

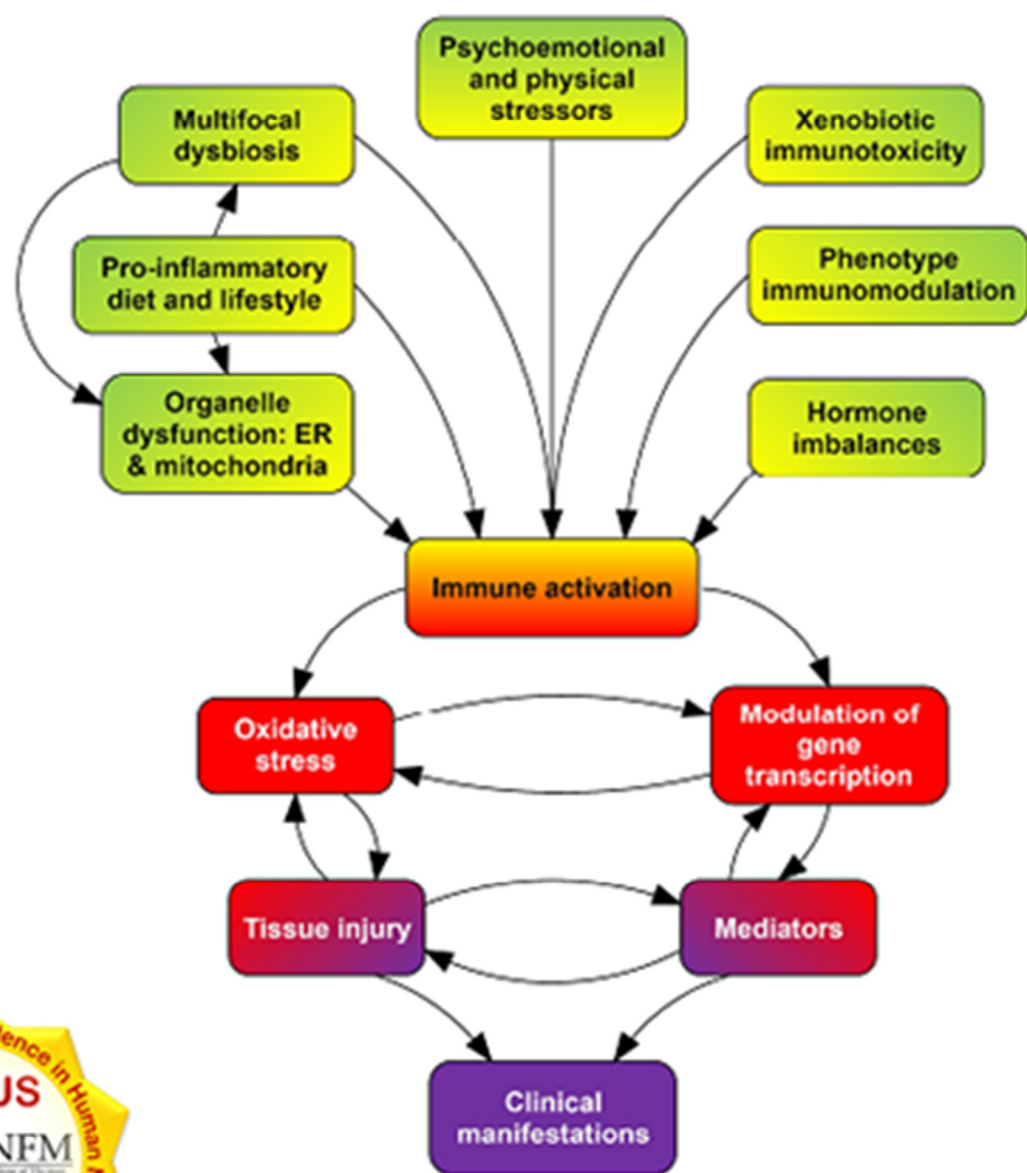
# INFLAMMATION MASTERY

## 4TH EDITION

CLINICAL NUTRITION, MITOCHONDRIAL DYSFUNCTION, MICROBIOME & DYSBIOSIS, FUNCTIONAL INFLAMMOLOGY, PAIN MANAGEMENT, INTEGRATIVE RHEUMATOLOGY, NUTRITIONAL IMMUNOMODULATION, IMMUNONUTRITION & ANTIVIRAL STRATEGIES

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

3-Part Learning System of Text, Illustrations, and Video



**DR. ALEX VASQUEZ**  
**ICHNFM.ORG**

INTERNATIONAL COLLEGE OF HUMAN NUTRITION AND FUNCTIONAL MEDICINE

# INFLAMMATION MASTERY

**4<sup>TH</sup> EDITION: THE COLORFUL AND DEFINITIVE GUIDE  
TOWARD HEALTH AND VITALITY AND AWAY FROM THE  
BOREDOM, RISKS, COSTS, AND INEFFICACY OF ENDLESS  
ANALGESIA, IMMUNOSUPPRESSION, AND POLYPHARMACY**

**A Three-Part Learning System of Text, Images, and Video**

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**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:

- "Alex is the master of painful conditions and metabolic treatments." *Public comment by an award-winning neurosurgeon and functional medicine practitioner, 2016*
- "I love this course and your approach to the material. I am learning so much. Each article you assigned was strategically chosen and offered support and insight. I was pleasantly surprised by the exam and thought it was very fair. ... Thank you for sharing your knowledge and experience with us!" *Doctorate Student under Dr Vasquez, 2016*
- "I appreciate the lecture yesterday and I am truly fascinated by your topic and your vast knowledge. ... I for one feel having people like you on our faculty can only strengthen the credibility of our school. ... I appreciate your education, knowledge and clearly you are the authority in your field. I have listened to all your lectures on YouTube - fantastic!" *University Faculty and Doctorate Student under Dr Vasquez, 2016*
- "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 Inflammalogy, 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*

notorious for inhibiting mineral absorption. Some supplements, like coenzyme Q10, should be administered with fatty food to enhance absorption. Other supplements, like amino acids, should be administered away from protein-rich foods and are often better administered with simple carbohydrate to enhance cellular uptake; this is especially true with tryptophan.

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

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

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

This article was originally published in the January 2011 issue of *Nutritional Perspectives*

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

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

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

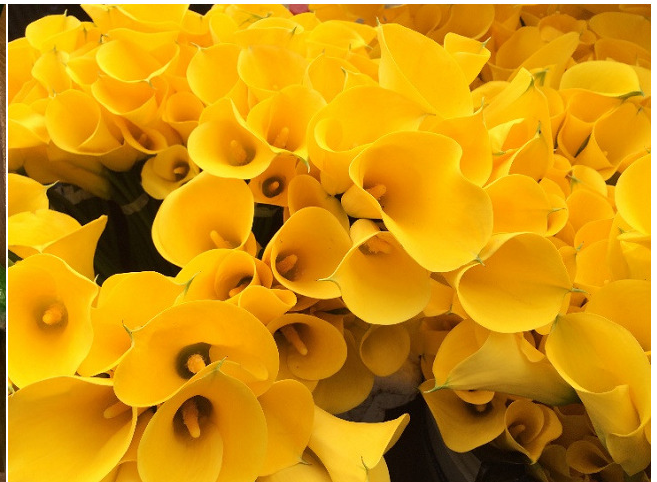
Of course, most diseases are multifactorial and therefore require multicomponent treatment plans, and some diseases actually require the use of drugs in conjunction with assertive interventional nutrition. However, while only a smaller portion of patients actually need drugs for the long-term management their problems, all clinicians should agree that everyone needs a foundational nutrition plan because nutrients—not drugs—are universally required for life and health. This five-part nutrition protocol is briefly outlined below; a much more

<sup>105</sup> Vasquez A. *Integrative Orthopedics: The Art of Creating Wellness While Managing Acute and Chronic Musculoskeletal Disorders*. 2004, 2007, 2012

<sup>106</sup> Vasquez A. Five-Part Nutritional Protocol that Produces Consistently Positive Results. *NutrWellness* 2005 Sep nutritionalwellness.com/archives/2005/sep/09\_vasquez.php

<sup>107</sup> Vasquez A. Common Oversights and Shortcomings in the Study and Implementation of Nutritional Supplementation. *Naturopathy Digest* 2007 June.

<sup>108</sup> Vasquez A. *Integrative Rheumatology*. IBMRC: 2006, 2009.



**Living color, more vitality:** The "colorization" process for the interior of this book began in April 2014 in Bogota (above) and Cartagena Colombia (below).



detailed substantiation of the underlying science and clinical application of this protocol was recently published in a review of more than 650 pages and approximately 3,500 citations.<sup>109</sup>

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

2. **Multivitamin and multimineral supplementation:** Vitamin and mineral supplementation has been advocated for decades by the chiropractic/naturopathic professions while being scorned by so-called "mainstream

<sup>109</sup> Vasquez A. *Chiropractic and Naturopathic Mastery of Common Clinical Disorders*. IBMRC: 2009

<sup>110</sup> Cordain L. *The Paleo Diet*. John Wiley and Sons, 2002

<sup>111</sup> O'Keefe JH Jr, Cordain L. Cardiovascular disease resulting from a diet and lifestyle at odds with our Paleolithic genome. *Mayo Clin Proc*. 2004 Jan;79(1):101-8

<sup>112</sup> Cordain L. Cereal grains: humanity's double edged sword. *World Rev Nutr Diet* 1999;84:19-73

<sup>113</sup> Cordain L, et al. Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr*. 2005 Feb;81(2):341-54

<sup>114</sup> "A high micronutrient density diet mitigates the unpleasant aspects of the experience of hunger even though it is lower in calories. Hunger is one of the major impediments to successful weight loss. Our findings suggest that it is not simply the caloric content, but more importantly, the micronutrient density of a diet that influences the experience of hunger. It appears that a high nutrient density diet, after an initial phase of adjustment during which a person experiences "toxic hunger" due to withdrawal from pro-inflammatory foods, can result in a sustainable eating pattern that leads to weight loss and improved health." Fuhrman J, Sarter B, Glaser D, Acocella S. Changing perceptions of hunger on a high nutrient density diet. *Nutr J*. 2010 Nov 7;9:51 nutritionj.com/content/9/1/51

<sup>115</sup> "The Paleolithic group were as satiated as the Mediterranean group but consumed less energy per day (5.8 MJ/day vs. 7.6 MJ/day, Paleolithic vs. Mediterranean, p=0.04). Consequently, the quotients of mean change in satiety during meal and mean consumed energy from food and drink were higher in the Paleolithic group (p=0.03). Also, there was a strong trend for greater Satiety Quotient for energy in the Paleolithic group (p=0.057). Leptin decreased by 31% in the Paleolithic group and by 18% in the Mediterranean group with a trend for greater relative decrease of leptin in the Paleolithic group." Jonsson T, Granfeldt Y, Erlanson-Albertsson C, Ahren B, Lindeberg S. A Paleolithic diet is more satiating per calorie than a Mediterranean-like diet in individuals with ischemic heart disease. *Nutr Metab (Lond)*. 2010 Nov 30;7(1):85.

<sup>116</sup> Liu RH. Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *Am J Clin Nutr* 2003;78(3 Suppl):517S-520S

<sup>117</sup> "With daily per capita consumption of HFCS in the US averaging about 50 grams and daily mercury intakes from HFCS ranging up to 28 µg, this potential source of mercury may exceed other major sources of mercury especially in high-end consumers of beverages sweetened with HFCS." Dufault R, et al. Mercury from chlor-alkali plants: measured concentrations in food product sugar. *Environ Health*. 2009 Jan 26;8:2 ehjournal.net/content/8/1/2

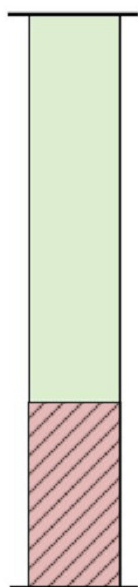
<sup>118</sup> Vasquez A. *Integrative Medicine and Functional Medicine for Chronic Hypertension: An Evidence-based Patient-Centered Monograph for Advanced Clinicians*. IBMRC; 2011. See also: Reungjui S, et al. Thiazide diuretics exacerbate fructose-induced metabolic syndrome. *J Am Soc Nephrol*. 2007 Oct;18(10):2724-31



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

### 3. Physiologic doses of vitamin D3:

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



#### **Excess vitamin D**

> 100 ng/mL (250 nmol/L) with hypercalcemia

#### **Optimal range**

50 - 100 ng/mL (125 - 250 nmol/L)

#### **Insufficiency range**

< 20- 40 ng/mL (50 - 100 nmol/L)

#### **Deficiency**

< 20 ng/mL (50 nmol/L)

#### **Image right: Interpretation of serum 25(OH) vitamin D levels:**

Updated from Vasquez et al, *Alternative Therapies in Health and Medicine* 2004 Sep

<sup>119</sup> Fletcher RH, Fairfield KM. Vitamins for chronic disease prevention in adults: clinical applications. *JAMA* 2002;287:3127-9

<sup>120</sup> Heaney RP. Long-latency deficiency disease: insights from calcium and vitamin D. *Am J Clin Nutr* 2003;78:912-9

<sup>121</sup> McKay et al. The effects of a multivitamin/mineral supplement on micronutrient status, antioxidant capacity and cytokine production in healthy older adults consuming a fortified diet. *J Am Coll Nutr* 2000;19(5):613-21

<sup>122</sup> Benton D, Haller J, Fordy J. Vitamin supplementation for 1 year improves mood. *Neuropsychobiology* 1995;32(2):98-105

<sup>123</sup> Coppen A, Bailey J. Enhancement of the antidepressant action of fluoxetine by folic acid: a randomised, placebo controlled trial. *J Affect Disord* 2000;60:121-30

<sup>124</sup> Wagner W, Nootbaar-Wagner U. Prophylactic treatment of migraine with gamma-linolenic and alpha-linolenic acids. *Cephalalgia* 1997;17:127-30

<sup>125</sup> Langkamp-Henken et al. Nutritional formula enhanced immune function and reduced days of symptoms upper respiratory tract infection in seniors. *J Am Geriatr Soc* 2004;3-12

<sup>126</sup> Barringer TA, et al. Effect of a multivitamin and mineral supplement on infection and quality of life. *Am Intern Med* 2003;138:365-71

<sup>127</sup> Fawzi WW, Msamanga GI, et al. A randomized trial of multivitamin supplements and HIV disease progression and mortality. *N Engl J Med* 2004;351:23-32

<sup>128</sup> Burbano X, et al. Impact of a selenium chemoprevention clinical trial on hospital admissions of HIV-infected participants. *HIV Clin Trials* 2002;3:483-91

<sup>129</sup> Abraham GE. Nutritional factors in the etiology of the premenstrual tension syndromes. *J Reprod Med* 1983;28(7):446-64

<sup>130</sup> Stewart A. Clinical and biochemical effects of nutritional supplementation on the premenstrual syndrome. *J Reprod Med* 1987;32:435-41

<sup>131</sup> Kaplan BJ, et al. Effective mood stabilization with a chelated mineral supplement: an open-label trial in bipolar disorder. *J Clin Psychiatry* 2001;62:936-44

<sup>132</sup> Kaplan et al. Treatment of mood lability and explosive rage with minerals and vitamins: two case studies in children. *J Child Adolesc Psychopharmacol* 2002;12(3):205-19

<sup>133</sup> Gesch et al. Influence of supplementary vitamins, minerals and essential fatty acids on the antisocial behaviour of young adult prisoners. *Br J Psychiatry* 2002;181:22-8

<sup>134</sup> Benton D. Micro-nutrient supplementation and the intelligence of children. *Neurosci Biobehav Rev* 2001;25:297-309

<sup>135</sup> Church TS, Earnest CP, Wood KA, Kampert JB. Reduction of C-reactive protein levels through use of a multivitamin. *Am J Med* 2003;115:702-7

<sup>136</sup> Vasquez A, Manso G, Cannell J. The clinical importance of vitamin D (cholecalciferol). *Alternative Therapies in Health and Medicine* 2004;10:28-37

Proof of the cause-and-effect relationship between vitamin D deficiency and chronic musculoskeletal pain comes from clinical trials among deficient patients showing that vitamin D monotherapy alleviates pain. The exemplary study by Al Faraj and Al Mutairi<sup>35</sup> showed that among patients with “idiopathic chronic low back pain,” 83% (n = 299) were vitamin D deficient, and supplementation with 5000 to 10 000 IU/d of cholecalciferol for 3 months alleviated or cured the low back pain in more than 95% of patients. The authors concluded that, in the evaluation of chronic musculoskeletal pain among populations with a sufficiently high prevalence of vitamin D deficiency, “Screening for vitamin D deficiency and treatment with supplements should be mandatory in this setting.”

Vitamin D has a wide range of safety according to an extensive review of the literature performed by Vieth.<sup>228</sup> Doses of 2000 IU/d of vitamin D<sub>3</sub> have been given to children starting at 1 year of age and were not associated with toxicity but led to a reduction in the incidence of type 1 diabetes by 80%, consistent with the vitamin’s anti-infective and immunomodulatory roles.<sup>229</sup> A 2004 review<sup>36</sup> on the clinical importance of vitamin D proposed that optimal vitamin D status is defined as 40 ng/mL to 65 ng/mL (100–160 nmol/L) and that “until proven otherwise, the balance of the research indicates that oral supplementation in the range of 1000 IU per day for infants, 2000 IU per day for children and 4000 IU per day for adults is safe and reasonable to meet physiological requirements, to promote optimal health, and to reduce the risk of several serious diseases. Safety and effectiveness of supplementation are assured by periodic monitoring of serum 25(OH)D and serum calcium.” Current data and laboratory reference ranges support a higher top limit for serum 25(OH)D of approximately 100 ng/mL (250 nmol/L). Vitamin D hypersensitivity is seen with primary hyperparathyroidism, granulomatous diseases (such as sarcoidosis, Crohn’s disease, and tuberculosis), adrenal insufficiency, hyperthyroidism, hypothyroidism, and various forms of cancer, as well as adverse drug effects, particularly with thiazide diuretics. Thiazide diuretics are known to potentiate hypercalcemia.

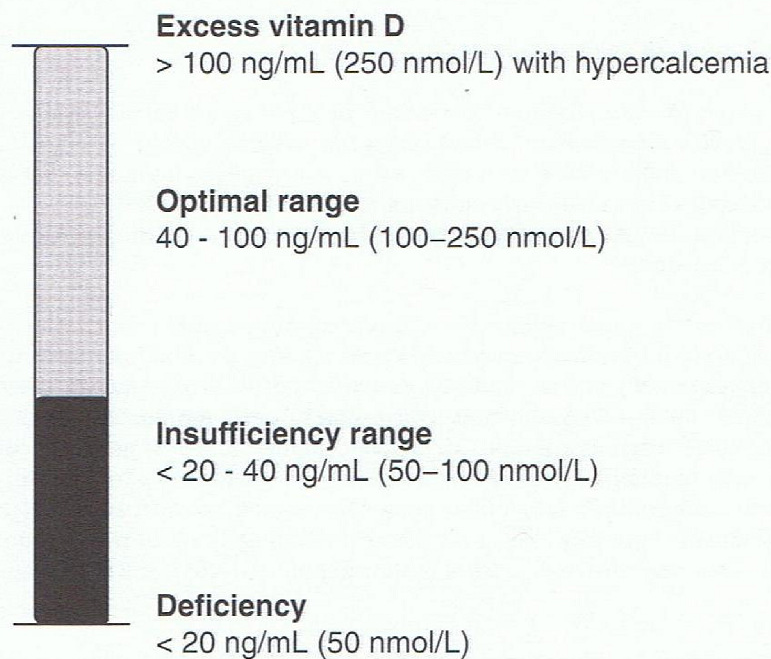


Figure 2.1—Interpretation of Serum 25(OH)D Levels

Adapted from Vasquez A, Manso G, Cannell J. *Altern Ther Health Med.* 2004;10:28-37.36

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

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

<sup>137</sup> Vasquez A. New Insights into Fatty Acid Biochemistry and the Influence of Diet. *Nutritional Perspectives* 2004; October: 5, 7-10, 12, 14

<sup>138</sup> Cleland LG, Gibson RA, Neumann M, French JK. The effect of dietary fish oil supplement upon the content of dihomo-gammalinolenic acid in human plasma phospholipids. *Prostaglandins Leukot Essent Fatty Acids* 1990 May;40(1):9-12

<sup>139</sup> Jantti J, Nikkari T, Solakivi T, et al. Evening primrose oil in rheumatoid arthritis: changes in serum lipids and fatty acids. *Ann Rheum Dis* 1989;48(2):124-7

<sup>140</sup> Oh da Y, et al. GPR120 is an omega-3 fatty acid receptor mediating potent anti-inflammatory and insulin-sensitizing effects. *Cell*. 2010 Sep 3;142(5):687-98

associated with complications such as pancytopenia, organ failure, and death<sup>407</sup>, it is not a treatment to be taken lightly nor should inexperienced physicians administer it. Colchicine can be administered orally, but its low therapeutic efficacy in relation to its moderate gastrointestinal toxicity limits its applicability. In a poorly designed study by Schnebel and Simmons<sup>408</sup>, orally administered colchicine was no better yet was more toxic than placebo; this study appears to have been designed specifically to show inefficacy and toxicity of colchicine since the patients were either given *no treatment* alternating with a *gastroirritative toxic dose* of colchicine.



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

<sup>407</sup> "Bone marrow depression has been reported, primarily in cases of acute colchicine intoxication, and intravenous administration of the drug has been associated with severe pancytopenia and death." Levy M, Spino M, Read SE. Colchicine: a state-of-the-art review. *Pharmacotherapy*. 1991;11(3):196-211

<sup>408</sup> Schnebel BE, Simmons JW. The use of oral colchicine for low back pain. A double-blind study. *Spine*. 1988 Mar;13(3):354-7 **Use of colchicine in this study varied from abstinence for 3 days followed by a toxic dose on day 4; therefore patients in the treatment group were subjected to no treatment for 75% of the time, followed by a dose that caused gastrointestinal toxicity—vomiting and diarrhea—the other 25% of the time. At neither phase of the study were patients exposed to a treatment that had any possibility of being effective in relation to the potential toxicity. This study was so poorly designed that its publication brings into question the editorial quality of *Spine* during this era.**

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

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

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

<sup>141</sup> Force M, Sparks WS, Ronzio RA. Inhibition of enteric parasites by emulsified oil of oregano in vivo. *Phytother Res* 2000;14:213-4

<sup>142</sup> Schuster BG. Demonstrating the validity of natural products as anti-infective drugs. *J Altern Complement Med* 2001;7 Suppl 1:S73-82

<sup>143</sup> Vasquez A. Integrative Rheumatology. IBMRC: 2006, 2009.

<sup>144</sup> Tuft L. Iodides in bronchial asthma. *J Allergy Clin Immunol*. 1981 Jun;67(6):497

<sup>145</sup> Falliers CJ, McCann WP, Chai H, Ellis EF, Yazdi N. Controlled study of iodotherapy for childhood asthma. *J Allergy*. 1966 Sep;38(3):183-92

<sup>146</sup> Tripathy S, et al. Rhinofacial zygomycosis successfully treated with oral saturated solution of potassium iodide. *J Eur Acad Dermatol Venereol*. 2007 Jan;21(1):117-9

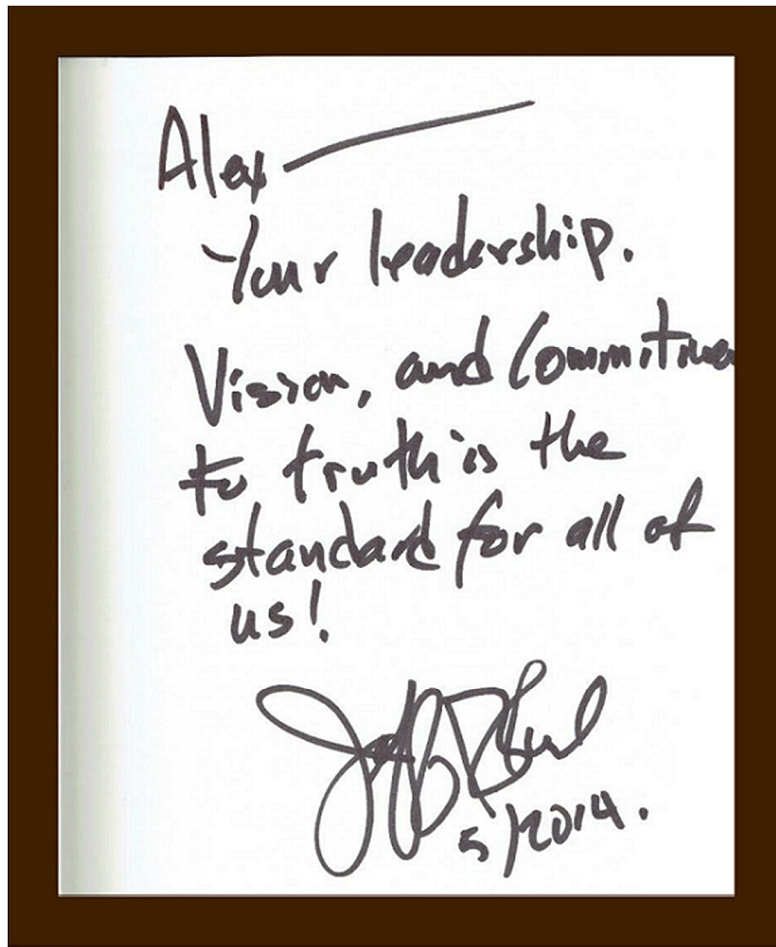
<sup>147</sup> Bonifaz A, et al. Sporotrichosis in childhood: clinical and therapeutic experience in 25 patients. *Pediatr Dermatol*. 2007 Jul-Aug;24(4):369-72

<sup>148</sup> Ghent WR, Eskin BA, Low DA, Hill LP. Iodine replacement in fibrocystic disease of the breast. *Can J Surg*. 1993 Oct;36(5):453-60

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

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

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



**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 publications in journals such as *Annals of Pharmacotherapy* (2005), *Alternative Therapies in Health and Medicine* (2004, 2014), *British Medical Journal* (2005), and *Nature Reviews Rheumatology* (2016). 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, clinical application and—most importantly for me: contextualization—that I could humanly muster while maintaining my own health, relationship, and other obligations. I will remain open to the 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.

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

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

<sup>150</sup> Indraccolo et al. Anaphylactic-like reaction to Lugol solution during colposcopy. *South Med J* 2009 Jan;102(1):96-7

<sup>151</sup> “Quantitative RT-PCR confirmed the array data demonstrating that iodine/iodide treatment increased the mRNA levels of several genes involved in estrogen metabolism (CYP1A1, CYP1B1, and AKR1C1) while decreasing the levels of the estrogen responsive genes TFF1 and WISP2.” Stoddard FR 2nd, et al. Iodine alters gene expression in the MCF7 breast cancer cell line: evidence for an anti-estrogen effect of iodine. *Int J Med Sci.* 2008 Jul 8;5(4):189-96

<sup>152</sup> Bonifaz A, et al. Sporotrichosis in childhood: clinical and therapeutic experience in 25 patients. *Pediatr Dermatol.* 2007 Jul-Aug;24(4):369-72

<sup>153</sup> Said of KI, “The standard dose was 1g, which contains 770 mg of iodine.” Miller DW. Extrathyroidal benefits of iodine. *J Am Physicians Surgeons* 2006;Winter,106-10

<sup>154</sup> Tripathy et al. Rhinofacial zygomycosis successfully treated with oral saturated solution of potassium iodide. *J Eur Acad Dermatol Venereol.* 2007;21:117-9

<sup>155</sup> Ghent et al. Iodine replacement in fibrocystic disease of the breast. *Can J Surg.* 1993 Oct;36(5):453-60

<sup>156</sup> Kessler JH. The effect of supraphysiologic levels of iodine on patients with cyclic mastalgia. *Breast J.* 2004 Jul-Aug;10(4):328-36



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

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

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

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

<b>Distinguishing iodine from iodide</b>	
<b>iodine</b>	<ul style="list-style-type: none"> <li>• <b>Natural</b> elemental form—diatomic.</li> <li>• <b>Nonthyrotropic</b>—no immediate adverse effects on thyroid function.</li> <li>• <b>Nuclear</b>—affects gene expression, for example by promoting estrogen detoxification and reducing estrogen responsiveness.</li> <li>• <b>Nixes microbes</b>, antimicrobial—very broad spectrum; povidone iodine is one of the most widely used topical antimicrobials in the history of microbiology and medicine.</li> </ul>
<b>iodide</b>	<ul style="list-style-type: none"> <li>• <b>Divided</b>—ionic, nondiatomic.</li> <li>• <b>Dietary</b> form, such as in iodized salt which typically contains potassium iodate, potassium iodide, sodium iodate, or sodium iodide.</li> <li>• <b>Dissolves mucus</b>—mucolytic benefits advantageous in the treatment of asthma, bronchitis and respiratory tract infections. Potassium iodide is thought to act as an expectorant by increasing respiratory tract secretions and thereby decreasing the viscosity of mucus; iodide levels increase in respiratory secretions within approximately 15 minutes after oral administration.</li> <li>• <b>Directly thyrotropic</b>—necessary for thyroid hormone production; high doses can cause thyroid dysfunction, which may be problematic (exacerbation of thyroid autoimmunity, hypothyroidism, or hyperthyroidism) or therapeutic (inhibition of thyroid hormone production during hyperthyroidism).</li> <li>• <b>Deals death to microbes</b>, antimicrobial—very broad spectrum, used in the form of potassium iodide (KI, SSKI) for the treatment of microbial infections such as zygomycosis and sporotrichosis.</li> </ul>

should appreciate that, especially regarding "~~chronic~~" (i.e., sustained) health problems, any treatment plan that allows the patient to resume his/her previous lifestyle is by definition doomed to fail because a return to the patient's previous lifestyle and activities that allowed the onset of the disease/disorder in the first place will most certainly result in the perpetuation and recurrence of the illness or disorder. Stated more directly: for healing to truly be effective, the comprehensive treatment plan must generally result in a permanent and profound change in the patient's lifestyle and emotional climate, which are the primary modifiable determinants of either health or disease.

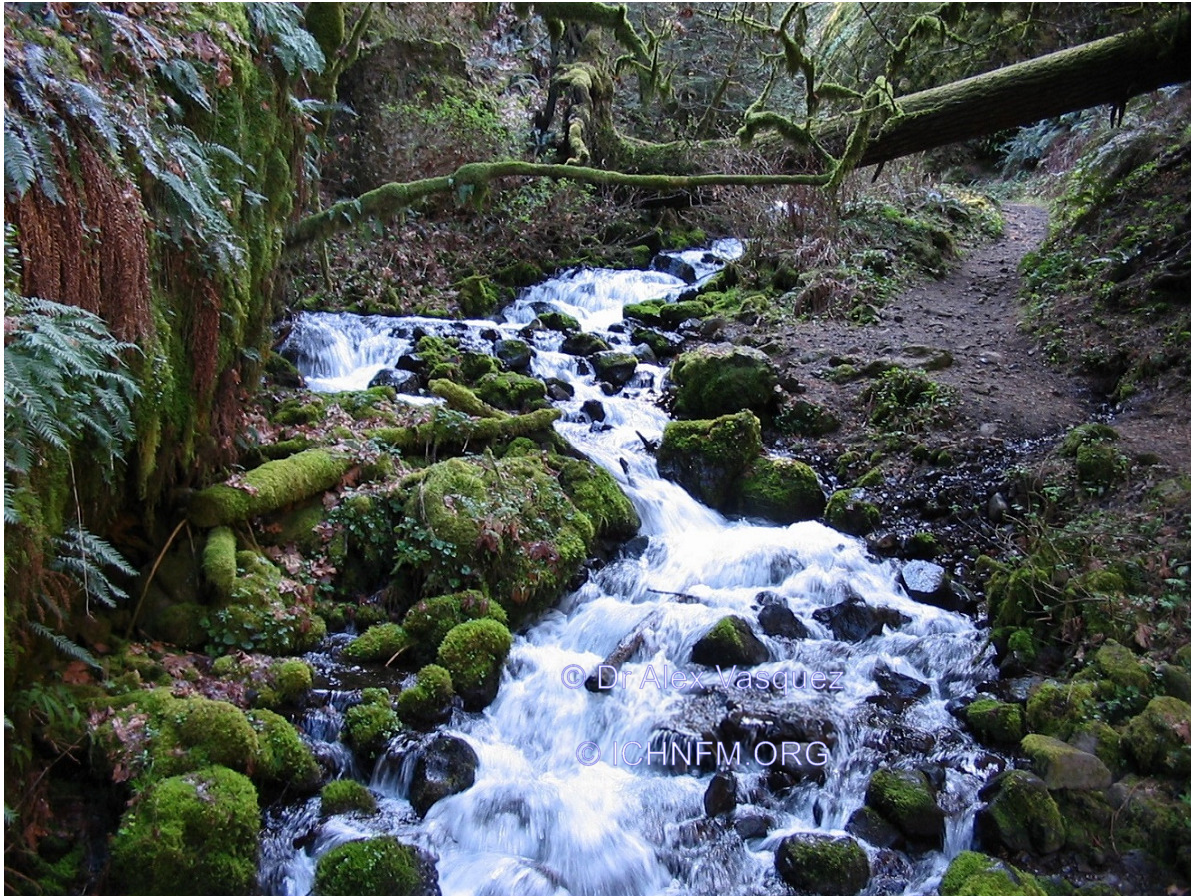


**Barcelona's tradition of honoring intellectuals—Plaça de George Orwell:** George Orwell is best known for his brilliant books *1984* and *Animal Farm* which creatively tell complex tales of herd mentality, politics, and various forms of social control and the manufacture of public consent and conformity. Less well-known is his *Homage to Catalonia*, in which he describes his experience as a volunteer in the Spanish Civil War (during which he was shot in the neck by a sniper) against the fascist regime of Francisco Franco, then supported by Hitler's Nazi Germany and Mussolini's Fascist Italy. His required-reading book *1984* has recently been summarized in a brilliant audio version<sup>66</sup> (and a short free video<sup>67</sup>) to increase its accessibility. In 2014, people protesting government surveillance and unjust imprisonments in Thailand were arrested for reading *1984*.<sup>68</sup>

<sup>66</sup> Moustaki N (Author), Podehl N (Narrator). *1984: CliffsNotes*. Audible. [cliffsnotes.com/literature/n/1984/book-summary](https://cliffsnotes.com/literature/n/1984/book-summary) and [amazon.com/1984-CliffsNotes/dp/B004S8NFZ2/](https://amazon.com/1984-CliffsNotes/dp/B004S8NFZ2/)

<sup>67</sup> Video SparkNotes: Orwell's 1984 Summary. <https://youtube.com/watch?v=pTqIVvUPAjw>

<sup>68</sup> Associated Press. 23 June, 2014. Protesting Thai reader of Orwell's *1984* dragged off by police in Bangkok. "Police in Thailand yesterday arrested eight people for demonstrating against the nation's increasingly repressive military junta, including a man dragged away by undercover officers for reading a copy of George Orwell's *Nineteen Eighty-Four*. The arrest was the first known case of anyone being detained for reading as a form of protest since the military seized power last month. ... A Thai reporter who witnessed the lone man reading Orwell's classic said he was taken away by half a dozen plainclothes police. The reporter said the man held the book up as officers approached. ... Another of the arrests was of a woman wearing a T-shirt with the words "Respect My Vote" on it." *South China Morning Post* [scmp.com/news/asia/article/1538616/protesting-thai-reader-orwells-1984-dragged-police-bangkok](http://scmp.com/news/asia/article/1538616/protesting-thai-reader-orwells-1984-dragged-police-bangkok). See also Campbell C. A Yellow Shirt Leader Says the Thai Coup Was Planned in 2010. *Time* 2014 Jun 23. [time.com/2910484/thai-coup-planned-2010-suthep-thaugsuban/](http://time.com/2910484/thai-coup-planned-2010-suthep-thaugsuban/). "My friends told me when they read *1984* for the first time they could never imagine there would be a country like that, but it's happening now in Thailand," says Pimsiri. "People are really watching you, your computers are being monitored... and many people have been detained in undisclosed locations." *Christian Science Monitor* [csmonitor.com/World/Asia-Pacific/2014/0530/Orwell-s-1984-suddenly-fashionable-on-Bangkok-streets](http://csmonitor.com/World/Asia-Pacific/2014/0530/Orwell-s-1984-suddenly-fashionable-on-Bangkok-streets)



**Columbia River Gorge:** Wahkeena Falls, Oregon *above*, Dog Mountain, Washington *below*.



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

**Progressive awakening**

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

Henry David Thoreau, *Walden*<sup>411</sup>

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

Nathaniel Branden, *Six Pillars of Self-Esteem*<sup>412</sup>

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

Friedrich Nietzsche, *Thus Spoke Zarathustra*<sup>413</sup>

<sup>411</sup> Thoreau HD. (Owen Thomas, Ed). *Walden and Civil Disobedience*. New York; WW Norton and Company: 1966, page 221

<sup>412</sup> Nathaniel Branden *The Six Pillars of Self-Esteem*, p. 67

<sup>413</sup> Nietzsche FW. *Thus Spoke Zarathustra*.

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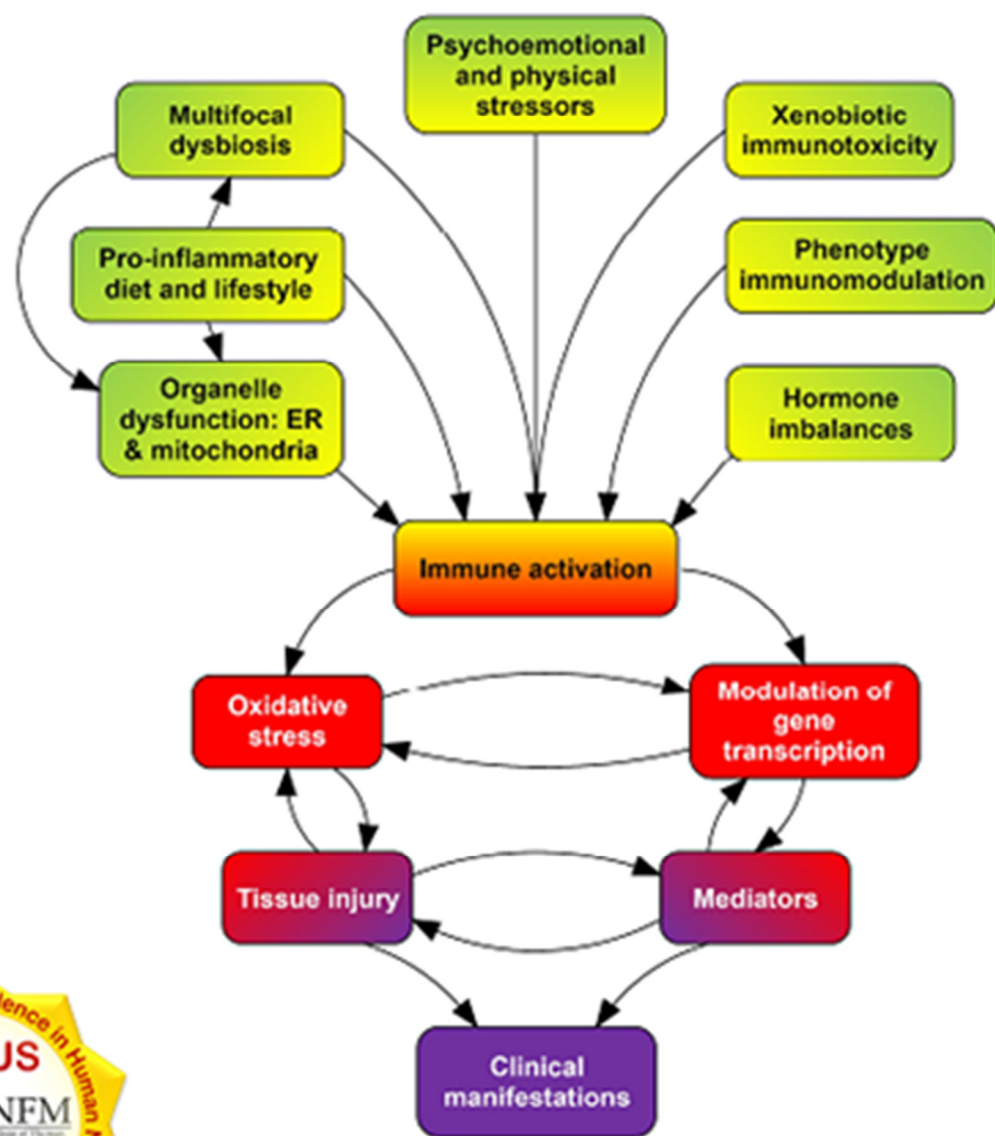
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