thing more do I know: I stand now before my last summit, and before that which has been longest reserved for me."
- "You have within you the power to merge everything you have lived through – attempts, false starts, errors, delusions, passions, your loves and your hopes – into your highest goal, with nothing left over."
- "At every step one has to wrestle for truth; one has to surrender for it almost everything to which the heart, to which our love, our trust in life, cling otherwise. That requires greatness of soul: the service of truth is the hardest service..."
- "With your love go into your isolation and with your creativity, my brother; and only later will justice limp after you."
- "What makes a person heroic?" Answer: "To simultaneously face one's greatest fear and one's highest hope."
- "My principle article of faith is that one can only flourish among people who share the identical ideas and the identical will."
- "Not around the inventors of new noise but around the inventors of new values does the world revolve."

Friedrich Nietzsche (German classical Scholar, Philosopher and Critic of culture, 1844-1900)



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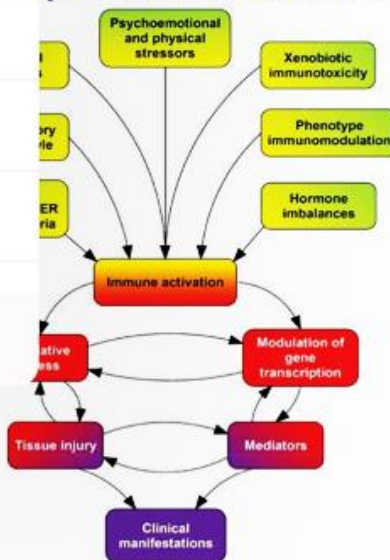
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3. [Basic Concepts and Therapeutics in \(Nondrug\) Musculoskeletal Care and Integrative Pain Management: Nonpharmacologic management of musculoskeletal problems is preferred over pharmacologic \(e.g., NSAID, Coxib, steroid, opioid\) management because 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 Inflammation Protocol” are reviewed here, from concepts and molecular biology to an emphasis on practical clinical applications](#)
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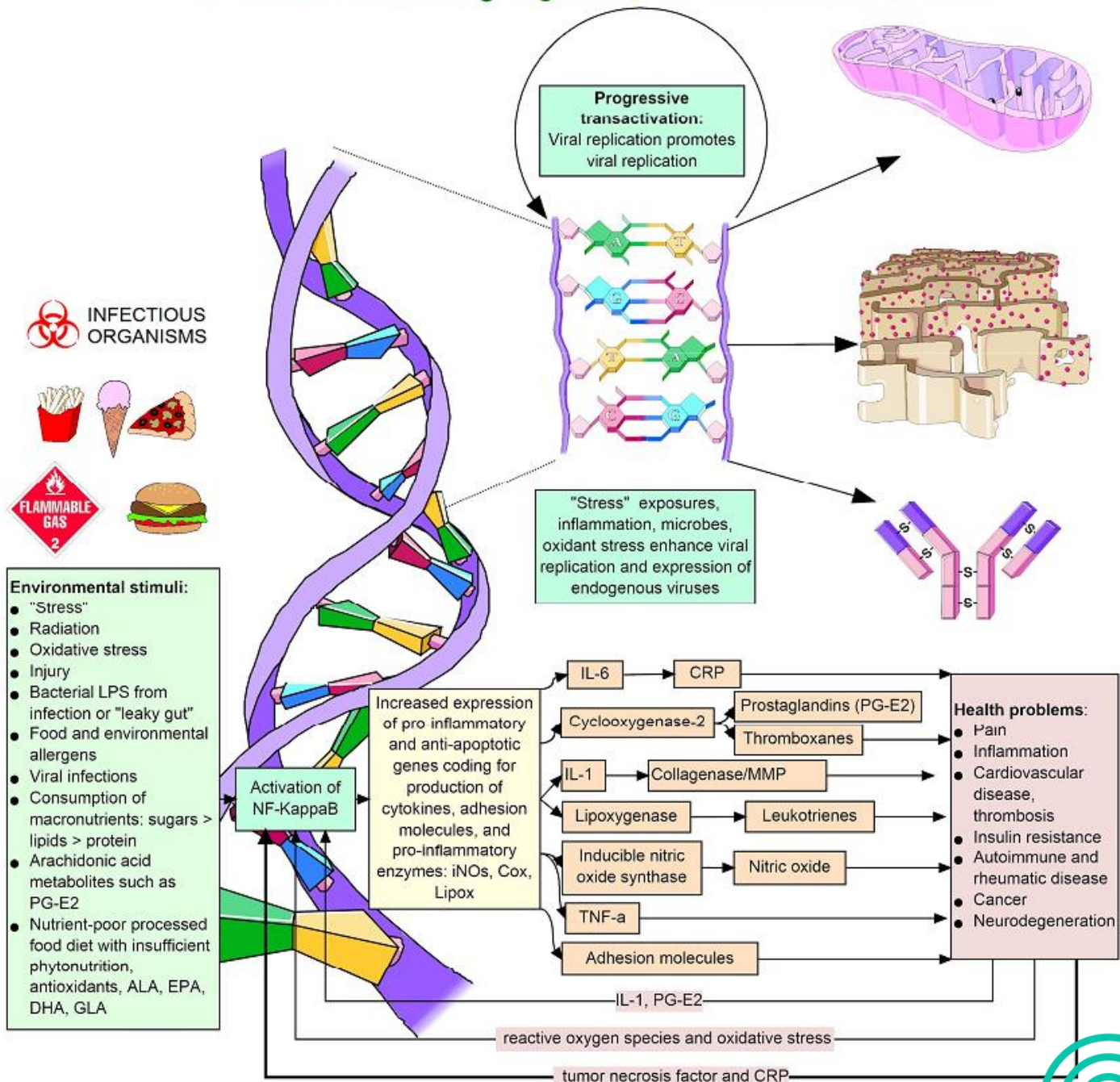




# ANTIVIRAL STRATEGIES AND IMMUNE NUTRITION

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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.<sup>1</sup> 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.<sup>2</sup> 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 gastroenterology<sup>7</sup> training in clinical proclaims itself as including the entire territory of clinical nutrition.<sup>10</sup> A major and serious problem arises when unskilled and invalid research is published by authors (including nonphysician journalists<sup>11</sup>) in major journals which mischaracterizes the validity of nutrition interventions (e.g., essentially always concluding that nutritional interventions are inefficacious

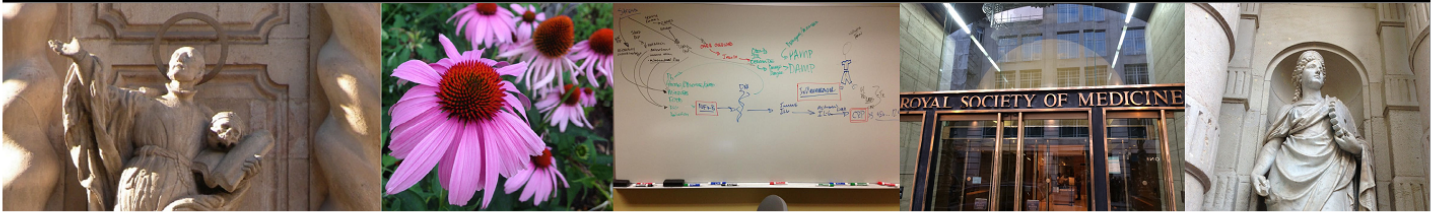
or potentially hazardous) and then such research is used politically and in the media to disparage, restrict and regulate practitioners and nutrition supplement industry<sup>12</sup> to the detriment of human health.

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 ublications, lists sed solutions. dependent upon stitative and ts of clinical rovements are gnorance in tion review recent 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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- VIDEO: BRIEF Critique of “Effects of n–3 Fatty Acid Supplements in Diabetes Mellitus: ASCEND Study” <https://vimeo.com/287650812>
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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 reality setting ablaze the passions of the they teach, lead, and supervise; I in flower fields like a professorial

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 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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**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 I had some kind of my entryway, I think, in that our assignment was to write a poem on and on, and—compared with some of my other experiences—I just realized that writing for me

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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# 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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E-mail address: [avasquez@ichnfm.org](mailto:avasquez@ichnfm.org)

## 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 clinical inflammatory disease such as disorders such as stated during Nutrition and September mitochondrial

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

ce—contains kinase and comparatively (n) and—like h active and that need to to appreciate the highest

importance; just as we have come to appreciate the

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### 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 1990s. I read the "nutrition" book that I read in high school, *Your Nerves* (1975) by Jonathan V Wright, MD, of this was followed immediately by the book *The Mind of Jonathan V Wright* (1975) by Jonathan V Wright, MD, of whom would later be my mentor at the University of Wisconsin-Madison. By the mid-1990s, I had read Jeffrey Bland PhD had read the book *Orthomolecular Medicine*, which was a personal<sup>3</sup> 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<sup>4</sup> and published in<sup>5</sup> 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 expect that competent healthcare (and adequate nutrition) are basic human needs. If you admit a counterargument to my assertions, they are more to the point, my goal is to share, regardless of personal position, the following: the following:

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• 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



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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<sup>1,2</sup> and articles<sup>3</sup> 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.<sup>4</sup> 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 become popular, but to do with it in *Functional Medicine* the complete Project, the that live in to anxiety a tantalizing therapeutic being integ

### "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

they only to suffering and

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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

**Alex Vasquez, DC, ND** is a licensed naturopathic physician in Washington and Oregon, and licensed chiropractic doctor in Texas, where he maintains a private practice and is a member of the Research Team at Biotics Research Corporation. He is a former Adjunct Professor of Orthopedics and Rheumatology for the Naturopathic Medicine Program at Bastyr University. **Gilbert Manso, MD**, is a medical doctor practicing integrative medicine in Houston, Texas. In prac-

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.

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 implement proper doses and with

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.<sup>1,2</sup> 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

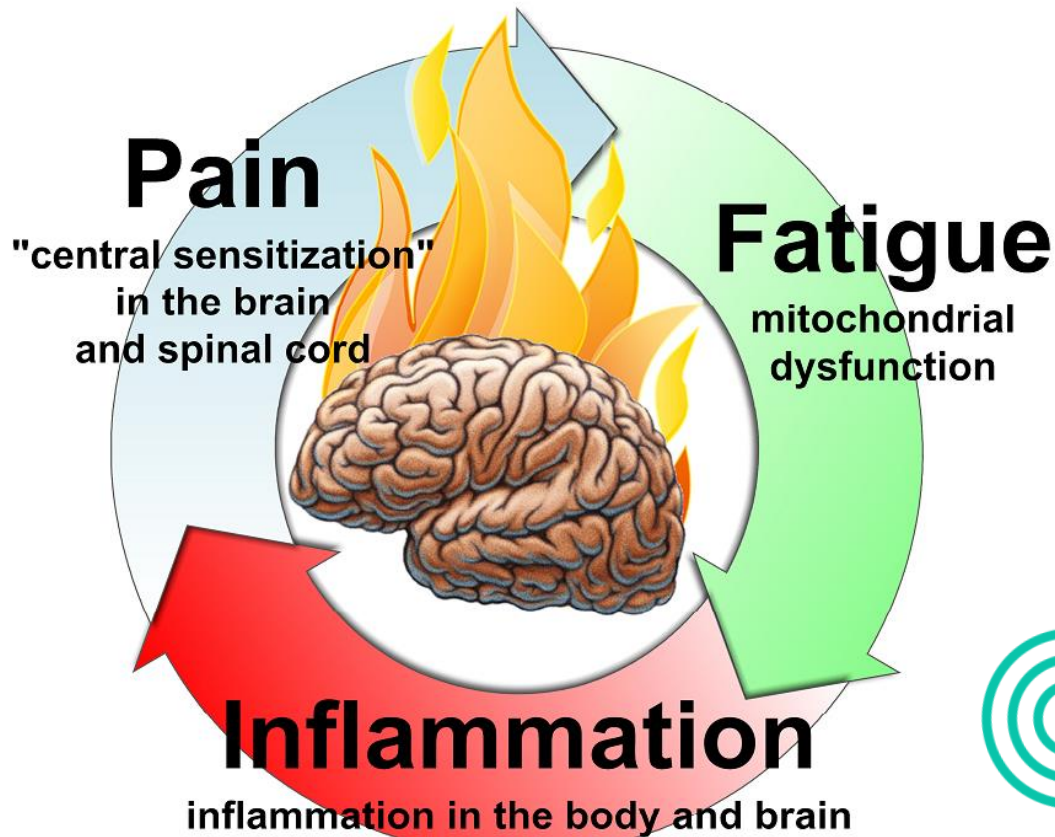
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# BRAIN INFLAMMATION IN CHRONIC PAIN, MIGRAINE AND FIBROMYALGIA

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



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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