

## Persistent inadequacies in nutrition education/training among physicians

**Introduction:** Despite the acknowledged importance of diet in the prevention of obesity, diabetes, hypertension and other components of cardiometabolic syndrome/disease, physicians are consistently and systematically untrained in nutrition. A few exemplary citations are summarized per the following:

- What do resident physicians know about nutrition? (*J Am Coll Nutr* 2008 Apr<sup>29</sup>): "OBJECTIVE: Despite the increased emphasis on obesity and diet-related diseases, nutrition education remains lacking in many internal medicine training programs. We evaluated the attitudes, self-perceived proficiency, and knowledge related to clinical nutrition among a cohort of internal medicine interns. METHODS: Nutrition attitudes and self-perceived proficiency were measured using previously validated questionnaires. Knowledge was assessed with a multiple-choice quiz. ... RESULTS: Of the 114 participants, 61 (54%) completed the survey. Although 77% agreed that nutrition assessment should be included in routine primary care visits, and 94% agreed that it was their obligation to discuss nutrition with patients, only 14% felt physicians were adequately trained to provide nutrition counseling. ... CONCLUSIONS: Internal medicine interns' perceive nutrition counseling as a priority, but lack the confidence and knowledge to effectively provide adequate nutrition education." These are impressive results showing that internal medicine doctors—specialists who commonly deal with diabetes, hypertension, obesity, and metabolic syndrome—do not have competence in nutrition, even by weak and basic standards.
- Relevance of clinical nutrition education and role models to the practice of medicine (*Eur J Clin Nutr.* 1999 May<sup>30</sup>): "Yet, despite the prevalence of nutritional disorders in clinical medicine and increasing scientific evidence on the significance of dietary modification to disease prevention, present day practitioners of medicine are typically untrained in the relationship of diet to health and disease."
- How much do gastroenterology fellows know about nutrition? (*J Clin Gastroenterol.* 2009 Jul<sup>31</sup>): "The mean total test score was 50.04%. ...CONCLUSIONS: Gastroenterology fellows think their knowledge of nutrition is suboptimal; objective evaluation of nutrition knowledge in this cohort confirmed this belief. A formal component of nutrition education could be developed in the context of GI fellowship education and continuing medical education as necessary."

**In sum:** The data consistently demonstrate that healthcare providers at the doctorate level are untrained in nutrition when assessed by rather simple standards; their knowledge of functional nutrition at the level of clinical intervention in the treatment of serious disease would reasonably be expected to be approximately zero. Thus, given that doctors are trained neither in musculoskeletal management (despite the fact that all patients have musculoskeletal systems and that related disorders represent no less than 20% of general practice) nor nutrition (despite the fact that all patients eat food and that such dietary habits (and/or the use of nutritional interventions) impact nearly all known diseases in the known universe), one might wonder as to the cause and perpetuation of this *systematically imposed ignorance* on such topics of major importance. Consistent faults in medical education are not accidental.

### Dumbing Us Down: The Hidden Curriculum of Educational Systems

"Look again at the seven lessons of school teaching: confusion, class position, indifference, emotional and intellectual dependency, conditional self-esteem, and surveillance. All of these lessons are prime training for permanent underclasses, people deprived forever of finding the center of their own special genius."

Such a curriculum produces physical, moral, and intellectual paralysis, and no curriculum of content will be sufficient to reverse its hideous effects. ... Schools teach exactly what they are intended to teach and they do it well."

Gatto JT. *Dumbing Us Down: The Hidden Curriculum of Compulsory Schooling*, p. 16

## Adverse effects of nonsteroidal anti-inflammatory drugs (NSAIDs), COX-2 inhibitors (coxibs)

**Introduction:** Nonsteroidal anti-inflammatory drugs (NSAIDs) have many common and serious adverse effects, including the promotion of joint destruction. Paradoxically, these drugs *cause* or *exacerbate* the very symptoms and disease they are supposed to treat: joint pain and destruction. In a tragic exemplification of Orwellian newspeak<sup>32</sup>,

<sup>29</sup> Vetter et al. What do resident physicians know about nutrition? An evaluation of attitudes, self-perceived proficiency and knowledge. *J Am Coll Nutr.* 2008 Apr;27(2):287-98

<sup>30</sup> Halsted CH. The relevance of clinical nutrition education and role models to the practice of medicine. *Eur J Clin Nutr.* 1999 May;53 Suppl 2:S29-34

<sup>31</sup> Raman M, Violato C, Coderre S. How much do gastroenterology fellows know about nutrition? *J Clin Gastroenterol.* 2009 Jul;43(6):559-64

<sup>32</sup> Orwell G. *1984*. Harcourt Brace Jovanovich: 1949. "Newspeak" is defined by the Merriam-Webster Dictionary (m-w.com) as "propagandistic language marked by euphemism, circumlocution, and the inversion of customary meanings" and as "a language designed to diminish the range of thought," in the novel *1984* (1949) by George Orwell.

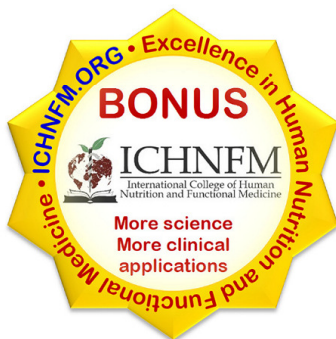
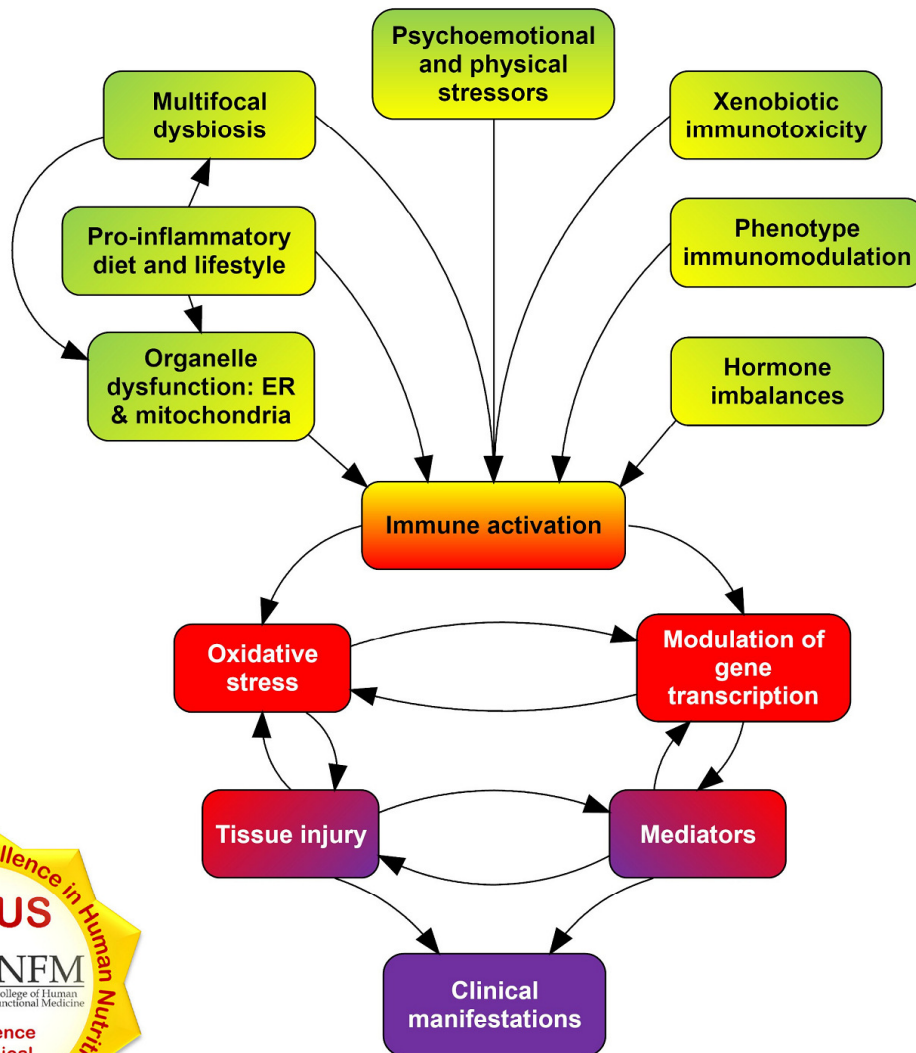
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# INFLAMMATION MASTERY

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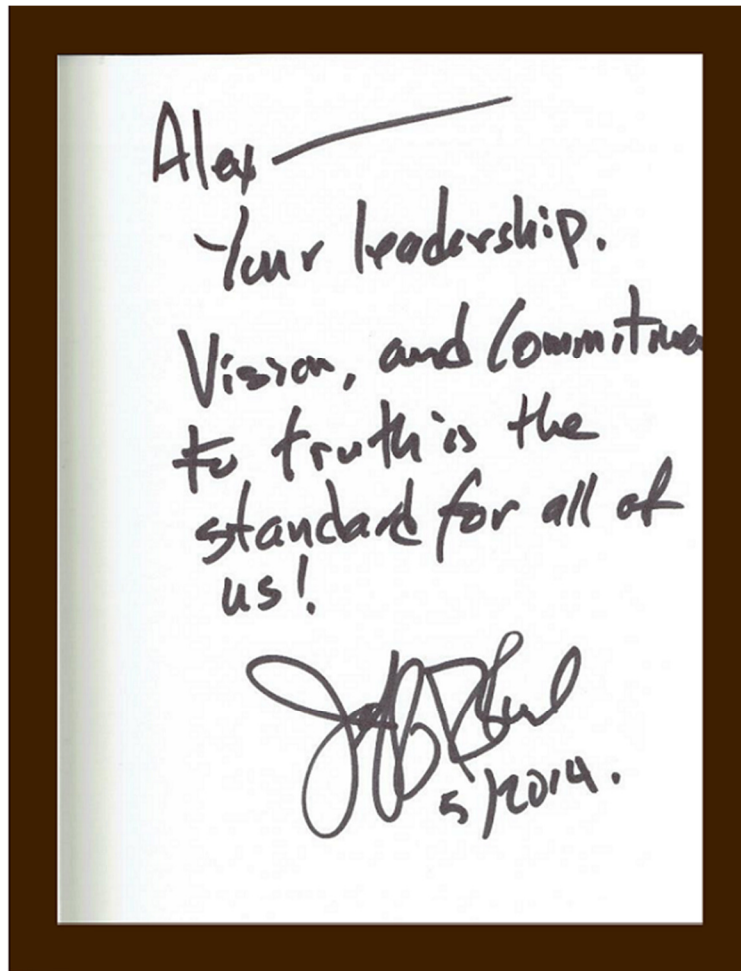
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**Pictured above—Personal inscription from Dr. Jeffrey Bland at a book signing event for his book *Disease***

**Delusion:** My inclusion of Dr Bland's personal note above is not meant to imply that he is endorsing this book; he might very well reject any or all of it. Further, this inclusion does not imply that he carries those same sentiments beyond the day that he wrote them to me in May of 2014. Rather, my inclusion signifies our mutual respect as colleagues, and my personal respect for his thought and demeanor, and his influence on my life and work. I have respectfully honored him in this book as the founder of what most clinicians in America know as Functional Medicine, and I have developed and extended my own version of his concept—that disease states are malleable rather than destined—to the clinical management of inflammatory disorders under the name of Functional Inflammalogy. Importantly and personally—but not paradoxically if one understands the true goals of mentorship, affiliation, and friendship—due to the support of friends and colleagues, this book also represents a departure from concern that I had for endorsement from or agreement with other people, professions, universities, or organizations. In this book, I have presented the truth as I see it—without apology—and without any filtering other than as the limitations imposed by time, space, my own abilities, and limitations imposed by human physiology. This work—now published as *Inflammation Mastery, 4<sup>th</sup> Edition*—has been "in progress" since its origin as course notes for Orthopedics and Rheumatology which I taught at Bastyr University in Seattle in 2000-2001 and through its previous publications in many books starting with *Integrative Orthopedics* (2004) and *Integrative Rheumatology* (2006) and peer-reviewed articles in journals ranging from *Annals of Pharmacotherapy* to *Alternative Therapies in Health and Medicine*. In addition to spanning more than 16 years, this work has also spanned various countries and cultures—including Houston, Fort Worth, Austin (Texas), Seattle (Washington), Portland (Oregon) in the United States, then to Bogota, Colombia and Barcelona, Spain. I consider this volume to be my highest presentation of truth, accuracy, and clinical application that I could humanly muster while maintaining my own health, relationship, and other obligations. I will always remain open to correction and the updating of this work as the weight of evidence indicates. The goals of healthcare should be the optimization of physical health and psychosocial-intellectual freedom.

**Dedications:** I dedicate this book to the following people in appreciation for their works, their direct and indirect support of this work, and for their contributions to the advancement of true healthcare.

- **To the students and practitioners of naturopathic/functional medicine**, those who continue to learn so that they can provide the best possible care to their patients
- **To the researchers** whose works are cited in this text
- **To Dr Alan Gaby and Dr Jeffrey Bland**, my most memorable and influential *personal* professors and mentors
  - Dr Gaby's diligent scholarship of the medical nutrition literature laid the evidence-based foundation for nearly all of us; his *Nutritional Medicine* is an excellent companion text to compliment this volume
  - Dr Bland deserves credit for being the primary developer of the American rendition of "functional medicine", a conceptual framework and clinical model used and discussed in this text. While development and continuous maturation of the functional medicine model has depended upon numerous researchers and clinicians, Dr Bland was clearly the pioneer for this concept circa 1993 and the nucleus around which many of us have worked (at least initially) in this regard.
- **To Henry Rollins**, in particular for his prose book *One from None*, which completely changed my life in 1991
- **To Dr Linus Pauling**, for modeling the combination of scientific scholarship (Nobel Prize in Chemistry 1954) and social engagement (Nobel Peace Prize 1962)
- **To Dr Friedrich Nietzsche and Dr Noam Chomsky**, my most memorable and influential *virtual* professors and mentors, both of whom exemplify profound scholarship and intellectual independence in favor of developing the highest possible human culture on earth
- **To Dr Robert Richard**, my clinical mentor in general outpatient medicine—a truly exemplary clinician
- **To Dr Bruce Ames<sup>1</sup> and Dr Roger J Williams<sup>2</sup>**, for proving the importance of biochemical individuality
- **To Dr Chester Wilk<sup>3,4</sup> and important others<sup>5,6,7</sup>** for documenting and resisting the organized oppression of natural, non-pharmaceutical, non-surgical healthcare
- **To Jorge Strunz and Ardeshir Farah**, for daily artistic inspiration since my first listen of *Primal Magic* in 1992

**Acknowledgments for Peer and Editorial Review of Earlier Versions of This Work:** Most of the sections that comprise the current work have been previously reviewed/published/presented; peer/editorial reviews are acknowledged below. Acknowledgement here does not imply that the reviewer fully agrees with or endorses the material in this text but rather that they were willing to review specific sections of the book for clinical applicability and clarity and to make suggestions to their own level of satisfaction.

- **2016 Edition of *Inflammation Mastery and the excerpt Pain Revolution for Migraine and Fibromyalgia*:** Sabrina Piper BSc (2016 ND candidate), John Bartemus DC BCIM CFMP DACBN, Elizabeth Busetto DC ND, Kenneth Cintron MD
- **2015 Edition of *Human Microbiome and Dysbiosis in Clinical Disease*:** Julie Jean BS BSN RN, Joseph Iaccino DC MSc
- **2014 Edition of *Antiviral Strategies and Immune Nutrition*:** Annette D'Armata ND, Elizabeth Busetto DC ND
- **2014 Edition of *Naturopathic Rheumatology*:** Annette D'Armata ND
- **2012 Edition of *Fibromyalgia in a Nutshell*:** Lisa Scholl BA, Annette D'Armata ND
- **2012 Edition of *Migraine Headaches, Hypothyroidism, and Fibromyalgia*:** Holly Furlong DC
- **2011 Edition of *Integrative Chiropractic Management of High Blood Pressure and Chronic Hypertension*:** Barry Morgan MD, Holly Furlong DC, Kris Young DC, Erika Mennerick DC, and J William Beakey DOM
- **2011 Edition of *Integrative Medicine and Functional Medicine for Chronic Hypertension*:** Erika Mennerick DC, JoAnn Fawcett DC, Ileana Bourland MSOM LAc, James Bogash DC, J William Beakey DOM
- **2010 Edition of *Chiropractic Management of Chronic Hypertension*:** Joseph Paun MS DC, David Candelario OMS4 (TCOM c/o 2010), James Bogash DC, Bill Beakey DOM, Robert Richard DO
- **2009 Edition of *Chiropractic and Naturopathic Mastery of Common Clinical Disorders*:** Heather Kahn MD, Robert Richard DO, James Leiber DO, David Candelario (UNT-HSC TCOM OMS4)
- **2007 Edition of *Integrative Orthopedics*:** Barry Morgan MD, Dennis Harris DC, Richard Brown DC (DACBI candidate), Ron Mariotti ND, Patrick Makarewich MBA, Reena Singh (SCNM ND4), Zachary Watkins DC, Charles Novak MS DC, Marnie Loomis ND, James Bogash DC, Sara Croteau DC, Kris Young DC, Joshua Levitt ND, Jack Powell III MD, Chad Kessler MD, Amy Neuzil ND
- **2006 Edition of *Integrative Rheumatology*:** Amy Neuzil ND, Cathryn Harbor MD, Julian Vickers DC, Tamara Sachs MD, Bob Sager BSc MD DABFM (Clinical Instructor in the Department of Family Medicine, University of Kansas), Ron

<sup>1</sup> Ames BN, et al. High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased K(m). *Am J Clin Nutr.* 2002 Apr;75:616-58

<sup>2</sup> Williams RJ. *Biochemical Individuality: The Basis for the Genetotropic Concept.* Austin and London: University of Texas Press; 1956

<sup>3</sup> Wilk CA. *Medicine, Monopolies, and Malice: How the Medical Establishment Tried to Destroy Chiropractic.* Garden City Park: Avery, 1996

<sup>4</sup> Getzendanner S. Permanent injunction order against AMA. *JAMA.* 1988 Jan 1;259(1):81-2

<sup>5</sup> Carter JP. *Racketeering in Medicine: The Suppression of Alternatives.* Norfolk: Hampton Roads Pub; 1993

<sup>6</sup> Morley J, Rosner AL, Redwood D. A case study of misrepresentation of the scientific literature: recent reviews of chiropractic. *J Altern Complement Med.* 2001;7:65-78

<sup>7</sup> Terrett AG. Misuse of the literature by medical authors in discussing spinal manipulative therapy injury. *J Manipulative Physiol Ther.* 1995 May;18(4):203-10



Test	Low	Normal	High	Reference Range	Units
Vitamin D, 1,25 + 25-Hydroxy			115.8	10.0-75.0	pg/mL
Calcitriol(1,25 Di-Oh Vit D)		53.1		30.0-100.0	ng/mL
Vitamin D, 25-Hydroxy					
Cmp14+Egfr					
Test	Low	Normal	High	Reference Range	Units
Glucose, Serum		90		65-99	mg/dL
Bun		20		6-20	mg/dL
Creatinine, Serum		0.93		0.76-1.27	mg/dL
Egfr # Nonafri Am		104		>59	mL/min/1.73
Egfr # Afri Am		120	22	>59	mL/min/1.73
Bun/Creatinine Ratio				8-19	1
Sodium, Serum		142		134-144	mmol/L
Potassium, Serum		4.8		3.5-5.2	mmol/L
Chloride, Serum		99		97-108	mmol/L
Carbon Dioxide, Total		26		18-29	mmol/L
Calcium, Serum		9.7		8.7-10.2	mg/dL

Cbc/Diff Ambiguous Default

Test	Low	Normal	High	Reference Range	Units
Wbc		5.8		3.4-10.8	x10E3/uL
Rbc		5.26		4.14-5.80	x10E6/uL

Ldh

Test	Low	Normal	High	Reference Range	Units
Ldh		123		121-224	IU/L

Homocyst(E)lne, Plasma

Test	Low	Normal	High	Reference Range	Units
Homocyst(E)lne, Plasma		10.7		0.0-15.0	umol/L

**Laboratory results for a 39yoM with psoriasis and psoriatic arthritis:** Abnormally increased conversion of 25-OH-cholecalciferol to 1,25-d(OH)-cholecalciferol is due expression of 25-hydroxyvitamin D3-1alpha-hydroxylase (1-OHase) in inflammatory tissue/cells. Note that serum calcium is normal, so no immediate threat is present (i.e., hypercalcemia) but of course the clinician has the responsibility to monitor periodically, inform the patient of symptoms of hypercalcemia such as headache and abdominal pain, and search for any predictive risk factors such as renal insufficiency or occult leukemia/lymphoma that could precipitate hypercalcemia. Assessment for hyperparathyroidism (eg, iPTH) is reasonable but not completely necessary; likewise, cancer screening is not absolutely indicated, as it would be in the case of idiopathic hypercalcemia. Also noted is the elevated homocysteine, common in patients with psoriasis; increased cell turnover—dermal hyperproliferation—likely contributes to draining/catabolizing nutrients such as folate. Since this patient's 25-OH-D is plenty sufficient, I had the patient temporarily reduce/discontinue vitamin D supplementation to reduce risk of hypercalcemia given that he is clearly vitamin D sufficient.

# CME

## CONTINUING MEDICAL EDUCATION

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

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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.

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 vitamin D supplementation in proper doses and with appropriate laboratory monitoring

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 that higher vitamin D levels provide protection from diabetes mellitus, osteoporosis, osteoarthritis, hypertension, cardiovascular disease, metabolic syndrome, depression, several autoimmune diseases, and cancers of the breast, prostate, and colon, we can now utilize vitamin D for a wider range of preventive and therapeutic applications to maintain and improve our patients' health.<sup>3</sup> Based on the research reviewed in this article, the current authors believe that assessment of vitamin D status and treatment of vita-

**Vasquez A et al. The clinical importance of vitamin D (cholecalciferol): a paradigm shift with implications for all healthcare providers. *Altern Ther Health Med* 2004 Sep-Oct.** This article indexed on Medline at [ncbi.nlm.nih.gov/pubmed/15478784](http://ncbi.nlm.nih.gov/pubmed/15478784) and is archived by the author online [ICHNFM.ORG/faculty/vasquez/profile.html](http://ICHNFM.ORG/faculty/vasquez/profile.html) and <https://ichnfm.academia.edu/AlexVasquez>





- **Thyroid assessment:** may show evidence of diabetes and hyperthyroidism in patients with iron overload.
- **Bone marrow biopsy:** unnecessary and archaic in this setting.
- **Liver biopsy:** traditionally considered the “gold standard” but is clearly unnecessary for the diagnosis, which can be established by phlebotomy, which is the treatment of choice.<sup>656</sup> **Life-savings should never be denied or delayed for lack of liver biopsy in iron overload.**<sup>657</sup>
- **Genetic testing, such as for the HFE mutation:** This is not recommended in most situations; these tests should be reserved for research purposes, especially children—of index cases. The only value that is of any support in supporting a diagnosis in a patient with elevated serum ferritin is phlebotomy; however, a negative result is meaningless in a patient compatible with iron overload. If the diagnosis is established by phlebotomy, genetic testing is unnecessary.

**Establishing the diagnosis:** Any *one* of the following three is sufficient:

- Diagnostic liver biopsy shows heavy iron deposits.
- Characteristic laboratory findings (ferritin >200 in women or >300 in men) *and* the ability to resist intractable anemia with serial/weekly phlebotomies.
- Characteristic MRI of liver *and* the ability to tolerate serial/weekly phlebotomies.

**Complications:**

- Patients diagnosed *and effectively treated* before the onset of liver failure.
- The most common causes of premature mortality in undiagnosed iron overload are liver failure, infections and/or complications of dialysis.

**Clinical management:**

- Treatment for severe iron overload is iron-removal therapy. Therapeutic phlebotomy—is the treatment of choice. Defective iron regulation in patients who refuse or cannot withstand phlebotomy (i.e., patients with severe liver failure) is treated with less effective, much more expensive chelation therapy.



**Persistent inadequacies in musculoskeletal education/training among physicians: The need to advance clinicians' knowledge in musculoskeletal care, pain management, and nutrition**

**Question:** What would be the expected clinical/financial outcome of physicians' being inadequately trained in musculoskeletal medicine and then given prescriptive rights for potent NSAIDs, coxibs, steroids, DMARDs, etc and placed in a position of ethical and professional responsibility for managing patients' pain?

**Answer:** We would reasonably expect the profession to misdiagnose various conditions, overuse drugs, overuse expensive (and with regard to computed tomography, dangerous) imaging technology to compensate for poor diagnostic skills, and to overuse procedures/surgery in an attempt to provide (the appearance of) competence in the clinical management of musculoskeletal problems. These are exactly the outcomes that we see in clinical practice: inaccurate diagnoses followed by inefficacious treatments, overuse of imaging, drugs, and surgery.

- Medical student musculoskeletal education (J Bone Joint Surg Am 2012 Oct<sup>20</sup>): "The survey contained a validated orthopedic examination of musculoskeletal competency (passing grade, 70% ... The mean score was 51.1%; only sixty-seven (19.3%) of the students passed. Fourth-year students scored significantly higher (59.0% [which is still an average grade of failure]) compared with first-year students (37.3%), but 65% of students in both groups failed. Only 34.2% of the graduating students had completed a musculoskeletal elective. Students who participated in elective musculoskeletal education had a higher pass rate (67.5%) than those who did not (43.9%)."
- Musculoskeletal education in US medical schools (Curr Rev Musculoskelet Med 2011 Sep<sup>21</sup>): "Despite the prevalence of musculoskeletal disorders in the United States, physicians have received inadequate training during medical school on how to examine, diagnose, and manage these conditions."
- Assessment of the musculoskeletal medicine attitudes and knowledge of medical students at Harvard Medical School (Acad Med 2007 May<sup>22</sup>): "Participants were asked to fill out a 30-question survey and a nationally validated basic competency exam in musculoskeletal medicine. ... Medical students rated musculoskeletal education to be of major importance (3.8/5) but rated the amount of curriculum time spent on musculoskeletal medicine as poor (2.1/5). Third-year students felt a low to adequate level of confidence in performing a musculoskeletal physical examination (2.7/5) and failed to demonstrate cognitive mastery in musculoskeletal medicine (passing rate on competency exam: 7%), whereas fourth-year students reported a similar level of confidence (2.7/5) and exhibited a higher passing rate (26%). ... These findings, which are consistent with those from other schools, suggest that medical students do not feel adequately prepared in musculoskeletal medicine and lack both clinical confidence and cognitive mastery in the field."
- Musculoskeletal cognitive competency in chiropractic interns (J Manipulative Physiol Ther 2007 Jan<sup>23</sup>): 123 fourth-year chiropractic students at a single school (Canadian Memorial Chiropractic College) were given a standardized musculoskeletal examination (basic competency examination [BCE], originally developed by Freedman and Bernstein, cited below, 1998 and 2002); very tellingly, these chiropractic researchers decided that twenty percent (5 questions) of the standardized musculoskeletal examination were not relevant to or were outside of the scope of chiropractic practice, i.e., that chiropractic practice scope is narrower than that of primary care and medical training. "Interns achieved a 51.2% passing rate (mean score, 73.2%) for the 25-item BCE,... For the modified 20-item BCE [narrowed for chiropractic education and practice scope], the interns' mean score was 80.8%..." This study is interesting in that, while chiropractic students performed better (51.5% for >73% passing grade; 64.7% for >70% passing grade) than their allopathic counterparts as would be expected for a four-year training program that focuses with near exclusively on musculoskeletal diagnosis and management, nearly half of them failed the exam if 73% accuracy is the standard; further, the researchers' modification of the exam appears to be an admission that chiropractic education/training scope is not on par with that of medical students and clinicians as they noted that 20% of questions "fell outside the scope of chiropractic practice." *What were the topics of these questions that were excluded?:* Congenital hip dislocation, knee dislocation following motor vehicle accident,

<sup>20</sup> Skelley NW, Tanaka MJ, Skelley LM, LaPorte DM. Medical student musculoskeletal education: an institutional survey. *J Bone Joint Surg Am.* 2012 Oct 3;94(19):e146(1-7)

<sup>21</sup> Monrad SU, et al. Musculoskeletal education in US medical schools: lessons from the past and suggestions for the future. *Curr Rev Musculoskelet Med.* 2011 Sep;4(3):91-8

<sup>22</sup> Day CS, et al. Musculoskeletal medicine: an assessment of the attitudes and knowledge of medical students at Harvard Medical School. *Acad Med.* 2007 May;82(5):452-7

<sup>23</sup> Humphreys et al. An examination of musculoskeletal cognitive competency in chiropractic interns. *J Manipulative Physiol Ther.* 2007 Jan;30(1):44-9

skin laceration and metacarpal fracture of the hand following minor trauma, appropriate indications for radiographs in patients with low-back pain, and simple clinical anatomy of the femoral neck and head. Thus, the admission by these researchers/clinicians that chiropractic students/clinicians are not prepared to deal with these issues is also a clear statement from them that they perceive that the profession is not prepared to deal with routine musculoskeletal issues at the primary care level.

- Insufficient musculoskeletal knowledge among academic primary care physicians (*J Bone Joint Surg Am* 2006 Jul<sup>24</sup>): "RESULTS: ... Fifty-nine (64%) of the ninety-two physicians scored < 70% [on an examination of basic musculoskeletal knowledge]. Higher examination scores were associated with male gender (p = 0.01) and participation in a musculoskeletal course (p = 0.009). Practitioners who took elective courses demonstrated higher scores compared with those who took required courses (p = 0.014). Greater musculoskeletal confidence was associated with the number of years in clinical practice (p = 0.045), male gender (p = 0.01), residency training in family practice (p < 0.00001), and prior participation in a musculoskeletal course (p = 0.0004). ... CONCLUSIONS: Although a large proportion of primary care visits are for musculoskeletal symptoms, the majority of primary care providers tested at a large, regional, academic primary care institution failed to demonstrate adequate musculoskeletal knowledge..."
- More evidence of educational inadequacies in musculoskeletal medicine (*Clin Orthop Relat Res* 2005 Aug<sup>25</sup>): "In their study, Freedman and Bernstein suggested that 80% of a group of graduates from many of the best medical schools in the United States were deficient in their knowledge of basic facts and concepts in musculoskeletal medicine. ... Despite generally improved levels of competency with each year at medical school, less than 50% of fourth-year students showed competency."
- Educational deficiencies in musculoskeletal medicine (*J Bone Joint Surg Am* 2002 Apr<sup>26</sup>): "Two hundred and forty (58%) of the 417 program directors of internal medicine residency departments responded. They suggested a mean passing score (and standard deviation) of 70.0% +/- 9.9%. As reported previously, the mean test score of the eighty-five examinees was 59.6%. Sixty-six (78%) of them failed to demonstrate basic competency on the examination according to the criterion set by the internal medicine program directors. ... According to the standard suggested by the program directors of internal medicine residency departments, a large majority of the examinees once again failed to demonstrate basic competency in musculoskeletal medicine on the examination. It is therefore reasonable to conclude that medical school preparation in musculoskeletal medicine is inadequate."
- Inadequacy of medical school education in musculoskeletal medicine (*J Bone Joint Surg Am* 1998 Oct<sup>27</sup>): "Seventy (82 per cent) of the eighty-five residents failed to demonstrate basic competency on the examination according to the chairpersons' criterion. In summary, seventy (82 per cent) of eighty-five medical school graduates failed a valid musculoskeletal competency examination. We therefore believe that medical school preparation in musculoskeletal medicine is inadequate."
- Training and clinical competency in musculoskeletal medicine (*Sports Med* 1993 May<sup>28</sup>): "Injuries and diseases of the musculoskeletal system account for more than 20% of patient visits to primary care and emergency medical practitioners. However, less than 3% of the pre-clinical medical school curriculum is devoted to teaching all aspects of musculoskeletal disease... Available elective training in musculoskeletal injuries and diseases is commonly taught by hospital-affiliated physicians and surgeons, with the result that this teaching case load is typically skewed towards serious and/or surgical problems."

**In sum:** The data and conclusions consistently report the fact that health professional education and training are both inadequate to ensure competence among (American) physicians in the understanding, diagnosis, and management of musculoskeletal disorders based on a verified and standardized *yet very basic* examination of musculoskeletal competence. The anticipated implications and consequences—inadequate care with overuse of invasive, expensive, and dangerous drugs, procedures, and surgeries—is well borne-out.

#### What purpose education?

"Education is a system of imposed ignorance."

Chomsky N. *Manufacturing Consent*, 1992 documentary film

<sup>24</sup> Lynch et al. Important demographic variables impact musculoskeletal knowledge and confidence of academic primary care physicians. *J Bone Joint Surg Am* 2006;88:1589-95

<sup>25</sup> Schmale GA. More evidence of educational inadequacies in musculoskeletal medicine. *Clin Orthop Relat Res*. 2005 Aug;(437):251-9

<sup>26</sup> Freedman KB, Bernstein J. Educational deficiencies in musculoskeletal medicine. *J Bone Joint Surg Am*. 2002 Apr;84-A(4):604-8

<sup>27</sup> Freedman KB, Bernstein J. The adequacy of medical school education in musculoskeletal medicine. *J Bone Joint Surg Am*. 1998 Oct;80(10):1421-7

<sup>28</sup> Craton N, Matheson GO. Training and clinical competency in musculoskeletal medicine. Identifying the problem. *Sports Med*. 1993 May;15(5):328-37

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



## Reviews of previous and recent works:

- "Thank you most kindly for your incredible dedication and kindness in sharing your knowledge with us. I am due to start med school next semester and thanks to you and all those who have taught you, I'll be way ahead of the curve." *Premedical/Medical student 2015*
- "Dr Vasquez, I have followed your work extensively and admire your intellect and passion. Thank you for your passion for teaching with integrity!" *Chiropractic doctor 2015*
- "I just wanted to tell you how much I appreciate the information I have received from you. I am still digesting most of it. I feel I have learned quite a bit already yet also feel I have barely scratched the surface." *Doctor and Graduate student under Dr Vasquez, 2013*
- "Dr. Vasquez, Thank you for all you do. **Your conference was simply amazing.** No one wanted to leave the room. I met medical professionals and very interesting lay people who were stimulated and invigorated to change their lives and the lives of others. **I am in awe at your intellectual integrity and veracity.** Best of luck to you in all of your future endeavors." *Medical physician and ICHNFM 2013 Conference Attendee*
- **2014 review of Functional Inflammolgy, Volume 1: "A truly comprehensive text on the vast subject of inflammation. I consider this book to be an essential addition to any health care practitioner who wishes to operate within the realm of Function Medicine. Please be aware that this book is dense in its content, and its 700 plus pages are full of deeply insightful information. I think Dr. Vasquez is one of the most prolific functional medicine contributors and books such as this should cement his reputation as such."**
- "I attended the last ICHNFM conference in Portland (and am still basking in the amazing information received)." *Email from Clinical Oncology Dietitian, in late February 2014*
- "Thanks for a fantastic conference!" *ICHNFM 2013 Conference Attendee*
- "Your discourse today reflected not only your passion and commitment to the wellness of our planet but most importantly the clarity and sincerity of your spirit/ heart/ mind. Always good to be with you and look forward to seeing you soon. Hope we can spend more time then." *Medical physician attendee 2014*
- "I was so refreshed by the **unfiltered excellence.**' What humanness. Breaths of fresh air." *ICHNFM 2013 Attendee*
- "Keep in mind Alex, that humanity is a better place because of you. I know you can't undo it all, but think about how many people would be worse off if it wasn't for your wonderful knowledge being shared with all us docs. Things that I have learned from you have changed peoples' lives for the better." *Naturopathic physician, 2014*
- "Just got back to Guam. Great experience at the International Conference on Human Nutrition and Functional Medicine. Exciting concepts on functional medicine. Thanks Dr. Alex Vasquez and team!" *ICHNFM 2013 Conference Attendee*
- "Already waiting in line to buy next year's ticket! **Dr. Vasquez you crushed it!** The future is looking fun already ☺" *ICHNFM 2013 Conference Attendee*
- "Had an incredible time at the 2013 International Conference on Human Nutrition and Functional Medicine. Got to meet some amazing people and hear from some of the top researchers/health professionals about human nutrition and functional medicine approaches. It was definitely worth every penny and can't wait to go back next year!" *ICHNFM 2013 Conference Attendee*
- "I miss you! Your confidence in a program you believed in. I miss your live classes where we would get off topic on a clinical pearl. I miss your way of teaching in a laid back atmosphere that made me feel comfortable, not intimidated. I just needed to let you know, this program is not the same, I am almost done, otherwise, I would have bailed out! I am grateful for the last 18 months I did have with you at the helm. ... You ignited in me my passion for learning again. You sparked the minds of all of us with your enthusiasm. Don't ever let anyone take that away. It has given birth to your new endeavor, and we will follow where you lead. Enjoy your new surroundings and celebrate your new beginnings. I know I look forward to what is ahead." *Doctor and Graduate student under Dr Vasquez, 2013*
- "Wonderful conference! Thanks so much." *ICHNFM 2013 Conference Attendee*
- "Really wonderful conference! Lots of material ready to implement Monday morning! **Congrats to Alex Vasquez on a herculean job very well done!**" *ICHNFM 2013 Conference Attendee*
- "Thanks for a great conference. I really enjoyed all of the speakers, but your lectures were by far the most useful for implementing ideas into my clinical practice. And the most entertaining." *ICHNFM 2013 Conference Attendee*
- "Thank you for your life-changing work." *Physician, 2011*
- "I want Dr. Vasquez to know that I have just received his book, *Chiropractic and Naturopathic Mastery of Common Clinical Disorders*. **It is a treasure. The best book in my library.** Thank you for the contribution that you are giving to the world of health care." *Clinician, 2010*
- "I appreciate the resources you offer the profession. I use your books and articles regularly." *Doctor, 2011*
- "Dr. Vasquez, I greatly appreciate your efforts. I am a student at \_\_\_, 8th trimester, and would like to express my gratitude for your research and works. After coming across your texts in the library, **I quickly found your insight and explanations of the current health care crisis, and in depth coverage and algorithms for inflammatory**



diseases as a profound inspiration and call to action. I appreciate your attention to detail, and have been taken back several times by the potency and meaning of your sentences. Thank you for your hard work, I will enjoy these books and will surely share with those that have the same drive for true and competent patient care." *Health Sciences Student, 2008*

- "I never told you this, but whenever I need to research a particular disease, **besides going on Pubmed and checking some classic Pathophysiology and Clinical Nutrition books, I use your books and I find them extremely well organized, concise, and up-to-date and with the functional/integrative medicine thinking I enjoy and believe it is the future of Health Care.**" *Nutrition Research Consultant and University Faculty in Europe, 2009*
- "Thanks so much. You are a great asset to our profession." *Doctor, 2010*
- "As a 7th trimester student quickly approaching 8th trimester and student clinic, I know I will be utilizing your books often. **Your "Chiropractic and Naturopathic Mastery of Common Clinical Disorders" book is referenced very frequently by many clinicians and faculty members at [our university]. Your work is highly regarded,** and I look forward to clinically utilizing the information I will obtain from your writings." *Health Sciences Student, 2011*
- "I am a chiropractic student at \_\_\_ Chiropractic College. I just wanted to drop a quick line thanking you for your thorough and accessible textbook Integrative Orthopedics. We are using it in our Differential Diagnosis class, and **it is the best book I've come across in Chiropractic College bar none. The writing is concise, informative and refreshingly eloquent. The material is super practical. I hope you continue putting out great resources.**" *Health Sciences Student, 2011*
- "I appreciate the resources you offer the profession. **I use your books and articles regularly.**" *Doctor, 2011*
- "**Your Integrated Orthopedics book is magnificent.** I wish all textbooks were structured and as thoughtful as that one." *Health Sciences Student, 2008*
- "By reading the introduction I realize that calling it an orthopedics book; does not do it justice. **It is far more than that. It looks to me that you have created, or are creating, the bible of Integrative Orthopedics and physical medicine.**" *Physician, 2007*
- "First of all let me say how honored I am that you have allowed me to review this work. You have done an amazing job! In my opinion **every healthcare provider SHOULD have this on their bookshelf.**" *Physician, 2007*
- "Your work on Chapter 12: Hip and Thigh is very good. The chapter is inclusive of the typical pathologies seen in private practice and I particularly liked the separation of juvenile from adult pathologies. Your choice of tests to assess hip and thigh pathology on page 320 is very nice and inclusive. I appreciate your use of algorithms and find them very useful in teaching and in practice. In general, **I thought this chapter represents a quality, state of the art presentation!**" *Clinician and Professor in Clinical Sciences, 2007*
- "I saw your books in a colleague's office and was really impressed. Really appreciate the thoroughness you've put into them." *Doctor, 2010*
- "**It is with great interest and fascination that I have been reading your material both in your two books (Integrative Orthopedics and Integrative Rheumatology) and online. I consider myself very fortunate to have come across your work,** as many of the basic elements of health which you discuss I never learnt or even heard about while in chiropractic college." *Doctor, 2010*
- "I appreciate the resources you offer the profession. I use your books and articles regularly." *Doctor, 2011*
- "**I'm so pleased with your books and was inspired to let you know they have already been incredibly useful! Good index; well organized algorithms. Sometimes I buy educational material and it just sort of sits there... Your books now live on my main desk. Thanks.**" *Physician and Journal Editor, 2009*
- "I just wanted to let you know how much I am enjoying reading **your book Integrative Rheumatology. It is having an extremely positive impact in the way I view health and am having a tough time putting it down. It is very inspirational.** I have long felt that it is very important to set a good example for your patients and now try my best to be one for my future patients. I like how you stress this in your book. In order to be the best example for my patients I am going to need to address some problems with my own health. I look healthy from the outside but I have been suffering from fatigue for about 4 years. It has a very negative impact on my health. People say that doing the same thing and expecting different results is the definition of insanity so I think it is time that I attempt to make some changes. ... **Thanks again for writing such a great book. I feel it is a must have for anyone in a musculoskeletal practice.**" *Health Sciences Student, 2010*
- "My name is [recent graduate], and I've been a fan of your books since I was in chiropractic college at [university] campus. Dr. [Author, Presenter] made your book, Integrative Rheumatology, required reading for his 9th quarter nutrition class. I never looked back, and have since purchased Chiropractic & Naturopathic Mastery of Common Clinical Disorders as well as Chiropractic Management of Chronic Hypertension." *Doctor, 2010*
- "I saw your books in a colleague's office and was really impressed. Really appreciate the thoroughness you've put into them." *Doctor, 2010*

- "Reading the new integrative management of high blood pressure book and I am thoroughly enjoying it; excellent job. **I am feeling so empowered I'm opening another office focusing on 'restoring the foundations of health' for the community** that I open it in. I am looking for a location and networking to find an internist and cardiologist that are forward thinking; I'm very excited!" *Doctor, 2011*
- "Thank you for the presentation at [the university] this past weekend. **My horizons about what can be done to help people were greatly expanded. I am now still studying the notes from the seminar and am looking forward to more study and learning on how to correctly manage diabetes and hypertension.**" *Doctor, 2011*
- "Thank you for exposing so many people to the results of our research on the treatment of hypertension. I hope you can pay us a visit during your next trip to our area so we can give you the tour of our new 50+ bed inpatient facility." *Dr Alan Goldhamer, Chief of Health Promoting Clinic, 2010*
- "**I always enjoy reading your work.** I personally gain a lot of knowledge through being a peer-reviewer for you and am better because of it!" *Doctor, Faculty Member, and Postgraduate Instructor, 2011*
- "**I attended your seminar at [University] in June and have been utilizing your hypertension protocols. In that short time, I have seen some marked progress with various patients.**" *Doctor, 2010*
- "I want to personally thank you for your expertise and books on...everything. I'm in my last year at SCNM (taking rheumatology right now) and I truly admire your research and ability to compile valuable information. Thank you." *Naturopathic Medical Student, 2014*

#### Work as love made tangible

"You work that you may keep pace with the earth and the soul of the earth.  
For to be idle is to become a stranger unto the seasons, and to step out of life's  
procession. ...  
Work is love made visible."

Kahlil Gibran (1883-1930). *The Prophet*, 1973

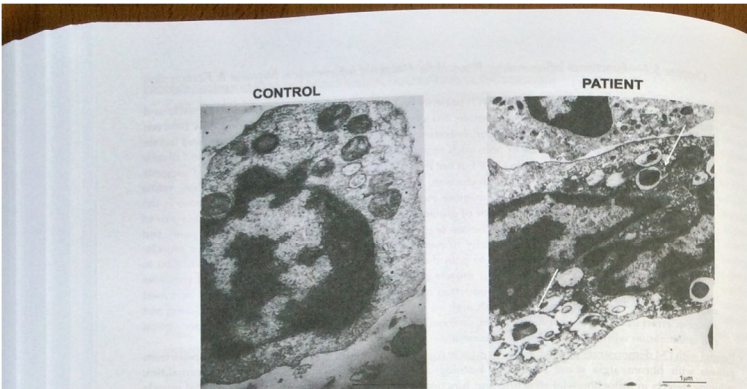
#### Begin at the beginning

"He who wishes one day to *fly*, must first learn *standing*  
and *walking*  
and *running*  
and *climbing*  
and *dancing*.

**One does not *fly* into *flying*."**

Friedrich Nietzsche (1844-1900). *Thus Spoke Zarathustra—A Book for All and None*, 1883-1885





**CONTROL** **PATIENT**

**Blood cells in FM patients show mitochondrial destruction (mitophagy), smaller size and lower number of mitochondria:** Structure of blood mononuclear cells (BMCs, cells of the immune system) from FM patients. The healthy/control BMCs show mitochondria with a normal structure. Autophagosomes (indicated by arrows), where mitochondria are destroyed (the process of mitophagy [mito-mitochondria, phagy-consumption]), are noted in the BMCs of patients with FM. [Bar = 1 micrometer]. This open access image is respectfully attributed to the brilliant research published by these researchers: Cordero MD, De la Haza M, Moreno Fernández AM, Carmona López JM, Garrido Maraver J, Cotán D, Gómez Izquierdo L, Bernal P, Campa P, Bullón P, Navas P, Sáiz de Añazar JA. Mitochondrial dysfunction and mitophagy activation in blood mononuclear cells of fibromyalgia patients. *Arthritis Res Ther*. 2010;12(1):R17. <http://arthritis-research.com/content/12/1/R17>

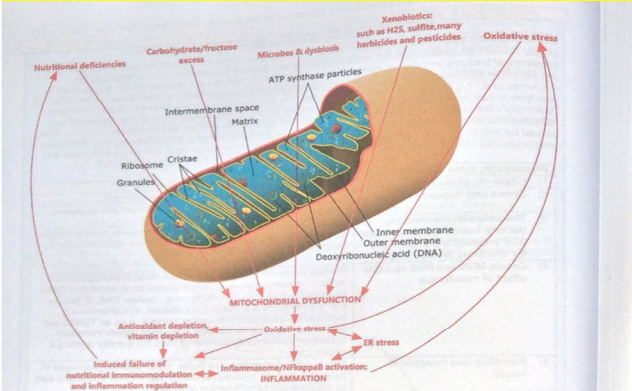
**Mitophagy: The body's inherent mechanism for the destruction of dysfunctional mitochondria**

**Concept:** Autophagic destruction of mitochondria is termed "mitophagy" and is the body's inherent mechanism for eliminating superfluous or dysfunctional mitochondria; this generally has a protective and life-sustaining effect. However, in the case of fibromyalgia wherein the mitochondrial dysfunction is persistent, prolonged mitophagy contributes to failure of adequate energy production and thereby contributes to clinical manifestations of fatigue, dyscognition, and impaired exercise/activity performance. Further, the consistent documentation of significant mitophagy in patients with fibromyalgia proves the biological/organic/real/pathophysiological character of the illness and refutes the pharmacocentric paradigm which holds that the condition is of psychogenic or neurologic origin and thus to be treated with so-called "antidepressants" and/or analgesic drugs, respectively.

- "The removal of damaged mitochondria that could contribute to cellular dysfunction or death is achieved through process of mitochondrial autophagy, i.e. mitophagy." Novak I. *Antioxid Redox Signal*. 2011
- "Mitochondrial number and health are regulated by mitophagy, a process by which excessive or damaged mitochondria are subjected to autophagic degradation." Rambold. *Cell Cycle*. 2011
- "Autophagy can be beneficial for the cells by eliminating dysfunctional mitochondria, but massive autophagy can promote cell injury and may contribute to the pathophysiology of FM." Cordero. *Arthritis Res Ther*. 2010

- **Pain in fibromyalgia originates peripherally and is amplified centrally.** The pain of fibromyalgia originates from the muscles<sup>252</sup> secondary to stimulation by oxidative and inflammatory mediators and is excessively amplified in the brain and spinal cord; another possible peripheral contribution to pain inputs is degeneration of nerve fibers in the skin.<sup>253</sup> To risk redundancy for clarity: FM pain originates *peripherally* in the muscles

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**Schematic overview of mitochondrial dysfunction's major causes and consequences:** Notice the presence of vicious cycles whereby cause becomes consequence, and then consequence becomes cause. Several dietary, nutritional, botanical, pharmaceutical/microbiologic, and sociopolitical interventions are obvious from the diagram.

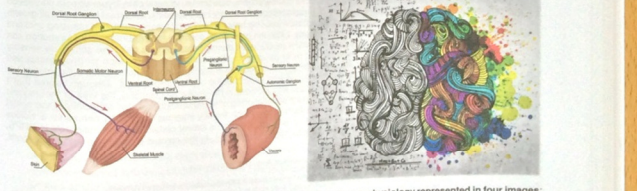
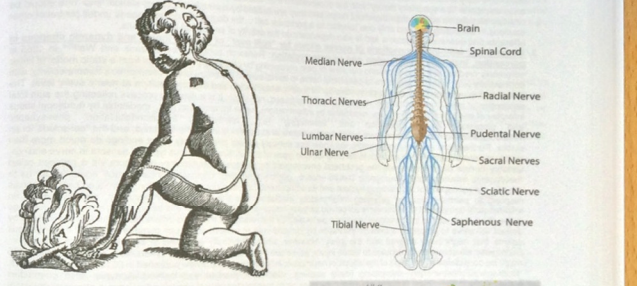
**Mitochondria – Re-Introduction and New Perspectives:**

- **Production of cellular energy in the form of ATP:** Mitochondria are organelles ("small organs") within each cell that produce the majority of cellular energy for biochemical reactions and cellular processes. The primary fuel used by cells of the body is ATP—adenosine triphosphate. Everyone who has studied mitochondria—ranging from high-school and undergraduate students of Biology all the way to doctorate-level medical/healthcare professionals—is familiar with the fact that mitochondria make ATP; in fact, for most people, whether they are general public or doctors, this is all they know about mitochondria. New research, however, has shown us that mitochondria have many roles in addition to their ability to produce cellular energy. Most importantly, microbial infections, triggering of cell death, and controlling various metabolic processes.<sup>1,2</sup>
- **Perpetuation of chronic inflammation:** Most relevant to the focus of this work on clinical conditions related to inflammation is the fact that mitochondria have the ability to trigger inflammatory responses via activation of the nuclear transcription factor kappa-B (NFkB). Transcription factors are intracellular molecules that bind to in this case the transcription factor kappaB is most notorious for its activation of genes that promote protracted and nonspecific. In this way, certain types of mitochondrial stimulation/activation/dysfunction can

<sup>1</sup> Flomench SB, Nemeroff B. Mitochondrial dysfunction and molecular pathways of disease. *Erg Med Pathol*. 2007 Aug;9(1):84-92  
<sup>2</sup> Green DR, Galluzzi L, Kroemer G. Mitochondria and the metabolic-inflammatory cell death axis in organismal aging. *Science*. 2011 Aug 26;333(6046):1109-12

(and likely in the skin as well, at least in some patients) and is amplified centrally in the spinal cord and grows both in size and intensity/hypersensitivity to include the skin, so that various skin inputs are perceived stimuli (as pain) and hyperalgesia (extended duration and increased intensity of pain).

- **Enhanced central pain processing of fibromyalgia:** patients is maintained by muscle afferent input (Pain, hyperalgesia in FM patients, emphasizing the important role of peripheral impulse input in maintaining central sensitization in this chronic pain syndrome; similar to other persistent pain conditions such as irritable bowel syndrome and complex regional pain syndrome."



**More than 400 years of the history and development of neuroanatomy and neurophysiology represented in four images:** These four images in sequence represent the history and development of the fields of neuroanatomy and neurophysiology. The starting with the drawing by Descartes in the 1600s. The tracing of nerves throughout the body. What might be called the findings suggest that some patients with chronic pain labeled as fibromyalgia have unrecognized SPN, a distinct disease that can be tested for objectively and sometimes treated effectively. Calklander et al. Objective evidence that small fiber polyneuropathy underlies some fibromyalgia cases. *Neurology*. 2013 Nov 14;81(20):386-394

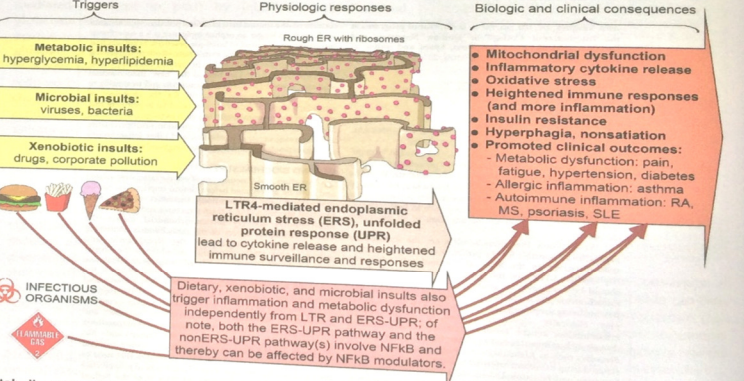
### Food-Induced Activation of Toll-like Receptors, Endoplasmic Reticulum Stress, and the Unfolded Protein Response:

#### An Integrated Model for Understanding Metabolic Inflammation

**Metabolic Inflammation: Diet-Induced Metabolic Impairment and Inflammation**

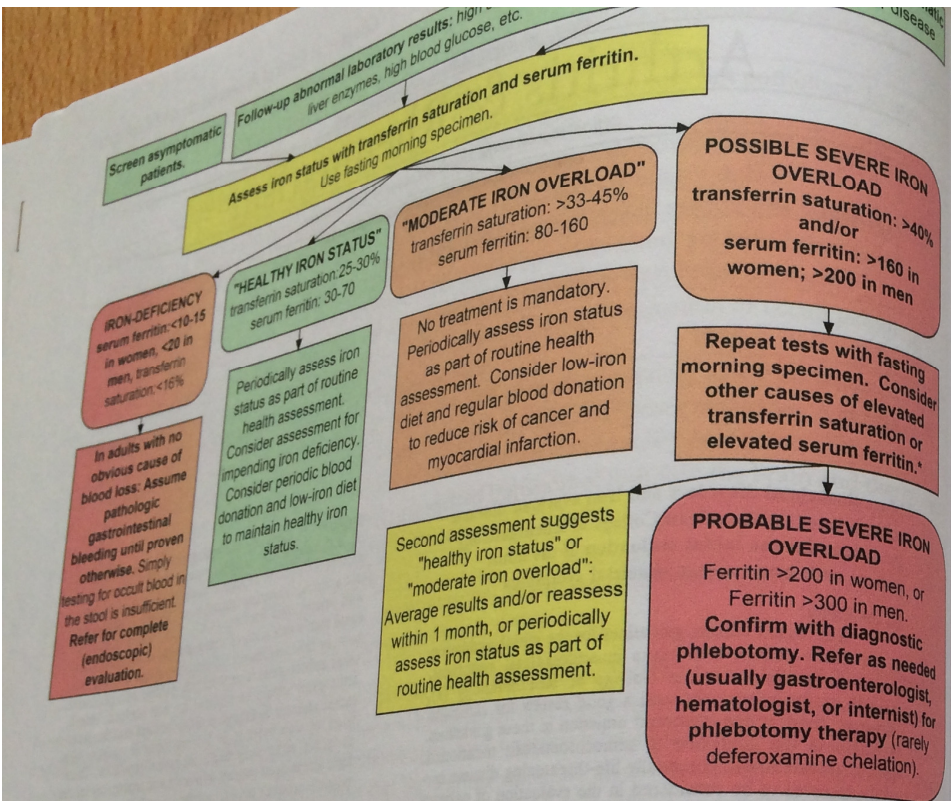
In this section, I will describe and give structure to a model for understanding what I have previously described—albeit intuitively—as metabolic inflammation.

**Introduction:** In my model presented starting in 2012,<sup>65</sup> I began differentiating/describing inflammatory conditions as existing along and within an *overlapping continuum* of metabolic inflammation, allergic inflammation, and autoimmune inflammation. The most basic definition/description of metabolic inflammation is simply that it is a pathophysiological state of nonacute metabolic disruption/dysfunction combined with a state of chronic/sustained mild/nonacute inflammation. What I have also stated is that "chronic inflammation" as most of us were taught in our Pathology coursework does not—for the most part—exist; except for a few rare diseases, the body does not perpetuate clinically significant states of inflammation. So-called *chronic inflammation* only occurs via a *sustained inflammatory response*. Another newer—and perhaps more direct way—of shattering the outdated paradigm of "chronic disease" is to state that such *diseases* do not exist—only *responses* and *accumulated damage* exist. Clinicians should experiment with the possibilities and implications of exchanging their conception of "chronic diseases" in favor of "sustained responses"; I think they will find the experience to be more illuminating/empowering/engaging than resignation to the chronic disease model and its subsequent indefinite noncurative (poly)pharmacotherapy. The illustration below introduces and summarizes several key concepts.



**Metabolic, microbial, and xenobiotic insults—often via TLR4—induce endoplasmic reticulum stress (ERS) and the subsequent unfolded protein response (UPR):** Consequences include vicious cycles of inflammation, oxidative stress, mitochondrial dysfunction, insulin resistance and hyperphagia—all consistent with sustained sterile nonacute inflammation and metabolic dysfunction/impairment termed here as *metabolic inflammation*.





**Algorithm for the comprehensive management of iron status:** The above flow-chart delineates patient management per iron status.

**Basic treatments for severe iron overload:**

- Iron-removal therapy is mandatory:** Phlebotomy therapy is generally performed weekly or twice-weekly. Deferoxamine chelation is reserved for patients who do not withstand phlebotomy (due to cardiomyopathy, severe anemia, or hypoproteinemia) or may be used concurrently with phlebotomy in some patients. Periodically assess hematologic and iron indexes. Continue with weekly iron removal therapy until patient reaches mild iron-deficiency anemia, then decrease frequency and continue phlebotomy as needed (e.g., 4 times per year).

**Laboratory tests and physical examination:** Assess general physical condition and hepatic, cardiac, endocrine, and general health status.

**Confirm diagnosis:** Liver biopsy ("gold standard") or diagnostic phlebotomy; perhaps MRI.

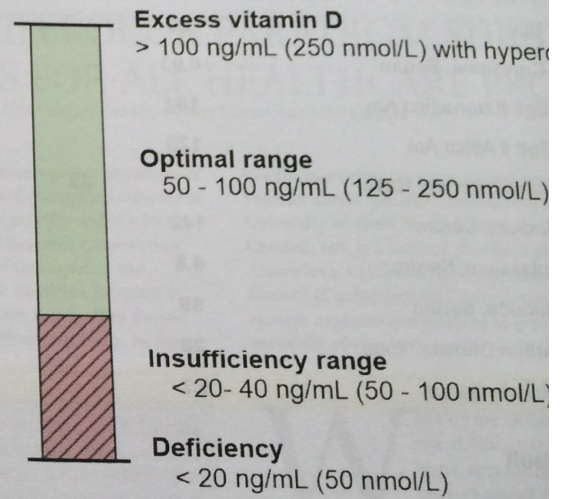
**Assess liver status:** Liver biopsy or perhaps MRI. Cirrhosis indicates increased risk of hepatocellular carcinoma and reduced life expectancy. Consider liver ultrasound, serum liver enzyme measurement, and serum alpha-fetoprotein to screen for hepatocellular carcinoma every 6 months. Hepatoma surveillance is mandatory in cirrhotic patients.

**Implement dietary modifications and nutritional therapies:** Avoid iron supplements, multivitamin supplements with iron, iron-fortified foods, liver, beef, pork, alcohol, and excess vitamin C. Ensure adequate protein intake to replace protein lost during phlebotomy. Diet modifications include antioxidant therapy.

**25(OH)D: serum 25(OH) vitamin D**

Overview and interpretation:

- Vitamin D deficiency is a common cause of musculoskeletal pain<sup>170,171</sup>. Deficiency is a significant risk factor for cancer, autoimmunity, diabetes, chronic pain and physical disability.<sup>173,174,175</sup>
- Measurement of serum 25(OH) vitamin D (or empiric treatment with vitamin D3 per day for adults) is indicated in patients with chronic musculoskeletal pain, particularly low-back pain.<sup>176</sup> Optimal vitamin D status correlates with levels of 50 - 100 ng/mL (125 - 250 nmol/L)—see our review article for details. Levels greater than 100 ng/mL are unnecessary and increase the risk of



**Interpretation of serum 25(OH) vitamin D levels.** Modified from *Alternative Therapies in Health and Medicine* 2004 and *Vitamin D and Pain: Expanded Clinical Strategies* 2008.

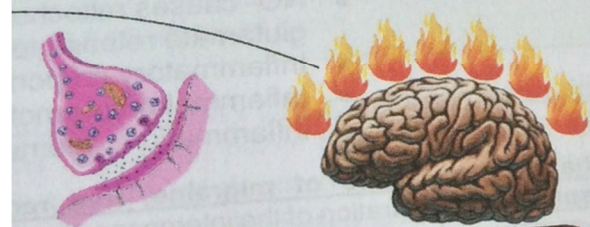
<b>Advantages:</b>	<ul style="list-style-type: none"> <li>Accurate assessment of vitamin D status.</li> </ul>
<b>Limitations:</b>	<ul style="list-style-type: none"> <li>Patients with certain granulomatous conditions such as sarcoidosis and patients taking certain drugs such as thiazide diuretics (hypertension) may develop hypercalcemia due to "vitamin D hypersensitivity" or "vitamin D toxicity" and patients require frequent monitoring of serum calcium while taking these supplements.</li> </ul>
<b>Comments:</b>	<ul style="list-style-type: none"> <li><b>Routine measurement and/or empiric treatment with vitamin D should be a routine component of patient care.</b><sup>178</sup></li> <li>Periodic assessment of 25(OH)D and serum calcium are required to ensure efficacy and safety of treatment, respectively.</li> <li>I'm increasingly convinced of the merit of measuring 1,25-dihydroxyvitamin D for the initial assessment of patients with inflammatory/autoimmune disease.</li> </ul>



and psychiatric disorders, such as pain and depression. The neurons themselves can also become inflamed because the inflammation is in the nerve cells. When **brain inflammation** becomes a self-reinforcing cycle, sometimes with severe consequences; for example, 1) inflamed neurons activate endothelial cells (thereby causing activation of mast cells and platelets causes release of proinflammatory metabolites (such as prostaglandins, leukotrienes, and other inflammatory mediators) and also promote neuronal inflammation and metabolic impairment seen in mitochondrial dysfunction which causes leakiness of the blood-brain barrier and release of inflammatory molecules from the blood.<sup>5</sup>

Excess glutamate triggers increased and constant stimulation of neurons, promoting constant discharge and "rewiring the brain" to become more sensitive to pain

Hyperexcitation (pain, depression, fatigue, migraine, seizure) and neurodegeneration



Excess glutamate triggers increased and constant stimulation of neurons, promoting constant discharge and "rewiring the brain" to become more sensitive to pain

Hyperexcitation (pain, depression, fatigue, migraine, seizure) and neurodegeneration

able to normal activity... and stressors... emotional stress... neurons, leading to neuron death: neurodegeneration.

ntly show evidence of mitochondrial impairment: 1) defects in CoQ10 synthesis, 2) defects in (ETC). The majority of these problems can be dysfunction promotes inflammation in microglia: mitochondrial dysfunction promote microglial activation.

al mitochondria promote microglial activation. Complex #4 in the electron...

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amplify, and exacerbate neuroinflammation caused by increased neuroactivity—the microglial cells; thus, neurogenic (in this context, including the microglia and astrocytes as components of the brain and spinal cord) neuroinflammation would be expected to participate in seizure disorders and vaccine-induced encephalomyelitis.

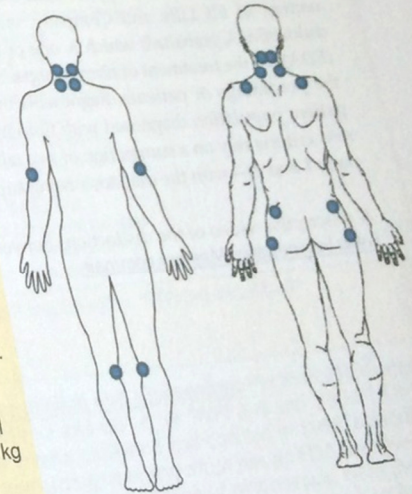
4. **Image lower right—The nervous system (represented by artistic brain image) is now appreciated as dynamic and interactive receiver and processor of sensory information;** in modern times, pain processing is appreciated as a dynamic, complex, and interactive process at every level, from 1) peripheral reception of stimuli (e.g., in the skin or muscles), to the 2) spinal cord, to the 3) brainstem, to the 4) subcortical structures especially the thalamus, to the 5) cortex. Generally appreciated is that much "spill-over", "misinterpretation", inhibition and amplification" can occur in the spinal cord, brainstem, and cortex. Generally, the brain is constantly adapting to input; for the neuron-neuron interconnections to increase pain processing—what facilitates the perception of pain, leading to enhanced pain perception, e.g.,

**Diagnosis**

- **Clinical criteria—description and contrast of the 1990 criteria and the 2010 criteria:** Per guidelines published in 1990 by the American College of Rheumatology (ACR), a diagnosis of fibromyalgia can be made in a patient with inexplicable, widespread myofascial pain of at least 3 months' duration; *inexplicable* denotes normalcy of routine laboratory and physical examination findings and failure to find an alternate explanation or diagnosis, while *widespread* denotes bilateral pain above and below the waist not attributable to trauma or rheumatic disease and with pain at 11 of 18 classic tender point locations (see illustration below).

**Illustration of the 9 paired locations of FM tender points:**

- Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites:
1. **Occiput:** at the suboccipital muscle insertions.
  2. **Low cervical:** at the anterior aspects of the intertransverse spaces at C5-C7.
  3. **Trapezius:** at the midpoint of the upper border.
  4. **Supraspinatus:** at origins, above the scapula spine near the medial border.
  5. **Second rib:** upper lateral to the second costochondral junction.
  6. **Lateral epicondyle:** 2 cm distal to the epicondyles.
  7. **Gluteal:** in upper outer quadrants of buttocks in anterior fold of muscle.
  8. **Greater trochanter:** posterior to the trochanteric prominence.
  9. **Knee:** at the medial fat pad proximal to the joint line.
- Per 1990 ACR guidelines, the diagnosis of FM is supported when at least 11 out of 18 of these locations are painful. Digital palpation should be performed with an approximate force of 4 kg (9 lbs). A tender point has to be painful at palpation, not just "tender."<sup>259</sup>



FM tender points are assessed bilaterally at 9 paired sites: (sub)occiput (below the head at the neckline), cervical spine (lower neck), trapezius and supraspinatus (two of the shoulder muscles), second rib (near costosternal [rib-breastbone] junction), lateral epicondyle, gluteal region, greater trochanter, and fat pad of the knees. Tender points are provoked by the clinician's application of approximately 9 kg of fingertip pressure, which is sufficient to cause blanching of the clinician's nail bed. The tender points in fibromyalgia are distinguished from myofascial trigger points (MFTP, described by Travell<sup>260</sup>) and counterstrain tender points (described in the osteopathic literature by Jones<sup>261</sup>). Pain must have been

1990 Criteria for the Classification of Fibromyalgia. [nra.net/Diagnost.htm](http://nra.net/Diagnost.htm) Accessed Nov 2011

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**Functional Inflammolgy (.com): Definition and Scope:** An evidence-based clinical approach to the prevention, management, comanagement, and cure of the majority of so-called “chronic diseases” that are increasingly in epidemic proportions worldwide; examples include diabetes, hypertension, obesity, migraine, neurodegeneration, fibromyalgia, and disorders of allergic and autoimmune inflammation. **Safety, Efficacy, Ethics:** Remarkable safety and efficacy; allows clinicians to meet all criteria of medical ethics: ① beneficence, ② non-maleficence, ③ autonomy, ④ informed consent, ⑤ distributive justice. **Refutations/Affirmations:** The “chronic disease model” is refuted and replaced by the view that **most so-called “chronic inflammatory diseases”** are simply **“sustained inflammatory responses”** to factors which can be clinically corrected; these seven primary factors are effectively addressed by the Functional Inflammolgy Clinical Protocol.

**Inflammation Mastery 4th Edition** combines the recently updated **Functional Inflammolgy** and Dr Vasquez’s previous **Integrative Rheumatology** into a new colorized updated textbook of almost 1,200 pages. This work is the culmination of several thousand research publications combined with Dr Vasquez’s many years of clinical experience and teaching graduate-level students and doctorate-level clinicians worldwide. With radiographs, photos, acronyms, illustrations, flowcharts, and detailed-yet-simplifying explanations, Dr Vasquez makes it easier than ever for clinicians to grasp important concepts in integrative care and functional medicine and then to translate the basic science research and molecular biology into treatment plans that can be explained and used in “the real world” of clinical practice with patients. The associated video tutorials and recorded live conference presentations further help students and clinicians “get it” via Dr Vasquez’s effective teaching style which embraces complexity while always emphasizing clinical applicability and psychosocial context. The **Inflammation Mastery & Functional Inflammolgy series of books and videos** translates important concepts and nutritional/biomedical science into easy and practical clinical applications for the prevention and treatment of disorders of sustained inflammation, which Dr Vasquez describes as “patterns of metabolic disturbance and inflammatory dysfunction” existing in three sequential and overlapping categories: 1) metabolic inflammation, 2) allergic inflammation, 3) autoimmune inflammation. This book includes access to video presentations which introduce the origin and components of the Functional Inflammolgy Protocol and **FINDSEX®** acronym. Post-publication updates to this information and important social and clinical contextualization are made available in videos and online repositories (access provided in the book), and the e-newsletter available from **InflammationMastery** and **FunctionalInflammolgy.com**. This textbook also provides access, via reprints or hyperlinks, to Dr Vasquez’s published articles—an example of which is his recent paradigm-shifting editorial published in the journal *Alternative Therapies in Health and Medicine* (2014 January). The updated section on pain management allows students and clinicians to understand and apply manual, pharmacologic, nutritional and botanical medicine treatments for musculoskeletal pain, thereby providing better relief for patients and avoiding the hazards of NSAIDs, coxibs, steroids, opioids, immunosuppressants and biologics.

**About the author—Dr Alex Vasquez:** Dr Alex Vasquez holds three doctoral degrees as a graduate of University of Western States (Doctor of Chiropractic, 1996), Bastyr University (Doctor of Naturopathic Medicine, 1999), and University of North Texas Health Science Center, Texas College of Osteopathic Medicine (Doctor of Osteopathic Medicine, 2010). Dr Vasquez is the author of many textbooks, including **Integrative Orthopedics** (2004/2012), **Integrative Rheumatology** (2006/2014), **Musculoskeletal Pain: Expanded Clinical Strategies** (published by the Institute for Functional Medicine, 2008), **Chiropractic and Naturopathic Mastery of Common Clinical Disorders** (2009), **Integrative Medicine and Functional Medicine for Chronic Hypertension** (2011), **Fibromyalgia in a Nutshell** (2012), **Migraine Headaches, Hypothyroidism, and Fibromyalgia** (2012), **Mitochondrial Nutrition and Mitochondrial Medicine for Primary Care Conditions** (2014), and **Dysbiosis in Human Disease** (2014), which is also an excerpt from **Functional Inflammolgy: Volume 1**. “DrV” has also written more than 110 letters and articles for professional magazines and medical journals such as *British Medical Journal (BMJ)*, *TheLancet.com*, *Annals of Pharmacotherapy*, *Journal of Clinical Endocrinology and Metabolism*, *Journal of the American Medical Association (JAMA)*, *Alternative Therapies in Health and Medicine*, *Journal of the American Osteopathic Association (JAOA)*, *Nutritional Perspectives*, *Journal of Manipulative and Physiological Therapeutics (JMPT)*, *Current Allergy and Asthma Reports*, *Integrative Medicine*, and *Arthritis & Rheumatism*, the Official Journal of the American College of Rheumatology. Dr Vasquez has lectured worldwide to healthcare professionals and provides expert consultations to physicians and patients internationally. All of DrV’s books are available on [Amazon.com](http://Amazon.com) with videos at [Vimeo.com/DrVasquez](http://Vimeo.com/DrVasquez) and audio recordings of lectures at iTunes.



Official Journal of the American College of Rheumatology. Dr Vasquez has lectured worldwide to healthcare professionals and provides expert consultations to physicians and patients internationally. All of DrV’s books are available on [Amazon.com](http://Amazon.com) with videos at [Vimeo.com/DrVasquez](http://Vimeo.com/DrVasquez) and audio recordings of lectures at iTunes.

**About the International College of Human Nutrition and Functional Medicine (ICHNFM):** International College of Human Nutrition and Functional Medicine was founded by a group of internationally-located world-class experts to provide higher-level training in nutrition and functional medicine to students and clinicians worldwide in Spanish, English, Portuguese, Catalan, and other languages. Originally founded in North America (Portland Oregon USA) and launched with the tremendously successful 2013 International Conference on Human Nutrition and Functional Medicine (described at [ICHNFM.ORG](http://ICHNFM.ORG) with select videos available at [Vimeo.com/ICHNFM](http://Vimeo.com/ICHNFM)), the organization is also now established in Europe (Spain) with several important publications also generated from in South America (Colombia). Dr Vasquez and his colleagues at ICHNFM provide educational courses, videos, written materials, and mentoring for students and clinicians to promote the expert-level application of clinical nutrition and functional medicine. Via forums and live interactive online classes, professors and students are able to interact, network, and share important insights, clinical experiences and case reports, effective doses of nutrients and prescription medicines, additional citations to research, important clinical pearls, and expanded discussions on various topics as the research and clinical practice of human nutrition and functional medicine continuously advance. International College of Human Nutrition and Functional Medicine®, *International Journal of Human Nutrition and Functional Medicine*® ([IntJHumNutrFunctMed.ORG](http://IntJHumNutrFunctMed.ORG)), and International Conference on Human Nutrition and Functional Medicine® are all registered trademarks™ legally held and internationally protected by the International College of Human Nutrition and Functional Medicine.

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- ◆ **Preface and Preamble:** Introduction, scope, perspectives, video access notice
- ◆ **Chapter 1: Concepts and Approach to Patient Assessment and Clinical Interpretation of Laboratory Tests:** Also includes sections on risk management, musculoskeletal emergencies, hemochromatosis and hypothyroidism
- ◆ **Chapter 2: ReEstablishing the Foundation for Health:** Evidence-based wellness promotion and lifestyle-based health optimization
- ◆ **Chapter 3: Basics of (Nondrug) Integrative Pain Management and Musculoskeletal Care:** Useful data, tools, and acronyms reviewing botanical medicines, ergonomics, nutritional supplementation, diet, neuromuscular stabilization, trigger point treatment, manual medicine; includes a complete clinical review of nutritional and manipulative treatments for carpal tunnel syndrome
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  - ◆ Fibromyalgia
  - ◆ Allergic Inflammation
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  - ◆ Psoriasis and Psoriatic Arthritis
  - ◆ Systemic Lupus Erythematosus
  - ◆ Scleroderma & Systemic Sclerosis
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  - ◆ Spondyloarthropathies & Reactive Arthritis
  - ◆ Sjögren Syndrome/Disease
  - ◆ Raynaud’s Syndrome/Phenomenon/Disorder
  - ◆ Clinical Notes on Additional Conditions: Behçet’s Disease, Sarcoidosis, Dermatomyositis and Polymyositis
- ◆ **Index and Appendix**

Family Medicine  
 Functional Medicine  
 Integrative Medicine  
 Internal Medicine  
 Pain Management  
 Preventive Medicine  
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This textbook is distributed via the International College of Human Nutrition and Functional Medicine based in Spain and United States: [NutritionAndFunctionalMedicine.org](http://NutritionAndFunctionalMedicine.org) and [ICHNFM.ORG](http://ICHNFM.ORG)

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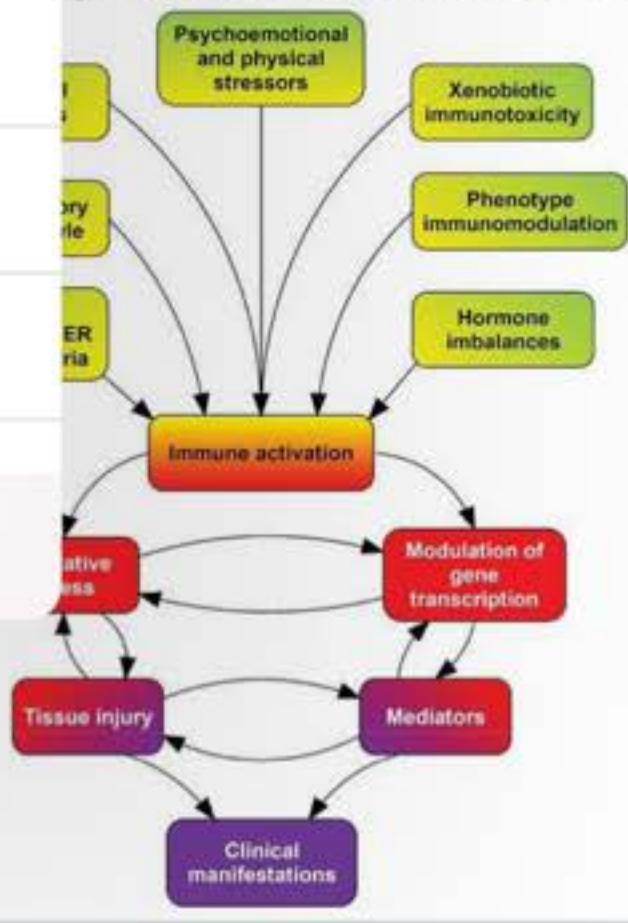


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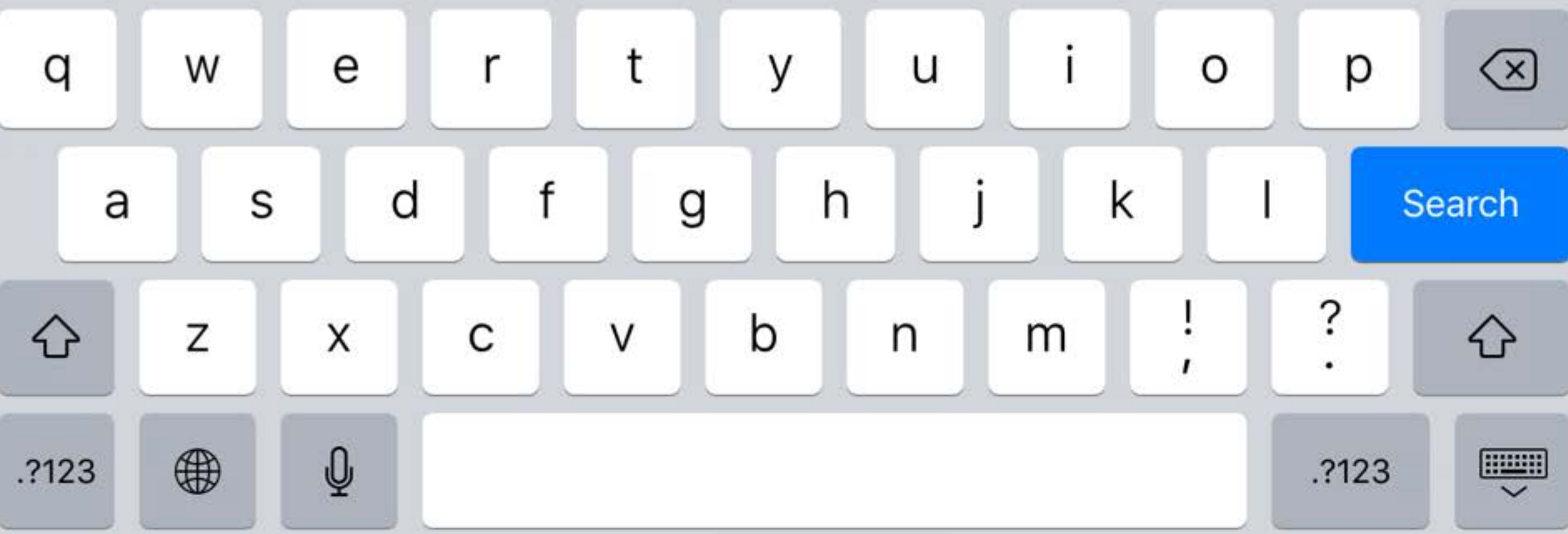
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## Chapter and Introduction

### Preamble

#### Volume 1

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

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#### Volume 2: Chapter 5—Clinical Applications of the Functional Inflammation Protocol



[1\) Hypertension](#)

[2\) Diabetes Mellitus](#)

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