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AAPI'S NUTRITION GUIDE TO

OPTIMAL HEALTH:
USING PRINCIPLES OF
FUNCTIONAL MEDICINE AND NUTRITIONAL GENOMICS

PART 2

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PART 2

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Introduction

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Person-Centered Diagnosis: Principles and Practice

Leo Galland, MD, FACP, FACN

The purpose of this chapter is to present an organizational structure for assessment of patients as unique individuals, an approach I have called Person-Centered Diagnosis[1]. The goal of Person-Centered Diagnosis is to enable healers to develop individualized treatment plans that are based upon an understanding of the physiological, environmental and psychosocial contexts within which each person's illnesses or dysfunctions occur. The information you need to effectively apply this organizational structure fills the remainder of this textbook. My goal here is to describe and illustrate the structure. To create it, you must start by eliciting all of the patient's concerns. In actively listening to the patient's story, you attempt to discover the Antecedents, Triggers and Mediators that underlie symptoms, signs, illness behaviors and demonstrable pathology. Functional Medicine is based upon treatment that is collaborative, flexible and focused on the control or reversal of each person's individual Antecedents, Triggers and Mediators, rather than the treatment of disease entities.

ELICITING THE PATIENT'S STORY

The first step in patient-centered care is eliciting the patient's story in a comprehensive manner. It is the Functional Medicine practitioner's job to know not just the ailments or their diagnoses, but the physical and social environment in which sickness occurs, the dietary habits of the person who is sick (present diet and pre-illness diet), his beliefs about the illness, the impact of illness on social and psychological function, factors that aggravate or ameliorate symptoms and factors that predispose to illness or facilitate recovery. This information is necessary for establishing a functional treatment plan.

The importance of understanding the patient's experience of her illness cannot be overemphasized. Extensive research on doctor-patient interactions indicates that doctors who fail to pay attention to the patient's concerns miss important clinical information. The conventional diagnostic paradigm, Differential Diagnosis, leads doctors to ignore or denigrate information that

patients consider important, or that influences individual prognosis [2] [3] [4]. Not only does this ignorance impair the effectiveness of treatment[5], it generates considerable dissatisfaction among patients.[6] [7] [8]

Extensive research done within the context of conventional medical care reveals what most patients know: doctors do not pay enough attention to what their patients have to say. A study done at the University of Rochester found that most patients have three reasons for visiting a physician, are interrupted within eighteen seconds of starting to tell their stories and never get the chance to finish.[9] Although doctors excuse this behavior by citing lack of time, it would have taken an average of one minute and rarely more than three minutes for a complete list of problems to be elicited.

Even when doctors know what their patients' concerns are, they typically ignore them[10]. Most patients have different ideas about their illnesses than their doctors and some form of clarification or negotiation is needed for an effective therapeutic alliance to be established[11]. A study that carefully analyzed taped transcripts of visits to a medical clinic found that patients attempted to clarify or challenge what their doctor had said in 85% of the visits. Their requests were usually ignored or interrupted[12]. Understanding the patient's perspective allows the doctor to work in a collaborative way with patients, giving information that helps the patient make healthful choices[13]. The more information that the patient receives from the doctor and the more actively the patient is involved in making decisions about treatment, the higher the level of mutual satisfaction and the better the clinical outcome[14] [15] [16] [17] [18]. A systematic review of randomized clinical trials and analytic studies of physician-patient communication confirmed a positive influence of quality communication on health outcomes.[19] Such a collaborative relationship depends upon the practitioner recognizing and acknowledging the patient's experience of the illness. Useful questions to ask include:

> How are you hoping that I can help you today? What do you believe is the source of your problems? What kind of treatment are you looking for? What do you most fear about your illness? What impact have your symptoms had on your life?

ORGANIZING AND ANALYZING THE PATIENT'S STORY

What modern science has taught us about the genesis of disease can be represented by three words: Triggers, Mediators and Antecedents. Triggers are discrete entities or events that provoke disease or its symptoms. Microbes are an example. The greatest scientific discovery of the Nineteenth Century was the microbial etiology of the major epidemic diseases. Triggers are usually insufficient in and of themselves for disease formation, however. Host response is an essential component. Identifying the biochemical mediators that underlie host responses was the most productive field of biomedical research during the second half of the Twentieth Century. Mediators, as their name implies, do not "cause" disease. They are intermediaries that contribute to the manifestations of disease. Antecedents are factors that predispose to acute or chronic illness. For a person who is ill, they form the illness diathesis. From the perspective of prevention, they are risk factors. Knowledge of antecedents has provided a rational structure for the organization of preventive medicine and public health. Medical genomics seeks to better understand disease by identifying the phenotypic expression of disease-related genes and their products. The application of genomic science to clinical medicine requires the integration of Antecedents (genes and the factors controlling their expression) with Mediators (the downstream

products of gene activation). Mediators, Triggers and Antecedents are not only key biomedical concepts, they are also important psychosocial concepts. In Person-Centered Diagnosis, the Mediators, Triggers and Antecedents for each person's illness form the focus of clinical investigation.

ANTECEDENTS AND THE ORIGINS OF ILLNESS

Understanding the antecedents of illness helps the physician understand the unique characteristics of each patient as they relate to his current health status. Antecedents may be thought of as congenital or developmental. The most important congenital factor is sex: women and men differ markedly in susceptibility to many disorders. The most important developmental factor is age: what ails children is rarely the same as what ails the elderly. Beyond these obvious factors lies a diversity as complex as the genetic differences and separate life experiences that distinguish one person from another.

Congenital factors may be inherited or acquired *in utero*. They can most readily be evaluated from a comprehensive family history, including mother's health before and during pregnancy. Genomic analysis, which is now commercially available, can supplement the family health history as a tool for investigating unique nutritional needs or individual variability in sensitivity to environmental toxins[20] [21]. The commonest single gene disorders in North America, celiac disease and hemochromatosis, may be confirmed by the presence of genetic markers, but should first be suspected from abnormalities in routine lab tests. Elevated serum ferritin concentration or transferrin saturation should prompt genetic testing for the alleles associated with hereditary hemochromatosis. [22] Increased small intestinal permeability, as measured by the inexpensive, non-invasive and under-utilized lactulose/mannitol challenge test, has a sensitivity approaching 100% for untreated celiac disease[23]. Abnormal intestinal permeability should prompt the measurement of celiac-specific immune markers in patients with chronic fatigue, autoimmune disorders or chronic gastrointestinal complaints of any type; normal intestinal permeability in patients consuming gluten virtually excludes gluten-sensitive enteropathy as a consideration, whatever the serological markers reveal. Because hemochromatosis and celiac disease are common, have protean manifestations and can be well controlled by nutritional interventions, ferritin and intestinal permeability should be routine components of the laboratory testing for antecedents of illness.

Some familial disorders may reflect intra-uterine rather than genetic influences. Twin studies of hypertension, for example, indicate a higher concordance for blood pressure between identical twins with a common placenta than identical twins with separate placentas.[24] Presumably, the shared placenta mediates subtle nutritional influences that affect a tendency toward chronic illness in adulthood.

Post-natal developmental factors that govern the predisposition to illness include nutrition, exposure to toxins, trauma, learned patterns of behavior and the microbial ecology of the body. Sexual abuse in childhood, for example, is associated with an increased risk of abdominal and pelvic pain syndromes among women[25] [26]. Recurrent otitis media increases the risk of a child developing Attention Deficit Disorder[27] [28], an effect that is not associated with hearing loss but may result from the effects of antibiotics on the microbial ecology of the gut.

Precipitating events are critical antecedents that closely precede the development of chronic illness. They represent a boundary in time: before this event the person was considered healthy; since the event, the person has become a patient.

Understanding the nature of the precipitating event may aid in unraveling the triggers and mediators that maintain the state of illness. The commonest precipitating events among my patients are a period of severe psychosocial distress, an acute infection (sometimes treated with antibiotics), exposure to environmental toxins at work or home or severe nutrient depletion related to illness or crash dieting. Useful questions for uncovering precipitating events include: When is the last time you felt really well for more than a few days at a time? During the six months preceding that date, did you experience any illness or major stress, change your use of medication or dietary supplements, or make any significant life changes? Cases in which cryptogenic illness was found to be precipitated by foreign travel, antibiotic use, dietary changes[29], smoldering infection or the illness of a spouse[30] have been presented elsewhere.

TRIGGERS AND THE PROVOCATION OF ILLNESS

A trigger is anything that initiates an acute illness or the emergence of symptoms. The distinction between a trigger and a precipitating event is relative, not absolute; the distinction helps organize the patient's story. As a general rule, triggers only provoke illness as long as the person is exposed to them (or for a short while afterward), whereas a precipitating event initiates a change in health status that persists long after the exposure ends. Common triggers include physical or psychic trauma, microbes, drugs, allergens, foods (or even the act of eating or drinking), environmental toxins, temperature change, stressful life events, adverse social interactions, and powerful memories. For some conditions, the trigger is such an essential part of our concept of the disease that the two cannot be separated; the disease is either named after the trigger (e.g., "Strep throat") or the absence of the trigger negates the diagnosis (e.g., concussion cannot occur without head trauma). For chronic ailments like asthma, arthritis or migraine headaches multiple interacting triggers may be present. All triggers, however, exert their effects through the activation of host-derived mediators. In closed head trauma, for example, activation of NMDA receptors, induction of nitric oxide synthase (iNOS) and liberation of free intra-neuronal calcium determine the late effects. Intravenous magnesium at the time of trauma attenuates severity by altering the mediator response [31]. Sensitivity to different triggers often varies among persons with similar ailments. A prime task of the functional practitioner is to help patients identify important triggers for their ailments and develop strategies for eliminating them or diminishing their virulence.

Although the identification and elimination of triggers is not a foreign concept in conventional medicine, many physicians neglect the search. A study was conducted by telephone in which practicing physicians were asked how they would treat a new patient with abdominal pain, who had a recent diagnosis of gastritis made by a specialist in another town. Almost half were ready to put the patient on acid-lowering therapy without asking about the patient's use of aspirin, alcohol or tobacco, all of which are potential triggers for gastritis. The authors of the study concluded, "In actual practice, ignoring these aspects of the patient may well have reduced or even negated the efficacy of other therapeutic plans implemented."[32]

MEDIATORS AND THE FORMATION OF ILLNESS

A mediator is anything that produces symptoms, damage to tissues of the body, or the types of behaviors associated with being sick. Mediators

vary in form and substance. They may be biochemical (like prostanoids and cytokines), ionic (like hydrogen ions), social (like reinforcement for staying ill), psychological (like fear) or cultural (like beliefs about the nature of illness). A list of common mediators is presented in Table I. Illness in any single person usually involves multiple interacting mediators. Biochemical, psychosocial and cultural mediators interact continuously in the formation of illness.

Cognitive/emotional mediators determine how patients appraise symptoms and what actions they take in response to that appraisal.[33]. They may even modulate the symptoms themselves. People in pain, for example, experience more pain when they fear that pain control will be inadequate than when they believe that ample pain management is available.[34]

Perceived self-efficacy (the belief in one's ability to cope successfully with specific problems) is a cognitive mediator that determines coping with illness. People with a high degree of health self-efficacy usually adapt better to chronic disease, maintaining higher levels of activity, requiring lower doses of pain medication, adopting healthier lifestyles, and cooperating with prescribed therapies, compared to people with low self-efficacy.[35] Self-management education is designed to enhance self-efficacy[36], and has been shown to improve the clinical outcome for patients with several types of chronic disease, including asthma[37], arthritis[38] and diabetes[39].

The biochemical mediators of disease (listed in Table 1) are best known for their ability to promote cellular damage. Most are organized into circuits and cascades that sub-serve homeostasis and allostasis. In these networks, each mediator is multi-functional and most functions involve multiple mediators, so that redundancy is the rule, not the exception. The most striking characteristic of biochemical mediators is their lack of disease specificity. Each mediator can be implicated in many different, apparently unrelated diseases, and every disease involves multiple chemical mediators in its formation.

Mediator networks that regulate inflammatory and neuroendocrine stress responses have been the subject of intensive research with important clinical implications. A detailed discussion of these networks is outside the scope of this chapter, but they are described in detail in Chapters..... Comprehensive reviews have appeared elsewhere[40][41][42][43]. Within the framework of Functional Medicine, a key feature of biochemical mediators is the natural rhythm of mediator activity, which is strongly influenced by the common components of life: diet, sleep, exercise, hygiene, social interactions, solar and lunar cycles, age and sex. Aging, illness and chronic psychological distress up-regulate activity of the inflammatory and neuroendocrine-stress response networks. Regular physical activity down-regulates both.

INTEGRATING THE PATIENT'S STORY

After listening to the concerns that led each patient to seek a consultation in Functional Medicine, make a series of distinctions:

(1) For patients whose main concern is optimal health and prevention, ask about present and past health problems and the family health history. If these supply no indication of illness susceptibility, then turn your attention to risk factors for future illness: weight, fitness, type and level of physical activity, dietary pattern, sleep habits, use of alcohol, drugs, tobacco, firearms, environmental exposures at home and work, travel, sources of stress and pleasure, degree of involvement with others, spiritual beliefs and practices, sexual relationships, hopes and fears for the future.

(2) For patients with an active health problem, always ask, "What was your health like before this problem began?" An intake questionnaire that asks about previous health problems is also helpful, because it gathers information about what the patient was like prior to the present illness in a different fashion, one that is condition-specific, not open-ended. The two approaches complement one another.

(a) Some patients will say that they were really healthy prior to their present illness. In that case, look for a precipitating event. If you or the patient can identify one, then ask about ongoing triggers that bear some relationship to the precipitating event. For example: if the precipitating event was marital or job stress, focus on stress-related psychological triggers. If the precipitating event was an environmental exposure, focus on on-going exposures to volatile chemicals or mold.

(b) The most challenging patients will usually indicate that their health was poor even before their present illness. In that case, take a detailed, chronological history from birth to the present that includes information about early life experience (including illness, injury and abuse), school and work performance, diet, drug and medication use, leisure activities, travel, family life, sexual experiences, habits, life stressors and places of residence. Because gathering this data can be very time-consuming, a self-administered questionnaire completed by the patient before the interview may help to prompt responses and improve memory of remote events. For many patients with complex, chronic health problems, it may be useful to take a detailed life history **before** seeking detailed information about present symptoms. Problems that emerge from such a review will have to be addressed for a successful outcome of treatment. Dealing with the present concerns by themselves will almost never succeed for patients in this group.

Whatever rapport you establish with patients initially, maintaining the therapeutic relationship usually depends upon significant improvement in symptoms or in a sense of well-being within a few days to a few weeks of the initial evaluation. This is most efficiently achieved by addressing the triggers that provoke symptoms and helping the patient decrease exposure to them. When triggers cannot be identified or avoided, then symptomatic improvement must rest on control of mediator activation. A combination of the two will usually produce the most satisfactory long-term benefits.

ASSESSMENT OF TRIGGERS

A comprehensive search for triggers requires that you know the following about your patient: each drug--prescription, over-the-counter or recreational--that the patient has used and when; nutritional habits and each dietary supplement used and when; what effects the patient noted from the use of each substance; sources of stress--life events, environmental exposures, thoughts or memories, and social interactions--and when they occurred in relation to symptoms. Elicit the patient's own ideas about possible triggers by asking, "What do you think causes or aggravates your symptoms." The patient's observations may be insightful and accurate in ascribing causality. Of course the patient's---and the clinician's—observations can also mislead, or focus on non-essential factors. Teach patients to challenge their own observations by looking for consistency and replicability, wherever possible. Suggest alternative theories for the patient to consider and explain that the search for triggers works best as a collaborative effort between patient and doctor. The patient's ability to recognize triggers is an important step in self-care.

Food and environment supply important triggers for the practice of Functional Medicine. Food intolerance is a very common phenomenon,

reported by thirty-three per cent of the population in one large study[44]. A minority of these reactions (4-14%) are due to true food allergies. Most food intolerance has no clear immunologic basis. Mechanisms include sensitivity to the pharmacological effect of alkaloids, amines or salicylates in food.[45] [46] [47] [48]Histamine poisoning from scromboid fish and tyramine-induced headache are dramatic examples.[49] Although most food intolerance is short-lived, severe chronic illness can occur, and the food trigger may elude identification unless the physician starts the investigation with a high index of suspicion. Gluten intolerance, with its protean manifestations, is probably the best example. Affecting about two per cent of people of European ancestry[50], gluten intolerance is common and often unrecognized. In addition to being the essential trigger for celiac disease, gluten sensitivity may be manifest in patients with neurological disorders of unknown cause[51], cerebellar degeneration[52], dermatitis herpetiformis[53], failure to thrive[54], pervasive developmental delay[55], inflammatory arthritis[56] [57] [58] [59] [60], psoriasis[61] [62] Sjogren's syndrome[63] [64], and schizophrenia[65] [66]. The different presentations of gluten sensitivity may derive from genetic differences among affected patients.[67]

Published studies on food intolerance and your patients' symptoms may be found through the National Library of Medicine. If the patient has a disease diagnosis, a Medline search may reveal previously observed associations between specific foods and the patient's condition. Access PubMed over the Internet (www.pubmed.gov) and run a search that cross-references the name of the patient's condition with "Hypersensitivity, Food" and also with "Food, adverse reactions". Both of these are Medline Subject Headings (MESH). There is no MESH listing for "Food Allergy" or "Food Intolerance". Your search will be more efficient if you list the patient's condition as it appears in MESH. A negative search does not eliminate food intolerance as a trigger for the condition being searched, but the number of positive findings may surprise you.

Health effects of ambient air quality are as important as those of foods. Numerous studies conducted in U.S. cities, demonstrate a close correlation between fine particle air pollution and daily mortality rates, even at levels of pollution considered safe by the World Health Organization[68] In the industrialized world, most people spend most of their time indoors, and indoor air pollution has become a serious cause of morbidity. Studies using experimental chambers have shown that volatile organic compounds (VOCs) released from building materials, furnishings, office machines and cleaning products, can cause irritation of the respiratory system in humans and animals at levels which are one hundred times weaker than permissible exposure levels or the World Health Organization Indoor Air Guidelines[69]. Controlled experiments with people who describe themselves as sensitive to VOCs confirm that VOC exposure causes headache, fatigue and difficulty concentrating. People who deny such sensitivity also experience symptoms but do not experience mental impairment when exposed. Air samples of buildings with and without Sick Building complaints have established an association between VOC exposure and human sickness.[70]

A questionnaire can elicit important information about environmental exposures at home and at work. The open-ended question, "Has your work or home environment been a concern to you?" should be accompanied by a checklist of potential exposures.

Microbial triggers for chronic illness present a particular challenge, as exemplified by the many facets of *Helicobacter pylori* infection. Originally isolated from the gastric mucosa of patients with gastritis and peptic ulcer disease, *H. pylori* has been implicated in the pathogenesis of NSAID

gastropathy[71], gastric carcinoma[72] and lymphoma[73] and a variety of extradigestive disorders, including ischemic heart disease[74], ischemic cerebrovascular disorders[75], rosacea[76], Sjogren's syndrome[77], Raynaud's syndrome[78], food allergy[79], vitamin B12 deficiency[80] and open angle glaucoma[81]. For elderly patients with open angle glaucoma and incidental H. pylori infection of the stomach, eradication of H. pylori by antibiotics was associated with improved control of glaucoma parameters at 2 years.[82] The mechanism by which *H. pylori* aggravates open-angle glaucoma is unknown, but may result from the ability of *H. pylori* colonization of the gastric tract to trigger the local and systemic release of Platelet Activating Factor, inflammatory cytokines, and vasoactive substances.

In the case of untreated *H. pylori* infection, non-invasive screening tests, including serum antibodies, stool antigens and C-14 breath testing, are available. For other types of infection, inquiring about the previous response of a given symptom or symptom complex to antibiotics may be useful. In 1988, physicians at the University of Minnesota conducted a study in which they administered intravenous cephalosoprins to patients with various types of arthritis who also manifested antibodies to *Borrelia burgdorferi*. Most of these patients were not thought to have Lyme disease. Some met diagnostic criteria for rheumatoid arthritis, some for osteoarthritis, some for spondyloarthropathies. The response to antibiotics was quite variable and ranged from no response to dramatic and sustained improvement. The authors noted that improvement in arthritis following antibiotics was not related to the patient's clinical diagnosis or the level of anti-*Borrelia* antibody. The best predictor of a positive response to the experimental treatment was a previous history of improvement of arthritis associated with the use of antibiotics[83].

The most comprehensive way to ask the antibiotic question is: "During the time you have had symptom X, have you taken antibiotics for any reason? Which antibiotic? Did symptom X change while you were taking the drug?" Among patients with chronic diarrhea of unknown cause, for example, some will report that their gastrointestinal symptoms improved when taking a specific antibiotic, others will report that they worsened. The first case suggests that bacteria or protozoa sensitive to the antibiotic may be causally related to the patient's gastrointestinal problems. Repeating the antibiotic prescription can establish if this response is replicable. If so, therapy can focus on treating the microbe and understanding why a single course of antibiotics was ineffective. The second case suggests that depletion of bacteria by antibiotics and concomitant increase in antibiotic-resistant organisms, including yeasts, may be contributing to diarrhea and treatment can focus on restoration of a normal intestinal flora.

ASSESSMENT OF PSYCHOSOCIAL MEDIATORS:

Useful questions for eliciting a person's beliefs about her illness are:

"What do you think has caused your problem?"

"What do you most fear about your problem?"

"How much control do you think you have over your symptoms?"

Useful questions for eliciting information about the nature and sources of social support include:

"Are there people in whom you can confide?"

"How satisfied are you with your marriage/family/friends/social life?"

"How much support do you receive in dealing with your health problems?"

"How often do you feel loved or cared for?"

ASSESSMENT OF BIOCHEMICAL MEDIATORS

Understanding the biochemical alterations associated with a conventional disease diagnosis can be helpful in understanding the biochemical mediators of each person's illness. Inflammation is believed to play a critical role not only in response to infection and in the classic inflammatory diseases, but also in the pathogenesis of coronary artery disease, diabetes, cancer and depression and the negative health effects associated with obesity and with aging.[84] [85] [86] [87] [88] [89] [90] The orchestration of mediator signals in the inflammation and neuroendocrine-stress networks, as they interact with one another, is critical for normal physiological functions, like the architecture of sleep, the repair of injury and the response to infection, and for the dysfunctional physiology central to the pathogenesis of most of the major chronic diseases.[91] [92]

Most chronic diseases is associated with chronic inflammation, but the patterns of immune response that underlie inflammation are not always the same. Patients with Type 1 diabetes mellitus, Crohn's disease or any other disorder categorized by granuloma formation or excessive cell mediated immune responses are likely to have an immune response to common triggers in which the TH1 component is upregulated and not subject to the normal downregulation provided by TH2 activity. Their mediator response to inflammatory stimulation produces excessive levels of gamma-interferon (g-IFN) and interleukin-12 (IL-12), key TH1-related cytokines.[93] Patients with severe depression often show a loss of negative feedback in the HPA axis. Urine free cortisol is elevated; the diurnal pattern may be disrupted, with increased P.M. cortisol secretion and blunting of dexamethasone suppression. This phenomenon appears to be driven at the level of the hypothalamus, not the adrenals, because spinal fluid Corticotrophin Releasing Hormone (CRH) is elevated.[94] Several groups of researchers have speculated that impaired synaptic function due to a deficit of omega-3 fatty acids may contribute to the CNS dysfunction of patients with depressive illness. Their Omega-3 fatty acid levels tend to be lower in blood samples than in control populations; administration of omega-3 supplements derived from fish oil has been shown beneficial in placebo-controlled studies of patients with depression, schizophrenia and attention deficit disorder. The key component appears to be eicosapentaenoic acid (EPA).[95]

To utilize the vast database of available information about biochemical disease mediators, integrative clinicians should consider three strategies. First, maintain up-to-date knowledge of disease pathophysiology by reading reviews in mainstream journals on mechanisms of disease or on specific mediators. In reading these, pay special attention to the types of mediators mentioned and their functions within the networks that subserve inflammation, oxidative stress, and neuroendocrine balance.

Second, attend workshops and courses that emphasize integrative physiology, sponsored by institutions like IFM, the New York Academy of Sciences, the Center for Mind-Body Medicine, and the American College for Advancement in Medicine [96]

Third, employ knowledge of the commonest biochemical imbalances in chronically ill North Americans and the influence of diet, nutrition and dietary supplements on these imbalances.

TREATMENT PLANNING

A Functional Medicine treatment plan should be collaborative and dynamic. Collaborative means that patient and practitioner work together to set

goals and priorities. Dynamic means that the treatment plan is adjusted as needed in response to feedback. Your knowledge of the patient's beliefs about her illness and perceived self-efficacy are essential for collaborative treatment. An appropriate therapeutic intervention for dysfunctional beliefs is the giving of information. Patients have an intense need for explanations about the causes of their diseases.[97] They want to know how they came to be sick, so that they can attach some meaning to the illness,[98] what to expect from the illness and what they can do to relieve symptoms or speed recovery. Information of this type can reduce anxiety, even when the diagnosis itself is frightening, may increase feelings of personal control, and improve the ability to cope with pain. People change their behaviors more readily when they receive information about the importance and the nature of the changes they need to make, help with setting goals and measuring progress. The kind of information needed is personal, not statistical. It must answer the question, "What can I do?"

The physician can help patients who are suffering from isolation by calling this isolation to the attention of family members or friends or by attempting to connect the patient with a support group or community agency. Possibly, there is nothing that can be done to relieve the patient's isolation, but the doctor's awareness and acknowledgment of it can be important to the patient and serve to enhance the therapeutic relationship[99].

If potential triggers have been identified, an assessment of the patient's ability to control exposure to them is important. For patients who are reluctant to make major dietary or environmental changes, explain that each avoidance is an experiment that the patient can direct with your guidance. If eliminating foods (and reintroducing those foods as a challenge) has no effect on symptoms or measurable physiologic parameters, do not encourage the patient to persist in the avoidance of those foods, whatever the results of *in vitro* allergy tests may be. The patient will have enough work to do following a healthy diet. Food intolerance is only meaningful if its effects can be demonstrated in real life.

For microbial triggers, the decision to use prescription antimicrobial drugs or natural products with antimicrobial activity may require negotiation. If the situation is not critical, it is usually worthwhile honoring the patient's preferences and intuition.

Understanding the ways in which mediators are modulated by diet enables creative nutritional therapies to be applied. Salicylic acid, the major metabolite of aspirin, suppresses activation of the nuclear transcription factor NF-kB, an anti-inflammatory effect that is independent of cyclooxygenase inhibition[100] and may be responsible for some effects of low-dose aspirin therapy.[101] Vegetables are rich sources of natural salicylates and vegetarians may have serum concentrations of salicylic acid as high as those of people ingesting 75 mg of aspirin a day.[102]

Dietary fatty acids may have profound effects on the network of inflammatory mediators, altering prostanoid synthesis, PPAR activity and the response to cytokines like IL-1[103]. They have subtler effects on the neuroendocrine-stress response network, modulating neuronal responses to serotonergic and adrenergic transmission.[104] Therapy with omega-3 fatty acids provides an excellent example of nutritional modulation of disease activity though alteration of biochemical mediators. Three principles can guide this type of therapy. The first utilizes knowledge of the pathophysiology of specific inflammatory and CNS disorders. Using this model, omega-3 therapy has been successfully applied to the treatment of patients with rheumatoid arthritis, inflammatory

bowel disease, coronary artery disease, peripheral vascular disease, dysmenorrhea, cyclic mastalgia, cystic fibrosis, migraine headaches, bipolar disorder, schizophrenia, attention deficit disorder, atopic eczema and multiple sclerosis[105]. Because the fatty acid composition of the contemporary Western diet differs significantly from paleolithic and ancestral diets, reflecting a marked decrease in omega-3 consumption relative to total fat, the response of so many unrelated disorders to EFA supplementation may indicate that EFA's are not merely working as nutriceutical agents, but that EFA dietary status is important for disease pathogenesis.

The second method rests upon the clinical evaluation of an individual's fatty acid status using clinical parameters that are independent of disease activity. Prasad has stated that the best test for nutritional adequacy is a functional test. Determine a parameter to follow and measure how administration of the nutrient(s) in question affects that parameter.[106] This method can be applied to the use of EFA therapy in clinical practice. Stevens et. al., studying boys with ADHD and a randomly selected population of schoolchildren, found a correlation between low concentrations of omega-3 EFAs, learning and behavior problems, and symptoms associated with EFA deficiency (thirst, dry skin and dry hair).[107] Evaluating the presence of these symptoms in patients and observing how they change with EFA supplementation is a quick guide to EFA status that may be used clinically to evaluate the EFA contribution to mediator imbalance. The author's method for doing this has been described elsewhere[108]. Finally, it is possible to measure the levels of fatty acids in plasma and erythrocyte phospholipids, although guidelines for level of change in fatty acid profiles needed to produce a known physiologic effect have not yet been developed.

The successful application of nutritional therapies, especially dietary interventions, and other self-care practices, as part of a therapeutic plan is very helpful in enhancing self-efficacy among patients. Enhancement of self-efficacy should always be a cardinal goal of treatment in Functional Medicine.

SUMMARY

Functional Medicine is essentially patient-centered, rather than disease-centered. A structure is presented for uniting a patient-centered approach to diagnosis and treatment with the fruits of modern clinical science, which has evolved to serve the prevailing model of disease-centered care. The core scientific concepts of disease pathogenesis are Antecedents, Triggers and Mediators. Antecedents are factors, genetic or acquired, that predispose to illness, Triggers are factors that provoke the symptoms and signs of illness, and Mediators are factors, biochemical or psychosocial, that contribute to pathological changes and dysfunctional responses. Understanding the Antecedents, Triggers and Mediators that underlie illness or dysfunction in each patient permits therapy to be targeted to the needs of the individual. The conventional diagnosis assigned to the patient may be of value in identifying plausible Antecedents, Triggers or Mediators for each patient, but is never adequate by itself for the designing patient-centered care.

Applying the model of Person-Centered Diagnosis to patients facilitates the recognition of disturbances that are common in people with chronic illness. Diet, nutrition and exposure to environmental toxins play central roles in Functional Medicine because they may predispose to illness, provoke symptoms and modulate the activity of biochemical mediators through a complex and diverse set of mechanisms. Explaining those mechanisms is a key objective of this textbook. A patient's beliefs about health and

illness are critically important for self-care and may influence both behavioral and physiological responses to illness. Perceived self-efficacy is an important mediator of health and healing. Enhancement of patients' self-efficacy through information, education and the development of a collaborative relationship between patient and healer is a cardinal goal in all clinical encounters.

This chapter provides a key foundation for the practice of functional and integrated medicine. For extensive information on integrated medicine, including Dr. Galland's articles on Leaky Gut Syndrome, Parasites, Detoxification and Magnesium, visit the Foundation for Integrated Medicine (http://www.mdheal.org/) In addition, Dr. Galland has created an extensive online resource featuring the wisdom of leading integrated physicians at Pill Advised (http://pilladvised.com), where you can also learn more about interactions between drugs and supplements, and between supplements, featuring highlights of published reports from research centers.

Table 1. Common Illness mediators

Biochemical	
	Hormones
	Neurotransmitters
	Neuropeptides
	Cytokines
	Free radicals
	Transcription factors
Subatomic	
	Ions
	Electrons
	Electrical and magnetic fields
Cognitive/emotional	
	Fear of pain or loss
	Feelings or personal beliefs about illness
	Poor self-esteem, low perceived self-efficacy
	Learned helplessness
	Lack of relevant health information
Social/cultural	
	Reinforcement for staying sick
	Behavioral conditioning
	Lack of resources due to social isolation or poverty
	The nature of the sick role and the doctor/patient relationship

This chapter provides a key foundation for the practice of functional and integrated medicine. For extensive information on integrated medicine, including Dr. Galland's articles on Leaky Gut Syndrome, Parasites, Detoxification and Magnesium, visit the Foundation for Integrated Medicine (http://www.mdheal.org/). In addition, Dr. Galland has created an extensive online resource featuring the wisdom of leading integrated physicians at Pill Advised (http://pilladvised.com), where you can also learn more about interactions between drugs and supplements, and between supplements, featuring highlights of published reports from research centers.

Leo Galland is internationally recognized as a leader in Integrative Medicine and Functional Medicine. An experienced and dynamic speaker,

he has lectured extensively to business and professional groups throughout the United States and the British Commonwealth, and in Europe. He is the author of three popular books, *The Fat Resistance Diet*, *Power Healing*, and *Superimmunity for Kids*. Dr. Galland is celebrated as a master clinician who has popularized innovative nutritional therapies for prevention and treatment of chronic conditions, including obesity, metabolic dysfunction, allergies, immune system disorders, gastrointestinal problems and neurological diseases. He maintains a private consulting practice in New York City, where he treats patients from all over the world. Dr. Galland is the author of more than 40 scientific articles and has contributed chapters and material to numerous textbooks including *Integrative Gastroenterology* (2011), *Textbook of Functional Medicine* (2010), *ACP Evidence-Based Guide to Complementary and Alternative Medicine* (2009), *Complementary Medicine in Clinical Practice* (2006), *Encyclopedia of Human Nutrition* (2005), the *Textbook of Natural Medicine*, (2005) *Integrative Medicine, Principles for Practice,* (2004), *Inside the Minds: The Art & Science of Being a Doctor* (2002), *Post-Viral Fatigue Syndrome* (1991), *Workers with Multiple Chemical Sensitivities* (1987), He is the coauthor of *Gastrointestinal Dysregulation: Connections to Chronic Disease* (2008). Dr. Galland has been honored with the Linus Pauling Award from the Institute of Functional Medicine for developing key concepts of Functional Medicine. He received the Seelig Magnesium Award from the American College of Nutrition, the Clinician of the Year Award from the National Nutritional Foods Association, and the Harold W. Harper Award in Preventive Medicine from the American College for Advancement in Medicine. He has been consistently selected for *America's Top Doctors*. Interviews with Dr. Galland or articles about his work have been featured in *The New York Times, The Washington Post, Newsweek, Reader's Digest, Redbook, Self, Bazaar, Men's Fitness, Allure, Bottom Line, The New York Daily News* and many other publications. He has appeared as a medical expert on The Today Show, Good Morning America, PBS, Fox News, CNN, MSNBC and dozens of local affiliates of the major broadcast networks. Dr. Galland graduated from Harvard University and completed his medical education and training at New York University Medical Center. Board certified in Internal Medicine, he has held faculty appointments at the Rockefeller University, the Albert Einstein College of Medicine, the State University of New York at Stony Brook and the University of Connecticut, and served as Director of Medical Research at the renowned Gesell Institute of Human Development in New Haven. Based on his extensive research of how supplements and medications interact, Dr. Galland developed Pilladvised.com, a web application where users can learn about interactions. In addition, he is the Director of the Foundation for Integrated Medicine (mdheal.org), a non-profit educational organization committed to integrating nutritional therapies into clinical practice.

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Reducing Under-Evaluation and Over-Treatment: An Opportunity for Functional Medicine

Keith Berndtson, MD

An office clerk suffers a bowel obstruction and a stroke, and survives only because of highly skilled emergency and intensive care. Her bill is over $50,000 but her insurance covers only $4,000. She works out an agreement with the hospital to pay $200 a month for the rest, but after a while the hospital says that isn't enough and raises it to $500 a month, forcing her into personal bankruptcy. She loses her house of 18 years to other creditors. The hospital gets nothing.

A diabetic woman arrives in an emergency room with no pulse in her foot. She needs to have two stents placed into an artery to keep blood flowing through her leg. The procedure goes well and she stays overnight for observation.

A month later she learns that the hospital billed her insurance for $50,000. Insurance paid about $20,000. Her family is responsible for the remainder. She showed the bill to the doctor who placed her stents. He sees that each stent was billed out at $14,000. Wholesale, they run about $900. Thinking it was a mistake the doctor takes the bill to the hospital's chief billing officer for review, who verifies that the hospital charges are correct.

A young mother obtains an integrative medicine consultation for help treating frequent and severe migraine headaches. She has tried various conventional and alternative medical treatments over six years without relief. She spent over one week as an inpatient in a headache unit. Her insurance and out-of-pocket payments during this time totaled over $60,000. Blood testing ordered by the integrative doctor reveals evidence of delayed reactions to dairy, wheat, and kidney

beans – staples in her diet. She stops eating them. Her headaches go away.

These cases illustrate three key reasons why health care costs us more than it should in America: underinsurance, overpricing, and what I call the over-under dynamic in our health care system – the over-treatment of under-evaluated problems.

All three of these patients had a chronic illness. The first two suffered acute health crises stemming from poor arterial circulation. The costs for treating these crises would have been lowered or avoided altogether in a system focused on wellness support and effective preventive medicine. The cause of the third patient's migraines was invisible to various specialists who, before her food triggers were found, had prescribed 17 drugs over 6 years.

In *Overtreated: Why Too Much Medicine is Making Us Sicker and Poorer,* journalist Shannon Brownlee sifts through the reasons why our health system costs more than it should, noting:

> We spend between one fifth and one third of our health care dollars, between five hundred and seven hundred billion dollars, on care that does nothing to improve health. Why do doctors and hospitals deliver so much unnecessary care? There are many reasons, but the most powerful reason doctors and hospitals overtreat is that most of them are paid for how much care they deliver, not how well they care for their patients.

The common view is that the main cause of the over-treatment problem is our willingness to pay physicians for whatever they do, not how well they do it. I contend that the main cause of the over-treatment problem is our unwillingness to grant physicians the time they need to fully evaluate the root causes of chronic illness. Three out of four health care dollars are spent pruning away the symptoms of chronic illness—a superficial approach that takes the habitual form of drugs and procedures. Prescriptions and referrals are the quickest and easiest options for busy doctors looking for reasons to draw a visit to a close to avoid falling farther behind. These "hurry up" prescriptions and referrals account for much over-treatment that Brownlee describes.

To address the over-treatment problem, Brownlee asks what kind of system would minimize it. She argues that such a health system would look something like our current Veteran's Health Administration (VHA) which, while no one was looking, has developed into an advanced, fully wired health system subculture. The VHA:

1. Rewards doctors who best interpret the evidence and translate it into good results.
2. Does a better job of coordinating care among the providers involved.
3. Uses electronic medical records.
4. Reduces excess capacity of hospital beds and medical specialists.
5. Makes sure every patient has access to a primary care physician *and* sees to it that these doctors are not overwhelmed with patients.
6. Delivers the best care it can for the lowest cost, measuring efficiency in terms of results achieved per dollar spent *over the entire course of an illness*.
7. Incorporates performance measures that assess which care processes reliably produce the best clinical outcomes for the least amount of money.

Based on the VHA higher quality-lower cost model, it appears that less disciplined practice dynamics account for most of the over-treatment problem. From an integrative standpoint, the key aspect of a clinically effective, cost-efficient approach to chronic illness care is a subculture that sees to it that doctors are not overwhelmed with patients. A practice system could meet every

other milestone met by the VHA and still generate wasteful spending and poor clinical outcomes if its doctors are routinely overwhelmed and forced into hurried decisions about prescriptions and referrals.

But even if all medical and hospital operations in the country were to similarly attack their over-treatment problems tomorrow, it would still take 10 years or more to see the hoped-for results. Why? Brownlee explains:

> Hospitals, nurses, specialists, and all the industries that produce medical goods have a vested interest in maintaining the status quo; they don't want to see health care shrink. Drug companies don't want doctors to write fewer prescriptions, and latex glove manufacturers don't want cardiologists to perform fewer angioplasties... Nobody would want to put thousands of people who are currently employed by the health care industry out of a job, unless it was absolutely necessary. But it is necessary, because the alternative to rightsizing health care is worse.

Brownlee wrote that last sentence before the Great Recession, when unemployment rates were lower than they are now. But her point still stands. Wasted health care spending drags our economy into a quicksand that stalls hiring.

Consider the business dynamics of medical imaging. In 2005, Ohio had more magnetic resonance imaging (MRI) scanners than all of Canada. So did many other states. Hospitals order new scanners because one of the levels on which they compete involves having the latest, greatest technologies. But as any hospital executive knows, the faster a profitable scanner runs, the more money it will make. Scanners are more often upgraded or multiplied for speed than for clinical reasons.

There are also political reasons for keeping the hospital stocked with the latest imaging technologies. Radiology departments drive profits ("surpluses" in not-for-profit institutions). If a radiology group wants a new toy, the administration will find a way to make it happen. No business wants its rainmakers feeling disgruntled.

In the 1990s managed care pressures bore down on medical practices. Medical technology companies sensed an opportunity. They developed office-based diagnostic and treatment systems and marketed them through mailings, journal ads, and conference exhibits. The best way to hook the attention of a doctor facing bottom line struggles is to offer a deal on a piece of equipment that will "make your practice more profitable and up to date."

Many doctors bought or leased hand x-ray units to measure bone density, semi-automated systems for measuring nerve conduction velocity, hand-held ultrasound units that can image blood flow to rheumatic joints, lower back traction units, infrared stimulation units for treating neuropathy, and so on.

Once a physician has leased a piece of equipment, its effect on the bottom line starts figuring into any clinical calculation where the equipment has a conceivable rationale in diagnosis or treatment. Procedures that, prior to the lease, had never been considered or were rarely recommended by the doctor now become part of the standard workflow for as many patients as possible.

Many of these machines generate information that falls into the category known as "TBU" – true but useless. Bottom lines do a little better early on, but enthusiasm often wears off and there sits a piece of stuff that collects more dust than money while generating a monthly lease payment.

Some doctors looking for ways to boost their bottom lines entered into contracts with

freestanding MRI clinics that would route a portion of any insurance reimbursement for a scan procedure back to the referring physician. Under these arrangements, if your handshake was weak, you needed an MRI. These deals were found to violate federal anti-kickback laws and Stark laws applicable to Medicare and Medicaid patients.

Brownlee's review of data from several sources indicates that if you include imaging tests billed to Medicare by radiologists and non-radiologists, the average Medicare patient undergoes 3 imaging tests per year. Let's say the cost of these studies (MRI scans, CT scans, PET scans, ultrasounds, x-rays, and so on) averages $200. There are some 50 million covered Medicare patients, so that's roughly $10 billion in imaging costs for Medicare annually.

The question then becomes, what percentage of these imaging tests were medically necessary? For purposes of addressing this question, let's define an imaging test as medically necessary if something significant and actionable was learned from the test.

For example, when a doctor has historical and physical evidence to cause legitimate concern about the possibility of multiple sclerosis (MS), whatever the scan shows will be useful. It may detect brain plaque consistent with MS, which would prompt the creation of a disease management care plan. It might also disprove MS for now, removing it as a cause for concern but prompting a search for ways to better explain the patient's clinical situation.

Yet many tests are ordered to rule a medical condition in or out and the results accomplish neither task. The results fall into the category of true but useless information that is of no medical value.

Based on several estimates, roughly one-third of medical procedures can be considered medically unnecessary or useless. Eliminating medically unnecessary imaging studies alone for Medicare patients would save Medicare roughly $30 billion dollars.

The Henry J. Kaiser Family Foundation reports that Medicare benefit payments for 2010 totaled $509 billion. By these calculations, Medicare could reduce its total annual payout by six percent just by denying payment for medically unnecessary imaging tests.

Yet it's not easy to simply issue a policy and collect the savings. Medical necessity is notoriously tricky to pin down ahead of the clinical decision. It's most often in retrospect that doctors realize that a test result didn't seem to matter one way or the other.

From a clinical standpoint, it is almost impossible to devise a rules-based algorithm for medical necessity when the task at hand involves setting up diagnosis and treatment plans for unique individuals whose chronic illnesses represent complex systems biology interactions. If clinicians are not allowed some flexibility to follow their hunches here and there, then it will feel to physicians that medical resources are being rationed by cost-reduction rules and that invisible third parties control clinical judgment. We need to clarify in advance the difference between a good clinical hunch and a profit-play. We're not there yet—but we have reached the point where affordability must take precedence by necessity. We need wiser ways to go about reallocating health care resources.

Health insurance companies, on the other hand, want more flexibility when it comes to defining the concept of medical necessity. Otherwise, they argue, doctors and hospitals are free to pee on their legs and call it medically necessary.

Doctors who use a clinical systems biology approach to chronic illness lick their chops at the thought of competing on an ability to turn

evidence into better clinical outcomes at less cost. Nowhere is our health care system more dysfunctional than in how it approaches the care and prevention of chronic illness. These dysfunctions trace to an overly costly routine for assessing the patient that, despite many tests and visits to multiple doctors, fails to produce a coherent systems biology-based way of explaining the patient's condition. The result is not an integrative care plan, but a conventional rubber-stamped care plan for a diagnosis rather than a unique person.

Chronic illness is a self-perpetuating loss of functional integrity. The reasons for lost health beg to be explained, not just diagnosed. Most diagnoses are illness labels, not explanations. Preventing or treating chronic illness poses a problem that differs for each patient in question. In the long run, the most cost-effective way solve problems is to understand their causes as fully as possible before moving ahead with a one-dimensional care plan.

Over 125 million Americans have one or more chronic illnesses. For many of them, over-treatment is a problem, but the deeper problem is under-evaluation—or too little evaluation based on a clinical systems biology approach to chronic illness.

In this context, under-evaluation does not mean that conventional doctors are doing too little testing to properly manage or prevent chronic illness. We just covered that. The problem is an over-reliance on diagnostic testing that does too little to help explain the root causes of chronic health decline, and the failure to deeply explore the patient's illness narrative. Doctors are not doing enough listening and history probing prior to making their diagnostic testing recommendations.

A systems biology perspective will help make doctors more effective in their work with chronically ill patients. Insurers don't' get this fact because it is in their interests not to get it. They already have doctors over a barrel with their policies, their way of defining medical necessity, and the way they enforce an outmoded process for the coding and documentation of procedures, known as the Current Procedural Terminology, or CPT system.

The American Medical Association (AMA) handed the CPT system to the insurance industry in 1966. Ever since, insurers have been exploiting the AMA's rules for how doctors must allocate the time they spend with patients if they want to get reimbursed. These rules have not kept up with the growing complexity of the physician's cognitive task.

When using a clinical systems biology approach to the chronically ill, meeting standard coding and documentation requirements steals precious narrative construction and problem solving time from both the patient and the doctor. Insurers benefit by making doctors to jump through irrelevant documentation hoops in order to justify their time, whereas the systems biology perspective allocates every necessary minute to explaining the problem before jumping to its solution.

Then there are the vague diagnoses that turn patients into medicine's second-class citizens, like chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome. These nametags create a false sense of precision when all they really do is confirm that your pattern of signs and symptoms meet experts' simplified criteria for a diagnosis. If you're chronically ill, a diagnosis is a place to start, but you'll want help solving the underlying systems biology puzzle using best working explanations for your particular illness experience.

Anyone who runs a solution shop of any kind, be it medicine or motorcycle repair, will tell you that the path toward a workable solution relies on a solid understanding of the problem. Under-evaluation is harder to grasp than over-treatment,

but it, too, is a serious cause of wasted money and bad clinical outcomes.

The mainstream approach to chronic illness races to a diagnosis that, once made, trips a cookbook-style disease management protocol. Use the cookbook recipe and disease markers may start floating in the right direction, giving the clinician a sense of accomplishment even though the patient may have made little or no progress toward her goal of normal function.

Say you visit your doctor because you're tired of being a fat, lazy, couch potato. Looking at your blood test results, the doctor diagnoses you with hypercholesterolemia, prescribes a statin drug, and puts you on a low-calorie diet. It made perfect sense. You'd been on the same statin before without any problems, but stopped refilling it because you lost your health insurance.

Two months later your doctor is all smiles. Your weight is down 9 pounds and your bad cholesterol (LDL) level is down 25 points.

You ask the doctor, "Then why am I feeling so bad?" You report muscle aches, difficulty sleeping, increased anxiety, and a new type of killer headache.

"Try this for the headaches, this for sleep, and this for anxiety. Let's see if your muscle aches improve. See me in 3 weeks."

In three weeks you report that you are sleeping through the night and that you feel less anxious, but you also feel too tired to exercise and the muscle aches and headaches are a little worse.

The doctor is thinking that the statin is not to blame since you've tolerated it before. You report that nothing about your life really changed since you started to lose weight. You and your doctor are stymied.

From a clinical systems biology standpoint, feeling worse while losing weight can mean that the patient is mobilizing stored fat-soluble toxins—also known as persistent organic pollutants (POPs)—at a rate that exceeds the capacity of the body's detoxification systems. The ability to tolerate mobilized POPs depends in part on lipoproteins like LDL and HDL and their ability to bind circulating molecules that are toxic and fat-soluble.

Supporting a weight loss and exercise routine with dietary supplements that support detoxification systems can reduce the toxicity symptoms that can accompany weight loss in people who are storing POPs in their fat cells. Another option is to pause statin, not because we think it is causing the muscle aches, but because the body relies on its lipoproteins to bind free-floating, fat-soluble toxins and escort them safely to the liver for processing and deportation. In this case, an option to help the patient feel better while losing weight is to let the LDL run where the body wants it to run for purposes of effective detoxification. When you reach your target weight and you're feeling more fit, we'll recheck the LDL and see if you still need support from a statin.

I know about this because it is part of my clinical experience as a functional medicine physician, not because a randomized, controlled clinical trial (RCT) proved it. Even if this issue were investigated using an RCT design, it could easily generate findings that are true but useless as far as patient care is concerned. The rap on RCTs is that their findings are often nearly impossible to translate into the medical care of uniquely individual patients.

To better accommodate a systems biology framework, our chronic illness model would have to transition from being doctor-and-disease-centered to being patient-and-wellness-centered. For a wealth of reasons this transition is overdue, but instead of a truly patient-centered, personalized approach to chronic illness, American health care is moving in the direction of selecting

for each patient more specific diagnoses from a list of codes that seem to lend precision, and selecting more overly simple treatments from a list of pre-packaged guidelines derived from studies that don't translate well to individual patients anyway.

To insurers, it's the coding and documentation methods that matter. To patients, it's the process and results of care that matter. Doctors are caught in the middle, unable to make their patients or third party payers happy at the same time. If the patient is paying, the doctor will try to make the patient happy. If the insurer is paying, the doctor will try to make the insurer happy. This may work fine assuming the insurer even remotely cares about whether the patient is happy. It is time for America's health care system to care more about what patients think.

ICD-9 codes are more accurate when they're describing acute conditions such as pneumonia or fractures, but they do a miserable job of capturing the systems biology dimensions of chronic illness. In fact, not one of the 14,000-plus codes in the ICD-9 collection comes close to a clinical systems biology description of what's going on in a given patient with chronic illness.

The net result: programmatic oversimplification of chronic illness and fragmentation of patient care into specialty silos where the only doctors in charge of evaluating the patient as a whole feel so rushed by the clock that they can't even afford to ask their patients open-ended questions anymore, let alone assemble a coherent view of the patient from a systems biology perspective.

A description of a clinical evaluation based on systems biology thinking would read more like a working explanation than a list of codes. The working explanation would reference the hypothesized root cause (or causes) of a person's chronic illness.

Consider the case of Emma, a young mother of two little boys who presented with a history of intermittent intestinal bloating fatigue, non-restorative sleep, weight gain, anxiety, and difficulty concentrating. Blood work showed a mild elevation of anti-thyroid antibodies though the thyroid hormone levels were fine. Her fasting blood sugar was 143 mg/dL, high enough to qualify her for a preliminary diagnosis of diabetes.

Her primary care doctor referred her to endocrinology, psychiatry, and gastroenterology, with instructions to arrange for help around the house, see what these doctors thought, and to follow up and see her again in 3 months.

The endocrinologist agreed that the thyroid findings could not account for her fatigue. He suggested annual follow-up for a thyroid physical exam and lab tests. He ran more blood tests and found that she did have mild diabetes that should be able to correct itself without medication if she would change her diet and get regular exercise. Otherwise, medication would be needed to control her blood sugar. Not wanting to take medication, she agreed to the lifestyle changes knowing she was too tired to exercise.

The psychiatrist prescribed a drug to enhance the action of serotonin in her brain. Within three days she felt worse from nausea, headache, and increased nervousness. At that point, he offered a drug to dampen anxiety, explaining it was for short-term use only due to tolerance and dependence issues that develops with long-term use. She declined the offer.

The gastroenterologist did endoscopies of her stomach and colon, which were normal. A blood test for celiac disease wasn't abnormal enough to make that diagnosis. She was told not to worry about gluten.

When she followed up with her primary care doctor to see what should happen next, the doctor suggested psychotherapy.

The ICD-9 record of this conventional primary care visit is summarized below:

CONVENTIONAL MEDICINE EVALUATION

Diagnostic Codes:

245.2	Autoimmune thyroiditis
250.0	Diabetes without mention of complication
300.02	Other anxiety disorder
780.52	Insomnia, unspecified

A friend of hers recommended that she see me. After our first visit, she commented that no other doctor had taken the time to hear the full story of what was happening in her life and show interest in what might explain why her symptoms unfolded the way they did. You'd never know from looking at her assigned ICD-9 codes that these four conditions were related to a cause that hadn't yet been detected or described.

I learned that her intestinal bloating began while on a 6-week course of antibiotic and oral steroid to get over a bout of severe sinusitis a year ago. She reported the bloating problem and the doctor advised that this was probably a complication of treatment and should resolve on its own afterward.

It didn't resolve. Within three months of the sinus treatment, fatigue became the next worrisome issue for her. Six months after that, she noticed that she'd wake up easily at night and have difficulty falling back asleep. She'd wake up tired and impatient. She developed intense sugar cravings and needed more caffeine to function. That's when her anxiety level seemed to skyrocket.

I ordered a celiac genotype test and it came back positive for the DQ2 marker – the most risky of the genes known to invite gluten intolerance and permit it to progress to its end stage—celiac disease. While she didn't have celiac disease, she could well be gluten sensitive, and the immune system reactions triggered in her gut could be affecting her thyroid, and possibly her pancreas and brain. Here's how I summarized her condition from a systems biology point of view:

SYSTEMS BIOLOGY EVALUATION

Narrative Summary 1:

Bloating, fatigue, anxiety, insomnia, difficulty concentrating, and high blood sugar levels.

Possible intestinal hyperpermeability triggered by prolonged antibiotic exposure, producing gluten sensitivity resulting in nutritional depletion and gastrointestinal, endocrine, psychiatric, and possibly neuroimmune complications.

Narratives have more explanatory power than a list of codes. Any health professional can make sense of it. The layperson's translation is easy too: the antibiotic-steroid use caused intestinal hyperpermeability, commonly called *leaky gut*. If your genes program your immune system to unleash a ferocious response to gluten fragments in your gut wall, and a leaky gut permits these fragments to enter your gut wall, then your system could well be headed for chronic health trouble at a rhythm and tempo that varies in ways explained by detailed narrative of your illness experience.

The overreaction to gluten in your gut wall can flip a switch from "gluten tolerant" to "gluten intolerant." You may or may not develop gut symptoms as a result, but the medical research literature shows how gut-based immune reactions can cascade to involve other parts of your system. In Emma's case, the best working explanation for her symptoms was that a fast-paced, gluten-mediated autoimmune cascade had come to involve not just her gut, but also her thyroid, and perhaps her brain and the insulin producing cells in her pancreas.

I checked for signs of autoimmune pancreatic disease, and these were negative, but her fasting insulin was slightly high, suggesting that she was

developing something called *metabolic syndrome*. Low-grade inflammation in her gut wall could produce enough of a systemic reaction to produce insulin resistance and explain her rising blood sugar level. Low-grade inflammation could put the system on yellow alert, including the brain, resulting in anxiety and disrupted sleep.

The treating endocrinologist, psychiatrist, and gastroenterologist might cry foul because nowhere did I established a chain of causal explanations for how antibiotics led to gluten intolerance, let alone how gluten intolerance led to anti-thyroid antibodies or possible immune-driven brain excito-toxicty. This is the way it is between the conventional standard of care and the clinical systems biology approach: what appears to be a series of groundless assumptions to one side, looks to the other side, like an explanation of best fit despite a number of blanks unfilled.

I had made assumptions, but they were made on grounds that meet a reasonable person standard. If gluten sensitivity had activated an inflammatory cascade that could explain her autoimmune thyroiditis, rising blood sugar, fatigue, anxiety, and disrupted sleep, then an integrative care plan comes into view. The care plan is not based on RCTs or expert guidelines. It is based on experience using a clinical systems biology approach to symptoms that elude explanation when left to usual and customary care. Emma says that in her little battle between conventional and integrative medicine, I won, at about one-quarter the price of the previously unhelpful care she'd received for the same set of problems.

I reassured her that a micronutrient-rich, gluten-free, low sugar diet would be of great help, and that she'd feel better, and that our nutritionist would help her make these changes. With our help, Emma eliminated gluten and sugar from her diet, ate more vegetables, and used supplements to boost her serotonin level and replete her stores of vitamin B12, magnesium, and vitamin D.

Within three months, she felt like her former, healthy self. Her energy was up, bloating and anxiety were way down, and she was sleeping well. Though her anti-thyroid antibodies were about the same, this was not unexpected. She was doing much better. Was this a case where the patient coincidentally got better on the lucky integrative doctor's watch? Or was it a case where clinical systems biology succeeded where usual and customary care had failed?

Emma is happy to be well again, but also a bit miffed about why her health insurance company refused to cover services that a Medical Director found to be medically unnecessary. That insurer had no problem covering thousands of dollars in procedures and specialty consultations that had failed to help her system restore full functional integrity.

The clues to solving most clinical puzzles are in the patient's history. The presence of a celiac permissive genotype supported the possibility of gluten intolerance with potential to progress toward celiac disease at an indeterminate rhythm and tempo, or the possibility of non-celiac gluten sensitivity, a condition that responds to a gluten-free diet but which has little potential to evolve toward celiac disease. Alessio Fasano, MD, and his colleagues at the University of Maryland's Mucosal Biology Research Center and elsewhere around the world established the distinction between these two types of gluten sensitivity. In March 2011, *BMC Central* published the paper by Sapone, et al proving that growing public interest in gluten-free diets is not a fad, but a serious matter of life and health.

A clinical systems biology approach worked. It blended knowledge of the latest medical literature demonstrating the causes of leaky gut and how a leaky gut can trigger for gluten sensitivity, with a narrative-building history and a care plan based

on experience and inductive logic. For want of a clinical systems biologist, how many times would Emma play 'around the horn' with specialists and primary care?

Gluten sensitivity is the poster disease for clinical systems biology. It demonstrates better than any other condition why incorporation of a clinical systems biology approach to chronic illness is justified. It also has the glam-factor of being reversible and being the illness that made it safe for physicians to use the long-derided term "leaky gut" in public.

A celiac disease panel typically looks for two specific antibodies in the blood. One antibody is formed against an enzyme in the gut wall called tissue transglutaminase (tTG). The other antibody is formed against gliadin, the indigestible portion of gluten protein that appears to be the main troublemaker.

The test ordered by Emma's gastroenterologist showed no antibody against tTG. Anti-gliadin antibodies were detected, but not at high enough levels to suggest celiac disease. In the context of Emma's illness experience it was a mistake to advise her not to worry about gluten. The most we could tell her about her test results was that if she was gluten sensitive, it looked like it hasn't progressed to a point anywhere near celiac disease yet. That's a clear difference of opinion that really mattered to Emma.

The endocrinologist missed his opportunity to draw a connection between her early stage autoimmune thyroiditis and her high blood sugar to the possibility of gluten sensitivity.

The psychiatrist was playing reasonable odds on going for serotonin enhancement using medication. She did not consider that Emma's serotonin levels could have dropped too low in response to constant use as a buffer against the toxic effects of low-grade inflammation on the brain.

Serotonin reuptake inhibitors help you squeeze more of a "don't worry, be happy" message out of whatever serotonin you're already making, but they do nothing to help you make more serotonin. When we checked Emma's urinary serotonin level, it was very low.

Emma's anxiety and insomnia were almost certainly caused in part by her low serotonin level. Serotonin acts like a *brake* on brain pathways whose neurotransmitters act like *accelerators* on the brain. These transmitters include norepinephrine, glutamate, and histamine, all of which were running high in Emma.

A leading explanation for why these transmitters run high in a case like Emma's is that immune system messenger molecules, known as *cytokines*, rain a constant pitter-pat of "yellow alert" messages onto the blood-brain barrier. Some of these messengers may leak through stressed points in the barrier, gaining access to the brain itself. A brain that would otherwise be orchestrating several cycles of deep sleep each night is instead kept on edge, resulting in daytime fatigue.

Her magnesium, vitamin B12, and vitamin D reserves were low. This is not unusual in someone whose gut absorbs things less efficiently. But each of these substances is neuro-protective in its own way, which means they help the nervous system less excitable and able to cope better with whatever stresses it happens to be under.

We repleted her stores of these nutrients, used 5-HTP to raise her serotonin level, and curcumin to suppress pro-inflammatory cytokine output. Along with her dietary and nutritional repletion changes, her energy improved to the point where she could exercise again. She felt like herself again with about three months—roughly sixteen months after the treatment for sinusitis that triggered her chronic health decline.

Her next systems biology summary looked like this:

SYSTEMS BIOLOGY EVALUATION:

Narrative Summary 2:

Apparent resolution of patient's gluten-mediated intestinal, neuroimmune, endocrine, and psychiatric complications, by virtue of a micronutrient-rich, gluten-free, low sugar diet, 5-HTP-based serotonin enhancement, anti-inflammatory extract of curcumin, nutritional repletion using magnesium, vitamin B12 and vitamin D, and exercise. Patient advised to use self-monitoring tools as part of a general self-care program based on diet, exercise, stress reduction, and learning the art of happiness. She will follow-up with me in 3 months or as needed.

Notice the emphasis on lifestyle medicine, natural therapies, self-care support, and the emphasis on the connection between happiness and wellness. It is probably harder to be happy when cytokine signals are annoying your brain. While it is the healer's job to engineer hope that voluntary self- regulation methods will prove helpful in almost any illness circumstance, it may be asking too much of self-regulation methods alone if underlying imbalances are driving inflammation, nutritional depletion, and neurotransmitter imbalance.

As you can see by this contrast between usual care and clinical systems biology, customary care is making the practice of medicine serve database format needs instead of the patient's need for in-depth evaluation and the doctors' needs for straightforward communication about patient care. All of the doctors involved in Emma's care are intelligent, compassionate, hard-working professionals. They happen to use a mind-set for clinical problem solving that follows conventional standards for medical care—standards primarily set by health insurers and their consulting medical experts.

The conventional standard of care commonly brushes aside the possibility of gluten intolerance as a factor in symptoms that are otherwise hard to explain, and it misses opportunities to help thousands of gluten intolerant patients every day.

I was a proud factory-issue family doctor for 10 years. My colleagues in family medicine were some of the smartest and hardest-working people I knew. Like me, most were a bit skeptical about alternative medical therapies, though I felt twinges of guilt for holding under suspicion something that I didn't really know much about.

When I joined an integrative medicine practice, it was to close my knowledge gaps about what tools the other side used to help patients. I did so with a chip on my shoulder because I didn't think the "other side" new science from a hole in the ground. The other side eventually became "this side." The main reason for this, in retrospect, was the emphasis on detailed narrative histories and respect for the deeply human nature of encounters whose task is supposed to be about healing.

You may have noticed that Emma's primary care doctor made no mention of intestinal hyperpermeability. This is unfortunate because leaky guts are linked to over a dozen autoimmune diseases and are suspected as root causes or complicating factors in a growing number of medically unexplained chronic illnesses.

But there's another reason why you don't see intestinal hyperpermeability listed as diagnosis in the records of patients like Emma: there isn't an ICD-9 code for it.

We can send people to the moon, but we can't enter a clinical diagnosis of leaky gut into the health record of the patient who has it because there is no ICD-9 code for it, even though it plays a major role in millions of cases

of chronic illness. Are we to discount narrative medicine and systems biology summaries because the higher priority is to fragment the story, as if it has no beginning, middle, or end, so we can shoehorn it into structured database? We are doing this because we think it will lead us to a more cost-effective approach to patient care? Are we spending hundreds of billions of dollars to digitize a flawed system for assessing, describing, and treating chronic illness? What was it that Linus Pauling said about doctors?

Enter ICD-10 – a monstrous set of codes that physicians, hospitals, and healthcare organizations around the country are scrambling to implement by October 1st of 2013. The ICD-10 codes won't improve on the ICD-9 system when it comes to describing chronic illness in narrative form using a systems biology point of view. Yet the lion's share of chronic illness may involve a few patterns of overlapping losses of functional integrity that are best described by a mix of narrative, genetics, lifestyle, environmental exposures, and metabolic pathway disruptions.

Figuring out how to pick from a list of hundreds rather than dozens of codes relevant to one's medical practice is going to eat into clinical problem solving time during encounters between patients and their doctors. This is especially true for already pressed primary care doctors because they deal with the widest range of diagnostic code sets compared to other forms of medical practice, and they have the least time to spare.

More importantly, to physicians anyway, is the real possibility that ICD-10 will create rampant new opportunities for claims processing delays and denials. What's needed to get more cost-effective results out of primary care is less, not more fragmentation of the physician's cognitive task; less, not more intrusion by third parties; less, not more of physicians having to second guess how they are being paid.

If you carry the logic of "the more detail, the better" to its conclusion, we'd need a million codes to reflect the complexity of chronic illness and what makes it different for each individual compared to another. Better to settle for simple narratives whose words reflect medical evidence, analysis, experience, and inductive logic in pursuit of explanatory power. Pay doctors for their time and factor in an adjustment based on the cost-effectiveness of their results and the clarity of their documentation. Don't hold them to CPT rules that are from the pre-systems biology age of medicine.

Let the competition in the health care sector unfold on a level playing field. Don't use customary care definitions of medical necessity to deny claims that reflect a functional medicine approach when customary care has already failed. Don't throw the good medical practice variations out with the bad. It'll make it look like health care reform is just another chapter in a book about how to kill disruptive innovations before they eat into the margins or market shares created by business as usual. Citizen-consumers are getting wise to that move. They're getting mad as hell and won't take it anymore.

Leaders will discover that hospital-run medical groups, independent multi-specialty medical groups, and the newer forms of collaboration we're seeing in the health sector—patient centered medical homes and accountable care organizations—will better compete if, somewhere within their conclaves, they've made room for a clinical systems biology-driven solution shop.

Doctors would have more time and freedom to probe the patient's narrative for clues as to which pattern of antecedents, triggers, mediators, and perpetuating factors applies to *this* person's chronic illness as opposed to *that* person's. There would be less time wasted dressing patients with codes that explain little and more time devoted to finding the words and concepts to communicate

why someone fell chronically ill. Working explanations, not mere diagnoses, should precede the creation of care plans whose goal is to restore functional integrity to a given patient's bodymind.

Modern medicine seems too content with the idea that millions of people can qualify for the *exact same* ICD code when each of these persons owns a unique illness narrative. So physicians are doing back flips to document their care using codes in a manner dictated by third parties – codes that don't begin to describe the systems biology of chronic illness, but codes that nonetheless must be used if the doctor wants to get paid.

With the right training programs, most doctors interested in practicing functional medicine could gain their credentials by attending trainings three or four times a year over two years. The *Institute for Functional Medicine* offers an excellent series of advanced practice modules and other support for physicians who'd like to incorporate a clinical systems biology approach into their practice model.

The most productive proving ground for the cost-effective care of chronic illness lays in the realm of a personalized approach to clinical systems biology, not in the realm of an assembly line, one-size-fits-all approach that jumps to a cookie cutter evidence-based practice protocol based on an ICD code. Resistance to change within our health sector may persist until consumers in the market for chronic illness care and prevention tell their health plans, "Hey! We found an innovative source of health value! It's not where you've been looking!"

Where you find teams skilled in applying the principles and methods of functional medicine, you will find many patients who are happy with the care process and its results, and many payers who are happy with cost-savings and customer satisfaction produced by the process.

Functional medicine physicians have the skills needed to reduce both over-treatment and under-evaluation of chronic health problems. Primary care and specialist physicians with an interest in functional medicine should take a look at the high quality training sources that are now available. But to advance the reach of a clinical systems biology approach to the care and prevention of chronic illness, interested doctors may have to change the way they think.

Keith Berndtson practices integrative medicine in Park Ridge, Illinois. In 1996, after ten years in family medicine and corporate health, he chose a road less traveled. On this road he came to realize the wisdom and value of the integrative and functional medicine traditions. He uses this experience to explore the wider implications of a clinical systems biology approach to wellness.

His medical practice, Park Ridge MultiMed, uses functional medicine principles to evaluate and treat patients with medically unexplained and non-responsive forms of chronic illness.

Berndtson founded *onebodymind.com* to supply innovative online tools for people interested in a deeper, more effective approach to health education, self-care support, and the stewardship of living systems. The website is also ground zero for a social network that will help prepare the way for the modern quest for health and sustainability.

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This previous essay appears in the upcoming book, *Value Health: The Modern Quest for Health and Sustainability*, by Keith Berndtson, MD.

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Nutritional Treatment of Fatigue (Excluding Chronic Fatigue Syndrome)

Alan R. Gaby, MD

Fatigue is one of the most common health complaints. It can be caused by a wide range of medical conditions and by various medications. In many cases, treatment of the underlying disorder results in an improvement in fatigue. However, in a large proportion of patients evaluated for fatigue, no underlying cause is identified. Conventional medicine has little to offer patients with unexplained fatigue, other than "reassurance" that their symptoms are not being caused by a serious illness.

Nutritional medicine, on the other hand, is frequently beneficial for patients with chronic, unexplained fatigue. In my experience, approximately 70–80% of these patients experience substantial improvement with nutritional therapy. Most of the common nutritional/metabolic disorders that are discussed repeatedly in this book (e.g., reactive hypoglycemia, food allergy, micronutrient deficiencies, hypothyroidism, and candidiasis) can cause fatigue. The astute practitioner, relying on a combination of clinical history, physical examination, and appropriate laboratory tests, can usually develop a nutritional program for chronic fatigue that has a high probability of success. Determining which interventions are most appropriate for any particular patient requires a fundamental understanding of the art and science of nutritional medicine. To paraphrase Sir William Osler, who made a similar comment regarding syphilis in 1897, to know chronic fatigue is to know nutritional medicine.

Dietary factors

Reactive hypoglycemia

Reactive hypoglycemia appears to be a common cause of fatigue.[1,2] Patients with fatigue caused by reactive hypoglycemia may experience a worsening of symptoms in the late morning or late afternoon (before mealtime) and an improvement after eating. They tend to crave sweets and may note that consumption of refined sugar relieves their symptoms transiently, only to be followed by an exacerbation. In my experience, a program that includes avoidance of refined sugar and other refined carbohydrates; consumption of small, frequent meals; and supplementation with nutrients

that help stabilize blood glucose levels often relieves fatigue in patients whose clinical picture is suggestive of reactive hypoglycemia. The evaluation and treatment of reactive hypoglycemia is discussed in chapter 6.

Food allergy

Numerous investigators have reported that hidden food allergy is a common cause of fatigue, both in children and adults.[3 4 5 6 7 8 9 10] Allergic fatigue may be associated with other symptoms of allergy, such as nasal congestion, abdominal pain, headache, body aches, hyperactivity, hyper-irritability, and edema. Some patients with allergic fatigue note that they feel better while fasting and worse after eating a meal. However, in other cases, fatigue improves after a meal containing a regularly ingested hidden food allergen, presumably because the patient is addicted to that food. Patients with allergic fatigue are frequently unaware that dietary factors are contributing to their symptoms. The evaluation and treatment of food allergy is discussed in chapter 7.

Caffeine

In case reports, 6 patients with severe sleepiness experienced an improvement or resolution of that symptom after they stopped consuming caffeine.[11] Mechanisms by which caffeine may cause sleepiness or fatigue include interfering with nocturnal sleep and triggering reactive hypoglycemia.

Nutritional supplements

Potassium magnesium aspartate

In 1959, a French scientist, Laborit, hypothesized that fatigue is caused by inefficient energy metabolism at the cellular level.[12] He suggested that enriching the cellular environment with appropriate substrates and cofactors could promote greater metabolic efficiency and thereby reduce the subjective symptom of fatigue.

Among the physiological compounds that were available at the time, the potassium and magnesium salts of aspartic acid (potassium magnesium aspartate) were considered likely candidates to enhance metabolic efficiency. Potassium regulates basic aspects of cellular functioning (i.e., transmembrane electrical potential and intracellular ionic strength) and is also involved in muscle contraction. Magnesium is required for the synthesis of the energy-yielding compound, adenosine triphosphate (ATP), and also enhances potassium transport into cells. Aspartic acid is converted *in vivo* to oxaloacetate, which is a substrate for the Krebs cycle.

After a study in rats supported Laborit's hypothesis by demonstrating that administration of potassium magnesium aspartate delayed the onset of exhaustion during a forced swimming test,[13] several uncontrolled and double-blind trials were undertaken in humans.[14 15 16 17 18 19 20 21] In these trials, 75-94% of patients experienced an improvement in fatigue after treatment with potassium magnesium aspartate. In contrast, only 5-27% of patients given placebo improved. In most studies, 2 g/day of potassium magnesium aspartate was administered, although one study used 4 g/day. These dosages refer to total weight: 2 g of potassium magnesium aspartate provides about 240 mg of potassium, 170 mg of magnesium, and 1.6 g of aspartate. Symptom relief was usually seen after 3-14 days. Fatigue of diverse etiologies (i.e., postoperative, post-viral, postpartum, menopausal, and nonspecific) responded to potassium magnesium aspartate. Adverse effects were uncommon and consisted mainly of mild gastrointestinal symptoms.

One hundred patients with chronic fatigue received potassium magnesium aspartate (1 g twice a day) for 2-18 weeks. Ninety-one percent of the patients improved within 5-14 days.[14]

One hundred forty-five patients complaining of fatigue received, in double-blind fashion (randomization not specified), potassium

magnesium aspartate (1 g 4 times per day) or placebo for 2 weeks. The proportion of patients in whom energy levels improved was 85% in the active-treatment group and 9% in the placebo group.[15]

Two hundred sixty-three patients with fatigue as their sole complaint were randomly assigned to receive, in double-blind fashion, potassium magnesium aspartate (1 g twice a day) or placebo for 2-4 weeks and then the alternate treatment for an additional 2-4 weeks. Seventy-nine percent of the patients improved while receiving active treatment, while only 27% improved while receiving placebo.[16]

The results of these studies are consistent with a more recent study in which 47% of 93 patients (median age, 38 years) with unexplained chronic fatigue had laboratory evidence of magnesium deficiency (i.e., they retained 20% or more of an intravenous magnesium load).[22]

In my experience, 2.0-3.35 g/day of potassium magnesium aspartate (i.e., 4 capsules per day of commonly available preparations) is one of the most frequently effective treatments for fatigue. Because of its high degree of efficacy and tolerability, it is often one of my first-line therapies for patients with unexplained fatigue who have no associated neuropsychiatric symptoms (if they do have such symptoms, then vitamin B_{12} may be tried first [see below]). Some patients who respond to potassium magnesium aspartate are able to discontinue treatment after about 6 weeks without experiencing a recurrence of symptoms, but they may need to resume supplementation during periods of increased activity or stress. Other patients require continuous treatment (with 50-100% of the initial dose) to maintain their improvement.

Vitamin B_{12}

Since shortly after its discovery in 1948, vitamin B_{12} given by intramuscular injection has had a reputation of being a "tonic," capable of improving fatigue, mood, and overall well-being in certain people who are not deficient in the vitamin.[23] [24] The popularity of this treatment is evidenced by the results of a survey conducted in the 1970s in which vitamin B_{12} accounted for 6% of all office injections, including allergy-desensitization treatments.[25]

Despite many impressive testimonials, the conventional medical community maintains that vitamin B_{12} injections are useless for patients who are not deficient in the vitamin;[25] [26] [27] that any improvement in symptoms is merely a placebo effect. To be sure, "getting a shot from the doctor" could produce a significant placebo response. However, the glowing reports from some patients strongly suggest that something more than a placebo effect is involved. I have heard comments such as, "I cleaned the house for the first time in 10 years;" or, "you gave me all this energy, now find something for me to do with it;" or, "this is the best I have felt in my entire life." Some patients who responded dramatically to vitamin B_{12} had previously noticed little or no improvement from injections of testosterone or other substances, indicating that receiving an injection per se did not evoke a placebo response in these patients. A double-blind trial provided some support for the empirical use of vitamin B_{12} injections.

Forty-eight subjects with fatigue, all of whom had normal hemoglobin concentrations and serum vitamin B_{12} levels, were randomly assigned to receive, in double-blind fashion, vitamin B_{12} (hydroxocobalamin, 5 mg intramuscularly twice a week for 2 weeks) or placebo. After a 2-week washout period, each person received the alternate treatment for an additional 2 weeks. Twenty-eight subjects completed the trial. The outcome measure

was the proportion of participants who preferred one treatment over the other for various subjective symptoms. Among subjects who received placebo before vitamin B_{12}, 12 preferred vitamin B_{12} and 2 preferred placebo with respect to "general well-being" ($p = 0.006$). For "happiness," 9 preferred vitamin B_{12} and 2 preferred placebo ($p = 0.03$). For "fatigue," 10 preferred vitamin B_{12} and 4 preferred placebo ($p = 0.09$). Among subjects who received vitamin B_{12} before placebo, there was no difference in response to the two treatments, apparently because the effect of vitamin B_{12} carried over to the second treatment period (serum vitamin B_{12} levels were still well above normal in 10 of 13 subjects 4 weeks after the last vitamin B_{12} injection).[28]

This study, while demonstrating that vitamin B_{12} has some degree of efficacy in non-deficient individuals, was not designed to be able to detect the dramatic improvement that occurs in a minority (perhaps 10-15%) of patients with unexplained fatigue.

In some patients, a positive response to vitamin B_{12} injections appears to be due to the correction of mild vitamin B_{12} deficiency (which can be demonstrated by a borderline-low serum vitamin B_{12} level and/or an elevated serum methylmalonic acid level).[29] [30] In those patients, the benefit may be relatively modest and the duration of the effect may be relatively long (reflecting the time it takes for vitamin B_{12} deficiency to recur). Effective vitamin B_{12} therapy for these patients may consist of 1,000 µg intramuscularly once a week for 4 weeks, then once every 3 months. In many of these patients, supplementation with vitamin B_{12} orally in doses of 500-1,000 µg/day may control symptoms and obviate the need for injections.

In another subgroup of vitamin B_{12} responders, there is no evidence of vitamin B_{12} deficiency. In this subgroup, the benefit from treatment is often substantial and the duration of the effect is relatively short (typically about 4-9 days, sometimes up to 2 weeks). These patients probably have some type of vitamin B_{12} dependency, in that they feel well only as long as their serum vitamin B_{12} level is well above the normal range. One possible explanation for the need to maintain an unusually high serum vitamin B_{12} concentration is a defect in the transport of vitamin B_{12} across the blood-brain barrier. Consistent with that explanation, some patients with neurasthenia have been shown to have subnormal vitamin B_{12} levels in cerebrospinal fluid in association with normal levels in serum.[31] Effective therapy for patients with presumed vitamin B_{12} dependency usually consists of 1,000 µg intramuscularly every 4 days to 2 weeks, depending on how long the treatment lasts. While the interval between injections varies from one patient to another, it is usually fairly consistent for any particular patient. To maintain the beneficial effect of vitamin B_{12}, injections may have to be continued indefinitely, unless another method of relieving the fatigue can be identified.

Hydroxocobalamin is preferable to cyanocobalamin for intramuscular administration, because it produces higher serum vitamin B_{12} concentrations and more prolonged elevations of these levels.[32] Methylcobalamin is also commercially available, but it is not known how its efficacy compares with that of other forms of vitamin B_{12}. For patients with presumed vitamin B_{12} dependency, oral, sublingual, or intranasal administration of the vitamin rarely improves fatigue, because these routes of administration cannot achieve the high serum concentrations that are attainable with intramuscular administration. When considering long-term use of vitamin B_{12}, the risks associated with repeated injections (e.g., tissue trauma or sterile abscess) should be weighed against the benefits. Many patients can be successfully taught self-injection, which saves them a considerable amount of time and money compared with injections at the doctor's office. Patients

administering injections frequently should be advised to rotate injection sites.

Because of its potential to produce substantial clinical improvement, intramuscular vitamin B_{12} is one of my first-line therapies for patients with unexplained fatigue. It is often tried first in patients who have associated neuropsychiatric symptoms such as anxiety, depression, insomnia, or decreased memory. In patients who do not have neuropsychiatric symptoms, potassium magnesium aspartate is often tried first (see above).

Iron

Anemia due to iron deficiency can cause fatigue, which is reversible with iron therapy. In addition to being a component of hemoglobin, iron is a cofactor for enzymes involved the electron-transport chain[33] (which plays a role in energy production) and in the synthesis of dopamine (which appears to modulate fatigue). In cases of mild iron deficiency, the activity of iron-dependent enzymes may be decreased before a reduction in hemoglobin levels occurs. Consequently, iron deficiency could contribute to fatigue even in patients who are not anemic.

Clinical trials have demonstrated that iron supplementation can improve fatigue in non-anemic iron-deficient patients.[34] [35] [36] Most of the improvement is probably due to an increase in the activity of iron-dependent enzymes, although some of the benefit might be due to an increase in hemoglobin levels within the normal range.[34]

One hundred forty-four non-anemic women (aged 18-55 years) with unexplained fatigue were randomly assigned to receive, in double-blind fashion, 80 mg/day of iron (as ferrous sulfate) or placebo for 4 weeks. Prior to treatment, 51% of the women had a low serum ferritin concentration (20 µg/L or lower). Mean severity of fatigue decreased by 29% in the group receiving iron and by 13% in the placebo group ($p = 0.004$ for difference in the change between groups). Subgroup analysis showed that only women with ferritin concentrations $\leq$ 50 µg/L improved with iron supplementation.[35]

Administration of iron to patients who are not iron-deficient may increase the risk of developing certain chronic illnesses, and it can harm people who carry an iron-overload gene. Therefore, iron supplementation should be reserved for patients with documented iron deficiency or borderline-low iron status.

Multivitamin-multimineral

Fatigue is one of the early manifestations of many different individual micronutrient deficiencies. The typical Western diet provides only marginal amounts of a wide range of vitamins and minerals. In some patients, fatigue could be caused either by a relatively poor diet or by an average diet in conjunction with a higher-than-normal requirement for one or more nutrients. In clinical practice, patients frequently remark that they have more energy when they take a multivitamin or multivitamin-multimineral preparation. The beneficial effect of a specific product was demonstrated with marginal statistical significance in a double-blind study of healthy volunteers.

Eighty healthy male volunteers (aged 18-42 years) were randomly assigned to receive, in double-blind fashion, 1 tablet per day of a multivitamin-multimineral formula (Berocca) or placebo for 28 days. One tablet of Berocca contains thiamine (15 mg), riboflavin (15 mg), niacin (50 mg), pantothenic acid (23 mg), vitamin B_6 (10 mg), biotin (150 µg), folic acid (400 µg), vitamin B_{12} (10 µg), vitamin C (500 mg), calcium (100 mg), magnesium (100 mg), and zinc (10 mg). Compared with placebo, active treatment was associated with a marginally significant decrease in tiredness ($p = 0.06$).[37]

As noted below, certain individual nutrients that are present in most multivitamin-multimineral products may be beneficial by themselves for some patients with fatigue. Other components of a broad-spectrum supplement might also be helpful, even though they have not been studied specifically as a treatment for fatigue.

Thiamine, vitamin B_3, and vitamin B_6

Several B vitamins play a role in energy production, and fatigue can result from a deficiency of various individual B vitamins. Studies on the treatment of fatigue with thiamine, vitamin B_3, and vitamin B_6 are described below.

Of 222 people aged 65 years or older from an urban general practice, 16% were found to have laboratory evidence of thiamine deficiency.[38] In 2 double-blind trials, supplementation of individuals aged 65 years or older with 10 mg/day of thiamine for 6 weeks and 3 months, respectively, improved fatigue when compared with placebo ($p < 0.05$ in one study, $p = 0.07$ in the other study).[38 39]

In an uncontrolled trial, 18 of 19 patients with chronic exhaustion and asthenia improved after receiving 40 mg/day of pyridoxine for 1 week.[40]

In a study conducted in 1940, prior to the enrichment of grains with B vitamins, supplementation with 100-200 mg/day of niacin decreased fatigue in some patients.[41]

While some apparently well-nourished patients have commented that taking B vitamins gives them more energy, those observations have not been confirmed by controlled trials. Nevertheless, moderate doses of B vitamins are safe and relatively inexpensive, so a trial of B-vitamin supplementation (as a component of, or in addition to, a multivitamin-multimineral preparation) should be considered for patients with fatigue.

Vitamin C

Fatigue is one of the symptoms of vitamin C deficiency. In a study of miners, supplementation with 150 mg/day of vitamin C resulted in a decrease in fatigue.[42] Although no controlled trials have been done, supplementation with vitamin C might improve fatigue in patients with suboptimal dietary vitamin C intake and in those subjected to stress.

L-Carnitine

Carnitine facilitates the transport of fatty acids into mitochondria, where they are metabolized to produce energy. Carnitine deficiency or suboptimal carnitine status would presumably lead to decreased energy production, potentially resulting in fatigue. Relative carnitine deficiency, resulting from decreased carnitine absorption, decreased endogenous carnitine synthesis, increased urinary carnitine loss, or an increased carnitine requirement could occur in various disease states, with the use of certain medications, or with advancing age. In double-blind trials, administration of 2 g/day of L-carnitine for 6 months decreased fatigue in patients with celiac disease who were on a gluten-free diet, and also improved fatigue in a group of centenarians ($\geq$ 100 years old).

Thirty patients with recently diagnosed celiac disease who had been on a gluten-free diet for 30 days were randomly assigned to receive, in double-blind fashion, 1 g of L-carnitine twice a day or placebo for 6 months. The mean severity of fatigue, as determined by a visual analog scale, decreased to a significantly greater extent in the L-carnitine group than in the placebo group ($p = 0.002$). At the end of the trial (7 months after commencement of the gluten-free diet), the mean serum carnitine concentration in the placebo group was 29% lower than in healthy controls, although the level was higher than before the start of the diet.[43] The results of this study indicate that patients with celiac disease have serum low

carnitine levels, even while consuming a gluten-free diet, and that carnitine deficiency is a cause of fatigue in these patients.

Seventy centenarians (aged 100-106 years) were randomly assigned to receive, in double-blind fashion, 2 g/day of L-carnitine or placebo for 6 months. Compared with placebo, L-carnitine significantly improved both physical and mental fatigue.[44]

In uncontrolled trials, L-carnitine supplementation (250-6,000 mg/day for 1-4 weeks) appeared to decrease fatigue in cancer patients, including patients with chemotherapy-related fatigue.[45] [46] [47] While a double-blind trial produced equivocal results in patients with cancer-related fatigue, the results were consistent with the possibility that L-carnitine produces a progressive reduction in fatigue over a period of 4-5 weeks.[48]

Vitamin D

According to one group of practitioners, vitamin D deficiency can cause fatigue, which is associated in some cases with aches and pains, especially in the shins and ribs.[49] Vitamin D deficiency should be suspected in individuals who have inadequate sun exposure (particularly if they are overweight or elderly or have dark skin) and do not consume significant amounts of vitamin D-fortified foods such as dairy products.

Intravenous nutrient therapy

In my experience, intravenous administration of a combination of magnesium, calcium, B vitamins, and vitamin C is effective for some patients with fatigue in whom other treatments (including intramuscular vitamin B_{12}) have failed. The usual treatment consists of 4 ml of 20% of magnesium chloride hexahydrate, 2 ml of 10% calcium gluconate, 1.3 g of vitamin C, 100 mg of pyridoxine, 1,000 µg of vitamin B_{12}, 250 mg of dexpanthenol, and 1 ml of B complex 100. This treatment, commonly referred to as the Myers cocktail, is described in chapter 340.

Other treatments

Thyroid hormone

Fatigue, often most pronounced in the morning, is a common manifestation of hypothyroidism. In hypothyroid patients, administration of thyroid hormone frequently improves fatigue. One group of investigators reported that 40% of 219 patients with chronic fatigue who underwent fine-needle aspiration of the thyroid gland had histologic evidence of lymphocytic (autoimmune) thyroiditis. In patients with lymphocytic thyroiditis, treatment with levothyroxine relieved the fatigue, even among the one-third of cases with TSH levels < 3.0 mU/L. Of note, only half of the patients with histologic evidence of lymphocytic thyroiditis had elevated blood levels of thyroid peroxidase antibodies.

Of 219 patients with fatigue for more than one year, 40% had histologic evidence of lymphocytic thyroiditis. TSH levels in patients with thyroiditis were widely scattered, with a median value of 3.8 mU/L and a range of < 0.9 mU/L to > 15 mU/L (normal range, 0.1-5.0 mU/L). In one-third of the patients with lymphocytic thyroiditis, the TSH level was < 3.0 mU/L, and in 59% of the patients the level was < 5.0 mU/L. The clinical response to levothyroxine therapy was "equally favorable" (details not presented) among patients with lymphocytic thyroiditis, irrespective of their initial TSH level.[50] Of the patients with definite histologic evidence of lymphocytic thyroiditis, only half had elevated circulating levels of thyroid peroxidase antibodies, thyroglobulin antibodies, or both.[51]

These findings are consistent with my observation that laboratory tests for thyroid function are frequently normal in patients who are clinically hypothyroid (chapter 8). In my experience, many patients with chronic fatigue who have clinical evidence of hypothyroidism but normal laboratory tests experience an improvement in fatigue after receiving an empirical trial of thyroid hormone.

Some of these patients may have had autoimmune thyroiditis, as noted in the above study (thyroid antibodies were only occasionally measured in my patients). However, others may have had tissue resistance to thyroid hormone, impaired conversion of thyroxine to triiodothyronine, or some other abnormality that increased their need for thyroid hormone. Consequently, the presence of lymphocytic thyroiditis may not be the only predictor of a positive response to thyroid hormone. Moreover, notwithstanding the study cited above, it is unclear whether the presence of autoimmune thyroiditis per se is an indication for treatment with thyroid hormone. For these reasons, clinical evaluation may often be the most reliable method of identifying those patients with chronic fatigue for whom a trial of thyroid hormone is appropriate.

Practitioners who are opposed to using thyroid hormone empirically have argued that tired patients may feel better when their metabolism is cranked up with thyroid hormone, but that does not mean they are hypothyroid or that the treatment is safe. However, that argument overlooks two points. First, people who are fatigued but not clinically hypothyroid often feel worse, not better, when they take thyroid hormone. Second, a specific set of symptoms, not just fatigue, usually improves when clinical hypothyroidism is treated. The evaluation and treatment of "sub-laboratory" hypothyroidism is discussed in chapter 8.

Dehydroepiandrosterone (DHEA)

In my experience, administration of dehydroepiandrosterone (DHEA) relieves fatigue in some patients whose serum DHEA-sulfate concentration is below or in the bottom 10-20% of the normal range for young adults of the same gender. Most of the patients who benefited from DHEA supplementation were elderly, but a few were middle-aged. The usual dosage is 5-15 mg/day for women and 10-20 mg/day for men. Further information and precautions regarding the use of DHEA are presented in chapter 56.

Candidiasis

According to clinical observations, fatigue is one of the symptoms caused by chronic candidiasis (also called *Candida*-related complex).[52] [53] Candidiasis should be suspected in patients with a history of recurrent *Candida* vaginitis, oral thrush, diabetes, or immunodeficiency. It should also be suspected in patients who have taken antibiotics (particularly if symptoms began after a course of antibiotics), oral contraceptives, or glucocorticoids. The evaluation and treatment of candidiasis is discussed in chapter 9.

Recommendations for chronic fatigue

1. Diet: Identify and treat reactive hypoglycemia and food allergies.

2. Potassium magnesium aspartate: 2.0-3.35 g/day.

3. Vitamin B_{12}: 1,000 µg intramuscularly once a week for several weeks in selected cases, then as needed if effective.

4. Iron: Identify and treat iron deficiency.

5. Other nutrients: Other nutrients that may be beneficial include B vitamins, vitamin C, L-carnitine, and vitamin D.

6. Intravenous nutrient therapy (Myers cocktail) in selected cases.

7. Thyroid hormone in selected cases.

8. DHEA in selected cases.

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Roundoc Rx

The Human Microbiome – Humans as Super-Organisms

Robert Rountree, MD

New discoveries in the human microbiome have led to the realization that humans are not the "simple" multicellular organisms that we thought they were—in fact, humans are super-symbionts who are completely dependent on a lifelong, mutually beneficial relationship with our microbial selves. Through new polymerase chain reaction (PCR) techniques, researchers have discovered that there are more bacteria cells on our bodily surfaces—collectively amounting to 100 trillion cells—than there are human cells in the entire body by a factor of 10:1. This means that humans are 90% bacteria! Furthermore, there are as many as two million distinct genes present on all the external and internal surfaces of our body. We have yet to identify all the different microorganisms that carry these genes, but there is no doubt that they are there. The implications of this finding are mind-boggling.

As a direct result of our ability to map these genomes we have come to the profound realization that here are all of these microorganisms living on us and, only a few years ago, we did not even know they existed. This begs the question: "What do all of these organisms do and how do they interact with our physiology?" For starters, they are absolutely essential for our health and well-being. Human beings cannot live without these organisms. They direct our immune and neurologic function, and profoundly affect digestion and metabolism. Now let's take a closer look at the human microbiome and the role these microorganisms play in our overall health.

The Human Microbiome Unraveled

The Nobel laureate Joshua Lederberg has suggested using the term "microbiome" to describe the collective genome of our indigenous microbes

(microflora), the idea being that a comprehensive genetic view of *Homo sapiens* as a life-form should include the genes in our microbiome.[1] As a result of new genomic sequencing techniques, which have allowed us to quantify, categorize, and otherwise determine what is actually growing on our bodily surfaces, we realize that the size and extent of this human microbiome is much more profound than anyone would have imagined.

Twenty years ago, if you wanted to know what microbes were growing in the crook of someone's elbow, you would swab the skin in that area, then transfer the sample to a Petri dish that contained a mixture of agar along with nutrients designed to make bacteria grow. This is a classic experiment that is still performed in biology classes across the country. After a few days of incubating the Petri dish, various species of *Staphylococcus,* gram-positive bacteria, would form colonies on the surface of the culture medium. The conclusion of the experiment based on this *prima facie* evidence is that the Staph species growing on the plate are the predominant bacteria growing on the skin.

What we have come to understand in recent years is that most of the species of bacteria that grow on the skin do not lend themselves very readily to this older culture technique, so we were actually missing most of what was there. An especially fascinating finding is that every region of the body has its own unique ecosystem of bacteria that is specific to that area. In other words, the types of bacteria found on the palm of the hand are distinctly different from those found in the axilla.

The same concept is true for a stool analysis. If someone with acute infectious diarrhea comes to see a doctor, the doctor might order microscopy to look for certain protozoan parasites such as *Giardia lamblia* or *Entamoeba histolytica*, or a stool culture for specific pathogenic bacteria such as *Salmonella*, *Shigella*, *Campylobacter*, and certain strains of *Escherichia coli*. We look for these organisms because *that is what we have known how to look for*, but the new reality is that, in fact, there are many other organisms not revealed through standard culture and microscopy techniques, and that DNA sequencing by PCR is going to replace the old way of doing things.

It is very similar to the old story of people looking for their lost keys under the light, and somebody asks: "Where did you lose the keys?" "Well, I lost them over there in the darkness." "Well, why are you under the street lamp?" "Because this is where the light is." That story very much applies to the evolution in microbiology. In the past, we have looked for organisms that we knew we could isolate, but, today, PCR techniques have become automated to the point where we can do a comprehensive analysis of the microbiota in the human body in a relatively short period of time, thus giving us a much more accurate picture of the composition of an individual's conglomerate microbial genome.

The five classes of microorganisms that have been found in the human microbiome include viruses, archaea, bacteria, microfungi, and protozoa. While the composition of normal microbiota varies from person to person, the majority of microorganisms found in and on the body are bacteria. These microbes exist on most bodily surfaces and wherever our body is interacting with "portals" to the outside world such as the respiratory, gastrointestinal (GI), and urogenital tracts.
For example, we used to think that the urogenital tract was mostly sterile, but now we know that is not the case. Interestingly, babies start out in the sterile environment of the womb, and then as soon as they are born they become colonized with microbes that are primarily derived from the mother's birth canal. In contrast, babies born by cesarean section are colonized with bacteria typically found on the mother's skin, as well as

the bacteria found on the skins of other infants, nursing staff, and even in the air in the hospital. This can have a lasting impact on the gut flora of these babies. The difference in initial colonization may explain why some studies have suggested that cesarean-section babies are more prone to developing food allergies and asthma in childhood,[2] although this association has admittedly not been a consistent finding.

Most of these organisms reside in the GI tract, which is, by far, the largest source of microorganisms in the human body. The next largest source is the surface of our skin. Current research suggests that there are between 500 and 1000 different species of oral and intestinal-tract bacteria. Gill and colleagues estimate that "the human intestinal microbiota is composed of 1013 to 1014 microorganisms, whose collective genome ("microbiome") contains at least 100 times as many genes as our own genome."[3] Humans, therefore, can really be viewed as "super-organisms" as our metabolism represents a mix of human and microbial attributes.

What Controls Microorganism Populations?

It is interesting to think about what keeps these microorganisms in balance. For instance, we wash our hands all the time and are naturally sloughing skin and mucosal cells, including cells that line our noses and mouths. When those cells slough off, they take with them any bacteria that might be attached. What is remarkable is that, if you temporarily sterilize the antecubital fossa by swabbing it with rubbing alcohol, within days—or even hours—it will be recolonized with a community of bacteria that is very similar to what was there before you sterilized the area. This tells us that there is something about every environment or "habitat" in the body that is set up to host a unique population of bacteria. The armpit is like a rainforest—damp and wet—so certain bacteria prefer that kind of environment and will grow there. Yet, the forearm, or the back of the hand, is much drier, so a different population will colonize there.

It is important to understand that, after a baby is born, the first group of bacteria that colonizes the skin or mucosal surfaces of the baby interacts with the DNA of the cells on those surfaces, and the bacteria send chemical messages back and forth. Based on those messages, the cells are signaled to make adherence factors, which make it easier for the bacteria to stick to the epithelium. For example, *Bifidobacterium*—one of the first bacteria on the scene—begin to colonize the baby's intestines and send messages to the DNA of the cells lining the gut that say: "Make this environment more hospitable for me."

This molecular dialogue takes place all over the body and continues throughout our lives. If something physically or biochemically disrupts that microecology, the result can lead to inflammation. Eczema is a good example of this phenomenon. Cold temperatures, insufficient moisture, or nutritional deficiencies can result in a breakdown of the normal skin barrier. That disrupts the microecology of bacteria that cover the skin so that pathogenic "bad guys," such as *Staphylococcus aureus*, can start to move in and wreak havoc.

In other words, chronic eczema results from a combination of an excessively permeable skin barrier along with an excessive immune response to the bacteria on or just underneath the skin's surface. This is very similar to what happens with ulcerative colitis, in which a deficiency of protective mucin allows certain bacterial populations to have access to immune cells that reside just underneath the surface of the gut mucosa. This increased exposure to "conditionally pathogenic" microorganisms activates those immune cells to generate an inflammatory response.

The bottom line is that disruption of the

microecology of the microbiota in the human body can lead to inflammation and chronic disease. Our microbiota may "Defend and Define Us" as one headline put it,[4] but, in the right conditions, they can also stir up a lot of trouble.

Microbiota Essential for Human Health

Healthy microbes in the human body are associated with significant health benefits including proper immune and neurologic functioning as well as optimal metabolism and digestion. The strongest line of evidence we have about the value of the microbiota and our health has been inspired by what is referred to as the "hygiene hypothesis."

The hygiene hypothesis began with the observation in 1989 by David Peter Strachan, MD, a British epidemiologist, that people in industrialized societies experienced higher incidences of asthma, allergy, and perhaps autoimmune disease.[5] An extensive body of research suggests that this increased incidence occurs as a result of excessive hygiene, vaccinations, and antibiotics, which make our internal and external environments "too clean." What the hygiene hypothesis basically tells us is that excessively clean or sterile environments may deprive the body of important information that it needs to function properly and remain in balance.

It wasn't that many years ago that the number-one cause of morbidity and mortality was pathogenic infections. This dropped significantly with the advent of synthetic antibiotic "wonder drugs." Yet, as a society, we have not been satisfied with our ability to simply control pathogens. We want to completely eradicate them—ALL of them—by doing everything possible to avoid exposure to infection or to stamp out infection in its earliest stages. We put antimicrobial compounds in soap, plastics, and toys. We treat babies aggressively with antibiotics for upper respiratory infections even though most of these infections are caused by viruses.

According to the Centers for Disease Control and Prevention, 30% of the 150 million antibiotic prescriptions in the United States are unnecessary.[6] Furthermore, at least 60% of manufactured antibiotics are used in animal feed as growth promoters.[6] The hygiene hypothesis says the net effect of all this is that the human immune system does not get adequate education, and the consequence of underexposure to infections is a rise in allergy, asthma, and perhaps autoimmune disease.

Let's take a little closer look at how this immunologic education works on a cellular level. Perhaps the single biggest influence on overall immune regulation has to do with a type of immune cell called the dendritic cell (DC). DCs are roving sentinels, whose specific task is to monitor the surfaces of the body for potential microbial threats. These sentinels do this by continuously sampling fragments of the microbes (and/or foods) that traverse the gut lining, respiratory tract, and skin.

DCs are found on every mucous membrane or epithelial surface on the human body—every place that human bodies come in contact with the outside world.

DCs start out in a naïve and relatively undifferentiated state. After exposure to certain antigenic structures (e.g., microbes, foods, pollens), they become activated to mature down a specific pathway of cellular differentiation. The resulting mature DCs can be proinflammatory, anti-inflammatory, or actively tolerant (anergic). Each type of mature dendritic cell then acts in turn to program naïve T-lymphocytes to follow its lead and become proinflammatory, anti-inflammatory, or tolerant. Given the huge number of foreign antigens present in the human microbiome, it is clear that tolerance of these antigens by immune cells is the norm rather than

the exception. The primary cells responsible for maintaining this tolerance are T-regulatory lymphocytes, often referred to as T-reg cells. T-reg cells develop from naïve T-cells that are programmed by DCs.

In order to mature down the tolerance pathway, DCs require continuous low-level exposure to "innocuous" bacteria known as commensals. If DCs do not get that exposure then they behave erratically. It is essential to have a two-way communication between the DCs and the microbiota. If an imbalance develops in the microbiota because of overgrowth of pathogenic bacteria or microfungi, this disruption activates DCs to mature down an inflammatory pathway instead of a tolerant pathway. The downstream consequence is that, instead of naïve T-cells becoming T-reg cells, these T-cells become activated into becoming Th1, Th2 or Th17 cells, all of which are highly inflammatory.

If the initial disruption leads to activation of Th-2 cells, then humoral (antibody-mediated) immunity is upregulated and allergic reactions can result. If the disruption leads to activation of Th1 cells involved in cell-mediated immunity then the result can be excessive inflammation. T-reg cells that are activated via the tolerance pathway tend to suppress overactivation of both Th1 and Th2 lymphocytes.

DNA mapping of the human microbiome has given us a much greater appreciation of the implications of the hygiene hypothesis. We are just beginning to realize to what extent the microbiome is influencing us in very powerful ways that we never expected.

Potential Effects of Disruption of Microbiota

If the human microbiome is essential for health, then disruption of the body's microbiota can lead to inflammation and disease. Numerous published studies show that disruption of gut microbiota has been associated with inflammatory bowel disease (IBD), obesity, autoimmune disease, asthma, allergies, cardiovascular disease, and other health problems.

Disruption of the body's microbiota can lead to inflammation and disease.

Inflammatory Bowel Disease

Let's look for example at IBD, a situation in which the immune system becomes overactivated and attacks the gut lining. There are two major types of IBD—Crohn's disease and ulcerative colitis. The current leading theory regarding the cause of Crohn's disease is that it is actually a type of immune deficiency. An immune defect in specific cells that normally keep bad bacteria in check allows these bacteria to overgrow. This leads to localized inflammation in the gut wall, microabscesses, and fistulas. In other words, Crohn's disease is not a disease of immune-system overreactivity, but rather a disease in which the normal balance of the microbiota in the GI tract is disrupted.

In contrast, ulcerative colitis is a condition in which the immune system overreacts to normal flora. The resulting inflammatory response damages the lining of the colon, causing ulcers and bleeding. In some ways, this is similar to what happens with periodontal disease. Periodontal disease is a chronic inflammatory condition in the tissue around the teeth that ultimately leads to bone loss. It turns out that it is not so much the specific bacteria that cause the problem, but

rather how the immune system overreacts to those bacteria.

Researchers have mapped the gut microbiomes of people with Crohn's disease and ulcerative colitis and compared them to the gut microbiomes of healthy individuals. The assumptions were that there would be overgrowth of one or two specific pathogens for each type of IBD and that these pathogens would not be found in healthy people. In other words, one organism would theoretically be responsible for each disease. Instead, the researchers found a distinctive overall *pattern* for each condition in which certain combinations of bacteria would predominate.[7] There appears to be a nonspecific disruption of the microbiome occurring that is saying something about the pathophysiology of the disease. Cracking the code that explains the pattern of the disruption may well lead to a cure for both forms of IBD.

As a consequence of these findings, researchers are looking at the cause of many chronic diseases differently now, especially chronic inflammatory diseases. Perhaps we should *always* be thinking of IBD, autoimmune disease, cardiovascular disease, asthma, and allergies as the consequence of an imbalanced microbiome that, in one way or another, has led to a loss of immune tolerance. That is what systems biology is all about—instead of looking for one cause, systems biology recognizes that the imbalances that lead to disease are caused by the interaction of many factors—both endogenous and environmental.

Obesity

An interesting new discovery is that there is a relationship between the GI microflora and body weight, and that the balance of microbiota in the gut may be an important predictor of obesity.[8–11] There are three major phyla of microbes that populate the gut (making up ~ 80% of total bacteria), which are *Bacteroidetes, Firmicutes*, and *Actinobacteria*. Jeffrey Gordon, MD, a molecular biologist at Washington University, initially determined that the gut flora of obese humans and obese mice have a lower percentage of *Bacteroidetes* (~ 5%) and relatively more *Firmicutes,* in contrast to lean individuals who had relatively more *Bacteroidetes* (~ 20%–30%) and fewer *Firmicutes*. In animal studies, Gordon and his colleagues (see Reference 8 for a study led by Ley) discovered that, if bacteria were taken from obese mice and put it into the intestinal tract of thin mice, the thin mice would become obese even though they continued to eat a regular diet.

This is a very profound finding because in the past there has been a tendency to assume that a person becomes obese simply because of overeating. However, the real question is *why* does a person overeat? Perhaps the patient's intestinal microecology has developed a microbial imbalance that disrupts the normal neurochemical feedback loops that control satiety. Or maybe he or she isn't really eating that much more food than a lean person, but intestinal bacteria are metabolizing that food in a different way.

Much of the research that followed the mice studies has been an attempt to figure out to what extent this difference in gut flora is a cause of obesity or a consequence of it. Gordon (in the study led by Ley) and others have postulated that *Firmicutes* bacteria possess a wider array of digestive enzymes that make them more efficient at extracting energy from food than *Bacteroidetes*, implying that higher concentrations of the former could lead to obesity even without increasing caloric intake.[10] It does appear to be true that certain bacteria are better at metabolizing food than other types. Bacteria also have a direct influence on satiety with certain bacteria increasing the appetite and others decreasing it.

When we say that obesity is "multigenerational" this may refer to the microbiome as much as it

refers to a lifestyle issue—if a mother is obese her child has more of a risk of being obese, because of inheriting her bacteria. This is an incredible realization. Of course, the major goal is to figure out whether there is a way to manipulate the gut flora (with probiotics or antibiotics or both) to alter a person's energy metabolism. Although the answer is still up in the air, the possibility that we could "treat" obesity with bacteria is astounding!

If a mother is obese, her child has more of a risk of being obese because of inheriting her bacteria.

The Role of Probiotics in Disease

If we can figure out how to manipulate these populations of microorganisms that take up residence in the human body, then we should theoretically be able to make a significant impact on the course of a disease. There are two ways we might achieve this: (1) alter the body's response and (2) actually change a person's microbiome, particularly in the GI tract.

An example of the first strategy comes from a published study, in which researchers found a lower prevalence of periodontal disease in people who had a higher dietary intake of omega-3 fatty acids (docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]).[12] One proposed mechanism is that the omega-3 fats have a mild immunosuppressive or anti-inflammatory effect. This is an example of how dietary changes can modify the immune response to the microbiome (by improving tolerance) and thereby alter the course of a chronic disease.

The second strategy represents the hope of probiotics as a therapeutic intervention. Research suggests that certain probiotics may induce DCs to mature down the tolerance pathway, with a resulting increased activity of toleragenic T-reg cells. Unfortunately, some of the new microbiome studies have actually pointed out the potential limitation of probiotic therapies. For instance, if a person with Crohn's disease has a major imbalance in the trillions of bacteria that make up the microbiome, it is unlikely that simply throwing a few billion CFUs [colony-forming units] of a couple of strains of *Lactobacilli* or *Bifidobacteria* in the GI tract for a few months is going to correct the underlying problem. This may explain why many of the clinical studies using probiotics for Crohn's disease have not shown much of an effect. In addition, these particular bacteria may not be as powerful for inducing tolerance as more-abundant commensal bacteria such as *Bacteroides fragilis*.[13] This may help explain the high degree of variability and inconsistent effectiveness found in clinical studies of probiotic formulas.

Interestingly, some of the best clinical results have not been obtained with more popular probiotics such as *Bifidobacteria* or *Lactobacillus* species, but rather with *Saccharomyces boulardii,* a type of nonpathogenic yeast that is not a normal denizen of the gut microbiome.[14] Similarly, a nonpathogenic strain of *E. coli* (*E. coli* Nissle 1917) shows significant promise for treating ulcerative colitis.[15] The good news about clinical studies of therapeutic probiotics for IBD is that they have an excellent safety record even if they don't always work that well.

Expecting probiotics to be an easy cure for chronic GI disorders (or other chronic diseases) is somewhat naïve. However, the concept continues to have merit. After all, the potential of

using therapeutic probiotics was based on decades of observation that people who eat yogurt, kefir, or other fermented foods tend to have healthier guts—and to be healthier in general. Instead of trying to "seed the clouds" by implanting the intestines with new strains of bacteria, a more-effective strategy might be to cultivate the growth of bacteria that are already there. A considerable body of research suggests that prebiotics—short-chain fatty acids such as inulin and fructo-oligosaccharides (FOS)—can act like fertilizer to enhance the growth selectively of certain beneficial strains of bacteria.

In contrast to the sometimes-mixed results seen with commercial probiotic products, fecal transplants (fecal bacteriotherapy) have been shown to have a very profound and lasting effect on gut flora. First pioneered by Thomas Borody,[16] a gastroenterologist in Sydney, Australia, a number of centers around the world are now doing this to treat people with severe imbalances of flora. Most of the transplants have focused on people with refractory *Clostridium difficile* colitis.

When *C. difficile* recurs (up to one third of cases) in patients or becomes resistant to vancomycin or metronidazole, there aren't a lot of other treatment options. Some of these people are in dire straits, because they have become cachectic and debilitated from persistent chronic diarrhea.

A number of published studies have reported profound recoveries from people who have had fecal transplants.[17,18] These studies show that it is possible to take an extract of fecal material from a healthy person, process it minimally, and then put the organisms into the GI tract of another person (by nasogastric tube, colonoscopy, or enema) and produce a significant and long-lasting alteration of new host's gut flora. Fecal transplants in these cases are being called, "human probiotic infusions." Most of the transplants have been in people with clostridia, but this is also being done increasingly for people with IBD. In fact, Dr. Borody has published case studies of people with ulcerative colitis who have gone into permanent remission after getting fecal transplants.[16]

This evidence from fecal transplants validates the concept that we can introduce healthy bacteria in a diseased gut and manipulate that person's microbiome for better health. It may be the mode of delivery that is important or the amount of probiotics or a particular strain that is important.

Conclusion

What we have learned about the human microbiome can be summarized in three main points: (1) the hygiene hypothesis provides a plausible theory as to why we are seeing an increase in allergies, asthma and certain autoimmune diseases in modern society: it is a result of "under-education" of our immune systems early in life; (2) a persistent disruption in the microbiome can lead to chronic inflammatory disease; and (3) we can alter the course of certain diseases by changing the composition of the microbiome or by altering our immunologic reaction to the microbiome (increasing or decreasing tolerance).

One of the major implications of our new understanding of the relationship between humans and microbes is that the consequences of overprescribing antibiotics are turning out to be much worse than we realized. We *really* need to get serious about stopping the inappropriate overuse of antibiotics.

Instead of chasing down every single outbreak of foodborne pathogenic *E. coli* or MRSA [methicillin-resistant *Staphylococcus aureus*] as if they were isolated events, we need to get to the real source of the problem, which is the routine

addition of antibiotics to grain feed as a growth stimulant. We need to follow Europe's lead and stop this practice completely.

The consequences of overprescribing antibiotics are turning out to be much worse than we realized.

Prescribing antibiotics like candy is disrupting our patients' microbiomes in ways that we never imagined, and makes a negative impact on human health. Even a recent review on the effects of helminths on the immune system and human microflora published in *The New England Journal of Medicine*, concludes with this statement: "We should therefore continue to advocate for a restrictive use of NSAIDs [nonsteroidal anti-inflammatory drugs], antibiotics, and food additives that will disturb microflora."[19] Yes, indeed, all of these things may profoundly disrupt the microflora.

We also need to improve our research protocols for studying the therapeutic effects of probiotics. We need further information about the effects of specific strains on specific diseases, and about optimal modes of delivery and dosages. We still don't know the answer to the perennial question of how many CFUs of a particular probiotic formula a person needs to take to have a significant long-term impact on the gut microflora. Is it a million CFUs? Ten billion? One hundred trillion? To get the best results, does the person need to take the formula for a month? Six months? A year?

I strongly believe that the general trend toward using probiotics in everyday life to maintain general gut health is a good thing; however, we need to get a lot better at determining how to appropriately *prescribe* probiotics for people who are ill. We have discovered a powerful principle, which is that the health of the body's microflora is essential to life, and, when the microecology is disrupted or when a loss of tolerance occurs, we have to restore the body's microfloral balance to prevent the development of chronic disease.

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Robert Rountree received his medical degree from the University of North Carolina School of Medicine at Chapel Hill in 1980 after graduating Magna Cum Laude from the University of North Carolina at Greensboro in 1976. He subsequently completed a three-year residency in family and community medicine at the Milton S. Hershey Medical Center in Hershey, Pennsylvania, after which he was certified by the American Board of Family Practice. He is currently board-certified by the American Board of Holistic Medicine.

Early on in his studies, he became deeply interested in a "patient-centered" approach to health and healing. Instead of following rigid protocols prescribed for specific diseases, he focused on the unique biochemical and emotional needs of individuals. To that end, he has augmented his training with extensive post-graduate studies in nutritional and herbal pharmacology along with certification as a master practitioner of Neuro-Linguistic Programming.

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Neurogenesis: Growing New Brain Cells

David Perlmutter, MD, FACN, ABIHM

On top of the finding that we can create new neural pathways into adulthood, a virtual revolution in neuroscience has been launched by the recent discovery of the process of neurogenesis, the ability of the brain to actually grow new neurons. Stem cell therapy, a hot button of political debate and the focus of leading-edge research, holds the promise of offering a powerful tool in neurodegenerative conditions. We now understand that the human brain is constantly undergoing its own "stem cell therapy" through the process of neurogenesis. Every moment of our lives, several critically important areas of our brains are being replenished with stem cells that are destined to become fully functional brain cells, and there's a lot we can do to enhance this process.

NEUROGENESIS IN ANIMALS AND HUMANS

Because neurogenesis had been noted in various other animals, scientists in the 1990s were hard at it, trying to demonstrate that humans indeed retained the ability to grow new brain neurons. In 1998, the journal *Nature Medicine* published a report by Swedish neurologist Peter Eriksson titled "Neurogenesis in the Adult Human Hippocampus." Dr. Eriksson had finally succeeded in launching what was to become a revolutionary paradigm shift.

As Sharon Begley remarked in *Train Your Mind, Change Your Brain,* "The discovery [of neurogenesis in the adult human brain] overturned generations of conventional wisdom in neuroscience. The human brain is not limited to the neurons it is born with, or even the neurons that fill it after the explosion of brain development in early childhood. New neurons are born well into the eighth decade of life. They migrate to structures where they weave themselves into existing brain circuitry and perhaps form the basis of new circuitry."[1]

Dr. Eriksson discovered that within each of our brains there exists a population of neural stem cells that are continually replenished and can differentiate into brain neurons. Simply stated, we are all experiencing brain *stem cell therapy* every moment of our lives, a concept that remains iconoclastic in a number of scientific circles. His Holiness the Dalai Lama has stated, "It is a fundamental Buddhist principle that the human mind has tremendous potential for transformation. Science, on the other hand, has, until recently, held to the convention not only that the brain is the seat and source of the mind but also that the brain and its structures are formed during infancy and change little thereafter."[2]

The revelation that neurogenesis was occurring in humans and that we retain this ability throughout our lifetimes provided neuroscientists around the world with a fresh and exciting new reference point with implications spanning virtually the entire array of brain disorders. Alzheimer's disease, characterized by a progressive loss of brain neurons, had long eluded researchers seeking to develop ways to slow the inexorable decline in cognitive function that so devastates patients and families. But with the idea of actually regenerating brain neurons, a new level of excitement and hope was raised in scientists who were dedicated to studying this and other neurodegenerative disorders.

So, now that neurogenesis was proven to be ongoing in humans throughout our lifetimes, the question became clear: What influenced this activity? Moreover, what could be done to actually enhance this process? And the fundamentally important question: What can we do to grow new brain neurons?

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David: Journey into Neurogenesis

During my college years, I had the opportunity to explore the brain using technology that was just in its infancy. It was in the early 1970s when the Swiss began to develop microscopes that could be used by neurosurgeons to perform delicate brain procedures. While this technology was evolving and eager surgeons in the United States were anxious to adopt this new approach to brain surgery, a problem soon became evident. Although learning to actually use the operating microscope was relatively easy, the neurosurgeons soon found they were becoming somewhat lost when it came to understanding the anatomy of the brain from this new microscopic perspective.

I was 19 and just starting my junior year in college when I received a phone call from Albert Rhoton, chairman of the Department of Neurological Surgery at Shands Teaching Hospital in Gainesville, Florida. Dr. Rhoton was leading the way for the expansion of the use of the operating microscope in the United States and wanted to create the first anatomy text of the brain, as seen through the microscope, to better aid surgeons as they began to embrace this new technology. I had applied for the position of student researcher and was surprised and gratified when he invited me to spend the following summer studying and mapping the brain. It was from this research that we eventually published a series of research papers and book chapters that gave neurosurgeons the needed roadmap to more carefully operate on the brain. In addition to anatomy, we also had the opportunity to explore and develop other aspects of microneurosurgery, including developing innovative instruments and procedures. Spending so much time behind the microscope, I had become quite adept at manipulating and repairing extremely small blood vessels that, prior to the

use of the microscope, would have been destroyed during brain operations, often with dire consequences.

Our lab had gained international recognition for its achievements in this new and exciting field and often attracted visiting professors from around the world. It was soon after a delegation of Spanish neurosurgeons had visited that I found myself accepting an invitation to continue my research at a prestigious hospital in Madrid, the Ramón y Cajal Center. Their microneurosurgery program was in its infancy, but their team was dedicated, and I felt honored to be assisting them in their groundwork efforts, especially in the work dealing with understanding the brain's blood supply.

The Spanish hospital was named to honor Nobel Laureate Santiago Ramón y Cajal (1852–1934), a great pioneer of neuroscience. Images of Dr. Ramón y Cajal were numerous in the hospital, and there was clearly a deep sense of pride among my Spanish colleagues that they could claim such an influential scientist as one of their own.

During my visit to Madrid, I felt compelled to learn more about Dr. Ramón y Cajal and came to deeply respect his explorations of human brain anatomy and function. One of his major tenets held that brain neurons were unique compared to other cells of the body, not only because of their function but also because they lacked the ability to regenerate. Thus, the liver, for example, perpetually regenerates itself by growing new liver cells, and there is similar regeneration of cells in virtually all other tissues including skin, blood, bone, intestines, and so on. But not so with neurons in the brain—or so stated Dr. Ramón y Cajal.

I admit that I was pretty well sold on his theory at the time, but I did wonder why it wouldn't make sense for the brain to retain the ability to regenerate itself, to have the ability grow new brain neurons. After all, researchers at the Massachusetts Institute of Technology had shown a decade before that neurogenesis, the growth of new brain neurons, occurred throughout the entire lifetime in rats.

Soon after I concluded my research in Spain, I was off to medical school at the University of Miami. And it was while learning histology, the microscopic study of tissues, that I realized how deeply entrenched in science was this notion that neurogenesis, while clearly defined in some animals, was not something that occurred in humans.

This teaching never sat well with me, especially when I thought back to my college years when the idea that "every beer you drink destroys 20,000 brain cells" was often kicked around late on a Friday night when surely more than that number had met their demise.

■ ■ ■

BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF)

A major component in this gift of neurogenesis—and it is a gift to be revered—is a protein called brain-derived neurotrophic factor (BDNF), which, as we read in previous chapters, plays a key role in creating new neurons. And it also protects existing neurons, helping to ensure their survivability while encouraging synapse formation—that is, the connection of one neuron to another—which is vital for thinking, learning, and higher levels of brain function. Studies have in fact demonstrated that BDNF levels are lower in Alzheimer's patients, which is no surprise, given our current understanding of how BDNF works.

But we gain an even greater appreciation for

the health benefits of BDNF when we consider its association with other neurological conditions, including epilepsy, anorexia nervosa, depression, schizophrenia, and obsessive-compulsive disorder.

BDNF Activation

We now have a very firm understanding of the factors that influence our DNA to produce BDNF. Fortunately, these factors are by and large under our direct control. Increasing your production of BDNF and thus increasing neurogenesis while adding protection to your existing brain neurons doesn't require that you enroll in a research study to determine if some new laboratory-created compound will enhance BDNF production. The gene that turns on BDNF is activated by a variety of factors, including voluntary physical exercise—animals forced to exercise do not demonstrate this change—calorie reduction, intellectual stimulation, curcumin, and the omega-3 fat known as docosahexaenoic acid.

This is a powerful message because all of these factors are within our grasp; they represent choices we can make to turn on the gene for neurogenesis. So let's explore them individually.

Physical Exercise: Laboratory rats that exercise have been shown to produce far more BDNF than sedentary animals. But, interestingly, animals forced to exercise produce considerably less BDNF than those who voluntarily choose to spend time on the running wheel. Researchers have shown that there is a direct relationship between elevation of BDNF levels in the voluntarily exercising animals and their ability to learn.

With the understanding of the relationship of BDNF to exercise, researchers have examined the effect of physical exercise in humans, both apparently healthy individuals as well as persons at risk or already diagnosed with Alzheimer's. The findings have been fairly remarkable. In a recent paper, Nicola Lautenschlager of the University of Western Australia found that elderly individuals who engaged in regular physical exercise for a 24-week period demonstrated an astounding improvement of 1,800 percent in memory, language ability, attention, and other important cognitive functions, compared with an age-matched group not involved in the exercise program. The exercise group spent about 142 minutes exercising each week—about 20 minutes a day.[3]

In a similar study, Harvard researchers found a strong association between exercise and cognitive function in elderly women and concluded, "In this large, prospective study of older women, higher levels of long-term regular physical activity were strongly associated with higher levels of cognitive function and less cognitive decline. Specifically, the apparent cognitive benefits of greater physical activity were similar in extent to being about three years younger in age and were associated with a 20% lower risk of cognitive impairment."[4]

These and other studies clearly indicate that exercise enhances brain performance and is directly associated with increased production of BDNF. Simply by voluntarily engaging in regular physical exercise, even to a relatively moderate degree, you can actively take control of your mental destiny.

Calorie Reduction: Another factor that turns on the gene for BDNF production is calorie reduction. Extensive studies have clearly demonstrated that when animals are fed a diet with reduced calories, typically by around 30 percent, their brain production of BDNF soars, along with a dramatic enhancement in memory and other cognitive functions.

But it's one thing to read research studies

involving rats in an experimental laboratory and quite another to make recommendations to human patients based on animal research. Fortunately, studies that show the powerful effect of reducing caloric intake on brain function in humans are now appearing in some of the most well-respected medical journals.

In a 2009 study, German researchers imposed a 30 percent calorie reduction on the diets of elderly individuals and compared their memory function with a group of a similar age who ate whatever they wanted. At the conclusion of the three-month study, those who ate without restriction experienced a small but clearly defined *decline* in memory function, while memory function in the group who consumed the calorie-reduced diet actually *increased* profoundly. In recognition of the obvious limitations of current pharmaceutical approaches to brain health, the authors concluded, "The present findings may help to develop new *prevention* and treatment strategies for maintaining cognitive health into old age."[5]

What a concept. Preventive medicine for the brain. While the tenets of preventive medicine have seemingly taken hold in so many other areas of health care, from heart disease to breast cancer, for some reason the brain has always been left out. Gratefully, with these new research findings, that is changing.

Further evidence supporting the role of calorie reduction to strengthen the brain and provide more resistance to degenerative disease comes from Mark P. Mattson at the National Institute on Aging Gerontology Research Center, who reports, "Epidemiological data suggest that individuals with a low calorie intake may have a reduced risk of stroke and neurodegenerative disorders. There is a strong correlation between per capita food consumption and risk for Alzheimer's disease and stroke. Data from population-based case control studies showed that individuals with the lowest daily calorie intakes had the lowest risk of Alzheimer's disease and Parkinson's disease. In a population-based longitudinal prospective study of Nigerian families in which some members moved to the United States, it was shown that the incidence of Alzheimer's disease among individuals living in the United States was increased compared to their relatives who remained in Nigeria."[6]

The Nigerians who moved to the United States were obviously genetically the same as their relatives who remained in Nigeria. Only their environment changed. And this research clearly focused on the detrimental effects on brain health as a consequence of the increase in calorie consumption.

While the prospect of reducing calorie intake by 30 percent may seem daunting, consider that Americans now consume an average of 523 more calories daily than in 1970. Current United Nations estimates show that the average American adult consumes 3,770 calories each day. In contrast, most health-care professionals consider normal calorie consumption (i.e., the amount of calories needed to maintain body weight) to be around 2,000 calories daily for women and 2,550 for men, obviously with higher or lower requirements depending on level of exercise. A 30 percent reduction of calories from an average of 3,770 per day provides 2,640 calories, still more than a normal minimum requirement.

Much of the calorie increase in Americans comes from our overwhelming increase in sugar consumption. The average American now eats and drinks an incredible 160 pounds of refined sugar each year, which represents a 25 percent increase in just the last three decades. This becomes particularly troubling in light of animal research done at UCLA showing a strong link

between "the typical diet of most industrialized Western societies rich in saturated fat and refined sugar" and reduced BDNF levels and, as expected, correspondingly reduced memory function.

Lowering sugar intake alone might go a long way toward achieving a meaningful reduction in calorie consumption; weight loss would likely be a side benefit. Indeed, obesity, in and of itself, is associated with reduced levels of BDNF, as is elevated blood sugar, a common consequence of obesity. Furthermore, increasing BDNF provides the added benefit of actually reducing the appetite.

We hope that this data and the desire to help your brain turn on BDNF production will motivate you to follow a reduced-calorie diet. But, if you want to do more, you can implement a program of intermittent fasting, which we will describe in Chapter 14.

Intellectual Stimulation: BDNF is described as a neuronal trophic factor, which means that it is a chemical that induces positive growth, health, and functionality in the target tissue—in this case, brain neurons. So it would only make sense to expect BDNF to increase when the brain is challenged. Just as muscles will gain strength and thus functionality when exercised, the brain also rises to the challenges of intellectually stimulating circumstances by becoming faster and more efficient as well as having a greater capacity for information storage.

These positive features are all facilitated by the increase in BDNF caused by stimulating activities. Inversely, it is likely that BDNF levels are low in individuals who spend several hours each day watching television, playing rote computer games, or otherwise engaged in mindless and passive activities.

An agile mind is also a good deterrent to help us avoid debilitating diseases associated with old age. Mark Mattson suggests that agility education and linguistics are two ways to keep an active, functional mind. He states, "In regards to aging and age-related neurodegenerative disorders, the available data suggest that those behaviors that enhance dendritic complexity and synaptic plasticity also promote successful aging and decrease risk of neurodegenerative disorders. For example, there is an inverse relationship between educational level and risk for Alzheimer's disease; people with more education have a lower risk. Protection against Alzheimer's disease, and perhaps other age-related neurodegenerative disorders, likely begins during the first several decades of life, as is suggested by studies showing that individuals with the best linguistic abilities as young adults have a reduced risk for Alzheimer's disease. Data from animal studies suggest that increased activity in neural circuits that results from intellectual activity stimulates the expression of genes that play a role in its neuroprotective effects. Levels of several different neurotrophic factors, including BDNF, are increased in the brains of animals maintained in complex environments, compared to animals maintained under usual housing conditions."[7]

Being involved in stimulating mental activities—such as problem solving, exploring novel environments, and, perhaps most important, meditating regularly—enhances BDNF production and creates a brain that is not only more resistant to deterioration but one that enables you to push the limits of day-to-day functionality. In this context, it is important to view meditation not as a passive activity but as an active, brain-stimulating exercise. Even among Alzheimer's patients, the rate of disease progression is dramatically slowed in those who engage in spiritual practices, which, again, is likely a consequence of increased BDNF.[8]

Meditation helps us visit the complex environment of the inner mind as well as the universal energy field. And, not surprisingly, this might well be the most powerful stimulant for BDNF production. Meditation-induced production of BDNF should be looked upon as the fertile ground into which seeds of spirituality-induced enlightenment are planted and flourish.

Curcumin: Curcumin, the main active ingredient in the spice turmeric, is currently the subject of intense scientific inquiry, especially as it relates to the brain. But curcumin isn't new to the medical research. In fact, practitioners of traditional Chinese and Indian (Ayurvedic) medicine have used it for thousands of years. Curcumin is known to possess a variety of biochemical properties that include antioxidant, anti-inflammatory, antifungal, and antibacterial activities.

But it is curcumin's ability to increase BDNF that has attracted the interest of neuroscientists around the world. Interestingly, in evaluating villages in India, where turmeric is used in abundance in curried recipes, epidemiological studies have found that Alzheimer's disease is only about 25 percent as common as in the United States. There is little doubt that the positive effects of enhanced BDNF production on brain neurons is at least part of the reason why those consuming curcumin are so resistant to this brain disorder.

Curcumin activates the Nrf2 pathway, a recently discovered "genetic switch" that works by turning on the genes to produce a vast array of antioxidants that protect mitochondria. We will discuss this more in depth in the next chapter. This ultimately protects the source of divine feminine energy that permeates our physiology and fosters well-being. But credit for this knowledge is best given to the ancients who describe in the Vedic texts turmeric's key role in cultivating relationships with the feminine form of divinity.

In contrast, Western civilization is only now recognizing that the feminine life force, in the form of life-sustaining mitochondria, are the conduits through which the healing, nurturing, loving energies of the biosphere flow. Interestingly, only recently have we begun to suspect that these seemingly simple intracellular particles may actually be thought of as cellular manifestations of qualities that were once ascribed to the Greek goddess Aphrodite, the Hindu goddess Shakti, the Buddhist goddess Kuan Yin, and Christianity's Mother Mary. With this knowledge, we become intimately connected with our history and rekindle our respect for the gift of feminine energy.
Docosahexaenoic Acid (DHA): Perhaps no other brain nutrient is receiving as much attention lately as DHA. Scientists have been aggressively studying this critical brain fat for the past several decades for at least three reasons.

First, more than two-thirds of the dry weight of the human brain is fat, and one quarter of that fat is DHA. From a structural point of view, DHA is an important building block for the membranes that surround brain cells. These membranes include the areas where one brain cell connects to another, the synapses. This means that DHA is involved in the transmission of information from one neuron to the next and thus is fundamental for efficient brain function.

Second, DHA is one of nature's important regulators of inflammation. Inflammation is responsible for a large number of brain maladies, including Alzheimer's, Parkinson's, attention deficit hyperactivity disorder (ADHD), and multiple sclerosis. DHA naturally reduces the activity of the COX-2 enzyme, which turns on the production of damaging chemical mediators of inflammation. This inhibits the enzyme and helps put out the fire in our brains.

The third and perhaps most compelling reason for studying DHA is its role in modulating gene expression for the production of BDNF. Thus DHA helps orchestrate the production, synaptic connection, and viability of brain cells while enhancing functionality.

In a recently completed double-blind interventional trial called the Memory Improvement with DHA Study (MIDAS), some members of a group of 485 healthy individuals with an average age 70 and mild memory problems were given a supplement that contained DHA made from marine algae and some were given a placebo. After six months, not only did blood DHA levels double in the group who received the DHA but the effects on brain function, compared with those who received the placebo, were outstanding. The lead project researcher, Karin Yurko-Mauro, commented, "In our study, healthy people with memory complaints who took algal DHA capsules for six months had almost double the reduction in errors on a test that measures learning and memory performance versus those who took a placebo. . . . The benefit is roughly equivalent to having the learning and memory skills of someone three years younger."[9]

Humans are able to synthesize DHA from a common dietary omega-3 fat, alpha-linolenic acid. But so little DHA is produced by this chemical pathway that many researchers in human nutrition now consider DHA to be an *essential* fatty acid, meaning that health maintenance requires a *dietary* source of this key nutrient. Data also show that most Americans typically consume an average of only 60 to 80 milligrams of DHA daily, less than 25 percent of what researchers consider to be an adequate intake of 200 to 300 milligrams each day.

BDNF and Brain Protection

BDNF is important not only in neurogenesis and neuroplasticity but also in protecting delicate neurons from being damaged by a variety of insults, including trauma, transient reduction in blood supply, and, perhaps most important, environmental toxins. Indeed, in laboratory studies, rats and even primates with higher levels of BDNF are far more resistant to brain-damaging toxins than animals with low or normal levels.

One important neurotoxin often used in laboratory animal experiments, especially those designed to evaluate the protective effectiveness of BDNF, goes by the abbreviation MPTP (which stands for its chemical designation). This neurotoxin has the relatively unique ability to specifically damage a part of the brain in humans, as well as in several animals, that is associated with Parkinson's disease. Therefore, MPTP is often used to measure the possible benefits of pharmaceutical preparations to defend the brain against neurotoxins. But, unlike many other investigations that are developed in laboratories, the MPTP street story is far more intriguing.

In the early 1980s, seven individuals ingested a street drug they thought was similar to heroin. Instead, due to an error in the illicit production of the heroin-like drug, the substance they took was contaminated with MPTP. Shortly thereafter, they were diagnosed with Parkinson's.

While this was devastating to these people, it opened the door for researchers to develop a powerful experimental model for the disease as described by neurologist J. William Langston in his book, *The Case of the Frozen Addicts: Working at the Edge of the Mysteries of the Human Brain* (1997), which later became the subject of two NOVA productions by the Public Broadcasting Service (PBS).

Langston found that treating squirrel monkeys with MPTP caused almost immediate development of Parkinson's, with damage to the animals' brains occurring exactly in the same area as in humans with the disease. Subsequent experiments with other animals generated the same results. Langston and others ultimately concluded that MPTP destroyed neurons by destroying their specific source of energy production, the mitochondria. Thus, MPTP proved to be a mitochondrial toxin specific for the area of the brain associated with Parkinson's.

Once it was discovered that MPTP selectively damaged mitochondrial function and produced Parkinson's, researchers focused their efforts to learn how they could block the damaging effects of this neurotoxin and, presumably, by extension, reduce the damaging effects of pesticides in general. Various drugs were developed, including Deprenyl, that, at least in animals, held promise of providing some protection for mitochondrial function against toxins like MPTP.

While human trials showed only modest benefit, the most dramatic neuronal protection against MPTP was not found in some extrinsic laboratory-produced, patentable drug, but with BDNF, a substance already within our physiology, encoded in our own DNA, a gift not purveyed on a prescription pad but from nature.

Study after study has since confirmed that BDNF provides almost complete protection of brain cells not only from MPTP but from a variety of other mitochondrial neurotoxins. And in many of the reports, the methods by which BDNF is increased also come naturally: increased physical exercise and calorie reduction.

Thus, turning on BDNF production, through natural means and lifestyle decisions, provides our brains with powerful protection against the ubiquitous onslaught of mitochondrial toxins, such as commonly used pesticides, to which we are exposed on a daily basis. Obviously, choosing to eat organic foods is helpful, but we cannot totally eliminate our exposure to these dangerous and, yes, brain-damaging chemicals.

David Perlmutter is a Board-Certified Neurologist and Fellow of the American College of Nutrition who received his M.D. degree from the University of Miami School of Medicine where he was awarded the *Leonard G. Rowntree Research Award*. After completing residency training in Neurology, also at the University of Miami, Dr. Perlmutter entered private practice in Naples, Florida. Dr. Perlmutter is a frequent lecturer at symposia sponsored by such medical institutions as Columbia University, the University of Arizona, Scripps Institute, New York University, and Harvard University. He has contributed extensively to the world medical literature with publications appearing in *The Journal of Neurosurgery, The Southern Medical Journal, Journal of Applied Nutrition,* and *Archives of Neurology.* He is the author of: *The Better Brain Book* and *Raise a Smarter Child By Kindergarten,* and is recognized internationally as a leader in the field of nutritional influences in neurological disorders. Dr. Perlmutter has been interviewed on many nationally syndicated radio and television programs including *20/20, Larry King Live, CNN, Fox News, Fox and Friends, The Today Show, Oprah, Dr. Oz, Montel Across America* and *The CBS Early Show.* In 2002 Dr. Perlmutter was the recipient of the *Linus Pauling Award* for his innovative approaches

to neurological disorders and in addition was awarded the *Denham Harmon Award* for his pioneering work in the application of free radical science to clinical medicine. He is the recipient of the 2006 National Nutritional Foods Association Clinician of the Year Award and was awarded the 2010 Humanitarian of the Year award from the American College of Nutrition on October, 2010.

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Functional Medicine and the Patient-Physician Relationship

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"I remember lying there and watching an anthill for hours. I would watch them scurrying back and forth, carrying things, digging new tunnels, and finally it hit me: they are the things that are biting me."

– *Jack Handey* (from *What I'd Say to the Martians*)

"The idea of autonomy denies that we are born into a world that existed prior to us... We are basically dependent beings: one upon another, and each on a world that is not of our making."

– *Matthew B. Crawford* (from *Shop Class as Soulcraft*)

What is it about ants? We're the geniuses, but you don't see them flailing to contain their health care costs. If America's health system were an anthill, and we laid around for decades watching how work got done, it would finally hit us: ants are better organized, and their bites don't come out of our wallets.

Societies succeed when their members can depend on each other. Businesses succeed when they make money by hook or by crook. Our health care system is increasingly dominated by corporate entities bent on maximizing their revenues. The system as a whole is torn between using best clinical practices to serve the health interests of people, and using best management practices to make hay while the sun shines.

In his book on the relationship between education, work, and the virtuous life, political philosopher and motorcycle mechanic Matthew Crawford makes clear that along any path to human flourishing, our best thinking will fail us unless we turn it into ethically disciplined action. Of the classes of wisdom gathered by humankind, we should expect our best medical traditions to uphold an ethic that recognizes our dependence on the world and each other.

If we shine the philosopher-mechanic's flashlight of truth over to our health system, we can see its deepest flaw: a physician workforce increasingly divorced from the mechanics of healing.

In this essay, I contrast the modern doctor-patient relationship with the age-old ideal of a tradesman whose primary aim is to develop effective solutions at a fair and reasonable price.

The covenant between physician and patient is more than a business relationship – it is a deeply personal and moral relationship whose success requires expertise, virtue, and, in many cases, protection from corporate models whose policies impede the mechanics of the healing process.

The Mechanics of Healing

Health is a state to be achieved. Wellness is a way of being and coping with life. In living systems, health and wellness are built on mechanisms that:

1. Minimize the loss of functional integrity in the presence of disruptive forces.

2. Avoid or escape disruptive tensions so healing systems can focus on repairing what's been damaged, allowing function and balance can be restored.

Wellness depends on coordinated fluctuations between phases of damage control and restoration. Balance within the system as a whole is served when the damage control and restoration teams have adequate resources and time to fully perform their roles. This is true whether the system as a whole is you, your family, your community, your society, or your planet.

Medical students are good at doing what they're trained to do. Because most are not trained to develop wellness promotion skills, most are not good at promoting wellness. They enter the profession with little exposure to the ways of wise self-care, which is unfortunate because wise self-care is emerging as a biological and ethical imperative for all of humanity.

Crawford concludes that an important part of living a dignified life of excellence in action is learning how to fix and maintain our stuff. This builds self-reliance in the art of maintenance and repair, and it builds expertise and skills that can be taught or shared – a capacity that is essential in a world whose interdependent systems and relationships define our wellness potential as a species.

As health care costs continue to inflate beyond what social systems are able to withstand, and with health care results awash in mediocrity, it becomes especially important to learn how to fix and maintain the stuff you're made of – the biophysical wetware, loaned to you by nature, that is your bodymind.

Perhaps the creative force that brought nature into being acted so in order to evolve interdependent living systems, from which an intelligent race of creatures might achieve a position of dominance, rise to the occasion, and become faithful stewards of health and wellness within their sphere of influence. Should such a species emerge wise enough to organize its members around principles of health and wellness, its functional role in the cosmic order, and its noble destiny within the earthly scheme of living systems, would be fulfilled.

If health and wellness are core issues for which humanity must seek wisdom in this turning point of a century, who are the experts to whom we should turn? For ages men and women have depended on physicians for advice on getting and

staying well. Now, when we need it most, our physicians are increasingly too busy fighting disease and insurance companies to give the subjects of health and wellness their due.

Medical specialists focus on specific parts of the system rather than the system as whole. Their expertise is deep, but too narrow to serve as a foundation for wellness. It is the medical generalists – internists, pediatricians, and family physicians – who are trained to assess each person as whole. They are taught to view each patient as a unique being whose roles in life are linked to a family, a community, and a job (paid or unpaid), as someone whose health depends on interactions happening at biological, psychological, and social levels.

In truth and practice, our primary care workhorses are allotted too little time to hone their integrative problem-solving skills. They're caught up in business models that won't grant them the space needed to fully engage the mechanics of healing.

If healing requires restoring metabolic balance that's been lost, the healer-mechanic's first task is to construct your health narrative – the arc of episodes that describe how wellness was lost, starting from the time you last felt perfectly well.

Rendered in this way, the healer-mechanic can scrub your health narrative for the clues behind the details, looking for patterns that point to when, how, and why given metabolic systems began losing functional integrity. The long arc of your history, along with a focused physical exam, will prompt recommendations for laboratory tests or diagnostic procedures whose purpose is to better clarify your health situation.

The mechanics of healing often go awry at this step in the process. The healer-mechanic limits himself to testing and procedures whose results have reasonable potential to guide the care process. The professional churner, on the other hand, places the interest of his franchise ahead of your health needs. Your procedural workup is ethically compromised and economically skewed toward the overuse of diagnostic testing and of treatments that serve little purpose beyond boosting the churner's bottom line.

The goal of the healer-mechanic is to achieve a sufficiently rich understanding of what's wrong in your individual case, and to accomplish this before jumping to a solution. Snap medical judgments contribute to the rising costs of managing chronic health problems. Under-evaluation is as expensive as over-treatment.

Another cause for healing to go awry at this step the doctor who feels pressured to minimize malpractice risks no matter the cost. This results in a defensive style of medicine where decisions are made after a fast-forward imagining of how a plaintiff's attorney will play your case to a jury. Ironically, the best way to lower the risk of malpractice is to practice like a healer-mechanic whose expertise and virtues aim for service excellence.

The healer-mechanic's assessment is integrative by nature, and it leads to an integrative care plan that addresses therapeutic lifestyle change, nutrition counseling, manual therapies, physical activity, stress management, the use of natural therapies and, when clinically warranted, medication or consultation with a specialist.

As your integrative care plan unfolds, you and your physician monitor what progress you're making toward your wellness goals. Using a systematic wellness support program to stay on track, you follow up with your physician or allied team members at scheduled intervals. Members of the team communicate and help analyze your observations about how you're responding to your care plan, looking for dials to adjust in ways that will keep you moving ever closer to your wellness goals.

Most primary care physicians have no trouble endorsing this way of conceptualizing the mechanics of healing. The difficulty arises when they try to implement a method of practice focused on wellness when they're already caught up in the chop shop pace of disease management interspersed with urgent health problems. Squeezed by the overhead it takes to offer their full basket of services, they are hard-pressed to offer a pace of service that does justice to the noble traditions of the healing trade.

This is not what the medical student who chose primary care bargained for. As residents, they are quick to grasp that the whole person rhetoric of primary care is highly inconsistent with facts and reality on the ground. An assembly line mindset fouls the habitats within which primary care doctors are expected to advance the ecology of health and wellness.

Within our primary care settings, from the smallest community storefronts to the most prestigious medical center office suites, you will find patients moving from place to place in search of wise clinical guidance. In these habitats you'll also find families, communities, and businesses small and large wading through a swamp of rising health costs where, if the crocodiles don't get them, the mosquitoes will.

Exploring Our Wellness Habitats

To survive, a species must either adapt to changing conditions within its habitat, or find a friendlier habitat. The species of medical professional known as the primary care physician is endangered because their habitats are under siege. These environments can defile the meaning of wellness. Too many patients, too much overhead, and working conditions that at times defile the meaning of wellness.

Primary care refers to a health care source that serves as someone's first point of contact with the health care system. In theory, primary care physicians evaluate and manage a wide scope of acute and chronic health problems; they offer periodic health evaluations and perform some early detection procedures; they provide some preventive counseling in bits and fragments, and they coordinate care in ways that address the health needs of the person as a whole, in the context of his or her family and community.

This makes them too busy to deeply engage the art and science of healing. Time pressures limit primary care doctors to a checklist style of revolving door care. As a result, patients turn to other species of health care practitioner, in search of habitats more conducive to an in-depth, personalized approach to wellness. This is a boon to practitioners of complementary and alternative medicine, yet demand for primary care services will balloon as millions without health insurance gain access to health care as a result of health care reform.

This creates demand for nurse practitioners and physician's assistants, but it's unclear how fast we can pump them into place when most states license these practitioners to provide billable medical services only under a physician's supervision, and the primary care physician base, which has been shrinking for more than a decade, will take years to recover.

Primary care doctors are outnumbered several thousand to one by patients needing primary care. With over thirty million new patients gaining access to care, overworked general internists, family physicians, and pediatricians will have to bar the doors or be swept away. Universal coverage does not equal universal access. Coverage does not equal cost-effective results.

By necessity we'll need to involve other species of community-based health practitioner in the

delivery of primary care. Nutritionists and dietitians, physical therapists, chiropractic physicians, naturopathic physicians, acupuncturists, and other health practitioners have for some decades now been delivering health services that overlap with primary care.

What good alternative health practitioners generally lack is credibility within the wider medical community. The reasons are mainly political, and this is unfortunate because there are thousands of highly capable and professional alternative health practitioners standing ready to complement primary care and help accomplish a shift to a wellness paradigm.

The people who become patients of alternative health practitioners are generally well satisfied with the process of care. In alternative health habitats, the pace of care is typically less hurried and it involves more active listening and closer follow-up than the primary care model.

Whether alternative health outcomes are the same, better, or worse is not clear, but studies of several common chronic medical conditions indicate that less invasive, natural approaches are capable of producing as good or better results at a significantly lower cost compared to conventional care.

Insurance coverage for alternative medicine services is spotty, but that hasn't stopped American health care consumers from spending upwards of fifty billion on alternative health products and services each year. With proper coordination and legislative support, alternative health and primary care professionals could become key allies in an effort to create wellness habitats that work for the American people.

So what are medical schools, residency programs, Congress, and health lobbies doing to shore up primary care and move the system toward wellness promotion?

Not much.

The Patient's Dilemma

Seen from one lens, the American health care system is an engine that runs one of American society's most productive economic sectors. Seen from another, it is a system run amok, an operation where cost-shifting and organizational inefficiencies daily trump the interests of patients and their need for wise health counsel, while neglecting the interests of primary care doctors and their need for adequate time to assemble deep and clinically meaningful narrative understandings of what's going on with each patient.

And so a divide is forming between primary care doctors and their patients, formed by third-party pressures on the doctor-patient relationship. High intensity third party pressures on doctors are less than a generation old. They persist because they enhance profit margins for the third parties.

The doctor-patient relationship is the core process by which humanity discovers paths to wellness. How can wellness operate as an organizing principle for our business and social institutions if we can't make it an organizing principle for decisions made in the very rooms patients enter in search of health wisdom from their primary care doctors? Most primary care physicians are forced to scribble or tap and make judgments in a hurry in order to meet third party demands. This is the root of the patient's dilemma.

Health care now accounts for one of every six dollars Americans spend in a year and it's projected to reach two bucks of every five within a few years. We' throw more than $2.5 trillion a year at a "name the disease, name the drug for the disease" approach to chronic illness. If we want better clinical results at a lower cost, we have to get primary care teams and their patients

together on the side of developing wellness habitats that support the mechanics of healing.

We're spending too much money on unnecessary drugs and procedures and too little time attending to our personal health and wellness responsibilities, wondering when somebody is going to fix our health system. Meanwhile our food chain, our waters, our soils, and our air are filling up with hazardous molecules that have no business in our bodies, courtesy of an industrialized, materialistic way of life that is progressively toxic to the living systems upon which we depend.

Our children are acquiring belly fat, allergies, asthma, attention deficits, and other health problems at record rates. Could their junk nutrition and toxic exposures be harming their metabolic integrity earlier in life than we've witnessed before? If so, our child health problems are early detection markers indicating that our technologies and consumer appetites are promoting biological dysfunction on an epic scale. The public has too few places to turn for wise medical guidance on what to do about these spreading environmental toxicities.

Our bodies, our families, our workplaces, and our communities are being physically, chemically, and emotionally stressed out of metabolic balance. What force of inertia allows our overfed health sector to keep greasing its chin at the expense of the American people?

The answer is the same force that would send our economy off a cliff by repackaging mortgage debt and selling it for ten times what it was worth; the same force that would split the relationship between doctor and patient into opposing sides because it helps a third party's bottom line; the same force that would have us pretend that in our search for solutions to complex health problems, we have no obligation to engage in wise self-care or responsible stewardship of the Earth.

There are no simple solutions for complex health problems. If metabolic systems are losing functional integrity, your health problems are complex, and they're headed toward becoming chronic. When metabolic systems lose enough degrees of freedom for solving problems on their own, the system as a whole becomes chronically ill. Only in a tortured corporate logic is turn-style medicine a match our nation's chronic illness burden.

When you present to a new doctor with a multidimensional illness, you are typically met with the question, "What brings you in today?" Medical students are trained to open visits this way, as doing so is a polite way to invite the patient to describe what's wrong.

For the hurried doctor it's a polite way to trap the patient into identifying the single issue that will be the topic of another rushed encounter – the doctor enters the room in hurry-up offense mode with a checklist of things to do that competes with your list of questions and your defensive abilities to get them answered. Third parties profit nicely on corrupted mechanics of healing.

Chronically ill patients don't have single issues. Navigating through the health care system to a wellness destination poses a major dilemma for those burdened with chronic illness. Though surrounded by doctors, they struggle to find a single one who possesses integrative expertise and whose practice design makes that expertise accessible.

People with a chronic illness want a clinical problem solver who can resist jumping to solutions before fully understanding the problem. To fully understand the problems of chronic illness, a physician must get the patient's whole story.

Getting stamped with a diagnosis is something far short of a deeply nuanced explanation for what went wrong and why. To move beyond diagnosis toward a working explanation of your chronic illness, wise health consumers settle for nothing less than a clinical problem solver who *wants* to hear your story from the beginning.

Your health narrative contains essential clues that help integrative problem solvers better understand what might be done to restore and maintain the functional integrity of your system as a whole.

Proper treatment and monitoring of chronic health problems cannot be shoehorned into bite-sized, widely spaced visits. With each trip to the office, your goal, as the owner of a chronic health problem, is to help your doctor or health practitioner extract a clinical impression that has some power to explain the root dynamics of your illness. A healer-mechanic will settle for nothing less than the best possible working explanation for why you became ill.

Where chronic illness is concerned, you and your doctor or health practitioner should come to reasonable agreement about your wellness goals, and about being accountable to each other in your efforts to reach them. Expect a few ups and downs as the care process unfolds. Lost prescriptions, phone delays, missed appointments, lab errors – a myriad of frustrations can stress the relationship.

Remember that you may not be the only one who gets worn down by your complex health problems – especially when you are unwilling to hold up your end of the bargain by changing the way you live, and perhaps the way you interact with your doctor. Since therapeutic lifestyle change is the foundation of nearly every integrative care plan, your job is to engage the task of making healthy lifestyle changes.

Natural therapies, including the targeted use of dietary supplements, often play a role in systematic efforts to achieve wellness goals. There are times when prescription drugs are warranted. When that's the case, you should feel confident that the prescription was needed because it fit an explanation of what's going on and what ought to be done about it, not because the doctor made a default judgment to avoid running behind.

It takes a doctor roughly thirty seconds to write or transmit a prescription, where it might take thirty minutes to explore the nuances of your illness and discuss what lifestyle changes and natural therapies might do to help your metabolic systems perform better as a team. For doctors in a hurry, prescription drugs have a way of winning by default. The cost curve bends ever upward.

Accepting responsibility for the lifestyle changes that wellness requires means changing certain behaviors. Wise health consumers must not only understand the pressures facing primary care doctors – they must develop the skills needed to obtain quality clinical assessments and care plans.

Since medical professionals are often too busy or too strapped to provide systematic wellness support, health consumers are often left to their own devices. Options here include finding the right online or community-based wellness support system.

The truth is, most doctors have plenty of wisdom to share – accessing this wisdom is the problem.

The Doctor's Dilemma

Surveys in the United States and elsewhere indicate that three out of four doctors now discourage their children from entering a career in medicine. In 2008, only two percent of internal medicine residents chose to practice general

internal medicine. The other ninety-eight chose to become medical specialists.

The reason for this plummeting interest in primary care medicine as a career path is clear. Medical students and residents see many primary care doctors scrambling to survive their decisions to attempt satisfying careers in the primary care trenches. The primary care doctor's dilemma is figuring out how to acquire the mindset and secure the practice systems needed to thoroughly assess which of your metabolic systems are losing functional integrity and why.

In the medical professional food chain, generalists are bottom feeders. The pay is low and the prestige is lower. Primary care doctors work as hard as most specialists but for considerably less reward. For many patients, the primary care experience is like being rushed through your dinner so more patrons can be seated.

The operational complexity of a typical primary care business far exceeds that of most specialty or hospital-based practices. Primary care practices generate more un-reimbursed work requests than any medical business known to man.

A typical day may entail a dozen or two phone calls and emails (a few marked urgent), requests for a letter of medical necessity or referral, responses to faxed prescription refills and calls from pharmacists about prescription denials, a trail of voice and emails, and a stack of pre-authorization forms for pills or procedures – poured on top of a brimming schedule in which each patient expects 100 percent of the doctor's attention, an extra few minutes for questions, and no errors.

Problems directly related to a specialist's care often fall into the lap of a primary care doctor when, despite bad outcomes, the specialist concludes that his work is done. To prevent their primary care operations from falling apart, practice managers hire support staff to keep up with the un-reimbursed workload, subtracting the cost of added help from the doctors' pay.

There are also billing and collection costs to absorb. Insurance company denials and underpayments create a drag on the month-to-month viability of many medical practices – and not just primary care. The documentation, coding, and billing requirements of each payer differ and their rules can change at any time.

Consumer-driven high deductible health plans and health reimbursement accounts force primary care doctors to become collections specialists; their staff make calls and pull teeth to sort out how much a patient owes when, with the practice absorbing the costs of delay. Practices slow to adapt to this change alone have gone belly up.

These pressures give many primary care doctors little choice but to adopt an assembly line style of care. A group may decide to pick up an already frenetic pace and become like a restaurant whose goal is to turn as many tables as possible. If the practice continues to operate in the red, it may consult a practice management expert. A few weeks and a few grand later, a report appears exhorting the doctors to "see more patients."

Another dilemma for the primary care doctor is figuring out how to get rewarded for delivering a personalized, in-depth approach to the evaluation and management of chronic health problems. Changing insurance reimbursement rules so primary care doctors get paid not by the duration of the visit, but by the medical conditions addressed during the visit, would be a more rational and socially cost-effective way to reward them for their expertise and service.

Let's say you have hypertension, joint pains, insomnia, and an irritable bowel. If your primary

care doctor tries to manage them all in a fifteen-minute visit, each problem is likely to get shortchanged.

If she takes the time needed to do a thorough job, she'll risk running behind, adding to her stress. If she schedules patients like you for forty-five minutes, she'll make less money because two forty-five minute visits don't yield as much insurance payment as six fifteen-minute visits – even though the total time spent on care is 90 minutes. From a medical practice management perspective, volume trumps value.

In many cases the busy primary care doctor will opt to refer to specialists for no other reason than she doesn't have time to manage your multiple problems and she doesn't want you to feel shortchanged. She'd take the time needed to address your concerns one by one if insurance companies paid her a separate fee for addressing each of your four problems.

The insurance company would save *big* money by preventing unnecessary referrals. Your doctor would see fewer patients in a day. Medical students might even become more interested in the field of primary care. Even with such healthy logic behind policy proposals like these, as our health care reform slugfest demonstrates, once cash flow channels are cut into the health system terrain, they're very hard to change.

A little empathy for the exasperation that primary care generalists are feeling can help the wise health consumer get more than an extra minute or two – it'll reinforce for your doctor why you deserve intense focus even on a bad day.

The sad truth is that most primary care doctors are wise generalists whose wisdom is inaudible in the breathless hamster wheel settings that primary care habitats have become. Empathy is an important form of reward for the harried but caring doctor.

Like all doctors, primary care doctors have to meet continuing education requirements to remain credentialed with their hospitals and health plans. Yet much of this education reinforces a "name the disease, name the drug for the disease" practice routine. Though integrative medicine education is making some headway, primary care physicians typically must go out of their way to find it.

Perhaps the biggest challenge faced by today's primary care doctors is figuring out how to avoid burnout. Imagine what will happen as the wise old generalists retire just as the twenty-year long, 75 million strong Boomer contingent hits the system demanding nuanced medical opinions for everything from heart disease to hangnail.

If Americans who've been neglecting their chronic health problems are able to get health insurance coverage, it will release a torrent of pent-up demand for primary care – a surefire recipe for burnout.

To shore up the primary care fleet's ability to handle this pent-up demand in a cost-effective way, primary care practice models should be exploring ways to incorporate an integrative medicine approach that uses allied health practitioners to support a wellness model for the prevention and care of chronic illness.

In February 2009, a group of integrative and functional medicine dignitaries including Mehmet Oz, MD, Dean Ornish, MD, Andrew Weil, MD, Mark Hyman, MD, and Jeffrey Bland, PhD, met with members of the Institute of Medicine, Congress, and the White House, where they made a compelling case for promoting a more personalized, integrative, science-based, wellness-oriented, results-driven approach to health care. They made a compelling case for an integrative, functional approach to health and wellness

If the health care sector resists, we'll have to wonder what forces are preventing integrative medicine from helping primary care groups compete for patients in mainstream medical habitats. Pity the front line generalists for the pounding they will take if health care reform unfolds without sending them integrative medical reinforcements.

Whatever desire they'll have to deliver integrative care to whole persons is going to be swept aside by the public's need for at least a few minutes of access to an overworked primary care provider every few months. Perhaps access to a harried, impersonal, checklist style of gatekeeper medicine is better than no access at all, but we can do better.

Finding a Path to Wellness

That we depend on a world that is not of our own making is no small point. Any discussion of health and wellness, or of expertise and virtue, must begin with the plain fact that some creative force acted first upon us, and that no matter how self-reliant we become, we remain dependent on each other and the living systems of the Earth.

The entirety of our non-fictional experience of the world exists in a fairly specific physical and historical context:

> Some ten billion years after the universe began under mysterious circumstances, self-reproducing living systems began jockeying for habitat on this planet. These habitats are now being fouled or destroyed in businesslike fashion by humanity. As the Earth's living systems tangle with our toxic industrial presence, humanity is bulldozing its way into the future with no apparent aim and with no effective means by which to discern and fulfill a unified sense of its functional purpose in the cosmic order.

Natural history is a tale about species and their various quests to find wellness and generational longevity within some kind of habitat. Most of the Earth is now our habitat. Though we dominate the world of living systems, we have yet to fully grasp the meaning of wellness as a healthy interdependence of widely connected systems.

When the implications of what wellness requires of us are finally understood, we will begin to discern humanity's functional purpose in the unfolding history of life on Earth. Only when we decide to make health, wellness, and ethics matter will we possess the wherewithal to fulfill our higher purpose – at home, at work, at leisure, and within the emerging cosmic order.

To find its path to wellness, humanity needs to close a few divides. The divide between doctors and patients is emblematic of the divide between humanity's industrialized, materialistically skewed relationship to the world, and the wellness we seek. But it is not the only divide in need of repair.

Congress cannot legislate root cause solutions to the root level problems in our health care sector. What's needed is an alliance of wise health consumers able to use their collective economic leverage to make health, wellness, and ethics matter in our national life, and in our globalizing world. The days where entrenched special interests and cost-shifters have the field to themselves must come to an end. Only by rewarding health value creators based on their results will wisdom and wellness prevail.

Our society needs a new health care game plan – one that nourishes, cultivates, and grows more sources of bodymind wisdom – more community-based medical homes where an integrative clinical

mindset can flourish in a habitat fenced off from the business and bureaucratic mentalities that corrupt the mechanics of healing. Only then can we create a health system that delivers more wellness at less cost.

We can start by supporting new forms of strategic partnership between primary care, integrative medicine, and the best talent in the alternative health community. This will help create new community-based networks where primary care and wellness support systems are fully aligned.

The fight for health and wellness is not just about the doctor-patient relationship – it's about the health of living systems and fate of future generations. If the principles of metabolic balance that balance damage control and restoration in biological systems don't begin to operate in the cultural, political, economic, and environmental dimensions of our lives, our legacy for future generations will be that we sat and watched as our presence became the driving source of inflammation and decay in the world.

As you learn more about how your metabolic systems work together to make health possible, a bigger picture begins to emerge. In this picture you'll see how the principles of metabolic balance that operate within you are the same principles that can underwrite global health, security, and prosperity.

Never has it been so necessary, or so possible, for people to pool their efforts to seek wisdom, value health, integrate, and aim higher.

Keith Berndtson practices integrative medicine in Park Ridge, Illinois. In 1996, after ten years in family medicine and corporate health, he chose a road less traveled. On this road he came to realize the wisdom and value of the integrative and functional medicine traditions. He uses this experience to explore the wider implications of a clinical systems biology approach to wellness.

His medical practice, Park Ridge MultiMed, uses functional medicine principles to evaluate and treat patients with medically unexplained and non-responsive forms of chronic illness.

Berndtson founded *onebodymind.com* to supply innovative online tools for people interested in a deeper, more effective approach to health education, self-care support, and the stewardship of living systems. The website is also ground zero for a social network that will help prepare the way for the modern quest for health and sustainability.

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Mending the Mind-Body Connection for Better Health

Susan Allen, RD, CCN

The integrative or functional medical professional appreciates the value of a dive-deep and go-broad approach to patient care. Unlike their traditional medicine counterparts, who rush their patients into sticking *only* to the 'problem of the day', these doctors actually encourage their patients to tell the whole story. This paradigm shift towards more comprehensive, patient-centered care is a breath of fresh air.

This section is written for these dive-deep and go-broad practitioners. The ones with fierce integrity; the ones who recognize the tremendous worth brought to their patients when they care enough to go against the insurance-mandated medical model. These practitioners are known by their first hallmark question, "When was the last time you felt perfectly well?"

Indeed, these are the healers who utilize a broader assessment process and sometimes unconventional means to treat the chronically ill. In many cases, they are more successful than their traditional medicine counterparts and often with less chemical and radiographic assault, resulting in fewer side effects. These doctors accept that nutritional status and toxic burden have a much stronger role in health and chronic disease and make this a large part of what is addressed in their patient care model.

We all know stress is connected to health. However, this may be the one area not addressed deeply or fully enough by practitioners. The missing piece, or at least underutilized in many settings, is the ability of the practitioner to tap into the power of the mind-body connection where stress hits hardest; to identify, and when necessary, mend the broken bond that many individuals have in this area.

The purpose of this article is to focus on this missing piece and to better position practitioners to help overturn patient roadblocks in the healing process. It will examine a different approach than just looking at the physical manifestations of symptoms. Instead, this article will discuss the often underestimated, under-addressed, ever intertwining, and seemingly infinite emotional and spiritual roadblocks to better health.

The mind-body-spirit connection is probably the most misunderstood and undervalued piece of the patient care model that can have the most profound effect when fully explored. Unfortunately, for many, this connection is addressed simply by a possible

referral to the psychotherapist and probably a prescription. Yes, of course, therapy and psychotherapeutic medications certainly have their role. It just seems that there is hardly any meaningful attention paid to the connection between emotional and physical health by health practitioners.

Mind you, I do not profess to have a specialty in psychology. However, I am pretty intuitive and have many personal and professional experiences that have shaped my thoughts and recommendations you will read here. I consider it a responsibility of the integrative or functional medicine professional to shine this light of awareness into their patient care model. It is a necessary part of a patient's "whole story" encouraged with a deep-drive approach. I also think nutritionists are well placed to explore this category as we typically have more time with patients — and just one reason (of many) why I believe all MDs should work in tandem with a nutritionist.

Of course, as a professional, you must stay within your comfort level and give out referrals as needed. However, if you at least take the time to have a better understanding of the mind-body-spirit connection, you will have a greater awareness of possible disconnects that have led to roadblocks that you may be able to help overturn.

The assessment process is your tool to discover more information for this task. Questions you might ask, either orally or on a written questionnaire, should cover subjects like happiness/satisfaction levels of work and relationships (love, social and family). Ask about stress levels, now and in the past, such as moving or a divorce. Ask about previous or current emotional traumas or losses, like the death of a loved one or a business failure. These are all areas where you may find potential connections and better understand how and why roadblocks are created.

Sometimes, your role will only be to introduce the concept of the possible connection. Remember to only operate at your comfort level. If you sense deep or more comprehensive work needs to be done, you certainly must refer out.

For the remainder of this read, I will detail connections for your awareness and discuss those places where you may be able to help overturn the roadblocks. These are basics that almost anyone can try. You may recommend your patient read a particular book. You may refer out for psychotherapy, and, if you think it may be related to an energy block, enlist someone who does clearing or other spiritual or energy practices to assist in the case. Bear in mind though, your work has only just begun. There is much you can do as a practitioner throughout the process. It is key to understand how roadblocks are created and how to break them down.

Roadblocks to Better Health

While roadblocks created by patients can make our job a little harder, it is almost never impossible to help our patients break through to relief and ultimately better health. People are often quite unconscious about their responsibility for these roadblocks, at least at first. It is important to understand that roadblocks are often created out of fear. [1]

As these roadblocks are influenced by outside and by deep inner stresses, this article addresses what I consider to be the top seven roadblocks:

1. Addiction and self-defeating behavior
2. Negative thinking
3. Judgment of others
4. Self-judgment, low self-esteem, blocking happiness and joy
5. Inability to forgive, guilt, and shame
6. Stuck in the past, worry of the future, unable to be "in the now"
7. Isolation, lack of faith, or spiritual disconnection

When referring to the roadblocks, there is some overlap. Nevertheless, they are all significant. Along the way you'll see interjected various suggestions on "what can you do to help your patient," while the last section of this chapter will detail more of "what your patients can do to help themselves."

Roadblock 1: Addiction and Self-defeating Behavior

One of the most complex roadblocks, because it involves so many other roadblocks, is addiction. This can include addiction to alcohol, drugs, food, shopping, gambling, etc. Why is it so easy for some to succumb to an addiction while others are resistant? Is it a lack of coping skills, a nutritional deficiency, a chakra energy block, a neurochemical imbalance, or all of the above?

Many health care professionals and much of the general population have a poor understanding of addiction. There tends to be a stigma associated with it. Whether it be destitute, rock-bottom, weak, illegal, or demoralizing, this stigma seems to further perpetuate an addict's behavior through their own self-loathing. Unfortunately, these days the sole solution lies too often in an abstinence program or a prescription rather than our having to cope or find solutions to our problems. In essence, it's really not even the addiction that is the core of the problem; the addiction is only the manifestation of something else going on.

Addictive behaviors relieve the pain of suffering. Yes, it can be as straight-forward as an addiction to pain killers to block agonizing physical pain, however for others the high they experience is a momentary relief for the healing of separation, either from someone or something physical but often from their very source or higher power. For some, the momentary experience of not being afraid, euphoria, or a sense of well-being is a glimpse of what is actually their true being and they keep going back to addictions to try to recreate that connection that they can't seem to get on their own.

For others, it is their way of escaping worry and anxiety — often because they don't know how to be in the now. In the now moment, there is nothing wrong. All is well. But this is unfathomable for many people. We can do our patients a big favor by helping them try not to feel guilty about leaving their worry behind. Still for others, addictive behaviors are a way of having control when they otherwise feel a lack thereof. We see this often with eating disorders and hoarders. [2]

Whatever the case, if the core of the addiction is not addressed, we are doing the patient a disservice. Time and time again, one additive behavior is simply replaced with another. Alcoholics turn to caffeine and sugar; as do smokers. The point is the answer does not lie merely in abstinence. The sooner we realize it, the quicker our patients can experience real freedom! [3]

True recovery from an addictive behavior or unhealthy coping behaviors requires work on many levels including changing how one thinks. This is why psychotherapy can play a crucial role. Yes, abstinence is necessary until a cycle is broken. My dietitian colleagues often say, 'Everything in moderation,' and while I agree with this in the long run, it rarely works when an addictive habit needs to be changed. For example, we don't always think of sugar as a true addiction but sugar can elicit the same dopamine response as cocaine. We know you can't just have a little bit of cocaine and still break an addiction!

Indeed, the addictive substance or habit needs to be blocked or abstained from as much as possible. We can aid the patient through withdrawal in any way we can but the real work begins from there. Addressing psychological factors and other roadblocks such as self-esteem issues and spiritual disconnectedness are key. Chakra clearing, acupuncture and other energy work may be quite

helpful. Likewise, assessing neurotransmitter imbalances and the physical stress response can also add a powerful component to success. Without this behind-the-scenes work, the root of addiction is not fully addressed and relapse rates skyrocket.

Teri's story

Teri was tired, not sleeping well, overweight, anxious, depressed, unmotivated to change, yet at the same time desperate for relief. She was caught in a vicious cycle of over-eating, with a definite sugar addiction, and bouts of over-drinking. She was easily intimidated and seemed to lack confidence or sense of self. She also had many digestive issues although nothing remarkable or specific came from GI and gluten testing. She did have a few food sensitivities. However, avoidance only made a small dent in her symptoms. I've seen this before. No amount of my nutritional counseling would be effective if she was unmotivated to actually implement the behavior and diet changes I'd recommend. She would try but her attempts would ultimately fail. This just served to put her in a deeper hole of despair.

Keep in mind, Teri had plenty of psychological counseling and medications prescribed. In fact, she came to us with a list that had built up over time, which included Welbutrin, Zoloft, Lamictal, Gabapentin, and Klonipin. In the end, this treatment plan bought her almost nothing as it had her numb to some degree. Interestingly, these drugs made her quite anxious at the same time. She was most certainly frustrated by her lack of progress and stuck in the same symptom set year after year. Furthermore, she felt shame for not being able to take care of herself and for being on all the medications. This only deepened her lack of self-esteem. There was clearly still a hidden, missing piece that kept her stuck.

It was time to call awareness to a possible disconnect, or block, that may have explained some of Teri's symptoms. When exploring her history, she told us the last time she felt like herself — pre-medication — was about age 10 or 11. However, this was also a difficult time in her life. She remembered wanting strongly to dance ballet but she started late in the game. Therefore, her desire was squashed by her teacher who told her that she would never really excel considering her late start. Even her friends, already in dance for years, mostly agreed with the teacher. Her parents had their own agenda for her as well. In fact, she remembered her father being very unyielding in his opinion that his daughter should participate in sports instead.

She recalled this time with sadness and frustration. All she wanted to do was express herself in a way *she* most desired. She felt intimidated, and in the name of making her dad proud, agreed to try sports instead. Not surprisingly, every sport she tried did not fit well. It was around that time she also remembers always having stomach aches. Her doctor never found anything wrong. It was diagnosed as stress and resulted in a prescription for her first medication. This quickly affected her self-esteem which led her to escape into food and alcohol. From there, it was a downward spiral into a deeper depression and a lack of self-care.

Together, her history, emotional issues, stresses and physical symptoms presented a strong picture. With Teri, we chose to use the Chakra system, where seven major chakras (often called energy centers) are associated with different parts of the body. Oftentimes blocks in a chakra are related to stressful events during a certain age period of one's life. In Teri's case, we saw a strong picture of a third Chakra issue. The third chakra allows us to form opinions to express ourselves in the world, which Teri had not been able to do. Using the Chakra system is only one method, but in some cases, like Teri, it can help explain a connection from the emotional to physical.[4,5]

Some patients will be resistant at first to acknowledging an emotional cause of illness, as this can be quite a foreign concept. They want the cause of their physical issue to be something separate, from the outside. That said, when awareness is accepted, even as a possibility, this piece alone can produce such an "aha" moment that healing can already begin.

Together with Teri's counselor, we worked with her on this block to healing. She did not even realize the connection at first. Soon she knew that she needed to process forgiveness for those who held her back from expressing herself. She even realized she needed to forgive herself for not doing more to push what she really wanted at the time. She also had to reconnect to her self-worth again. We helped her with many exercises in this respect, like visioning and affirmations. We also encouraged her to consider taking a dance class to see if she could reconnect with her once-lost desire.

Alongside this work, my MD colleague and I were able to identify and address adrenal stress markers and neurotransmitter imbalances through urine and saliva testing.[6] With this help, her continued counseling, and all the self-work she contributed, she was able to successfully abstain from sugar and alcohol. Over a year's time, we were able to get her off one medication at a time while bringing in more natural amino acid, nutrient, and herbal support when necessary to bridge any gaps until all medications were discontinued. On a side note, it may not always be possible to discontinue medications, but often it is possible to decrease the dosage. This can also contribute to the success of the cases we see.[7]

As Teri's head cleared from the decrease in medications and neurotransmitter-balancing work, she was able to get back in touch with her feelings and she found motivation. She was able to learn how not to use food and alcohol for love or escape. She had no trouble including a little sugar without letting it get out of control and although she chose not to drink alcohol for the most part, she did imbibe on holidays and special occasions with perfect control even to this day many years later.

Teri needed to learn how to set the example of how the world should love her by showing how she loved herself first. It was an uphill climb, but for every step forward her faith grew and she became more determined to reach her goals. She continued to work with her team of caregivers, and over time she even started dance classes again. She also meditated regularly, went back to school, and had the motivation to stay on track with the healthy diet I recommended. For the first time since she was a child, she felt free, empowered, motivated, focused, and healthy. But more importantly, she felt a joy and self-love she couldn't ever remember feeling before. She could hardly believe it herself.

This is the kind of success you want in your practice and for your patients! Not just Band-Aids but *real healing*. Not just top-layer treatment but deep-to-the-core-of-the-issues treatment. Whether or not specialty testing is needed and whether or not patients are on medications, I have many cases of success. They are often through collaboration. If you are a nutritionist, find an ordering physician you can team up with to order testing. I'm convinced the team approach is the most effective way to get the job done. There are many integrative medicine professional organizations with member databases to search for a local like-minded physician. One in particular is the Institute for Functional Medicine. Visit www.functionalmedicine.org.

Roadblock 2: Negative Thinking

By helping patients understand how fear and negativity affect their health, barriers can be overcome and successes can be achieved on a

larger scale. For most practitioners, there is a type of patient that is a mystery for many of us, the patient that seems to enjoy having an illness. We all have them from time to time. Instinctively, you can usually spot them quickly. They are the ones who have been to many practitioners and they have a long story for all that is wrong with them and the rest of the world, why nothing has worked, and why they have lost hope that anything will ever make them better.

Many of us get drawn into these cases. After all, who doesn't like a good challenge? And some really do have a valid plea. The root of their malady simply has not been identified because it is so obscure. We have had a few of these in our clinic recently as we embark on the mysterious realm of biotoxin-related illness. However, it does not take long to identify the "energy vampires" — the clients who may talk desperation but they do not always make the life changes needed to make themselves feel better. They are often the ones least likely to follow recommendations. I refer to this group as the "make-me-well, but-do-not-ask-me-to-do-anything-for-it" group. It is so counter-intuitive! Why on earth, you ask, would someone want to stay ill?

Healing from an illness often requires great change. Change is a very scary thing for people. Sometimes, the fear of change is harder to deal with than the illness itself and so one stays in the "safety net" of the illness. Your greatest gift to anyone who resists healing is to allow them time, at least until they are more secure and ready.

To be fair, this type of patient, or negative emoter, does not desire illness and there is technically no enjoyment of the process of being ill. By the way, illness can also be used interchangeably with eating disorders, addictions and any self-defeating behaviors. It is important to note that negative emoters can benefit from their actions. For example, if negative emoters are looking for attention, having an illness garners the attention they may be wanting from others. We must be very gentle with these folks. We need to help them learn self-love and gather the courage to be reborn into an unknown and often brand new identity.

No matter what your professional practice, you can have a role in helping your patients ready themselves for change. I can think of quite a few cases where the first several visits, sometimes lasting months, were all about preparation. In the beginning, with these kinds of cases, I felt very ineffective and it appeared nothing much got accomplished. As a nutritionist, I would repeatedly give the recommendations: eat more or less of this, exercise more, drink more water, etc. There would be some attempt to take one step forward that would result in taking two steps back. It is easy to blame the patient in these cases and to think they might not really care.

Over the years, I have learned that the patient needs this time to explore and to gain confidence. If it is attention they need, I give them attention and take every opportunity to explore their fears and their potential roadblocks. Many times, it also requires a referral to a therapist of some kind. With each visit, there is an increased trust to go to those vulnerable places and gradually the patient sees success. None of this is wasted time. No real progress may have been made if the case had not been approached in this manner.

One of the most important considerations when helping someone in a negative state is that you must avoid falling into negativity yourself. Empathize for a moment and move as quickly as you can into the better feeling place. You know how you feel after spending time with very positive people; you'll tend to feel energized, uplifted, and inspired. You can be this person for your patient.

Remember, no matter how unconscious a person is when making the decision to sink into negativity, in this moment they still have the power to choose otherwise. In deciding to help such a person, your primary role is to help guide him or her to make a more conscious choice, one that will likely be much more empowering. So, how can we help negative people?

An effective tool is to help patients define the gentler form of two feelings still closely related. Ask, "Do you feel more angry or fearful?" Followed by, "Do you feel despair or hopelessness?" Find the less-charged emotion going up the ladder as far as possible in that moment — always at least to the next better feeling place. Ask, "Can you see what to do about it?" "Can you change your view of it?" "What will it mean to you tomorrow, next week, or next year?" Help them put it into perspective. Often, we can find a way to move from hopeless to hopeful as we help them change their thought process and work toward potential solutions. Kind words, positivity, and attention can turn things around. [8]

Give your patients suggestions for "time-outs" such as taking five or 10 minutes to take space from a stressful work situation to close their eyes and to listen to their favorite music. There are so many time-out exercises to draw from if one has their awareness called to the exercises and can then utilize them in times of need.

Perhaps there is a friend or family member that will help intervene. Ask your patients to identify and enlist their supporters. You should give them fair warning, oftentimes it is not who they initially think. If appropriate, write or call to remind the patient that you care. Remind your patients they can do the same with others to help facilitate solutions to problems. It is true that helping others can go a long way to helping yourself.

As a last resort with those more vulnerable or fragile, you can consider working one-on-one with the person yourself to help lift them out of their negativity. This requires a delicate combination of genuine caring and detached awareness. Because we all have free will, it is not always possible to help someone who refuses to accept your assistance. It is important to release your attachment to any particular outcome and remain open to all possibilities. If you become too attached to specific outcomes, you'll drag your own awareness down, drain your energy, and ultimately diminish your capacity to help even others as well. Sometimes, the best thing you can do is to let go with love and have faith that everything will turn out for the best. Turn your attention to helping those you are able to help.

Roadblock 3: Judgment of Others

Debbie Ford in her book, "Dark Side of the Light Chasers," describes a level of judgment as the concept that what we most dislike in others is often unconsciously what we dislike about ourselves. [9] What about traits we don't care for in others, like insecurity, disorganization, overly critical, frugal, selfish, or weak? Could these just be parts of ourselves we're not proud of either? According to this author, it is a good bet. Although not openly admitted, this lack of self-esteem comes to us very covertly.

Judging can be a tool of awareness if we look inside and use it to self-assess. This will help us to grow and garner better self-perception. After all, we cannot change others only ourselves. Here is a novel thought. Instead of saying something judging, we should use a compliment instead.

Hate is probably the most toxic and strong of all judgments. Yet much of our society underestimates this fact, and we allow the word to be used far too flippantly. For example, we *hate* to go to work, *hate* to drive in traffic, *hate* to exercise, *hate*

following rules, and even *hate* the color red. It starts at an early age when we might hate to eat our vegetables, hate to go to school, or hate our little brother for breaking our toy. Oh, sure, you might counter with, "Hate is a strong word. Don't you mean dislike?" But in reality, how many parents and teachers actually counter any more? Because many times the conditioning while we're young goes unchecked and many people head into adulthood with a blind eye.

Though the lack of gratitude in people has been touted repeatedly by Oprah Winfrey and countless others, it is still a trend that needs much coaxing. Why is gratitude so hard to realize? Why is it so easy for people to get stuck far in the opposite direction? Is it because we stopped trying long ago? Here are two ideas. 1) For every time you heard someone say, "I hate..." you can ask back: "Tell me what you like," "What are you grateful for," or "What do you love?" 2) Writing thoughts down helps to embed them more solidly in a reality consisting of positive thoughts. Have your patients start by using journaling as an outlet for negative thoughts. Thinking positive thoughts is great but it is easy to get sidetracked. Have you ever tried to meditate when so many thoughts keep popping into your mind? It is hard to stay focused. The exercise of journaling brings a strong intention to your thoughts. It also brings the element of routine, which is the key for successful change. (10,11)

Roadblock 4: Self-Judgment, Lack of Self-Esteem, Blocking Happiness and Joy

Self-judgment is useful up to a point. However, once it becomes draining to self-esteem, it is destructive. Consider the fact that we are conditioned from an early age to compare ourselves to others. It is not socially acceptable to be fabulous all on our own. Instead, we know this as being self-centered, narcissistic, conceited, and selfish.

Jealousy is an emotion that we all experience, and it's a good barometer if we use it wisely. We can stop ourselves short and turn it around. By seeing what others have, it may help you see what you want to aspire toward becoming as a person. This self-judgment should never result in seeing yourself as not good enough!

It does not help that many of us were not brought up in the most perfect way. In fact, many have experienced an upbringing where love had to be earned as though it were conditional. It is easy to grow up feeling like there is always a price to pay for love. With conditional love comes the pressure of having to measure up. Because many of us were not raised without condition, we have to learn anew. We need to release the belief that there are consequences when we come up short. We need to let go of the belief that it is not enough even when we are perfectly good at what we do. Our mantra for our patients should be, "Do not simply conclude you are wrong if something is not going right!"

Another exemplification of low self-esteem is perfectionism. In our stress to hide our perceived inadequacies, it is easy to adapt the "Superman/Wonder Woman" smoke screen persona. Know anyone like this? They do not know how to say "No." They take care of everyone else but themselves. It is easier to feel good about yourself and certainly others must admire you if you are selfless. In the end, this is what separates you from yourself. For some, this is a better fate than looking in the mirror and dealing with what they see. Many do not know the feeling of constant joy. First, the "do-it-all" syndrome must be escaped and the perfection must be overcome. Learning how to say, "No," will lead to learning how to delegate.

By taking one gentle, healing step at a time, it is like learning how to walk all over again. You have to remind your patients that they'll fall a lot in the beginning. It *will* feel uncomfortable, but eventually they'll get better. They'll have more confidence. It will even get to be fun when that walk turns into a skip, a jump, and eventually, an all-out sprint.

As an exercise, I ask my patients to surrender the energy that holds them back and to just let it go. I ask, "Who are you now that you're free?" so they can start to envision what they can become. Natural inspiration will come once the space has been cleared. We create our experience in this world much the same way a child creates on an etch-a-sketch. We should hold no more stock in it than this child does when they shake it, and make it disappear, and start over. In other words, do not take your form too seriously.

I'll say things like, "Recognize and welcome your spirit, strive for balance, share your gifts, remember what you love, and know that you deserve love. Accept life's lessons with grace, and always choose to treat yourself and others with kindness."

I give the exercise of policing self-talk. Having the awareness first is the only way to change. How many times have you heard someone say, "I'm so stupid," "I'm so slow," or "I look ugly or fat in that." We might think we're exaggerating when we say stuff like this, but our soul believes it to the very core. For every time my patients catch themselves in negative self-talk, I ask them to stop themselves and immediately counter with a positive statement instead, such as the following statements: "I am good at my job," "I have beautiful eyes," or "People admire me for having courage."

They can also make a declaration: "*By the power of my word, I declare that I am worthy of love and forgiveness. The thought that I was not is done. It is finished. There is no more room here for that thought anymore. Through the power of my connection to my source, I let go. I receive love. I am forgiven for judging myself. I love myself.*" Feels good just saying the words, doesn't it?

Lastly, I remind patients to experience laughter every day. Choose where they want to be when it comes to being fun, alive, in love, and in joy. Take time to go dancing, to explore the world, and to empower others with the knowledge of connectedness of spirit and health. I ask, "What is the color of this freedom?" so they can better own the concept. I ask them if there's anything that needs to move out of the way for their vision to have more room, to get unstuck, clear their energy, or de-clutter. I remind them a new life is being birthed, and it's now alive to express!

Roadblock 5: Inability to Forgive, Guilt, and Shame

Many times our patients are stuck in a space of hurt. If you think about it, we have all been a victim at one time or another. For some, it is just a matter of time for healing to occur. For others, the time does not come and their inability to forgive manifests in a chronic emotional or physical response. I've noticed this especially with those who are repressed or avoid processing. For example, these individuals might have chronic depression, chronic pain conditions, digestive troubles, sleep, or fatigue issues.

Forgiveness issues are tricky. Often, patients need the aid of psychotherapy while others will benefit from energy-clearing work. What about those who have experienced a traumatic event where it seems forgiveness is seemingly unfathomable? These are some of the hardest cases as most can easily justify the lack of forgiveness. [12]

What is also challenging is when we have a patient who is still very connected to their event but refuses to acknowledge this fact. A natural tendency is to want to "be well." In doing so, it is tempting for patients to talk themselves into believing that they have fully moved past that which needs forgiving or resolving. Sometimes, the

breakthrough moment occurs just with the realization and acceptance that more healing or full resolution has yet to happen.

The flip side of this is the patient who repeatedly lives the story. You will hear it over and over. Living in the victim role has its benefits. For some, it affords them attention. For others, it is a convenient excuse to justify an action or lack thereof. An example of this might be the person who cannot practice positive self-care (exercise, take vitamins, eat right, etc.). Staying in the victim role is also a convenient excuse to stay stuck. Some would also say the negative energy of a victim is what prevents the very opportunities that can help them move forward. [13]

As a practitioner, you can help people see past their stories. Hear the story. Use it to your advantage and then move past it. You can't change form or condition but you can lift them up and allow healing.

Lack of self-esteem often comes with, or from, shame. "Taking the blame" is often associated with feelings of guilt. These are probably the two most self-destructive emotions one can have. The toxicity of guilt and shame comes from our false beliefs that have kept us separated from our good. Guilt re-triggers the belief system that holds us back. Shame or guilt only serve one purpose and that is to block our full attainment of joy, happiness, and unconditional love. Guilt and shame are some heavy emotions. As an aside, it's funny how many cases of back pain manifest in those who feel like the weight of the world is on their shoulders. Eventually, you feel the physical pain. In order to release shame and guilt, we often need to forgive ourselves.

Here is an example of a homework assignment I might give a patient experiencing guilt and shame:

Assignment: Have a week of grief and really feel the loss of that piece of you that you are letting go. Allow the grieving process to move though you and feel sad if you want. Nurture yourself as you would a little child. Give yourself a little gift in the same way you would to help a child feel special. You are loosening a perceived loss. Be angry if needed. Take a bubble bath to feel better. Hug yourself like you are hugging that child. Really feel it. Play both roles. Feel the child's feelings and then be the parent who nurtures and forgives, exhibiting unconditional love.

Many fail to realize that forgiveness is freedom. It is a release from the pain of victimhood. We do ourselves no good by continuing to manifest the pain. Our pain certainly does nothing to "punish" our abusers. It does not make them change, and it will never erase the event. Punishing ourselves has no purpose if we ever expect to move forward and realize our potential for love and happiness. There is a fine line that exists between forgiving and excusing. Forgiving is NOT forgetting. Forgiving is freedom! [12]

Even if a patient is getting outside help, you can also have a role in helping to clear the playing field of resentments and finding what has not been forgiven. Here is another idea:

Set an intention. *Intend to forgive.* Release the need to know how, just know you want to. Practice or try it on for size until you get it right. Another effective form of intention is through affirmation or a positive statement. You can affirm something more powerfully by saying or writing your statement of knowing. Affirmations must be stated in the place where you expect to be. That's the beauty: you don't have to know but you do want to be in the energy of knowing. An example of an affirmation of forgiveness is: "I allow the power of forgiveness to move through me and set me free from any belief I have about myself that says _____." As a bonus, this example may tie into self-esteem as well. Affirmations are good for those who need to break free from their rut

beliefs that things always happen to them or this is the way it always is for them. [14,15]

Roadblock 6: Stuck in the Past, Worry of the Future, Unable to be "in the Now"

This roadblock is big and universal. It is practically impossible to stay in the present. Our egos are much too strong. Only the very few, fully spiritually evolved like the Dalai Lama, are capable of living in the present continually. For the rest of us, it is a worthy goal to at least try for living in the present — to not be stuck in the past or to continue to wait for the future to happen.

As Eck hart Tolle would tell us, "Operate in the now." [16] Take the good from your past and carry it into the now. The past is over, the future does not exist yet, and therefore the good is in the now. Your filter is your beliefs and perceptions. How do the past and the future steal our ability to transform? Free yourself of worry to propel yourself into action. Otherwise, you are crippled. The past is our gift and our teacher. When things don't work out, why do we look at it like failure rather than a learning experience?

Put yourself in the company of people vibrating the energy you would like to project. Practice walking in the "let go." *Let go* of the past. *Let go* of what you think life is supposed to look like in the future. Ask for help if you need it.

Recognize the past is where shame is and the future is fear. The present is where your imagination is — don't let the ego get in the way. When you have an idea or desire, the ego comes in and asks, "How will you get it?" If you say you want something the following way: "I am going to get..." Then, you're in an energy position of not having, or just short of having, because you're still getting. Put yourself where you want to be. Don't worry about the how. Just know you'll be there and the universe will align. Be open to all possibilities. The universe may have a way that you aren't aware of right now. Do not block. Just be open to whatever comes your way.

For patients with this roadblock, I encourage them to the following affirmation daily: *"Today I release the past. It is over and it has no power. Today, I release the future. It is only a dream. Today, I live in the* **now** *moment where my source is and where I am free to choose, free to love and be loved, free to express and free to be me."* Then, I have them list all the things they release from their past and likewise their future. Indeed, living in the **now** moment take a lot of practice, but the rewards are infinite. I also recommend my patients practice visioning, as it has a purpose to bring the energy of what you want into the now. Planning is a **now** event. It is okay to plan for the future. Catastrophizing is getting lost in the future. It is dangerous territory. Enjoy what you have now and celebrate it. Do not let your happiness be conditional on your future.

Roadblock 7: Isolation, Lack of Faith, or Spiritual Disconnection

We are not our body; we are so much more. Some accept this concept freely, while others think this statement is very controversial. For example, we either believe when we die that it is all over or we believe we move on to reconnect with a higher source, who or whatever that is for each individual does not matter. Many believe that spiritual disconnection is a roadblock. If you cannot connect with your higher source, you cannot heal.

This same group finds relief in knowing they are not alone or isolated in this vast universe. Many feel that faith is their freedom from the burden of the responsibility of being in total control. We learn from an early age, most of us, that there is much we have no control over at all. Some call it God's will. Some call it the higher order. It doesn't always make sense. We cannot see it or touch it,

we just trust. It is fearful not knowing, this is true. But, somehow, they feel it is okay to be afraid and still find a place inside that says, "I will do it or get through it. All is fine." [17]

The rest stay stuck in the bond of control. They believe they control life and others exclusively. They see the world through their five senses. If they can't see it, smell it, touch it, taste it, or hear it, it therefore doesn't exist. They rely less on intuition and more on facts as they can be proven. Some would call these young souls, if you even believe in a soul.

The problem is, without faith, it is hard to believe you have any help in healing. It is a heavy burden to believe you have to do the job all on your own. At the base level, it is about having faith in others to help you. At the highest level, it is having faith that what is meant to be, will be, no matter what you say — as though there was a grand order in things.

Indeed, there is something to be said about giving up the driver's seat and taking your hands off the wheel. It is a trust, a knowing that you don't control, and an understanding that outcomes are not always what we wish for or plan. It is knowing that good will come from any outcome even if it first appears not to be good at all. Yes, it is scary. You must trust that you really do not lose your uniqueness in the process. You only lose your ego, the master controller.

I ask my patients to find their passion, commitment, and also to think about a global commitment. When you give yourself up or engage in service to others, you feel so much fuller. The ego lives in fear. If we hold on to our faith, I believe we can overcome the ego. In the oneness consciousness all problems dissolve, they may not go away, but they can transform.

The exercise here is to pray, to whatever or whomever you choose, it doesn't matter. Yes, there is research that shows it has effectiveness but it seems almost ironic that we even need research to tell us this at all. Prayer has the same frequency as play. When you play dress up as a kid, you become that person, if only for a short time. Prayer is like that; become who you want to be. Wish that for others. Have faith in what you don't know, yet at the same time trust in your knowing. Find harmony. Find peace. It's the ultimate intention.

A Practitioner's Role

So now that we've gone through what I consider to be the seven most powerful roadblocks that get in the way of our patients' better health, let's summarize the general points of what you can do as a practitioner to help those you work with.

Look for the underestimated disconnects in the mind-body-spirit triad that might delay or represent a full barrier to healing. When necessary, work as a team in concert with other healers to help your patient address *all connections* more fully and come to their fullest potential for success.

Hold someone in their greatness, don't judge them if they slide back. Just know they will do what they do and they are great anyway, no matter what. Oh, and be sure to tell them so! Help them erase their checklist of lack and believe instead in their ability for abundance. Remind them to laugh, find joy and have gratitude for what they have every day. Cheer them on as they take small steps in their new beliefs.

Promote freedom from dependence. Anyone dependent on help from others is not free. This doesn't mean we can't ever accept the graciousness or guidance from others; we just shouldn't be dependent on it to the point of giving up our own identity or our power to help ourselves.

On that same line of thinking, encourage your patients to stop identifying with their sick self, but instead to act as if they are well. Bruce Lipton, in his book, *Biology of Belief*, describes how neurochemistry is influenced by genetics, inflammation, toxic burden, etc., but points out it is also influenced by belief." [18] This explains spontaneous healing. If you can make it disappear, therefore you can make it appear. I often say, "Lose the need to name your illness, instead claim your wellness." A hard concept, some say. I say further, "Fake it until you make it. You just might surprise yourself!"

Just as you can't help your patients move forward without knowing where they're moving from, equally important in knowing where they can go from here. Many practitioners will approach things from this point in a very different way — and that's okay as long as the patient gets where they need to be in the end. There's certainly no one-size-fits-all approach!

Throughout the article, I have offered many practices your patients may enlist to help them move forward on their healing journey. If you haven't experienced most of these yourself, you owe it to yourself and your patients to try them on for size. How better to speak to their virtues anyway? Oh, and if you're feeling the need to find scientific research for the validity of these practices, release the need please. Yes, some are well-researched but others may not be. Remember when we all thought the world was flat? The lack of research does not automatically bring discredit. As long as no harm is done, even a placebo has benefit if it gets a patient up the ladder one step further. I don't know why this is such a hard concept in medicine, but it is. It's time we opened our hearts and our minds. I know *you* have if you've read this far.

All I can say is keep learning and growing and spreading the good word!

Resources: What patients can do further

Acupuncture

Acupuncture is a method of encouraging the body to promote natural healing. It is done inserting needles and applying heat or electrical stimulation at very precise acupuncture points does it. The classical Chinese explanation is that channels of energy, called meridians, run in regular patterns through the body and over its surface. An obstruction in the movement of these energy streams is like a dam that backs up in others. The acupuncture needles unblock the obstructions by stimulates the nervous system to release chemicals in the muscles, spinal cord, and brain. This reestablishes the regular flow and therefore helps the body to correct imbalances in many area including digestion, energy production, pain conditions and more. The end result is a stimulation of the body's natural healing abilities, and promotion of physical and emotional well-being. (http://www.medicalacupuncture.org)

Aromatherapy

Aromatherapy is the art of utilizing naturally extracted aromatic essences from plants to balance, harmonize and promote the health of body, mind and spirit. It works through the physiological, psychological and spiritual realm of the individual's response to aromatic extracts to enhance the individual's innate healing process. As a holistic practice, Aromatherapy is both a preventative approach as well as an active method to employ during acute and chronic stages of illness. It is a non-invasive modality designed to affect the whole person not just the symptom or disease and to assist the body's natural ability to balance, regulate, heal and maintain itself.
(http://www.naha.org)

Biofeedback

Biofeedback is a technique that trains people to improve their health by controlling certain bodily processes that normally happen involuntarily, such

as heart rate, blood pressure, muscle tension, and skin temperature. Electrodes attached to your skin measure these processes and display them on a monitor. With help from a biofeedback therapist, you can learn to change your heart rate or blood pressure, for example. At first you use the monitor to see your progress, but eventually you will be able to achieve success without the monitor or electrodes. Biofeedback is an effective therapy for many conditions, but it is primarily used to treat high blood pressure, tension headache, migraine headache, chronic pain, and urinary incontinence. (http://www.aapb.org)

Dance/Movement Therapy

Similar to music therapy and of course, often combined, dance/movement therapy is the psychotherapeutic use of movement to further the emotional, cognitive, physical and social integration of the individual. It is focused on movement behavior as it emerges in the therapeutic relationship. Expressive, communicative, and adaptive behaviors are all considered for group and individual treatment. Body movement, as the core component of dance, simultaneously provides the means of assessment and the mode of intervention for dance/movement therapy.
(http://www.adta.org)

Emotional Freedom Technique (EFT)

EFT is a form of psychological acupressure, based on the same energy meridians used in traditional acupuncture to treat physical and emotional ailments but without the invasiveness of needles. Instead, simple tapping with the fingertips is used to input kinetic energy onto specific meridians on the head and chest while you think about your specific problem - whether it is a traumatic event, an addiction, pain, etc. -- and voice positive affirmations. The combination of tapping and voicing affirmation works to clear the "short-circuit" - the emotional block -- from your body's bioenergy system, thus restoring the mind-body balance, which is essential for optimal health and the healing of physical disease.

Massage Therapies

Massage therapy often referred to as bodywork or somatic therapy, refers to the application of various techniques to the muscular structure and soft tissues of the body that include applying fixed or movable pressure, holding, vibration, rocking, friction, kneading and compression using primarily the hands, although massage therapists do use other areas of the body, such as the forearms, elbows or feet. Massage positively influences the overall health and well-being of the client. Far reaching benefits affect the musculoskeletal, circulatory-lymphatic, nervous, and other systems of the body. (http://www.amtamassage.org)

Meditation

Practiced in a variety of ways, mediation allows contemplation and reflection through freeing or quieting of the mind. It can be an exercise in releasing troubling thoughts to just be in the moment. Regular meditation can provide many benefits such as lowing blood pressure and heart rate, improved breathing, relaxation and over all stress reduction thereby improving mood and decreasing depression. No one form of meditation is right or wrong; none is better or worse. There are many sources of guided meditation that are often good for beginners.
(http://www.meditationsociety.com)

Mentor/role model

Look for a mentor or role model who has already walked the walk. Maybe this is a religious or spiritual guide, a healer, or a best friend. The premise in general is to surround one's self with as many positive, successful people they can. Likewise, to release the negative people that influences their life as much as reality will allow. Role models will be found in personal relationships but also indirectly as authors of motivating books and as uplifting speech-givers.

Music Therapy

Music Therapy is an established health profession in which music is used within a therapeutic relationship to address physical, emotional, cognitive, and social needs of individuals. After assessing the strengths and needs of each client, the qualified music therapist provides the indicated treatment including creating, singing, moving to, and/or listening to music. Through musical involvement in the therapeutic context, clients' abilities are strengthened and transferred to other areas of their lives. Music therapy also provides avenues for communication that can be helpful to those who find it difficult to express themselves in words. (http://www.musictherapy.org)

Qigong

Qigong (pronounced "chee-gung") is an ancient Chinese exercise that integrates physical postures, breathing techniques and focused intention. Qi is translated to mean the life force energy that flows through all things in the universe. Gong, means accomplishment, or skill that is cultivated through steady practice. Together, Qigong means cultivating energy, it is a system practiced for health maintenance, healing and increasing vitality. Qigong can be classified as martial, medical, or spiritual. Practices vary from the soft internal styles such as Tai Chi; to the external, vigorous styles such as Kung Fu. However, the slow gentle movements of most Qigong forms can be easily adapted, even for the physically challenged and can be practiced by all age groups. (http://nqa.org)

Reiki

Reiki is a Japanese technique for stress reduction and relaxation that also promotes healing, It is administered by "laying on hands" and is based on the idea that an unseen "life force energy" flows through us and is what causes us to be alive. If one's "life force energy" is low, then we are more likely to get sick or feel stress, and if it is high, we are more capable of being happy and healthy. (http://www.reiki.org)

Visioning:

Helps develop a clear sense of purpose and goals to focus and drive creative energy. Visioning can be done like brainstorming, in meditation or via a vision board that one creates using drawings and/or pictures.

Yoga

The classical techniques of Yoga date back more than 5,000 years. The word Yoga means "to join or yoke together," and it brings the body and mind together into one harmonious experience. The whole system of Yoga is built on three main structures: exercise, breathing, and meditation. The exercises of Yoga are designed to put pressure on the glandular systems of the body, thereby increasing its efficiency and total health. Regular daily practice of all three parts of this structure of Yoga produces a clear, bright mind and a strong, capable body.
(http://www.americanyogaassociation.org)

Susan Allen has been evolving her nutrition career for over two decades. Now, nationally recognized as a functional nutrition expert, she provides a unique and very successful approach to personalized health and wellness as she incorporates an overall focus on the mind-body-spirit connection in her work as a speaker, mentor, author and nutrition consultant. Susan earned her nutrition degree in Medical Dietetics from the University of Illinois, became a Registered Dietitian (RD), and completed post-graduate level training to become a Certified Clinical Nutritionist (CCN), which designates her specialty in the nutritional aspects of functional medicine, which is personalized medicine that deals with primary prevention and underlying causes instead of symptoms for chronic health conditions.

Ms. Allen has worked in many settings in addition to her own private practice. She was involved in

one of the first free standing nationally based Integrative Medicine Clinics, then called American Whole Health where she worked with well know physician and author, David Edelberg, MD and many other doctors pioneering the Integrative Medicine path. She also consulted for the start up of The Center for Integrative Medicine affiliated with prestigious Northwestern Memorial Hospital in Chicago.

Ms. Allen has held board appointments with The International and American Association of Clinical Nutritionists, the American Dietetic Association's sub-specialty group: Nutrition in Complementary Care (NCC), now known as Dietitian's in Integrative and Functional Medicine (DIFM), on the Nutrition Board of the Institute for Functional Medicine (IFM) and on the Scientific Advisory Board of Integrative Therapeutics, Inc., one of the largest natural medicine manufactures in the United States.

Susan lectures nation-wide, has been a consultant to the natural vitamin industry and is a respected mentor/trainer to registered dietitians and other healthcare professionals. Considered an authority, she has appeared on numerous radio and television programs, has been quoted extensively in the press, and is also a published author.

While she currently speaks, trains and consults coast-to-coast, Susan's home is in the Chicago area where she enjoys a thriving practice as Director of Nutrition and Wellness at Park Ridge MultiMed (www.parkridgemultimed.com) with noted Integrative Medicine Physician and author, Keith Berndtson, MD. She also serves as Director of Nutrition for *OneBodyMind.com*. Founded by Dr. Berndtson, this website supplies innovative online tools for people interested in a deeper, more effective approach to health education, self-care support, and the stewardship of living systems. It is also ground zero for a social network that will help prepare the way for the modern quest for health and sustainability.

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Healing Emotions in Children

Stephen Scott Cowan, MD, FAAP

The Diagnostic Statistical Manual (DSM), the bible of conventional Western psychiatry, has been relatively effective in providing detailed categorization of what's *wrong* with us, but it doesn't really tell us what is *right* with us. This presents a significant problem when it comes to growing a healthy child in your house or your practice.

The explosive rise in the diagnosis of children with mental disorders over the past 20 years has led to significant overuse of strong psycho-pharmaceutical medications originally intended for adults and not FDA approved for pediatric use.[i] This has several untoward effects. It puts clinicians in the difficult position of *having* to treat a child once a diagnosis has been given or run the risk of malpractice. A recent report in the Harvard Medical Letter has gone so far as to suggest that the availability of psycho-pharmaceuticals may actually be influencing the clinician's process of diagnosis.[ii] But DSM diagnoses are based on the collection of symptoms not pathophysiology, and treatment options give the impression that a symptom has a distinct neurochemical association. Contrary to what pharmaceutical companies would like you to believe, the promise of "better living through chemistry" can leave us crippled by a life-long dependency on pills without ever probing the deeper roots of our emotional problems.

Another complication of the rise in clinical labeling of emotional disorders in children has led to an over-identification with their diagnosis. It is not uncommon these days to hear kids say "I'm ADD " or "I'm bipolar." Identifying ourselves with a disease is a serious problem that actually prohibits full recovery. The use of "adult" psychiatric diagnoses in labeling children gives the impression that children are simply "little adults." This negates the unique quality that defines children, namely their intense process of growth and development. A child is constantly adapting to his environment in an ongoing process of shaping his internal structures known as neural plasticity. The vibrancy of these changes is what makes children so much fun to be around. Their wondrous sense of exploration and creativity makes a child much less predictable particularly when it comes to labeling emotional states.

There is a subtler problem in labeling children. The DSM gives labels to clusters of symptoms but these are often taken to mean that they are somehow permanent disease conditions. Treating

symptoms as if they are diseases can lead to quick fix interventions that ignore the causes underlying those symptoms. But perhaps the most problematic issue presented in the DSM is the complete absence of any definition of "emotional health," giving the impression that health is simply the absence of a diagnosis. But there is more to living a healthy emotional life than *not* having symptoms or labels.

Resilience

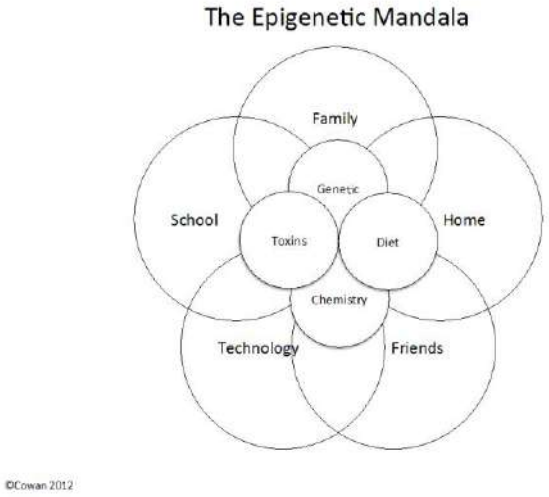
The plasticity of our nervous system highlights the epigenetic phenomena that have revolutionized our understanding of the interrelationship between our hereditary influences and environmental factors. Rather than seeing ourselves from the perspective of hardwired genetic determinism, we now have a broader ecological view of what it means to be healthy. This is particularly important in defining emotional health.

Mark Greenberg, the noted psychologist at the Penn State University has done groundbreaking work in searching for the factors that determine how we cope with what Hans Selye calls "the stress of life."[iii] Stress is a necessary stimulus for growth, and adaptation and resilience can be defined as how well we bend and recover from the winds of change. Our coping mechanisms are influenced by the epigenetics of our circumstances. The more labels there are for emotional illnesses in children, the less tolerance there is for children who don't "fit in" neatly to rigid expectations of how a child should behave. The smaller the box, the more kids fall out of it. The epidemic use of psychiatric medications in children has its roots in such narrow perspectives. The first step in understanding how to improve a child's emotional health is to look beyond chemistry at all the factors that either support or interfere with resilience.

The Mandala of Epigenetic Fitness

We are walking communities. 99% of the proteins made in the human body derive from non-human microbial cells. The food we eat contains micro-RNA that dictate how our genes are read. The health of our gut flora has a direct effect on the balance of our neurochemistry. Over 80% of the serotonin produced in the body comes from the gastrointestinal system. Thus our gut is a brain that regulates our mood.

But a holistic perspective goes far beyond simply giving supplements instead of pharmaceuticals. That is still buying into the quick-fix mentality of drug companies. To truly appreciate the big picture, we must expand our perspective and take into account everything that influences our genome. The new field of behavioral epigenetics championed by Moshe Szyf at Mcgill University is just beginning to scratch that surface.[iv] In exploring factors that contribute to what I call "epigenetic fitness" we need to look at the mandala of influences in our life (see diagram). *Mandala* is an ancient Sanskrit word that means relationship. How we are related determines our epigenetic fitness. This is the key to promoting emotional wellbeing.



Food: The quality of the food our children eat certainly affects their emotional

stability. The current obesity epidemic is directly related to the rise in high-energy, nutrient-poor foods that alter blood sugar balances, shorten frustration thresholds and drive compulsive behaviors. But it's not just what we eat but where we eat, how much we eat, when we eat and why we eat that determine our emotional wellbeing. Hunger can be a positive motivator or a distraction depending on the degree of intensity. Many children today have become over-indulged with fast food and have lost the deeper meanings in eating linked to social relations and stress-reduction.

Toxins: We are exposed to toxic environmental factors every day. Our physical and emotional health is directly affected by the levels of toxic burden that come from living in a modern industrialized world. The air we breathe, the food we eat, the noise we are exposed to, the extended exposure to artificial light, heat and cooling all disrupt our connections to the natural rhythms of life. Lack of sleep, exercise, and proper digestion can all lead to excess stress hormone production that can overload the biomedical detoxification system causing chronic physical and mental suffering. Supporting detoxification is a fundamental aspect of emotional health maintenance. But toxic exposures extend beyond chemicals to the emotional stressors of our daily life.

Family: Our family serves as our first support system. Family dynamics can also certainly become as toxic as chemical exposures. Indeed, our family relationships trigger neurochemical effects that can be contagious. How well we resonate within our family will contribute to our state of wellbeing or discomfort.

Friends: How often does a clinician consider asking friends to participate in the treatment of a child with emotional disorders? There are many times in my career when a patient's friends have come forth with valuable information that helps illuminate what is actually going on in my patient's life. This is particularly true with teenagers who have evolved their own supportive social network. The recent rise in online bullying has highlighted the dark side of such exposures and need to be investigated carefully.

Home: The structure and setting of the house where a child lives can have powerful effects on a child's moods and emotions. Which side of the bed she sleeps on, the color of the walls, where she eats, where she watches TV all contribute to the level of stress or resilience in any child. The ancient Chinese study of Fengshui looks at the ways we can make subtle shifts in the energy and mood of one's home to promote greater harmony and positive emotional states.

Technology: Perhaps the most underappreciated influence on our childrens' emotional resilience lies in their exposure to modern digital technology. Our children are considered "digital natives," having grown up fluently speaking the language of the internet, cell phones and videogames. We adults are "digital immigrants." We may be able to speak the language but it is not necessarily natural to us. Adapting to the highly visual, over-stimulating world of technology can leave children feeling bored

and apathetic in environments like school where they do not have access to the same kind of feedback.

School: We must not forget the effect our schools have on our children's emotional wellbeing. As our schools become more rigid in their standardized institutionalization of learning, there is less and less tolerance for the diverse ways children adapt, grow and express themselves. This is one of the most prominent causes of over-labeling in children.

Each of these factors is critically important in considering a holistic approach to improving a child's emotional fitness. One is not more important than the others and each can be used therapeutically to enhance a child's ability to recover from emotional stress effectively without medication.

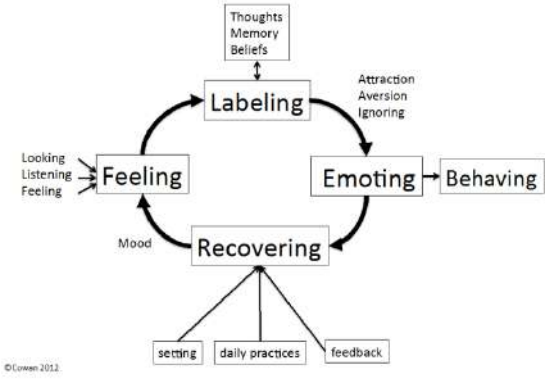
Tong: the meaning of health

The classical Chinese symbol *Tong* shows the image of a bell ringing. It means to connect, to communicate, or free-flowing communication. In Chinese medicine it is one of the defining words for health. How we resonate in the world gives a deeper sense of what emotional health means. This gives a sense of the constant dialogue that is taking place with our environment. In ecological terms, emotional health therefore means that we exist as unfinished business. Our "emotional immunity" does not rest on building a shell so one ever gets upset, but rather is defined by the free-flowing flexibility that gives the power to bounce back.

In speaking about emotional immunity, there are important parallels with our physical immune system. As a holistic pediatrician, it is not uncommon to encounter parents seeking ways to "boost their child's immunity" because their child is always getting sick. But all too often, when we examine the situation more closely, I find that the child is getting sick, recovering and then getting sick again. When looked at another way, parents begin to realize that their child is actually always "getting better." Immunity does not mean one never gets sick. That would actually be abnormal. A healthy immune system is constantly exercising as it resonates with the world. Just as physical health does not mean the absence of sickness, a healthy emotional immune system does not mean never feeling upset. It simply means you are able to recover quickly.

The Cycle of Emotional Recovery

Emotional recovery is directly linked to our flexibility in responding to the circumstances we find ourselves in. Let us take a look at the powerful relationships between feelings, emotions and behaviors. (see diagram)



In the developing child, feelings, emotions and behaviors happen so quickly they often seem to be the same thing. This can lead to considerable

confusion when a child is told to stop behaving in a particular way, and she takes it to mean "stop feeling." This is the path to suppression that will manifest in deep-seated psychological pathologies later in life. One of the important first steps in enhancing emotional recovery in children comes with being able to separate these aspects of our emotional life.

Neuroscience has shown that there is a gap of about 200 milliseconds between our sensory feelings and the moment when we begin to categorize these feelings. Resonating with the world involves that act of listening, looking and feeling, which very quickly become hearing, seeing and touching *something*. That *something* is a conceptual idea based on language, memory and beliefs that make up our reference system. Once labeled (recognized), we are motivated towards or away from the stimulus, or to simply disregard it. Such movements of attraction, aversion and ignoring are expressed as a kind of ringing or reverberation in an attempt to communicate (*tong*) with the world. The motion of our facial expressions and body language is what Antonia Dimassio calls our emotion[v]. We emote not just in response but in order to evoke something from the world, to stake our claim, whether it is passion for what we are attracted to, aggression for what we are averse to or by simply ignoring what seems neutral to us.

There is another brief gap between the rising emotion and the ways these expressions are enacted as behaviors. For instance, we may form an angry face to evoke our aversion to a situation but this may not always propagate into behavioral actions. For the immature child, the lightning speed with which these impulses arise and become behaviors can be frightening. It takes time and experience to begin to modulate the speed of emotion-to-behavior. This is one of the great problems with current conventional diagnosis and treatment. By suppressing the symptom-behavior, there is little opportunity for a child to distinguish feelings from behaviors in order to develop mature emotional regulation. It is of paramount importance for children to realize that there are good and bad behaviors but no such thing as a bad feeling.

During the heat of an emotion, however, there is a refractory period that makes intervention extremely difficult. But once the peak of the emotion passes, there is a recovery period that allows a child to return to simply listening, looking and feeling clearly again. The power of emotional recovery is directly influenced by the setting, feedback and personal practices that promote our habits. Much of my work with parents and children is developing strategies that shorten recovery time and return to feeling in order to enhance emotional immunity.

Often when the setting does not provide opportunity for a child to "let go" of an emotion, we will see lingering moods that can distort sensory perceptions. This can set up a vicious cycle that fuels chronic pathological behaviors and interferes with the natural exchanges necessary for learning, memory and a sense of wellbeing.

Our job as health practitioners is, in its truest sense, to prepare our patients for getting sick and to shorten their recovery time, rather than to simply stop illness from ever arising. This is a revolutionary concept in health care. Shortening recovery time puts a different spin on how you live your life and interact with others. Preparing to be emotionally upset and then practicing recovering is an active engagement with the natural processes of the heart. This changes the mood of medicine and clarifying goals of therapy. There are critical points along the cycle of feeling-labeling-emoting-recovering that represent opportunities to empower the patient to recover and return to clarity of perception. This begins with the power of attention that creates the space

and time to develop flexible communication with the world (*tong*).

Xin: The Triune Heart

We are wired to pay attention. As the eminent father of psychology, William James said, "That which I choose to pay attention to, shapes my brain." This lies at the heart of emotional epigenetics. But we do not pay attention with one brain, we use three brains to do it. In the early 1970's, Paul MacClean, working at the National Institute of Health, first described the structure of the brain as a reflection of our evolutionary progression. He called it "the Triune Brain."[vi] At that time, emotions were thought to originate in the structures situated between the brain stem and neocortex known as the "limbic system." As a long-time student of classical Chinese medicine, I have adapted this view of the brain to help parents and clinicians understand the emotional states of a child in ways that are less focused on pathologizing symptoms and more geared to helping each child maximize his strengths and virtues.

In Chinese medicine, the idea of mind and heart are held within one term: *xin*. This ancient character shows what some believe to be a lotus blossom opening with a stem and three leaves. Others say it represents the major chambers of the heart. There is deep meaning in this imagery. As a pediatric neurodevelopmental specialist, I find that something marvelous happens when we replace the word "mind" with "heart." Suddenly paying attention with all our heart begins to reflect our emotional state of mind. What I call the Triune Heart is made up of "the frog heart, the puppy heart and the big heart."

The frog heart pays attention to the basic connections to our world, the cycles and rhythms that maintain our basic life support: circulation, breathing, eating, sleeping, and eliminating. The heart connection in charge of circulation is one of the prime representations of *tong* (communication). Indeed studies have shown that when heart rate is synchronized with respiration, it can enhance emotional wellbeing and improve the flexibility of attention. Like the little frog that waits and then simply snaps the fly reflexively, we pay particular attention with our frog heart in order to develop a synchronized resonance with the world.

Sitting on top of the frog heart is what MacClean described as the limbic system and what I call the puppy heart. We all have a puppy living inside us that drives our immediate urges to find security in the moment. The intensity of these urges fall into five expressions: excitement, hostility, fear-withdrawal, routine-compulsion and separation-anxiety. When we are in a threatened state, we each have a particular style of barking that lets the world know we are insecure. When the puppy heart is charged up, it has a downward influence on the frog heart: we overeat or don't eat at all, we hyperventilate or hold our breath, we can't sleep or we sleep too much and we are unable to let go, getting constipated or developing loose stools. These are the physical manifestations of the over-stressed state; the puppy heart bears down on the frog heart causing loss of synchrony.

Above this we have evolved the neocortex, what I call the big heart. Big heartedness allows us to see ourselves within our context. This drives the character that Martin Seligman describes as our character strengths and virtues. It is here that through our power of imagination, we can regulate our puppy heart impulses and shorten recovery time.

One of the most profound developments in neocortical imagination is symbolic language. When we can name our feelings, we are able to increase the time between feelings and emotional expressions. I teach parents to practice simple exercises with their children in order enhance attention to a wider range of shifting feelings. This provides children with more effective tools that they can use to communicate their feelings with greater security and less need for wild puppy barking.

Creative play is an important way child can practice using their big-hearted imagination to effectively communicate with the world. Being able to imagine what others are feeling is the root of empathy. Imagining the effect one is having on others is the root of deep self-reflection. Imagining the consequences of ones actions is the root of heroic perseverance. Imagining one's own death is the root of ethical judgment and moral behavior. Each of these big-hearted emotions enables a child to be master of her puppy heart. A recent study that followed children for 30 years clearly demonstrated the importance of developing emotional regulation in ultimate outcomes of economic success, social success and physical health.[vii] I teach children to use the power of their imagination in visualization-meditation exercises to help them return to a state of clarity in feelings. This is the key to mindfulness practices that can shorten recovery time from strong emotional states.

In my book, *Fire Child Water Child*, I describe my holistic approach to helping children develop their virtues and become masters of attention.[viii] To be truly effective, I have found it essential that we embrace each child's unique nature. Nature favors diversity. It is the key factor in our survival as a species. When we deny our diversity, we are forced to constrain our expressions and suppress our emotions. This leads to deeper distortions in emotional expressions. Using the naturalistic language of classical Chinese medicine, I describe the five adaptive styles: *wood*, *fire*, *earth*, *metal* and *water* that offer parents an ecological approach to enhancing each child's attention and self-esteem. By seeing a child's urgent emotional expressions as a barking cry for help rather than something broken, we open our own big hearts to compassion which is contagious to everyone around us. This is the therapeutic power of healing emotions. By empowering our children to resonate with the world, we empower the world in healthy and enduring ways.

Stephen Scott Cowan completed his pediatric training at St. Luke's-Roosevelt Hospital Center in NY in 1987 and went on to complete a 2 year fellowship in Child Development at the Developmental Disabilities Center at Roosevelt Hospital. He is long-standing member of the American Board of Pediatrics, a fellow in the American Academy of Pediatrics and serves on the AAP committee of Developmental Disabilities. He is a clinical instructor at NY Medical College and has lectured internationally on the holistic management of chronic problems in children. He is certified in Medical Acupuncture and is a member of the American Academy of Medical Acupuncture. He is a long time student of Chinese medicine, studying with Efrem Korngold OMD and Stephen Aung MD. He is a member of the Autism Research Institute's Defeat Autism Now practitioners. Dr. Cowan is a co-founder and advisory board member of the Holistic Pediatric Association and serves on the advisory boards of the Integrative Health Symposium and the TCM World Foundation Building Bridges Conference. In 1991 Dr. Cowan founded Riverside Pediatrics, in Croton, NY with Larry Baskind MD where he incorporates alternative therapies in the treatment of common childhood disorders. He is also the founder of The Westchester Center for Holistic

Families in Mt. Kisco, NY, where he offers holistic developmental consultations and treatments that include nutritional and biomedical interventions, acupuncture, biofeedback, and meditation. He specializes in the diagnosis and treatment of chronic pediatric problems such as Attention Deficit Disorder, Autistic Spectrum Disorders, Tourette's syndrome, Asthma and Allergies and Digestive disorders.

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Atherosclerosis, Functional Foods, and Nutritional Genomics

Micheline Vargas, DrPH, CNS, RCEP, CSCS

INTRODUCTION

The leading cause of mortality in both men and women in the United States is cardiovascular disease (CVD) due to atherosclerosis. Atherosclerosis involves chronic inflammation and a progressive buildup of lipids and fibrous elements in the arterial walls. It begins with the formation of "fatty streaks". Fatty streaks can be found in the aorta by 10 years of age, in the coronary arteries by age 20, and in the cerebral vasculature by the age of 40.[1] Early intervention is imperative. Preventive interventions focused on managing cholesterol, blood pressure, and weight, have been found to favorably alter atherosclerotic progression. Unfortunately, less that 50% of the cardiovascular events are prevented in the treatment groups of the most successful clinical trials.[1,2] In fact, most myocardial infarctions (MI) occur in individuals with normal cholesterol levels.[3] Greater focus on contributing factors (i.e., inflammation) involved in the atherosclerotic disease process may be helpful in preventing cardiovascular events.

Biological data now demonstrate that most MIs occur after atherosclerotic plaque rupture and thrombosis (clot) formation. Inflammation can threaten plaque stability and increase its propensity to rupture and in turn cause thromboses that trigger a cardiovascular event. Approximately two-thirds to three quarters of all fatal coronary thromboses are due to rupture of the fibrous cap.[4] Autopsies show that rupture is more likely to occur in plaques with a soft lipid core and a thin inflamed fibrous cap.[5] Therefore, the contributing factors that lead to the lipid core and inflamed cap need to be addressed in an intervention. Nutrition therapy can play an integral role in the prevention of atherosclerosis and should aim to

reduce contributing factors such as low density lipoprotein cholesterol (LDL-C) deposition, LDL-C oxidation, and chronic inflammation.

Nutrition plays a key role in reducing risk of CVD in populations. Individuals, however, differ significantly in the degree to which beneficial changes occur.[6] This individual response is likely due to differences in genetic makeup, known also as genotype. Only recently have medical researchers begun to understand how variations in genes affect an individual's health. Personalized nutrition, or "nutritional genomics", uses an individual's unique genetic makeup to make recommendations that will potentially reduce risk for diseases and/or more effectively manage diseases such as atherosclerosis.

This article will review the importance of nutrition in reducing risk for atherosclerosis. Specifically it will: 1) review the atherosclerotic process, 2) review heart healthy guidelines, 3) discuss how functional foods may modulate atherosclerosis and CVD risk, and 4) briefly touch on the role of nutritional genomics, as it relates to the atherosclerotic disease process and CVD.

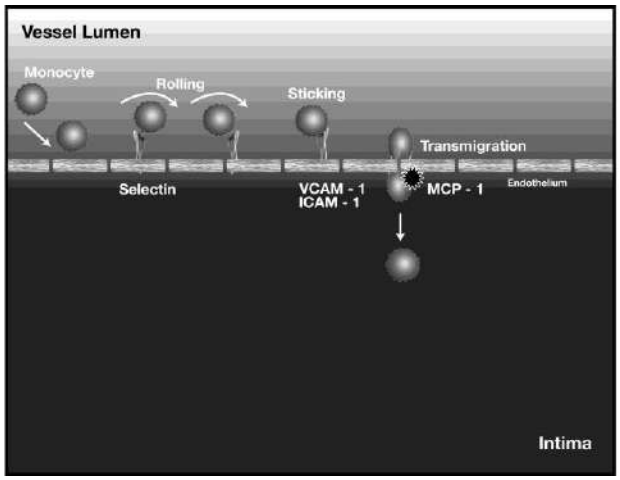
Review of the Atherosclerotic Disease Process

Chronic inflammation of the arterial wall is a well-established theory in the atherosclerotic disease process.[7,8] Advances in basic and experimental science have established that inflammation is involved in mediating all stages of this disease from initiation through progression and, ultimately, to atherosclerotic plaque rupture.[9,10] These findings not only enhance one's understanding of atherosclerosis, but also aid in more appropriate targeting of therapy.[8] Preventive therapies (i.e., dietary) that reduce chronic inflammation also appear to reduce the risk of CVD.

The atherosclerotic disease process will be described in the steps and figures below as it is the basis for dietary treatment approaches.[5,9]

1. Injury to the arterial wall, which may be due to one or more risk factor(s) (i.e., hypertension, smoking, etc.), triggers an inflammatory cascade. Once injured, the endothelium (layer of cells that line the inside of the artery) will express adhesion molecules such as: selectins (E, P, L); vascular cellular adhesion molecule -1 (VCAM-1), intracellular adhesion molecule-1 (ICAM-1), and integrins. Adhesion molecules facilitate monocyte (white blood cells that are part of the immune system) attachment to the endothelium. Their function is just as their name implies. They act like an adhesive and hold the monocyte down to the endothelium.
2. The injured endothelial cells will begin producing chemoattractants, such as monocyte-chemoattractant protein-1 (MCP-1), interleukin-8 (IL-8), platelet-activating factor (PAF), and leukotriene B_4 (LTB_4). Chemoattractants "attract" the monocyte to migrate through the endothelium into the subendothelial space of the artery wall. Here is where much of the action will take place.

Figure 1: Recruitment of Blood Monocytes

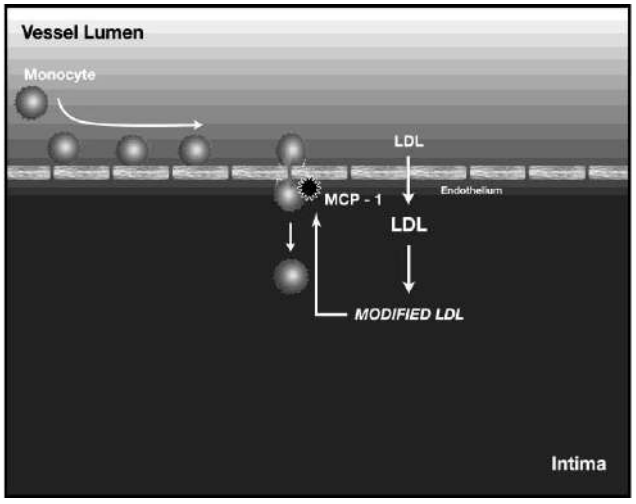


3. The monocyte, now in the subendothelial space, can directly influence the endothelium by secreting growth factors, chemotactic

substances, and cytokines (signaling molecules involved in cellular communication).

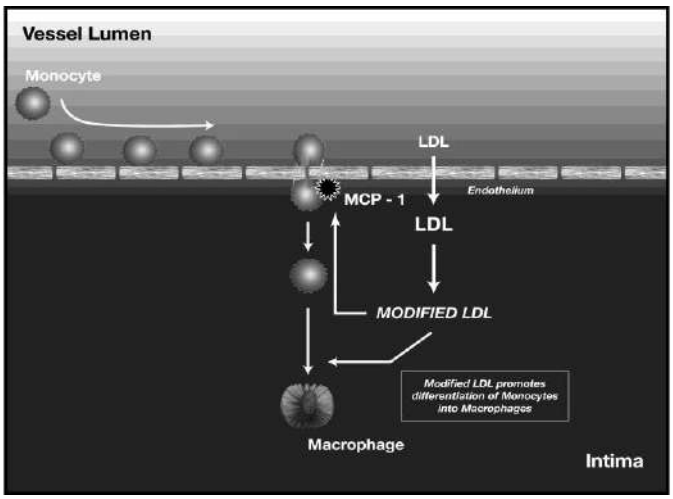
4. Once in the subendothelial space, monocytes differentiate into macrophages. Activated macrophages express cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin-1 Beta (IL-1β). These inflammatory cytokines further stimulate endothelial cells to express adhesion molecules (i.e. VCAM-1, ICAM-1) as well as additional proinflammatory cytokines. An inflammatory cycle is created.
5. LDL-C infiltrates the extracellular matrix of the subendothelial space via passive diffusion and the action of specific receptors. Elevated serum concentrations of LDL-C, along with proinflammatory cytokines, enhance this process. The trapped LDL-C become exposed to reactive oxygen species (ROS) and undergoes oxidation.

Figure 2: Modified LDL-C Stimulates Chemoattractants from Endothelial Cells



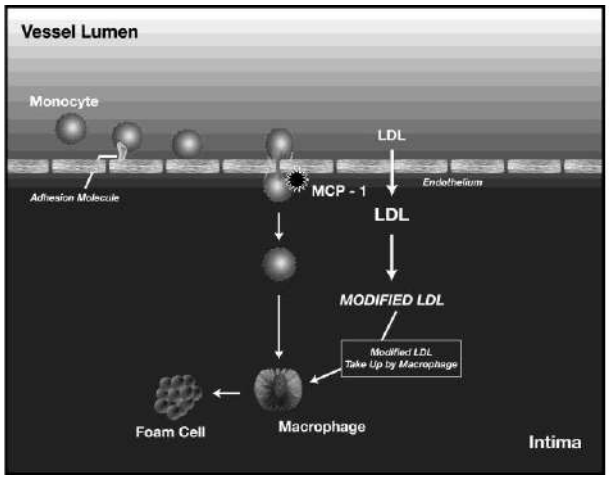
6. Oxidation of LDL-C is a major physiological mechanism behind the pathophysiology of atherosclerosis. The oxidized LDL-C (ox-LDL-C) is a powerful inducer of inflammatory molecules. It can initiate and promote proinflammatory responses within the artery wall. The ox-LDL-C can induce chemoattractants such as IL-8 and TNF-α. These chemoattractants will recruit more monocytes to the arterial wall which will be bound to the artery wall by adhesion molecules. The ox-LDL-C will stimulate the differentiation of monocytes into macrophages by inducing macrophage colony-stimulating factor (M-CSF).

Figure 3: Monocytes Differentiate into Macrophages



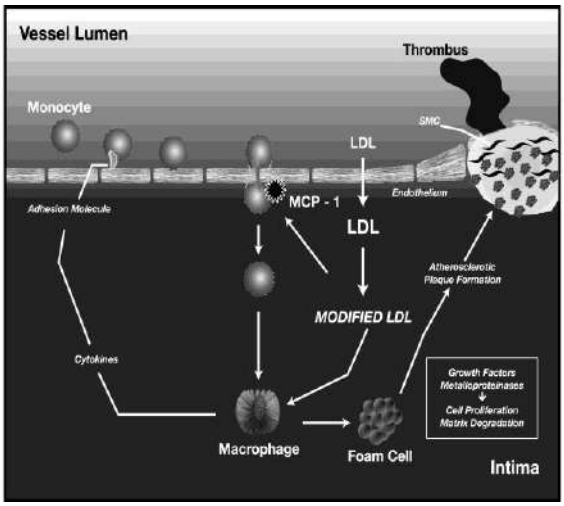
7. Macrophages express scavenger receptors, which gives them the ability to "scavenge" or ingest the ox-LDL-C. The scavenger receptors are up-regulated by proinflammatory cytokines. The uptake of ox-LDL-C by the macrophages results in "foam cells", a hallmark of atherosclerosis. The foam cells die and form the soft lipid core of the atherogenic plaque.

Figure 4: Foam Cell Formation



8. Cytokines released from foam cells and macrophages stimulate smooth muscle cells to migrate to the intima. The intima is the innermost layer the artery wall. The fibrous cap that covers the soft lipid core is created by the smooth muscle cells and extracellular matrix secretion. Cell proliferation is directly stimulated by cytokines and growth factors from macrophages, interferon-gamma (IFN-γ) from T-cells, elevated homocysteine, and increased angiotensin II (a vasoconstrictor).
9. The vessel is further compromised by alterations in vasoactive substances. An imbalance between endothelial-derived vasodilating (i.e., nitric oxide) and vasoconstricting substances (i.e., endothelin-1, angiotensin) impairs regulation of vascular tone. Normally nitric oxide (NO) inhibits leukocyte adhesion, helps maintain non-proliferative vascular smooth muscle, and limits platelet aggregation.[11] As production or availability of NO is diminished, its ability to protect against vascular injury, inflammation, and thrombosis is diminished.
10. As the process continues, macrophages and foam cells release fibrogenic mediators (i.e. peptide growth factors). These mediators can promote smooth muscle cell (SMC) replication and contribute to proliferation and production of dense extracellular matrix, creating a fibrous cap.[5,8,12] IL-8, which is present in macrophage dense areas of the atheroma, can also induce proliferation and migration of SMC.[13]
11. The vascular smooth muscle cells (VSMC) that accumulate in the intima play a key role in the development of the arterial lesion. These cells synthesize collagen that stabilizes the fibrous cap. However, as the lesion progresses VSMC apoptosis occurs, contributing to plaque vulnerability.[5]
12. As the atherosclerotic disease process continues, the plaque becomes more unstable. Foam cells and macrophages produce metalloproteinases that contribute to matrix degradation.[11] As the proteolytic enzymes degrade the collagen in the fibrous cap, it becomes thin, weak, and susceptible to rupture.[5,8] T-lymphocytes are also involved in the degradation of the fibrous cap. They produce IFN- γ, which can halt the synthesis of collagen by the SMC, thereby limiting the renewal of collagen and increasing susceptibility of the fibrous cap to rupture.[5,12]
13. Once the plaque has been disrupted excessive apoptosis of the VSMCs can increase thrombogenicity.[5,10] The VSMCs produce active thrombin, which activates platelet adherence.[12] Macrophages produce tissue factor, which is a major procoagulant and can trigger thrombosis. Thrombus formation can lead to vessel occlusion and trigger a cardiovascular event (i.e. MI).[5]

Figure 5: Release of Fibrogenic Mediators and Plaque Rupture with Thrombosis



Inflammation and Adipose Tissue

Adipose tissue plays an important role in the atherosclerotic disease process. Although it will not be discussed in detail, it has been briefly addressed because of its contributing role in the inflammatory and atherosclerotic disease processes.

Maintaining a healthy body weight, specifically maintaining a healthy body composition, is important in the prevention and treatment of atherosclerosis. Obesity has long been considered a risk factor for CVD, due in part, to adipocyte

secretion of cytokines that induce a proinflammatory state.

It is now recognized that adipose tissue functions in part as an endocrine organ.[14] It secretes many immunomodulatory factors and sends inflammatory signals.[15] Elevated concentrations of TNF-α and IL-6 have been found in obese subjects.[16] This proinflammatory state may contribute to the atherosclerotic disease process. Dietary interventions that aid in body fat reduction may reduce proinflammatory cytokines and the inflammatory response. This may in turn reduce atherosclerotic disease risk.

General Nutrition Recommendations

Basic heart healthy dietary practices should be encouraged. The National Cholesterol Education Program (NCEP) has developed dietary guidelines (Table 1) for individuals with elevated cholesterol, those at risk for cardiovascular disease, or those with known cardiovascular disease. It should be noted that these guidelines are undergoing a revision and should be available in 2010. The goal of the current guidelines is to decrease total cholesterol (TC) and LDL-C levels, while maintaining or increasing high density lipoprotein cholesterol (HDL-C) level. Desirable/optimal levels of TC, LDL-C, and HDL-C can be found in Table 2. The following basic principles should be adhered to:[1]

- Eat a variety of fruits, vegetables, and whole grain or high fiber foods.
- Minimize the intake of salt and sugary foods and beverages.
- Dairy products should be fat-free or low-fat.
- Legumes, lean meats, and poultry without the skin are good protein choices. Soy protein may be used to replace some animal protein.
- Fatty fish (i.e., salmon, tuna, mackerel, sardines) should be consumed at least twice per week.
- Saturated fat found in butter, cheese, and animal fat should be limited.
- Trans fat, in processed snacks and sweets should make up less than 1% of total calories.
- The majority of dietary fat should come from monounsaturated and polyunsaturated fats such as nuts, seeds, fish and vegetable oils.
- Most people should limit cholesterol intake to less than 300 mg per day.
- If the LDL-C level is over 100 mg/dL or the individual has heart disease, cholesterol intake should be less than 200 milligrams a day and the individual should follow the "Therapeutic Lifestyle Changes (TLC)" diet created by the NCEP (Table 1).
- Maintain a healthy body weight and body composition.
- The use of functional foods and the support of nutritional genomics can further strengthen the basic dietary intervention.

Table 1: TLC Diet

Nutrient	Recommendation
Saturated Fat*	Less than 7% total calories
Polyunsaturated Fat	Up to 10% of total calories
Monounsaturated Fat	Up to 20% of total calories
Total Fat	25-35% of total calories
Carbohydrate	50-60% of total calories
Fiber	20-30 grams per day
Protein	Approximately 15% of total calories
Cholesterol*	Less than 200 mg per day
Plant Stanols/Sterols**	2 grams per day
Increased viscous (soluble) fiber**	10-25 grams per day
Total calories (energy)	Prevent weight gain - balance energy intake and expenditure

*LDL-raising nutrients

**Therapeutic options for LDL-lowering

Source: American Heart Association[17]

Table 2: Cholesterol Classification (mg/dL)

Total Cholesterol	LDL Cholesterol	HDL Cholesterol
Desirable < 200	Optimal <100	High(good) ≥ 60
Borderline high 200-239	Above Optimal 100-129	Low (poor) < 40
High ≥ 240	Borderline high 130-159	
	High 160-189	
	Very high ≥ 190	

Source: US Department of Health and Human Services[18]

The Role of Nutrition and Functional Foods

Evidence suggests that dietary factors play an important role in the prevention and treatment of atherosclerosis. Nutritional therapies should target traditional cardiovascular disease risk factors (i.e., elevated cholesterol, hypertension, and obesity). This article will, however, focus on four key components in the atherosclerotic disease process: 1) LDL-C deposition, 2) oxidation of LDL-C, 3) inflammation, and 4) thrombosis. Functional foods appear to provide protection in each of these areas and can help tailor a diet to address the special needs of an individual.

What are Functional Foods?

Although there is not a legal definition of a functional food, the Institute of Medicine's Food and Nutrition Board has defined functional food as "any food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains."[19,20] Generally speaking, functional foods have a positive impact on one's health. These foods might, for example, aid in the prevention or treatment of a specific disease such as atherosclerosis.

The health benefits or desirable physiological effects attributed to functional foods may be due to their biologically active components. Table 3 highlights functional foods or food components that are thought to have cardiovascular benefits. Selected functional foods and supplements will be discussed for their roles in reducing LDL-C deposition, LDL-C oxidation, inflammation, and/or thrombus formation (Table 4).

Table 3. Functional Foods with Cardiovascular Benefits

Functional Food/Component	Food/Dietary Sources
Dietary Fiber	
○ Soluble fiber	Apples, beans, citrus fruit, peas, psyllium seed husk
○ Whole grains	Brown rice, cereal grains, oatmeal, whole wheat bread
○ Beta glucan	Barley, oatmeal, oat bran, rye, mushrooms
Fatty Acids	
○ MUFA	Avocado, canola oil, olive oil, tree nuts
○ PUFA (ALA)	Flaxseed, walnuts
○ PUFA (EPA & DHA)	Calamari, mackerel, salmon, tuna
Plant Stanols & Sterols	
○ Free stanols/sterols	Sterol-fortified foods/beverages, corn, soy, wheat
○ Stanol/sterol	Sterol-fortified spreads,

esters	dietary supplements
Soy	
○ Soy protein	Soy beans, soy foods, soy protein isolate
Phytoestrogens	
○ Lignans	Flaxseed, some vegetables, rye
Sulfides/Thiols	
○ Allyl methyl trisulfide, diallyl sulfide	Garlic, leeks, onions, scallions
Flavonoids	
○ Anthocyanins	Berries, cherries, red grapes
○ Flavanols (i.e., catechins, epigallocatechin)	Apples, chocolate, grapes, black tea, green tea
○ Flavanones (i.e., naringenin, hesperetin)	Citrus foods
○ Flavonols (i.e., kaempferol, quercetin)	Apples, broccoli, onions, tea
Isothiocyanates	
○ Sulforaphane	Broccoli, cauliflower, cabbage, kale, horseradish
Minerals	
○ Potassium	Bananas, beans, citrus juices, cereals, low-fat dairy, nuts, potatoes, tomatoes, whole grain breads
○ Selenium	Brazil nuts, garlic, grains, eggs, fish
Phenolic Acids	
○ Caffeic acid, ferulic acid	Apples, citrus fruits, coffee, pears, some vegetables
Vitamins	
○ Vitamin C	Acerola cherry, citrus fruit, kiwi, strawberries, sweet red/green pepper
○ Vitamin E	Almonds, hazelnuts, sunflower seeds, turnip greens

ALA – *a*-linolenic acid; DHA – docosahexaenoic acid; EPA – eicosapentaenoic acid; MUFA – monounsaturated fatty acids; PUFA – polyunsaturated fatty acids

∗Adapted from International Food Information Council Foundation Functional Foods Component Chart.[21]

Table 4. Functional Foods Involved in Reducing LDL-C Deposition, LDL-C Oxidation, Inflammation, and Thrombosis

Benefit	Food or Food Components
Improve Cholesterol Concentration	Oats, soy, psyllium, flaxseed
Reduce LDL Oxidation	Garlic, CoQ10, antioxidants (i.e. vitamin C, E), rosehips, green tea
Improve Antioxidant Defense/Neutralize Free Radicals	CoQ10, vitamin C, vitamin E, Beta-carotene, selenium, grapes, rosehips, blueberries, blackberries
Reduce Inflammation	Omega-3 fatty acids, grapes, blackberry, blueberry
Reduce Thrombosis	Garlic, onion, flaxseed

Beyond the TLC: Functional Foods with Cardiovascular Benefits

Oats. Oatmeal and oat bran have been widely studied for their cholesterol lowering capabilities. Statistically significant reductions in TC and LDL-C have been seen in hypercholesterolemic patients. Based upon a meta-analysis of 20 trials, the

intake of 3 grams of soluble fiber (from oats) per day resulted in a 5-6 mg/dL reduction of plasma cholesterol in hypercholesterolemic subjects.[22] This small reduction in plasma total cholesterol has been suggested to be clinically significant and likely to reduce risk for coronary heart disease by 27%.[23] A health claim has been approved by the U.S. Food and Drug Administration (FDA) stating that soluble fiber from oat bran may reduce the risk of heart disease when added to a diet that is low in saturatedfat and cholesterol. Beta glucan, a soluble fiber found in oat and barley products, is credited for the lipid lowering effects.

Soy Protein. Hypercholesterolemic patients that fortify their diets with soy protein are able to significantly lower TC and LDL-C.[1] Evidence exists for the role of soy protein in reducing blood cholesterol.[24] In fact, the FDA has approved a health claim based on scientific evidence for soy protein and reduced risk of cardiovascular disease. The claims reads, "25 grams of soy protein a day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease." It should be noted that the FDA is re-evaluating this claim due to recent mixed evidence.

Stanols and Sterols. In 2001 the American Heart Association (AHA) released a science advisory for healthcare professionals. This advisory discussed the possible health benefits of plant stanols and sterols in conjunction with a low fat diet. The FDA has approved a health claim stating that diets low in saturated fat and cholesterol that include plant sterol and stanol esters may decrease the risk of heart disease through the direct link of blood TC and LDL-C. Plant sterols and stanols reduce LDL-C by interfering with cholesterol absorption.[25]

Consumption of plant stanols and sterols has been reported to reduce LDL-C concentrations by 5-20%.[24,26] A recent meta-analysis showed an association between plant stanol and sterol intake and a significant reduction in LDL-C (-12 mg/dL). This study found a positive dose response relationship between LDL-C reduction and plant sterols and stanols intake up to 2.5 gram per day. Doses higher than 2.5 grams per day showed little additional benefit.[25] This dose is similar to 2 gram per day dose recommended by the AHA.[13]

Psyllium. Psyllium is an excellent source of soluble, viscous fiber. Psyllium has been found to decrease serum TC and LDL-C. It has consistently been shown to normalize or decrease blood lipid concentrations in patients with hypercholesterolemia and/or type 2 diabetes. The FDA has approved a health claim that consuming soluble fiber from foods such as psyllium seed husk (PSH) in conjunction with a diet low in saturated fat and cholesterol may decrease the risk of heart disease. To carry this claim a food must provide at least 1.7 grams of soluble fiber from PSH per serving.[27]

Garlic. Over the last several decades, scientific research has been examining the health benefits of garlic. Early clinical trials demonstrated very promising results. Recently, several of the early trials have been criticized for poor design, and lack of adequate controls. More rigorous clinical trials examining garlic's efficacy have failed to reproduce the same magnitude of effects reported in some of the early studies. However, when the entire body of research is considered, the benefits of supplemental garlic powder are apparent, albeit of less impact than previously thought. Garlic does appear to exert beneficial effects on cardiovascular health.[28]

Many clinical trials and several meta-analyses have reported significant reductions (2%-25%) in TC levels with garlic use.[29-36] Garlic, however, has a number of protective effects independent of cholesterol related concentration changes, such as

reduced triglycerides, blood pressure, decreased platelet aggregation, improved blood flow, decreased fibrinogen, and reduced atherosclerotic plaque volume.[31,37] Animal studies have demonstrated that purified allicin, an important bioactive compound in garlic, can reduce atherosclerotic plaque without lowering LDL-C concentration.[38] Other bioactive compounds, such as ajoene, allixin, erubosides, *S*-allyl cysteine, and *N*-acetyl *S*-allyl cysteine, exist in garlic. Many of these compounds have antiplatelet effects, antithrombotic effects, and affect the expression of endothelial adhesion molecules elevated during endothelial injury. In vitro studies have demonstrated that several isolated garlic compounds reduce the oxidation of LDL-C.[39]

A dose ranging from 600 mg to 1,200 mg per day is often seen in clinical trials. This amount corresponds to approximately one to two cloves of garlic per day. Garlic powder is, however, typically used in clinical trials and the dosage is based upon the biomarker, alliin. It is recommended that the garlic powder be standardized to 1.3% alliin for observable health benefits.[40] In most studies garlic powder was taken in multiple doses throughout the day rather than as a single dose. This may enhance absorption.

Coenzyme Q_{10}. Coenzyme Q_{10} (CoQ_{10}), commonly known as ubiquinone, is a vital cofactor in the electron-transport chain. Therefore, CoQ_{10} plays an important role in the energy metabolism of food as well as cellular energy production.[41,42] Tissues with high energy needs or high metabolic activity, such as the heart, contain high levels of CoQ10.[43] It is therefore not surprising that the therapeutic effects of CoQ_{10} have been studied in patient with cardiovascular disease. It has been reported that individuals with cardiovascular disease have abnormal concentrations of CoQ_{10}.[44]

Preliminary research demonstrated an association between tissue levels of CoQ_{10} and congestive heart failure (CHF). Some studies found improvements in ejection fraction, stroke volume, cardiac index, and exercise tolerance. Unfortunately, not all studies have shown improvements. This may be attributed to poor study design in early research. Additional evidence from in-vitro, animal, and human studies, however, does suggest CoQ_{10} supplementation improves cardiovascular health.[45-49]

Benefits of CoQ_{10} may be attributed, at least in part, to its antioxidant capabilities. In its reduced form, CoQ_{10} (ubiquinol), acts as an antioxidant protecting biological membranes from free radicals.[50,51] It effectively scavenges superoxide radicals.[52] CoQ_{10} is effective in protecting against oxygen-generated damage to cellular membranes and lipid transport molecules (lipoproteins).[53-55]

Preliminary evidence suggests that supplemental CoQ_{10} may also mitigate statin (HMG-CoA reductase inhibitors) induced myotoxicity. Blood CoQ_{10} concentrations are reduced by statin therapy. Statins inhibit cholesterol synthesis by inhibiting HMG-CoA reductase and the mevalonate pathway.[53] CoQ_{10} is synthesized from mevalonate and tyrosine. It is one of several end products of the mevalonate pathway. Hence, the inhibition of the mevalonate pathway by statins will reduce CoQ_{10} synthesis. This reduction in CoQ_{10} may contribute to myotoxicity via reduced mitochondrial metabolism. CoQ_{10} supplementation has been found to increase CoQ_{10} concentrations and may lessen the muscle damaging effects of statins. Routine use in all patients taking statins is, however, not recommended due to a lack of clinical documentation.[53]

Normal plasma levels typically fall between 0.7-1.0 µg/mL.[56] A 30-60 mg per day dose appears to maintain this level.[57] Plasma levels

typically need to reach a level between 2-3 µg/mL to stimulate a clinical effect.[56,58] A 100-200 mg per day dose appears to be required to reach a clinically effective plasma level.[58] It may take several weeks to reach a value greater than 2.5 µg/mL.[56]

Omega 3 Fatty Acids. Unsaturated fatty acids are receiving increasing attention as potential anti-inflammatory and anti-atherogenic agents.[60] Omega-3 polyunsaturated fatty acids (PUFA) in particular appear to possess the most potent immunomodulatory activities. Among the omega-3 PUFA, the long-chain PUFA from fish oil, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) appear to be more biologically potent that *a*-linolenic acid (ALA).

Effects brought about by omega-3 PUFA may be due to their ability to modulate the amount and types of eicosanoids made, but they also elicit eicosanoid-independent mechanisms.[61] Omega-3 PUFA appear to reduce endothelial expression of inflammatory markers such as, VCAM-1, ICAM-1, E-selectin, IL-1β, IL-6, IL-8, and TNF-α.[62-66] Based on these anti-inflammatory effects, supplementation with omega-3 fatty acids theoretically has an antiatherogenic and plaque stabilizing effect.

Numerous studies have found supplementation to reduce cardiovascular disease risk. Population studies globally have shown protective relationships between omega-3 fatty acids and CVD. Results from large-scale epidemiological studies and clinical trials suggest fish consumption or fish oil supplementation lead to reduced incidence of coronary heart disease,[67] reduced risk of sudden cardiac death,[63,68,69] and reduced all-cause mortality and coronary mortality.[70] Based on existing evidence the FDA permitted a qualified health claim for foods and dietary supplements containing EPA and DHA and the reduced risk of coronary heart disease.[71,72]

The amount of omega-3 fatty acids that should be consumed depends on an individual's health status. The American Heart Association makes fish and omega-3 fatty acid recommendations based on the population. These recommendations can be found in the following Table 5.[17]

Table 5. Recommendations for fish and omega-3 fatty acid intake

Population	AHA Recommendation
Patients without documented CVD	Eat a variety of fatty fish at least 2 days per week.
Patients with documented CVD	Consume approximately 1 g of EPA + DHA per day†
Patients who need to lower triglycerides	Consume approximately 2-4 g of EPA + DHA per day‡

†Consult physician prior to supplementing
‡Provided in capsules under a physician's care

Antioxidants. Antioxidants are thought to inhibit atherogenesis and improve vascular function. They improve biologic activity of endothelial derived NO and help to dispose of reactive oxygen species (ROS).[1] In-vitro studies have found α - tocopherol to directly inhibit atherogenic mechanisms including monocyte release of ROS, monocyte-endothelial cell adhesion, IL-1 and TNF-α cytokine release, LDL oxidation, , platelet adhesion, and smooth muscle cell proliferation.[1] Consumption of both vitamin E and vitamin C appears to provide greater antioxidant benefit than ingestion of either vitamin alone.[1,73,74] The antioxidant selenium has an inverse relationship with both atherosclerosis[75] and cardiovascular mortality.[76] Selenium is a cofactor for glutathione

peroxidase, a critical enzyme involved in catalyzing the reduction of endothelial cell membrane oxidants (i.e., lipid hydroperoxides) to less reactive alcohols.[1] Grapes (wine, juice, skins, seeds, resveratrol). Red grape skins and red wine contain many polyphenolic compounds, including pro-anthocyanidins, trans-resveratrol, and flavonoids such as kaempferol, catechins, and quercetin.[77] These act as antioxidants. Resveratrol, in addition to its antioxidant effects, has anti-inflammatory properties, can cause blood vessel dilation, and can inhibit platelet aggregation. Resveratrol has been shown to reduce inflammation in animal studies, in part, by reducing IL-1β, TNF-α, and PGE2.[77]

Grapeseed extract has been found useful in ways similar to other grape products. Grape seeds have a high content of catechins and pro-anthocyanidins; both are members of the flavonoid family and function as powerful antioxidants.[78-80] The ability of grape seed extract to scavenge free radicals is reportedly better than that observed with vitamins C, E, and beta-carotene.[81] Grape seed extract has also been shown to relax the endothelium via release of nitric oxide.[82-84]

Pro-anthocyanidins, found in grape seed extract, scavenge free radicals and prevent peroxidation of lipid membranes.[85,86] Pro-anthocyanidins may help protect the integrity of vascular structures and they may reduce atherogenic factors such as blood pressure, cholesterol levels and the aggregation of clotting factors (platelets) in the blood.[87,88]

Rosehips, Blueberries, and Blackberries. Rosehips, blueberries, and blackberries have a number of heart healthy benefits.[89,90] Rose hips are high in vitamin C, have high phenolic content, and scavenge free radicals (i.e. superoxide).[91] Rose hips extract may also support cardiovascular health by limiting lipid oxidation and reducing the chemotaxis of leukocytes.[92,93] In an animal model, blackberry extract reduced ICAM-1 expression. This may be one mechanism by which blackberry extract reduces the inflammatory process.[94] In vitro studies further show that blackberry extract scavenges peroxynitrite free radicals to protect against endothelial dysfunction and reduces C-reactive protein (CRP).[91,95,96] Blueberry extract contains anthocyanins and hydroxycinnamic acid, which impact the inflammatory response in vitro.[97] Anthocyanins appear to inhibit the expression of IL-8, MCP-1, and ICAM-1, while hydroxycinnamic acids inhibit the expression of IL-8 and ICAM-1.[98]

One botanical formulation discussed in the nutritional genomics section of this article found a botanical formulation containing rosehips extract (1200 mg/d), grape extract (40 mg/d), blackberry powder(165 mg/d), and blueberry powder (330 mg/d) effectively targeted mediators involved in the atherosclerotic disease process.[94]

NUTRITIONAL GENOMICS

What is Nutritional Genomics?

The wealth of information generated by the Human Genome Project combined with recent advances in molecular biology have fostered the emergence of nutritional genomics. Nutritional genomics is a new discipline in the field of nutrition science. This new discipline is paving the way for personalized nutrition as more associations between dietary components and gene variants are identified.[99] It is anticipated that nutritional genomics will play a major role in disease prevention. Research in this area will lead to greater use of existing foods, food components, and novel foods in the prevention and treatment of atherosclerosis and other chronic disorders.

There is a two-way interaction between genes and components in food. A person's genetic

makeup determines how well they can use various food components to support health. The study of how individual genotypes determine a person's response to food components is called nutrigenetics. Conversely, nutrients and other food components influence gene expression and the production of the proteins encoded in the genes. Essential nutrients (i.e. macronutrients, micronutrients), other bioactive substances (i.e. phytochemicals), and metabolites from food components (i.e. eicosanoids), and xenobiotics are all dietary components that can influence gene expression.[100] Genes are exposed to nutrients in foods throughout life. Hence, diet is a critical environmental factor that influences gene expression. Bottom line, gene expression plays a major role in our very existence. Nutrients affect gene expression and formation of proteins that serve as hormones, enzymes, oxygen transporters, and building blocks for cells. Hence, the amount and the form of nutrients present during gene expression can alter protein synthesis and thereby affect health. The study of how food components influence gene expression is called nutrigenomics.

Nutritional Genomics, Inflammation, and CVD

Dietary recommendations, such as those set forth by the NCEP, have been found effective in populations. Individuals, however, respond differently to the treatment. This may be due to genetic variations within the population. Recent scientific evidence indicates that some CVD, including MI, is due to inherited gene variations. Genetic susceptibility may lead to more severe or earlier CVD. Some of these variants are susceptible to dietary intervention.[93,101] Nutritional genomics, sometimes called "personalized nutrition", uses an individual's unique genetic makeup to make recommendations.

Some individuals have a genetic predisposition for over-expression of inflammation. Genetic susceptibility to overexpression of the IL1 genes, for example, may lead to more severe or earlier CVD.[7] IL1 plays a key role in regulating and coordinating inflammation.[102] In an inflammatory response the IL1 gene is one of the first to be activated. It activates other proinflammatory cells, proteins and other molecules. It is responsible for activating other cytokines and chemical messengers that will maintain the inflammatory response.[93] Small differences in the activation of the IL1 gene can have a significant effect on how powerfully the inflammatory system responds.[93,103] Evidence now shows that people that test positive for the IL1 risk pattern also have elevated CRP levels and individuals with elevated CRP levels are at increased risk for CVD.[104,105] This knowledge can help the nutrition or healthcare provider develop a personalized nutrition plan.

What's Out There Now?

Scientists are discovering new ways to uncover diet-gene interactions at the molecular level. One company, for example, has created a genetic test that analyzes two IL1 genes that lead to over-expression of inflammation and risk for CVD. Testing positive for these genes does not mean that the individual will develop cardiovascular disease, but it does let them know they are at greater risk. Nutritional interventions, including nutritional genomics supplements, designed to target these genes and reduce inflammation may improve cardiovascular health.

Scientists are discovering gene-disease associations at a steady pace, investigating the molecular mechanisms, and identifying the influence of gene variants on disease susceptibility. The goal here is to identify gene variants that are strongly associated with risk for particular diseases so that disease susceptibility can be detected early in life and appropriate action taken to minimize risk. Additionally, gene-diet associations

are being detected that link gene variants and diet and lifestyle approaches that provide guidance for decreasing disease susceptibility.

Numerous genes, gene variants, disease, and diet/lifestyle approach associations have been detected to date. Since inflammation is a major predisposing factor in the development of cardiovascular disease, the IL1 gene family is being studied in an attempt to identify gene variants that increase the risk of developing cardiovascular disease and diet and lifestyle approaches that target these gene variants, thereby decreasing this risk.

Nutritional genomics is also facilitating research and development of novel nutraceuticals and functional foods that target mediators involved in the atherosclerotic disease process. One study demonstrated that a botanical formulation containing rosehips extract (1200 mg/d), grape extract (40 mg/d), blackberry powder (165 mg/d), and blueberry powder (330 mg/d) could influence expression of the IL1B gene.[93] The mixture significantly decreased IL1B gene expression and CRP levels in healthy individuals with gene variants associated with over expression of the IL1 cytokine. These results suggest that dietary approaches can influence gene expression and thereby, decrease the magnitude of inflammation and risk of developing CVD.[93]

Evolving and powerful genomic technologies are shaping the field of nutritional genomics. As this research advances and the mystery behind gene-diet interactions unfolds, strategies for more personalized and more effective nutrition therapies will be developed. A few novel products have already hit the market place. As the science behind nutritional genomics evolves, we can expect new strategies for preventing and treating atherosclerosis.

TAKE HOME MESSAGE

Prevention and treatment of atherosclerosis is accomplished by interventions that attempt to reduce LDL-C, oxidation of LDL-C, inflammation, and thrombogenesis. Functional foods appear to provide protection in each of these areas and can help tailor a diet to address the special needs of an individual. The emerging field of nutritional genomics can further help a dietitian determine a patient's individual needs based on his or her unique genetic makeup. This knowledge will allow for a more personalized and effective nutrition plan.

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Dr. Vargas was a Research Scientist in the Supplement Product Development Department at the Nutrilite Health Institute. Her research emphasized the development of botanical products with functional properties designed to maintain health and well-being. She supported many product lines including, sports supplements, weight management, heart health, women's health, and men's health.

Prior to joining Nutrilite, Dr. Vargas was a professor at California State University, Fullerton. She taught courses in nutrition, clinical exercise physiology, and health. She was also an adjunct faculty member at Loma Linda University where she taught a course in electrocardiography (ECG). Dr. Vargas worked as a Clinical Exercise Physiologist in Cardiac Rehabilitation. She also worked as a Preventive Care Specialist, where she provided lifestyle therapy to weight management patients. Dr. Vargas has authored manuscripts on weight management; atherosclerosis, functional foods, and nutritional genomics; and the relationship between CRP, metabolic syndrome, and exercise.

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Integrative Cardiology: Nutrition, Nutraceuticals and Enhancing Resiliency in Cardiovascular Disease

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Introduction:

Cardiovascular disease is one of the most prevalent lifelong diseases, affecting over 50% of the population, and increasing in incidence every year. Despite major medical advances such as coronary stenting and statin therapy, cardiovascular disease still accounts for one out of every six deaths in Americans. The risk factors for having an acute myocardial infarction were clearly summarized in the Interheart Study (Ogden et al. 2006). These factors (smoking, elevated ApoB/ApoA1 ratio, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruits and vegetables, regular alcohol consumption, lack of regular physical activity) were found to account for over 90% of cardiovascular risk. If you review Interheart, you will note that the identified risk factors extend beyond what is currently assessed by the Framingham score. Psychosocial risk in Interheart was as powerful a predictor of a cardiac event as mid-line obesity and hypertension.

At the Scripps Center for Integrative Medicine we have used Interheart as a road map to design programs that address all risk factors for cardiovascular disease from nutrition and physical activity to depression, anxiety and maladaptive responses to stress and tension. We take a holistic approach which addresses the entire person; body, mind, emotions and spirit. When considering an integrative holistic approach, one takes into account not only genetic and social predispositions, but emotional, environmental, and spiritual contributions as well. We now know that epigenetics plays a crucial role in manifesting and preventing disease and that seventy to ninety percent of chronic disease is related to lifestyle. Only when the entire spectrum of disease causing factors is addressed can we achieve a true and effective strategy for the care of patients with cardiovascular disease, and effect a true improvement in their quality of life.

Nutrition:

There is no question that diet and nutrition are the essential building blocks of good health. Hippocrates the father of medicine taught "food is medicine" and an ancient Ayurvedic proverb states "with proper food, medicine is of no need". With regard to cardiovascular health the effects are tangible and apparent, with hard clinical endpoints such as myocardial infarction, heart failure, hypertension, obesity and cardiovascular mortality. There have been numerous epidemiologic studies highlighting the effect of diet on individuals even after accounting for genetic predisposition and variations among ethnic groups.

One of the largest early epidemiological studies was conducted by Chen et al. in 1990, which followed over 10,000 individuals in China and the United States. The U.S. diet was found to be twice as high in fat, three times lower in fiber in and significantly higher in animal protein. This study also demonstrated that there was a 16.7 fold increase in deaths from heart disease in men, and a 5.6 fold increase for women with notably higher rates of cancer, diabetes and hypertension in the U.S. population. More importantly, Asian immigrants adapting a standard American diet matched the American levels of heart disease within just two generations (Chen et al. 1990).

The impact of diet was also highlighted by the pivotal Lyon Diet Heart Study, a randomized control trial which assessed the benefits of a Mediterranean diet for secondary prevention in cardiovascular disease. Individuals with a prior myocardial infarction (MI) were placed on a Mediterranean diet rich in fruits, vegetables, fish, oils high in α-linolenic acid, and less red meat (n=302) compared to a standard diet (n=303). The benefits of the Mediterranean diet were profound, with a 50-70% reduction in recurrent cardiac events at as early as 46 months. The results were so compelling that the study was actually terminated early (Kris –Etherton et al. 2001). These findings were reproduced in subsequent studies such as the HALE project, which concluded "Among individuals aged 70 to 90 years, adherence to a Mediterranean diet and healthful lifestyle is associated with a more than 50% lower rate of all-causes and cause-specific mortality" (Knoops et al. 2004).

Earlier trials, simply evaluating the benefits of increasing dietary fruits and vegetables demonstrated similar positive health impacts in several risk factors for cardiovascular disease. In one study of 459 adults, the investigators found that "A diet rich in fruits, vegetables and low fat dairy foods and with reduced saturated and total fat can substantially lower blood pressure ($p < 0.001$) (Appel et al. 1997.) Similarly, the Nurse's Health Study and Health Professional's Follow up study conducted in over 84,000 women for 14 years and over 42,000 men for 8 years demonstrated, observationally, that "Consumption of fruits and vegetables, particularly green leafy vegetables and Vitamin C

rich fruits appears to have a protective effect against coronary heart disease" (Joshipura et al. 2001). Other studies have shown similar benefits in the reduction of stroke.

The similarity among all these nutritional approaches is the emphasis on incorporating high amounts of whole foods that are low on the glycemic index, low in saturated fat and anti-inflammatory. Inflammation is a risk factor for cardiovascular disease and is clearly linked to nutrition. Foods such as cured red meats, sugar, simple carbohydrates and food sensitivity can lead to inflammation. The Mediterranean diet which is high in fruits, vegetables, beans and olive oil has been shown to decrease markers for inflammation such as IL6, IL 18, hsCRP and improve insulin resistance. The Mediterranean diet has also been shown to slow progression of Alzheimer's disease which has also been linked with inflammation (Scarmeas et al 2006). The inclusion of whole foods and beneficial bioactive or medicinal foods (almonds, fiber, green tea, soy, oats, berries, dark chocolate) can help decrease cholesterol, blood pressure and blood sugar.

Natural Supplements:

Unfortunately, the industrialization of food has left the Standard American Diet void of micronutrients and high in sodium and omega 6. The omega 6/omega 3 ratio is as high as 50:1 largely due to the high utilization of high fructose corn syrup as a food additive. Furthermore, the industrialized food system and current agricultural practices have significantly depleted the soil of essential vitamins and minerals. Refined foods have lost their medical quality and are high on the glycemic index leading to inflammation. Over 68% of the population is deficient in minerals such as magnesium and an equal percentage is deficient in vitamin D.

Certain supplements are fundamental to our cardiovascular practice. The approach we take in lipid management is: disorders determine treatment. All patients are treated with an anti-inflammatory, low glycemic index diet. Protein sources are preferably plant based. Physical activity is essential to maintaining ideal body weight and to decrease blood pressure, blood sugar and triglycerides. Supplements and pharmaceuticals are used to further achieve lipid goals. For example, an isolated LDL elevation may be managed with statin therapy, Zetia, red yeast rice, artichoke extract, citrus bergamot, plant sterols and fiber. A low HDL and high triglycerides would be managed with omega three fatty acids, niacin and on occasion fenofibrates. Combination therapy is frequently used. The following vitamins, minerals and supplements are commonly used in our cardiology practice but represent only a small sample of what is currently available to achieve our goals.

- *Omega Three Fatty Acids*

One of the most commonly used supplements for cardiovascular health is omega three fatty acids. Observational and epidemiological studies in the past have demonstrated the association of fish consumption with reduced cardiovascular events. A review by Stone el al indicated that men who consume fish at least three times weekly had lower rates of coronary heart disease and mortality then men who did not (Stone 1996). Further observational studies have also shown a positive dose response with fish consumption and cardiovascular disease risk factors such as obesity, hypertension, and diabetes. More recently, the Nurses' Health study demonstrated a dose responsiveness as well, comparing coronary heart disease death rates in women who consumed fish or omega3 less than one time per month, to those women who consumed fish or omega3 one to three times per month, once per week, 2-4

times per week, and greater than five times per week. The reduction in CHD related death for those who consumed the omega3 was found to be 21%, 29%, 31%, and 34% respectively as the fish consumption was increased (Kris-Etherton et al 2002).

The positive associations and potential health benefits of omega 3, are also apparent when reviewing the randomized controlled trials. The strongest evidence in the form of randomized controlled trial is gleaned from the DART, GISSI, and JELIS trials. The DART trial demonstrated a 29% reduction in all-cause mortality with 200-400g of fish per week, estimated to provide 500-800mg per day of omega3. A post hoc-analysis of those who received fish oil supplements (900mg per day of EPA+DHA) suggested a cardioprotective effect (Burr et al. 1989). These findings were supported by the GISSI- Prevention Study wherein 11,324 patients were treated with Vitamin E 300mg versus Omega3 850mg. At 3.5 years, there was a 15% reduction in the primary endpoint of death, nonfatal myocardial infarction, stroke, a 20% reduction in all-cause mortality, and 45% reduction in sudden cardiac death in the Omega3 group (Hooper et al. 1999). Similarly, the Japan Eicosapentaenoic acid (EPA) Lipid Intervention Study (JELIS) was conducted in 18,645 patients in Japan with hyperlipidemia who consumed large amounts of fish at baseline. Individuals were treated with a statin plus 1800mg EPA versus statin alone for 5 years. Those on combination statin and EPA therapy had a 19% relative reduction in major adverse cardiovascular events (Yokoyama et al. 2007).

These generally widely accepted benefits were recently called into question with the publication of the recent New England Journal of Medicine trial in 2010 (n-3 Fatty Acids and Cardiovascular Events after Myocardial Infarction). In this randomized controlled trial of 4,837 post MI patients age 60-80, subjects were randomized to receive omega3 in the form of margarine - EPA/DHA 400mg, α-linolenic acid 2g (plant based), EPA/DHA & α-linolenic acid, and placebo margarine. As expected, at such small doses, no benefit was apparent in the primary endpoint of fatal and nonfatal cardiac events or need for cardiac interventions (Kromhout et al. 2010).

What these important trials high light, is that there is not only a benefit, but perhaps there is a true dose threshold of the ideal amount of EPA/DHA. Unfortunately, these studies did not measure omega6/omega3 ratios which can vary significantly from person to person. Currently, the recommended dose of EPA and DHA is 900 mg per day for primary or secondary prevention, but for treatment of hypertriglyceridemia 1000-4000mg per day is recommended. Lovaza is FDA approved for the treatment of hypertriglyceridemia. A 4 gram dose of Lovaza per day is associated with a 45% reduction in triglycerides. Of course, one of the greatest challenges we face in the use of fish oil is the exploitation of our ocean resources. More sustainable omega 3 sources will have to be obtained in addition to limiting the amount of omega 6 in the diet. The later seems more reasonable.

- *Niacin (Vitamin B3)*

Niacin has recently received some unfavorable press with the publication of the recent AIM-High data in the NEJM, in 2011. This trial, set out to assess the rate of coronary heart disease, non-fatal myocardial infarction, ischemic stroke, hospitalization > 23hr for ACS and symptom driven coronary or cerebral revascularization over a 36 month period in 3,414 patients randomized to niacin 1500-1800 mg per day in addition to simvastatin 40-80 as compared to statin alone.

The trial was terminated early due to a lack of clear benefit in the niacin group. However, when examined more closely, it appears that the event rate overall was much lower than anticipated, and the population chosen was relatively low risk overall (average LDL=60) when compared to prior studies and compared to the general population. There was in fact a favorable benefit in the lipid profile with an increase in HDL from 35-42 at 2 years, a reduction in triglycerides from 164 to 122, and reduced LDL from 74 to 62, with the bulk of benefit occurring within the first year. Many questions have been raised regarding this research because of the low LDL at baseline from statin therapy and the small increase in HDL. Prior well established studies, such as Framingham, the Coronary Drug Project, the HATS trial, and ARBITER 2 have all pointed toward increased cardiovascular events in people with low HDL. The Coronary Drug Project, an early randomized controlled trial with long term follow up compared 5 drug regimens in males with prior MI, one of which was niacin. With 3 grams of Niacin per day (n=1119) versus placebo (n=2787) there was a notable reduction in total cholesterol by 10%, triglycerides by 27% and a reduction of MI at 5 years. Over 15 years there was a 4% absolute reduction in mortality (Canner et al. 1986).

Previously, Niacin has been shown to have a broad range of beneficial effects on the lipid panel, lowering LDL and Lp(a), shifting to more favorable particle size, and raising HDL. These benefits appear to be dose-dependent, and the current recommendation is 1000-2000 mg per day.

- *Red Yeast Rice*

Red Yeast Rice (RYR) is a useful alternative for LDL lowering, particularly for those patients who are reluctant to take statin medication. RYR is an end product of the yeast (Monascus purpureus) which grows on certain grains of rice. Red yeast rice acts as an HMG-CoA reductase inhibitor, and is in fact chemically identical to lovastatin in some purifications. Numerous studies have validated its use, demonstrating reductions in LDL of 20-30%. RYR is well tolerated. Halbert compared RYR 2400mg daily to pravastatin 20 mg daily in 43 patients with a history of statin induced myalgia. At 12 weeks, the rate of discontinuation due to myopathy was 5% in the RYR group versus 9% in the pravastatin group, both demonstrating a 27-30% reduction in LDL (Halbert et al. 2010)

RYR has the same side effect profile as statin therapy. Patients should be monitored for myopathy and liver enzyme abnormalities. In patients with a history of statin induced myopathy red yeast rice should be used with caution and at lower doses.

- *Garlic*

Garlic's greatest role is in hypertension, with research demonstrating a reduction in systolic blood pressure by ~8%, and diastolic blood pressure by ~7%. The current recommendation for garlic is 600-900mg/day powder, or 2400mg daily of aged garlic extract. For those who prefer garlic as a food this is equivalent to four cloves of raw whole garlic per day.

- *Vitamin D*

Although the mechanism is not fully understood, a number of previous epidemiological studies have associated low vitamin D levels with increased adverse cardiac events and increased mortality. Proposed mechanisms range from impaired cardiac contractility to effects on the renin-angiotensin-aldosterone system, and even in glycemic control. The NHANES study 1998-1994 surveys found that Vitamin D < 20 was associated with a higher level of self-reported angina, myocardial

infarction or congestive heart failure. A more recent follow up NHANES survey from 2000-2004, corroborated this, in addition to adding peripheral vascular disease. Cohort studies support this data; in the Health Professionals Follow up study, a 10 year follow up of men with Vitamin D < 15 were found to have a 2 fold increase in myocardial infarction (Giovannuci et al 2008). Similarly, in the Framingham offspring study, individuals with severe Vitamin D deficiency <10 and no cardiac history were noted to have a hazard ratio of 1.8 (95% CI 1.05-3.08) for development of a cardiovascular event in 5 years when compared to individuals with Vitamin D >15. Additional studies have demonstrated that low Vitamin D levels are associated with hypertension, as in the Nurses' Health Study (Forman et al. 2007).

With regard to randomized control trials, the data is still inconclusive regarding the benefit of supplementation. Not only is the dose unclear, but the target serum levels are not agreed upon. There have, however been studies demonstrating a reduction in systolic blood pressure with 800IU of Vitamin D supplementation (Pfeifer et al. 2001). The most recent RECORD trial (Avenell et al. 2012) which randomized over 5000 individuals to either 800 IU of Vitamin D, 1000mg of calcium, both, or placebo did not show a statistically significant benefit in the reduction of all-cause mortality, vascular mortality, or cancer incidence. Again, however the target dose and ideal serum level is still not well established.

At the current time, there are no clear guidelines regarding the use or proper dose of Vitamin D for primary or secondary prevention of cardiovascular disease, despite the numerous observational studies linking vitamin D deficiency to increased adverse cardiovascular events. In our practice, we recommend a goal of at least 55ng/mL for serum levels, particularly for those at an increased risk for osteoporosis and breast cancer. Low vitamin D levels have been linked to depression, an independent risk factor for cardiovascular disease making treatment even more compelling.

- *Magnesium*

Magnesium is one of the most important cardiovascular minerals. In the acute care setting, magnesium is used to treat malignant arrhythmias, preeclampsia, and constipation. Magnesium has a critical role in nearly all cellular functions, and oral magnesium has been shown to act as a calcium channel blocker, increase nitric oxide, and improves endothelial function. Magnesium has a role in the reduction of arrhythmia, sudden death, ventricular ectopy (DelGobbo et al, 2012 PVCs), palpitations, hypertension, hs-CRP, and metabolic syndrome. As with vitamin D, there is no consensus on the ideal amount or levels to attain with routine supplementation. This is complicated by the fact that serum magnesium levels do not reflect intracellular magnesium concentration. For an accurate assessment of bioavailable magnesium we measure intracellular RBC magnesium levels. In observational studies, a dietary intake of 500-1000mg per day appeared to be associated with reduced blood pressure (Houston 2011).

- *Micronutrients in CHF*

In addition to the nutrients achieved through a diet rich in fiber and whole foods many individuals still have nutritional deficiencies. Our approach is to measure an individual's antioxidant and micronutrient levels and to supplement accordingly. This is of particular importance when addressing patients with congestive heart failure or cardiomyopathy. The heart is a highly metabolic organ, reliant upon many macro and micronutrients to effectively maintain its activity and function. While healthy fats and dietary carbohydrates

provide the main substrate and sources of ATP, several micronutrients such as Coenzyme Q10, L-Carnitine, Thiamine, and Taurine are essential cofactors in the process of energy conversion into efficient continuous cardiac function (Soukoulis et al. 2009)

CoEnzyme Q10, an essential component in cellular respiration in the mitochondria, has been shown to have significant benefit in individuals with congestive heart failure with regard to left ventricular (LV) function, cardiac output, exercise capacity and functional class. Early studies demonstrated decreased serum and tissue levels of CoQ10 in individuals with heart failure, with the degree of deficiency correlating to the level of LV dysfunction. In one of the largest studies 2,664 patients with NYHA class I and II CHF were treated with 50-150mg of oral CoQ10 with clinical assessments at three months. This observational study demonstrated that 54% of individuals had demonstrated improvement in at least 3 of the 9 symptoms assessed, including cyanosis, edema, pulmonary rales, hepatomegaly, hepatojugular reflux, dyspnea, sweating, arrhythmia, and vertigo. Additional smaller studies have been conducted, which imply modest benefit, although the results are variable due to variations in study population, and in barriers to determining actual myocardial CoQ10 levels. CoQ10 has been advocated as an adjunct to statin therapy for prevention or reduction of statin-induced myopathy. The data are conflicting with regard to benefit, however one study (Caso et al. 2007) did show a 40% reduction in statin related muscle pain after 30 days of treatment with 100mg per day of CoQ10 ($p<0.001$) when compared to placebo.

In all studies, there were no reports of adverse events associated with the use of CoQ10.

L-Carnitine, which is essential for fatty acid transport into the mitochondria, has also been used in the management of congestive heart failure. Like CoQ10, serum levels do not reflect true tissue concentrations, however studies have shown potential benefit from L-Carnitine supplementation. The CEDIM Trial, a randomized controlled trial of 472 post myocardial infarct patients, explored the effects of L-Carnitine on left ventricular remodeling post myocardial infarction. Patients received L-Carnitine (n=233) at a dose of 9g/day for the first 5 days, followed by 6g/day for 12 months, compared to placebo (n=239). Results by echocardiography demonstrated a significant attenuation in left ventricular remodeling in both end-systolic and end-diastolic volumes in the L-Carnitine group (Iliceto et al. 1995). Smaller studies have shown potential benefits with increases in exercise capacity, reduced pulmonary artery pressure, and favorable reductions in cardiac chamber size in patients with dilated cardiomyopathy and NYHA class III or IV functional class.

Thiamine (vitamin B1) Severe thiamine deficiency manifests as "wet" beri beri. Recent findings, have demonstrated profound thiamine deficiencies in patients with NYHA III and IV heart failure compared to class I and II, with thiamine deficiency exacerbated by diuretic use. Thiamine deficiency, in small studies, does appear to respond to oral supplementation. Hanninen et al. 2006 demonstrated that oral supplementation with 1.5mg per day in 100 hospitalized patients showed improved diuresis and ejection fraction, which correlated with increased thiamine levels. Shimon et al demonstrated a profound 22% increase in EF at seven weeks in heart failure patients receiving 200mg per day versus placebo, with improvements in ejection fraction noted as early as one week.

Whether there is a role for these micronutrients in prevention has not yet established, but as with any supplements, they must be tailored to the

individual's unique spectrum of illnesses, nutritional deficiencies, epigenetics and environmental risk.

Exercise & Cardiac Rehabilitation:

Exercise is one of the most powerful and effective methods for reducing cardiovascular morbidity and mortality, and for improving general health overall. Patients avoid exercise for a multitude of reasons. This is particularly true with regard to secondary prevention, as cardiac patients are often deconditioned, sedentary, or simply too frightened to begin exercising after a cardiac event. Well documented studies show up to a six fold decrease in cardiac death in post PCI and CABG patients who participate in a comprehensive cardiac rehabilitation program. (Taylor et al 2004). Earlier studies demonstrated that even modest exercise, such a daily walking, decreases death in both men and women by 50%. Exercise not only decreases weight, lowers blood sugar and triglycerides but improves general well-being and is a cure for stress and insomnia.

It should be emphasized that, alternatives and adjuncts to traditional exercise should be presented to patients. Ancient modalities, which have made a recent resurgence, may often better suit the needs and preferences of the individual. There have been a multitude of studies highlighting the health benefits of yoga, on a wide range of physical parameters, including cardiovascular disease. Benefits of yoga include enhancing resiliency in post myocardial infarction patients and improvement in heart failure, metabolic syndrome, blood pressure and overall quality of life (Jayasinghe 2004). Similarly, Qigong and Tai Chi, components of traditional Chinese medicine, have been shown to improve flexibility, strength, symptoms of congestive heart failure, hypertension, stress and anxiety.

In addition to these modalities, meditation, (in particular Transcendental Meditation) has shown significant health benefits with improvements in blood pressure, anxiety, and insulin resistance. Transcendental Meditation and Mindfulness Meditation are powerful medicine in helping patients find inner peace. These forms of meditation not only reduce anxiety, stress and worry but have been shown to decrease alcohol use and cigarette consumption. It is no surprise that finding inner peace leads to less addictive behaviors (Rainfort et al. 2007).

Social Support, Emotional & Spiritual Health

- *Connections with parents*

Research confirms that our social connections are a key component to health. How we live our lives, our coping skills, habits and perception of the world all have a profound impact on health outcomes. Our first relationship is in utero with our mother and from there we begin to have relationships throughout our life. These relationships have been extensively studied and offer insight into health and illness.

In the context of studying the personality traits and relationships that contribute to a physician's health and well-being, 126 male Harvard students were asked questions regarding anxiety and related mental health issues. Included were questions about their relationships with their mother and father. They were then followed for 35 years regarding their own development of health risks and illness. One of the key predictive questions was the following: *Would you describe your relationship with your mother and with your father as very close, warm and friendly, tolerant, or strained and cold?* On follow-up, 35 years later, the outcomes were:

If relationship with Mother was:

Tolerant or strained - 91% had significant health issue

Warm and close - 45% had significant health issue

If relationship with Father was:

Tolerant or strained - 82% had significant health issue

Warm and close - 50% had significant health issue

If relationship with both parents was:

Strained - 100% incidence of significant health issue

Warm and close - 47% had a significant health issue

These findings indicate a correlation between the subjects' parental relationships and their subsequent adult health. The authors offered the following explanations for the above outcomes, and why they are so striking:

1. Nutrition, stress, loving energy, both before and after birth, will contribute to the health of the individual.
2. Healthy and unhealthy lifestyle behaviors develop in childhood.
3. Coping styles develop in childhood: anxiety, anger, optimism, self-esteem.
4. Choices of stable relationships in adulthood are often mirrors of parental relationships.
5. Healthy relationship with a parent in childhood usually means the presence of a supportive parent in adulthood.
6. Spiritual values and practices are developed in childhood.

(Russek et al. 1990)

In a similar study, 1,100 male medical students were surveyed using a "Closeness to parents scale." Follow-up occurred 50 years later. The degree of closeness to parents strongly correlated with cancer rates, suicide rates, coronary artery disease rates, hospitalization for mental illness, and interpersonal difficulties. These findings were independent of smoking, alcohol use, or radiation exposures. The correlation was strongest for the development of cancer. (Thomas et al. 1974)

These two studies strongly suggest a relationship between the connection of parent to child and the subsequent health of that child as an adult. It is also important to note that these studies accounted for other disease risk factors, and the results were independent of these risk factors.

- *Connection in Marriage*

Ten thousand men were surveyed and followed for 5 years. The key outcome was the development of angina. Men with substantial risk factors for CAD (elevated cholesterol, age > 45, HTN, diabetes, EKG abnormalities) were 20 times more likely to develop angina than men without those risks. When asked, "Does your wife show you her love?" men within the high-risk group who said "Yes" had half the rate of angina as those who answered "No." This study indicates that men who perceive themselves to be loved gain comfort in that fact. It is postulated that these men have less elevations in their stress hormones such as adrenaline, noradrenaline and cortisol (Medalie et al. 1976).

Nearly 1,400 men and women who underwent cardiac catheterization and were found to have coronary artery disease were followed for 5 years. Social issues were monitored. Two key questions were (1) "Are you married?" and (2) "Do you have someone in whom you can confide?" After 5 years, roughly 15% of those who were married or had a confidant had died, while the mortality

rate was 50% for those who were unmarried or had no confidant (Williams et al, 1974).

These two studies are good examples of the power of marital relationships.

Other studies have shown the following:

- Men who are shown love by their wives have fewer gastric ulcers.
- Married men and women live longer.
- People who are in happy marriages live longer than people who are not.
- Couples who argue more have lower immune function and more frequent respiratory infections.
- People with CAD who live alone have twice the rate of MI as people who live with someone else.

All of these studies point to one fact: that happy marriage and companionship are good for your health, *independent of other risk factors.*

Contrast this to the effects of poor relationships, and similar correlations are noted. One study evaluated the effect of a relationships reported as "bad" on the individuals' health. It involved 6,114 male and 2,897 female British civil servants, with a 12-year follow-up. Adjustments were made for covariates, including age, sex, marital status, employment grade, obesity, hypertension, diabetes mellitus, and cholesterol level, as well as psychosocial factors (negative affectivity, depression, and work stress) and health behaviors (smoking, alcohol intake, exercise, and fruit and vegetable consumption). Unhappy marriages led to 34% more coronary events regardless of gender and social status (De Vogli et al. 2007).

The qualification of a relationship as "good" or "bad" however, is also reliant on the individuals' perceptions of their situation. The degree of optimism with which a situation is approached has a significant impact on outcomes as well. In a longitudinal study of dating couples, the authors tested whether optimists (who have a cognitive disposition to expect positive outcomes) and their romantic partners are more satisfied in their relationships, and if so, whether this is due to optimists' perceiving greater support from their partners. In cross-sectional analyses, both optimists and their partners indicated greater relationship satisfaction, an effect that was mediated by optimists' greater perceived support. When the couples engaged in a conflict, optimists and their partners saw each other as engaging more constructively during the conflict, which in turn led both partners to feel that the conflict was better resolved. In a one year follow-up, men's optimism predicted relationship status. Effects of optimism were mediated by the optimists' perceived support, which appears to promote a variety of beneficial processes in romantic relationships (Srivastava et al. 2006).

Another study set out to examine whether optimistic individuals live longer than patients who are pessimistic. Participants were aged 65 to 85 years (999 men and women) and completed a 30-item questionnaire on health, self-respect, morale, optimism, and relationships. Of the participants, 941 (466 men, 475 women) had complete information on questions regarding optimism. These patients were divided into four groups based on their level of optimism. Over the follow-up period of 9.1 years (1991 to 2001), there were 397 deaths. Compared to participants who reported a high level of pessimism, participants reporting high levels of optimism had a 55% lower risk of death from all causes, and a 23% lower risk of cardiovascular death. The researchers also found an inverse relationship between level of optimism and risk of death, with a stronger protective effect of optimism in men than women for all-cause mortality (Giltay, 2004).

Optimism reduces the risk of cardiovascular death through mechanisms largely unaffected by baseline values of physical activity, obesity, smoking, hypertension, and lipid profile. Pessimistic subjects may be more prone to changes across time in risk factors that affect the progression of cardiovascular disease (e.g., the development of smoking habits, obesity, or hypertension) than optimistic subjects. In addition:

- Optimism is associated with more physical activity, moderate alcohol use in women, and less smoking.
- Optimism is associated with better health in general. People in poor health tend to report more pessimism.
- Optimists may cope with stress differently and more effectively than pessimists do.

- *Social Isolation and Lack of Connection*

Social isolation seems to contribute significantly to adverse health outcomes in many disease states. Several studies in the literature have documented this phenomenon. Depression, for example, is linked with multiple diseases, such as cancer, sudden death and coronary artery disease. Nancy Frasure-Smith, in multiple studies, demonstrated that social support ameliorates the effect of depression on patients with cardiovascular disease. Social support does not necessarily eliminate the depression, but it does eliminate the adverse health outcomes of the depression (Frasure-Smith et al. 2000).

With regard specifically to coronary disease, 149 men and women undergoing cardiac catheterization were questioned about the extent they felt loved and supported. The number of blockages found on subsequent angiography correlated positively with the degree of love and support (Seeman et al. 1987).

A separate, much larger study of sixty-nine hundred individuals were surveyed and followed for 17 years. Key issues were contact with friends and relatives, church membership, membership in clubs or groups, and marriage. Those without close ties or frequent social contact had an overall death rate 3.1 times higher than those who did have these contacts. Both men and women in the low-connection category had higher cancer death rates. An analysis was done in breast cancer patients and it was found that those with low connection had twice the death rate, regardless of race (Kaplan et al. 1987).

These studies, and others, indicate that social isolation and a perceived lack of connection, is a significant risk factor for coronary artery disease, cancer, and all-cause mortality. Nobel Prize winner Elizabeth Blackburn evaluated perceived stress in women. She concluded that those women with the highest perceived stress had cells that were on average 10 years older than their biological age when compared to women with low perceived stress. Her research is one of the greatest contributors to understanding the link between stress and aging. Furthermore, these women were more prone to major risk factors for chronic disease (Epel et al. 2010) It is important to note that social isolation and stress in these studies is self-reported, and this risk is therefore related to the individual's perception.

- *Connection in the community*

The need for connection and support extends beyond the simple unit of family and friends. The collective support of one's community plays a surprisingly significant role the prevention of disease. A remarkable 50-year observational study of the towns of Roseto, Bangor, and Nazareth, Pennsylvania (PA) demonstrate this concept. In the 1930s and 1940s, it was noted that the town of Roseto, PA had a significantly lower rate of acute MI than its neighboring communities,

despite equal prevalence of diabetes, obesity, and high-fat diet in the three towns. During the follow-up in the 1970s, the rate of MI and overall mortality substantially increased in Roseto, but not the other towns. When health behaviors were analyzed, there were still no significant differences in the three communities as to smoking, weight, diet, diabetes, or other risk factors. What had changed, however, was the social structure of the town. Roseto had been populated by descendants from southern Italy in the late 1800s. In the 1930s and 1940s, it still retained a much greater number of three-generation households, close family ties and traditional religious values. As these ties began to disintegrate in the late 1960s, the rates of MI and mortality began to rise. This is the longest of the multiple studies of communities showing a clear relationship between community activity, social structure, and the rates of disease. It also points toward the role of religious practice and its effect on disease prevalence (Kaplan et al. 1987).

- *Lifestyle Change*

The Ornish lifestyle change program was one of the earliest instances in which this entire spectrum of potential health risk was studied and addressed in large scale observations and trials. This series of studies has included up to 477 patients. The Ornish intervention includes a low-fat vegetarian diet, exercise, yoga, and group support. Although these trials have had remarkable success in reversing coronary artery disease and diminishing adverse events, procedures, and cost of care, they do not specifically address the effect of group support. However, an interesting observation (yet unpublished) is that patients in the program improve (or do not improve) by group. This is referred to as the "cohort effect." Individuals in groups that bond well and interact well in their group sessions tend to have greater improvements on subsequent angiograms and fewer adverse outcomes than those in groups that become dysfunctional. This is only an observation at this time, but will be tested for significance in the future.

The group model (intentional connectedness) is clearly one of the most powerful tools we have to combat illness-related depression and anxiety. It is also one of the most potent effectors of behavioral change, as documented in chemical dependency programs. The above observations clearly suggest that group support significantly affects the clinical course of disease.

- *The Healing Physiology of Connection*

To further explore the possible mechanisms for the health benefits of connection studies regarding the role of social connection have been undertaken. Intentional connection (group support), interpersonal connection (marriage, friendship, pets), and community connection (participation in church groups and social groups) have all been shown to decrease life stress. Life stress is internally mediated through the release of catecholamines, cortisol (if chronic) and other neuro-hormonal mechanisms. Social isolation is associated with elevated catecholamines and cortisol (Cacioppo JT, 1994). Catecholamines and cortisol contribute directly to cardiac risk through the following mechanisms:

- Increased blood pressure
- Increased blood viscosity
- Increased platelet adhesion
- Decreased heart rate variability
- Increased endo-vascular reactivity and endothelial inflammation
- Increased production and release of VLDL (triglycerides) from the liver
- Increased conversion of VLDL to small dense LDL (highly atherogenic)

The stress hormones (adrenaline, nor adrenaline, cortisol and aldosterone) that ultimately increase cardiac risk can arise from a multitude of sources, highlighting the importance of teaching people how to transform stress and anger. The devastating Northridge, California earthquakes in 1996 were followed by a 5- fold increase in cardiovascular death during the acute period. Fear, anger, anxiety were clearly risk factors for these cardiovascular events. Consider Takatsubo cardiomyopathy, a well-known cardiac disease entity that by definition is precipitated by severe emotional stress, resulting in significant and often severe cardiac dysfunction. One study of 1,623 cardiac patients asked the question, "What happened during the 26 hours preceding your heart attack?" Particular attention was focused on arguments and anger, both of which were shown to trigger myocardial infarctions in both men and women (Mittleman et al. 1995). The authors concluded that an anger outburst increased the risk of a myocardial infarction 230%.

Regardless of the source, stress leads to a clear negative cardiovascular outcome, which can at times have catastrophic consequences if not recognized and treated appropriately.

Conclusions:

While western medicine excels in acute care, it falls short in cardiovascular disease prevention and chronic disease treatment. Getting to the underlying cause of disease is the essence of Integrative Medicine which utilizes approaches from all global healing traditions. Treating the whole person, body, mind, emotions and spirit is essential to achieving optimal health. Interheart has provided us a roadmap to frame the direction we need to take. This direction is not one-dimensional relating only to the physical body. Rather, it is multidimensional requiring multi-disciplinary teams of practitioners dedicated to coaching, guiding and inspiring individuals to transform their lives. We recognize that information leads to knowledge but practice leads to transformation. Providing the tools and guidance for transformation is our goal in Holistic Integrative Medicine.

Erminia "Mimi" Guarneri is board-certified in cardiology, internal medicine, nuclear medicine and holistic medicine. Dr. Guarneri is the founder and medical director of the Scripps Center for Integrative Medicine. Dr. Guarneri was an English Literature major as an undergraduate at New York University. Her medical degree is from SUNY Medical Center in New York, where she graduated number one in her class. Dr. Guarneri served her internship and residency at Cornell Medical Center, where she later became chief medical resident. She served cardiology fellowships at both New York University Medical Center and Scripps Clinic.

Dr. Guarneri served as an attending in interventional cardiology at Scripps Clinic, where she placed thousands of coronary stents. Recognizing the need for a more comprehensive and more holistic approach to cardiovascular disease, she pioneered the Scripps Center for Integrative Medicine where she uses state-of-the-art cardiac imaging technology and lifestyle change programs to aggressively diagnose, prevent and treat cardiovascular disease. She is a fellow member of the American College of Cardiology, Alpha Omega Alpha, the American Medical Women's Association, and a diplomat of the American Board of Holistic Medicine. In 2009, Dr. Guarneri was honored as the ARCS scientist of the year. She is now president-elect of the American Board of Integrative and Holistic Medicine.

Dr. Guarneri has authored several articles that have appeared in professional journals such as the Journal of Echocardiography and the Annals of

Internal Medicine. Dr. Guarneri participated as a member of the writing committee for the American College of Cardiology Foundation Complementary Medicine Expert Consensus Document. This expert consensus statement on integrating complementary medicine into cardiovascular medicine was published in 2005.

She is the author of The Heart Speaks, a poignant collection of stories from heart patients who have benefited from integrative medicine approaches. The Heart Speaks and her clinical work have been featured on NBC Today and PBS 's To the Contrary and Full Focus. In her book Dr. Guarneri takes the reader on a journey of the heart – exploring the emotional heart, able to be crushed by loss; the intelligent heart, with a nervous system all its own; and the spiritual heart, which yearns for a higher purpose. With groundbreaking new research and unparalleled experience, Dr. Guarneri skillfully weaves the science and drama of the heart's unfolding. Her work was also featured in a two-part PBS documentary, The New Medicine. Dr. Guarneri is regularly quoted in national publications such as the Yoga Journal, Body+Soul, Trustee magazine and WebMD.

She has been recognized for her national leadership in integrative medicine by the Bravewell Collaborative and now serves as chair of the Bravewell Clinical Network for integrative medicine. In 2008 Dr. Guarneri was honored by Project Concern International for her work in Southern India. She currently serves on the International sub-committee for Direct-Relief International. Dr. Guarneri served on an advisory panel for the Institute of Medicine to explore the science and practice of integrative medicine for promoting the nation's health. The summit's findings were released Feb. 25-27, 2009 in Washington, D.C. In 2011, Dr. Guarneri was the winner of the Bravewell Leadership Award which honors a physician leader who has made significant contributions to the transformation of the U.S. health care system.

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A Non-invasive Thermal-wrap Technique for Inducing Calorie Burning and Weight Loss

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Abstract

Context: With excessive weight being the second-most-important, preventable cause of premature disease and death in America, a new way to reduce weight could provide important benefits to overweight or obese individuals who find exercising or dieting difficult.

Objective: To determine if thermoregulation, in conjunction with the consumption of a well-balanced Mediterranean diet, can increase calorie burning and weight loss.

Design: This 8-week pilot study examined the effects of thermal-wrap technique on weight, percentage of fat composition, body mass index (BMI), basal metabolic rate (BMR), circumference of waist and hip, and water loss.

Setting: The study took place between November 2004 and January 2005 at the Vivinlinea Clinic in Great Neck, New York.

Patients or Other Participants: The study included 70 subjects who were either overweight or obese as determined by BMI. The study was nonrandomized, with the researchers assigning subjects to one of two groups based on the services the participants selected while attending the clinic—50 to the Thermal Group (TG) and 20 to the Control Group (CG). The distribution of subjects was self-selected in that those who requested the thermal-wrap technique received it plus nutritional planning and those who did not received only the nutritional planning.

The researchers recorded baseline morphologic measurements and personal data, including height, weight, age, and menstrual status. The groups were not matched but did not differ on baseline measures. Researchers also calculated the baseline BMI and BMR (using the Sterling-Passmore equation[14]). In the TG, 4 participants stopped the program due to claustrophobia and 3 stopped due to lack of compliance with the nutritional plan. In the CG there were no dropouts All participants who remained active through the 4-week point completed the study.

Intervention: Intervention consisted of two, 50-minute sessions each week for eight weeks, consisting of thermal-wrap technique. The thermal wrap uses electromagnetic energy to create heat, directing it to specific tissue areas. A trained professional applied the thermal wrap. Intervention for the TG and mock intervention for the CG both employed a thermal wrap; the wrap for the TG group was heated to a temperature of 44°C, while the wrap for the CG was not. The study used the thermal wrap in 2 configurations, depending on the participant's BMI. Members of both groups also received a series of dietary counseling sessions providing guidance on individualized eating programs based on a well-balanced Mediterranean diet of between 1600 and 2000 Kcal.

Outcome Measures: The researchers examined cumulative weight loss over eight weeks as the primary outcome. Secondary outcomes included changes in percentage of fat composition, BMI, basal metabolic rate (BMR), circumference of waist and hip, and water loss.

Results: At the end of the 8-week study, the CG had lost an average of 1.0 (0.7) kg while the TG had lost an average of 5.2 (1.3) kg (95% CI (Δ): 3.7-4.7, *P*<.0001). During the 8-week treatment, the CG lost a mean (sd) of 758.6 (558) kcal/week while the TG lost 5105.2 (1191) kcal/week (95% CI (Δ): 3928-4765, *P*<0.0001)). The average BMI in the CG declined 0.4 (0.4) kg/m^2 and the TG 2.0 (0.5) kg/m^2 (95% CI (Δ): 1.4-1.8, *P*<.0001). The mean BMR of the CG decreased 18.5 (17.8) compared with 34.3 (23.8) in the TG (95% CI (Δ): 19.9-29.6, *P*<.01). Mean percentage of body fat decreased 0.5% (1.0) and 3.7% (1.1) in the CG and TG respectively (95% CI (Δ): 2.7%-3.8%, *P*<.0001). Waist circumference declined an average of 0.7 (0.6) cm in the CG and 5.8 (1.9) cm in the TG (95% CI (Δ): 4.5-5.6, *P*<.0001), while the hip circumference declined an average of 1.0 (0.8) cm in the CG and 6.3 (2.0) cm in the TG (95% CI (Δ): 5.2-4.6, *P*<.0001). Water decreased 0.2% (0.9%) in the CG and increased 3.1% (0.6%) in the TG (95% CI (Δ): -3.8 to -2.9, *P*<.0001). No adverse events were observed or reported.

Conclusion: Although preliminary, this pilot study suggests that thermal-wrap technique may provide a safe and effective mechanism for inducing weight loss in overweight and obese women. Further research is needed to confirm this finding.

Author Disclosure Statement

This study has been possible thanks to the contribution of the Vivinlinea Corporation, which sponsored the clinical study and accepts responsibility for the analysis and interpretation of the data.

Obesity, defined as a BMI ≥30 kg/m^2, is rapidly increasing among Americans. In 1990, no state in the country had an obesity prevalence >15%; in 2008, all states but one had prevalence rates surpassing 20%, with 32 states having obesity rates >25%.[1] In the period 2006 to 2008, 25.6% of the US population was overweight

(25≤BMI<30) and 32.2% was obese. Another 4.8% was considered extremely obese (BMI≥40).[2]

Excessive weight is the second-most-important, preventable cause of premature disease and death in America, second only to smoking.[3] Diseases associated with being overweight or obese include cardiovascular disease, diabetes, certain cancers (endometrial, colorectal, prostate, kidney, and breast), arthritis, complications of pregnancy and delivery, and surgical complications.[4] Obesity is also associated with an increased risk of premature death. The Framingham Study found overweight males lived 3.1 fewer years and overweight females 3.3 fewer years on average than their normal-weight peers, and obese men and women lost 5.8 and 7.1 years of life respectively.[5]

While patients may achieve weight loss through diet alone, maintaining the loss in the long term is difficult.[6] Studies have shown that high-intensity exercise is effective in promoting weight loss; however, its utility in individuals with cardiovascular, joint, or other health problems is often limited.[7,8]

A unique approach to weight loss involves thermoregulation. Physiological thermoregulation in humans comprises changes in heat dissipation (cutaneous vasodilatation and sweating) and heat generation (shivering) in response to various internal and external thermal stimuli. A strong relationship exists between tissue physiology and the response of that tissue to heating.[9] As the temperature of the tissue increases, its blood supply also increases, heating it and increasing metabolism to burn more calories.[10]

Each degree of elevation of body temperature (Celsius) increases oxygen consumption by 13%,[11] resulting in a loss of 0.586 kcal for each gram of sweat that evaporates.[12] Indeed, one study demonstrated a loss of 300 to 800 kcal after 20 minutes in a sauna, resulting in a net weight loss of 500 grams or more of water and fat.[13]

In this report, the authors present the results of a study designed to evaluate the effects of thermoregulation on weight. The study achieved thermoregulation using a thermal-wrap technique.

Methods

Between November 2004 and January 2005, 70 healthy female subjects visited the Vivinlinea Clinic in Great Neck, New York. Subjects gave their consent to participation in the study, and the researchers assigned them to one of two groups based on the services they selected while attending the facility—50 subjects to TG and 20 to CG.

The researchers recorded baseline morphologic measurements and personal data, including height, weight, age, and menstrual status. They also calculated baseline BMI and BMR (using the Sterling-Passmore equation[14]). They measured the circumference of the waist, hips, right thigh, and right knee while the subject was in a standing position, with the waist measured at the level of umbilicus; the hips at the level of the superior aspect of the hipbone; the right thigh at 1 inch below the inguinal flexure of the inner thigh; and the right knee at 1 inch above the popliteal fossa.

One drawback of the BMI is that high muscle mass can yield high BMIs even though body fat is not excessive. Therefore, to determine whether an individual with a high BMI is overfat, the researchers performed a body composition analysis (BCA) with a bioelectrical impedance analysis (BIA) (Model 310 Biodynamics Corporation) to address any overestimation (or underestimation) of body fat in high (or low) BMI individuals. Fauci AS, Braunwald E, Isselbacher K, et al;

Guida B, Trio R, Pecoraro P, et al; and Sartorio A, Malavolti M, Agosti F, et al have shown this approach to be accurate in assessing body fat, lean body weight, and body water content.[11,15,16]

One kg of fat tissue burned is equivalent to 9000 kcal, and one kg of lean tissue is equivalent to 4000 kcal. After weight loss was measured, the BCA allocated a loss of fat and lean tissue. Calorie expenditure was calculated by multiplying the number of fat kg lost by 9000 and the number of lean kg lost by 4000 and summing the two products.

Initially, each participant received a 30-minute assessment with a nutritional counselor during which they received guidance on an individualized eating program based on a well-balanced Mediterranean diet. The nutritional counselor was available throughout the 8-week study. This program emphasized fresh, fiber-rich fruits, vegetables, and whole-grain products but did not exclude nutrient-rich choices from the dairy and protein food groups.[17] The program included 3 well-balanced meals per day with 1 or 2 snacks. Subjects were also urged to consume at least 1 L of fresh water daily. The diet also permitted participants to drink 4 ounces of wine up to 3x/week and a cup of coffee or tea once per day.

The nutritional counselor personalized each participant's eating program based on her BCA-determined BMR, with a 15% increase in kcal. For instance, if a subject's BMR was 1600 kcal at rest, her total daily intake was set at 1840 kcal. Overall daily calorie intake was from 1600 to 2000 kcal with 25 to 30 g fiber, an adequate intake for sedentary females.[18] The counselor also encouraged all participants to participate in light exercise, such as walking 20 minutes at a time, 2x/week.

Materials

Intervention for the TG and mock intervention for the CG both employed a thermal wrap with that of the TG using electromagnetism to create heat directed to specific tissue areas. The researchers used the wrap in 2 configurations, the use of which depended on the participant's BMI. For those with a BMI<30 they used 3 wraps for the localized exposure of torso/abdomen/waist/hips and both thighs (Figure 1). A total-body wrap for whole-body exposure represented the second configuration for those with a BMI≥30.

The actual wrap employed, (Thermal-Wrap5000™, Great Neck, N.Y.) has been shown to be safe with no adverse effects (Lovisolo G.A., Marino C., c/o ENEA labs, Casaccia Research Center, report available upon request). Its design uses a conductive heating system with resistive elements causing the heat to gently penetrate deeper into the skin in safe and controlled manner. During testing, the researchers observed an increase of 7°C or more on the superficial layer of the skin and up to 10 mm of depth. Core temperatures increased 0.6°C, typical of that observed during sporting activity.[19]

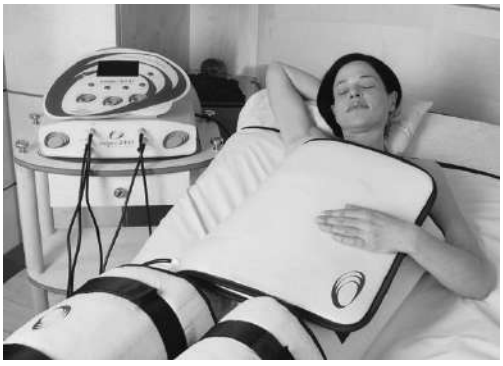

Figure 1: Localized Thermal-wrap configuration

The apparatus comprises 2 parts: (1) a transformer or control board operated by a trained individual and (2) 3 heating structures, called

thermal wraps, that induce modulated and gentle heat in cutaneous and subcutaneous areas. Maximum extremely low-frequency electric field (ELF) was 11 µT.

Each thermal wrap contains a series of insulated electrical resistances that the transformer controls to provide a 50 to 60Hz current at 24V and a power of 600W at maximum.

All participants received 2 weekly, 50-minute thermal-wrap sessions for 8 weeks, with at least 48 hours between each session. In the TG, the researchers heated the wraps to a mean temperature of 44°C; in the CG group, they did not heat them. They weighed all participants prior to and after each session.

The TG and CG could drink up to 100 ml of water during each session. At the conclusion of each session, participants remained supine for at least 5 minutes after the removal of the wrap to allow vital-sign equilibration. They then showered and were weighed after urination. After eight weeks and 16 thermal-wrap sessions, the researchers completed another total set of measurements.

Statistical Methods

Research using this modality is quite novel, and little data is available to help plan scientifically meaningful studies. A major goal of this study was gathering data to help the field to design future studies that are properly powered. Despite this problem, the effect of treatment was large, and the researchers were able to detect significant differences in weight loss and other measures between the two groups. The study was powered to detect at least 0.5 BMI units of differential change between the groups (assuming a standard deviation of the difference of the change scores of 0.6, power exceeded 85%).

Statistical analyses: The researchers analyzed each dependent (outcome) variable using a 2x2, repeated-measures analysis of variance. They fit a model to estimate the interaction effect between the groups (TG vs. CG) and the repeated-measures effect for time (before treatment vs. after treatment). The study tested appropriate model assumptions, and no transformations or nonparametric analyses were necessary. The study analysis was on an intent-to-treat basis. The study reported a 2-tailed *P*-value of .05 as statistically significant for all statistical tests. It made no adjustment for multiple comparisons or multiple tests and presented confidence intervals (95%) for all parameters of interest. The study used the SAS System 9.2 (SAS Institute, Inc., Cary, NC) for all statistical analyses.

Results

Table 1 shows all baseline characteristics of the study's participants, including postmenopausal status and ethnic heritage. Subjects' ages ranged from 20 to 70 years. The initial mean weight and BMI were similar in the 2 groups. In the CG, 7 (35%) participants were obese and 13 (65%) were overweight, while in the TG, 19 (38%) were obese and 31 (62%) were overweight. The researchers observed no significant differences in demographic characteristics. (See Table 1 on next page)

Table 1 - Mean (Standard Deviation) Baseline Measurements

Parameter [a]	Control Group (CG) (n=20)	Treatment Group (TG) (n=50)
Age, y (SD)	45.4 (12.6)	47.3 (13.0)
Weight, kg (SD)	75.0 (7.7)	74.4 (11.3)
Postmenopausal Status No. (% Postmenopausal)	11 (54)	30 (60)
Ethnicity, No. (%)		
Caucasian (non-Iranian)	17 (85)	39 (78)
Iranian	2 (10)	8 (16)
East Indian	1 (5)	2 (4)
African-American	0 (0)	1 (2)
Body Mass Index, kg/m^2 (SD)	29.1 (2.4)	28.9 (4.0)
Basal Metabolic Rate kcal/day (SD)	1503.5 (129.0)	1457.8 (177.3)
Body Fat, % (SD)	35.2 (3.3)	35.6 (4.5)
Waist, cm (SD)	93.5 (7.0)	89.8 (10.9)
Hips, cm (SD)	104.8 (7.9)	107.8 (10.1)
Right Thigh + Knee, cm (SD)	107.8 (7.5)	110.5 (9.4)
Body Composition Analysis: Lean mass + Water % (SD)	48.9 (4.3)	48.9 (9.1)

[a] *No significant or clinical differences between groups.*

Table 2 shows all changes in body composition and weight; i.e., the effects of treatment. During the 8-week treatment, the CG lost a mean (SD) of 758.6 (558) kcal/week while the TG lost 5105.2 (1191) kcal/week (95% CI for difference (Δ): 3928 to 4765, *P*<.0001), calculated using the independent t-test. After the 8-week study, the CG lost significantly less weight than the TG (*P*<.0001). As a result, the average BMI in the CG declined less than TG. The average BMR of the CG decreased 18.5 (17.8) kcal/day compared with 34.3 (23.8) kcal/day in the TG (95% CI (Δ): 19.9- 29.6, *P*<.01). Mean percentage of body fat decreased 0.5% (1.0) and 3.7% (1.1) in the CG and TG respectively [95% CI (Δ): 2.7%-3.8%, *P*<.0001].

Waist circumference declined an average of 0.7 (0.6) cm in the CG and 5.8 (1.9) cm in the TG (95% CI (Δ): 4.5-5.6, *P*<.0001), while the hip circumference declined an average of 1.0 (0.8) cm in the CG and 6.3 (2.0) cm in the TG (95% CI (Δ): 5.2-4.6, *P*<.0001). Water (as a percent of body mass) decreased 0.2% (0.9%) in the CG and increased 3.1% (0.6%) in the TG (95% CI (Δ): -3.8 to -2.9, *P*<.0001).

Table II: Measurement of Changes After 8 Weeks of Twice-Weekly Thermal-Wrap (negative sign denotes a decrease from baseline)

Change Parameters	**Control Group: Change (SD)***	**Thermal Group: Change (SD)***	***P*-value for Group x Time Interaction**
Calories Burned/Week	758.6 (558)	5105.2 (1.191)	<.0001
Weight, kg	-1.0 (0.7)	-5.2 (1.3)	<.0001
Body Mass Index, kg/m^2	-0.4 (0.4)	-2.0 (0.5)	<.0001
Basal Metabolic Rate kcal/day	-18.5 (17.8)	-34.3 (23.8)	<.01
Body Fat (%)	-0.5 (1.0)	-3.7 (1.1)	<.0001
% of Weight Loss Due to Fat	49.5 (22.3)	78.2 (10.2)	<.0001
Waist, cm	-0.7 (0.6)	-5.8 (1.9)	<.0001
Hips, cm	-1.0 (0.8)	- 6.3 (2.0)	<.0001
Right Thigh + Knee, cm	-0.6 (0.6)	-5.4 (1.9)	<.0001
Lean Mass + Water (%)	-0.5 (0.5)	-1.4 (1.3)	<.0001
Water (%)	-0.2 (0.9)	3.1 (0.6)	<.0001

No difference exists in weight loss between premenopausal or postmenopausal subjects, nor was any relationship with the menstrual cycle evident.

Safety: No adverse events were observed or reported.

Compliance: Perhaps due to the motivations of the 70 subjects in choosing the services they received and due to the comfort of the procedure, only 7 participants dropped out of the study (an attrition rate of 10%).

Discussion

To the researchers' knowledge, the study is the first to demonstrate that thermoregulation technique, in conjunction with consumption of a well-balanced Mediterranean diet, can result in a significant amount of weight loss and a reduced percentage of overall body fat, without strenuous physical activity for overweight and obese female subjects. The women in the TG lost an average of 5.2 kg and 3.7% of body fat during the 8-week intervention.

The researchers did not design the study to elucidate the mechanism by which the thermal wrap leads to weight loss; however, that mechanism is likely related to the increased blood flow, vasodilatation, and capillary recruitment that occurs during application—a series of events that improves lymphatic and blood circulation in the area of application.[20,21] It has been shown that blood flow in the human skin can increase more than 15-fold when the skin is heated to 43°C. Such heating induces arteriole dilation and recruits capillaries, activating lipolytic enzymes in adipocytes.[22] These changes greatly stimulate the thermoregulatory system of the body, which is under hypothalamic control, leading to heat dissipation to avoid systemic hyperthermia, and in the process, consuming energy.[23] The mechanism also may involve mechanically and thermally enhanced blood flow, generally improved vascularization, lymphatic drainage, and an increase in interstitial metabolic oxygenation to the fat tissue with a resultant decompression in the lipolymphedema and decreased connective sclerosis and fibrosis.[24]

The reduction in body fat likely occurred not just through lipolysis but also through fatty-acid oxidation and thermogenic elimination of the reducing energy generated in brown adipocytes or through similar processes in other cells.[25]

Limitations to this study include the fact that it was not randomized or blinded. In addition, the actual caloric intake and daily physical activity of the subjects were not independently verified; thus, it is possible that the differences between the groups were due to differences in compliance rather than to the treatment per se. The researchers conducted no laboratory studies to indicate the effect of the intervention on lipids, blood glucose, and other risk factors for cardiovascular disease. Finally, long-term follow-up beyond 8 weeks is of interest. The field needs future studies that use a randomized, controlled design with measures of dietary compliance to confirm the hypothesis that the thermal wrap significantly impacts body weight.

Conclusion

This article reports on a study that used thermoregulation, to achieve a non-invasive approach to weight loss. As this pilot study shows, combining this technique with a healthy diet (Vivinlinea Methodology) over 8 weeks can lead to significant weight loss and body-fat reduction. Further controlled trials will be

necessary to further assess the efficacy of the methodology.

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30

New Ideas for the Treatment of Pain

Hal S. Blatman, MD, ABIHM, DAAPM

Introduction

Pain is something we all have experienced. Most people are fortunate to experience pain as a warning of bodily injury that stops as we recover. Others are not so lucky and continue to suffer from chronic pain despite the best of medical care.

This chapter first reviews what we are taught about pain with insights toward why many common treatments do not work as well as we would like. New information follows that elaborates how muscle and fascia generate most of the pain in our bodies. The next section discusses how food choices contribute to chronic pain, and the last section discusses the future of pain and rehabilitative medicine and what can be done now to stop pain and help the body heal like never before.

Medical students are taught several theories about what is thought to cause pain. One of these theories is inflammation. Doctors use words like arthritis, tendinitis, and bursitis to describe pain from such inflammation.

Let's consider George, an imaginary patient with shoulder pain. George has had shoulder pain for 10 years and all of his friends have turned into doctors. He has been advised about food, vitamins, magnets, and other things that have helped his friends when they have had similar ailments.
Finally, George hurts bad enough to go and see Dr. Jones. Dr. Jones was taught to do an x-ray and an MRI scan of the shoulder, and on the next visit points out to George how there are bones too close together and that spurs have formed in his joint. By the evidence of the studies, George is advised that he has arthritis. He gets a prescription for arthritis medicine, and he is a content patient--not because he gets any better, but because he knows what he's got.

Dr. Jones on the other hand, took a leap of faith. He was taught when he went to school that if he could demonstrate an abnormality on an x-ray or MRI scan that was close to where the patient complained of pain and symptoms, that he could attribute the pain and symptoms to the abnormality on the study. Unfortunately, this requires a leap of faith doctors have no right to make. Some people with bone-on-bone x-rays have no pain in their

bad joint. Indeed, x-ray findings correlate with range of motion; they do not correlate with pain.

Another theory students are taught in school is that radiating pain comes from a pinched nerve. For example, if a patient has pain that radiates from their neck down to their hand, doctors are taught to look for a pinched nerve in the neck. Similarly, if a patient has pain that radiates from their low back down to their foot, doctors are taught to look for a pinched nerve in the lower back. While there are many people who have had successful surgeries for such disc injuries, there are many more people who fail surgical treatment and continue to experience severe radiating pain. In addition, medical studies show that 30% of normal 40 year old men have at least one herniated disc in their lower back. These facts make us question what else might be causing the pain that mimics a herniated disc.

Medical students are also taught that depression causes pain. Indeed, they are taught that if a woman is 40 years old and has had pain for a couple of years, she has pain because she is depressed and she should be prescribed antidepressant medication. Contrary to this thinking, more recent information teaches that pain causes depression. Pain signals from muscle and fascia go through the mood and depression centers in the brain on their way to the cortex where we become aware of the location of the pain. Bombarding these brain centers with pain darts is enough to cause depression--even in otherwise normal people who do not have a history of depression.

One of the most arrogant theories young doctors are taught is the "supratentorial" theory of pain management. This refers to the idea that if all the medical tests are negative and the patient still complains of pain, he or she must be making it up.

More modern theories in pain medicine include neuroplasticity, wind-up, the role of neurotransmitters, and the science of how nerves transmit and modify pain information signals. The science and current thinking on these issues are not the topic of this chapter. Even with these newer theories, there is so much more that can be done to decrease pain and heal from injury when muscle and fascia are taken into account.

Myofascial Pain

In the 1930's and 1940's, Janet Travell, MD was introduced to the idea that pain comes from muscle and fascia. Fascia is the tissue that holds muscles together, connects muscles to muscles, muscles to bone, and bone to bone. It also holds organs like the heart, lungs, liver, and intestines in place. When steak fibers are separated, fascia is the thin film between the fibers. Fascia is also the thick tissue called gristle that holds muscles to bone. Doctor Travell learned that all qualities of pain could come from muscle and fascia--numbness, burning, tingling, aching, stabbing, and cramping. She also learned that the pain was actually generated by small knots that formed in the injured muscle and fascia tissue as a physiologic reaction to injury. As she developed the physical examination skills to be able to feel these knots, she learned that they were capable of referring pain to distant sites in the body[i]. Knots in the buttocks muscles would refer pain down the leg to the foot, and knots in the upper shoulders and neck would refer pain to the head and down the arm. Dr. Travell called these knots "trigger points," and the pain generated by these trigger points is called "myofascial" pain.

As Dr. Travell discovered, each trigger point in the body generates both localized and referred pain patterns (see diagram). Humans and also animals have trigger points in most, if not all of their muscles.

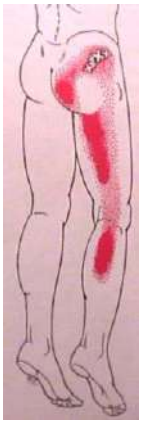
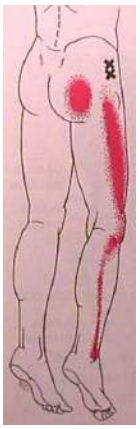


Diagram X's represent the trigger points, and the red shadowing represents location of the referred pain pattern.



Awareness of the pain patterns from these trigger points depends on how "active" they are. The more active the trigger point, the more pain signals it transmits. Trigger points that generate pain outside of the mind's awareness are termed "latent." Even latent trigger points restrict motion, cause muscle weakness without atrophy, and predispose the body to acute attacks of pain. Common examples of re-activating latent trigger points include:

- Throwing one's back out by doing too much yard work
- Waking up in the morning with a stiff neck

These examples of sudden onset pain are often attributed to a pinched nerve or inflammation. Indeed the pain is neither...it is usually myofascial pain from activated latent trigger points.

Pain patterns are usually generated by groups of trigger points in several injured muscle and fascia areas. Pain levels vary with how loudly the ensemble or orchestra of trigger points plays and which solo artist stands up to sing. This typically varies with the following:

- What the person has physically done in the past 3 days that has aggravated his/her muscles
- How well the person slept last night
- What the weather is going to do tomorrow
- How much stress the person is under
- What the person has eaten in the past 1-4 months

These things are more important in healing from pain than most anything else, including discs, nerves, depression, and inflammation. At least 70% of most pain patterns are caused by muscle and fascia. And what is most important is Doctor Travell's discovery that making the trigger points less active will also make the pain they generate go away.

What was more important was her discovery that making the knots go away would also make the pain go away.

Indeed, most of the pain in our bodies comes from groups of these knots or "Trigger Points" that "sing" together to create a pain pattern.

Some common examples of trigger point pain patterns include:

- Migraine is generated by knots in the muscles of the jaw, neck, shoulder, and upper back.
- Shoulder pain and upper back pain are generated by knots in the muscles and fascia of the neck, shoulder, upper back, and upper arm.
- Lower back pain is generated by knots in the muscles and fascia of the abdomen, lower back, buttocks, pelvis, and thighs.
- Pelvic pain and prostate pain are generated by knots in the muscles and fascial of the thighs, pelvis, buttocks, and abdomen.
- Lower back pain is generated by knots in the muscles and fascia of the lower back, abdomen, pelvis, and thighs.
- Plantar fascitis pain is generated by knots in the muscles and fascial of the calves and feet.

This list is not complete, but it makes the point. Trigger points in muscle and fascia can also refer pain to joints. Thigh muscles can cause such intense and sharp pain in the knee joint that it is not possible to distinguish between joint and muscle pain. What confuses practitioners even more is that there is no pain sensation describable that cannot come from muscle and fascia. Doctors and nurses are taught that the patient's description of pain symptoms provides a solid clue as to the cause of the pain. This is unfortunately not true. All the sensations of burning, radiating, knife-like stabbing, numbness, and tingling can come from muscle and fascia. They do not have to come from pinched nerves.

All of these pain patterns have much in common. The differences are the different muscles and the different areas of the body. The pain patterns all share the same origin for pain. In fact, pelvic pain has been called a "migraine" in the pelvis, and lower back pain has been called a "migraine" in the lower back. Is it any wonder that diagnostic testing is not more helpful? Trigger points do not show up on EMG, MRI scan, or CAT scan testing. They are most detectable by physical

examination, and most health care education programs do not teach examination or treatment techniques for this ubiquitous myofascial pain.

Fascia

The knowledge base and understanding of fascia has rapidly grown during the last several years.

In 2009, Thomas Myers published the second edition of his book titled "Anatomy Trains." The book teaches about the anatomy of fascia and how it is contiguous throughout the body[ii]. He has been able to demonstrate the dissection of a single string of fascia tissue that goes from the bottom of the toes, up the back of the legs, up the back of the torso, continuing up the back of the neck, and then over the top of the head to stop at the eyebrow.

Indeed, there are such strings all over the body. And the fascia planes exist in the form of sheets more than strings. These sheets of fascia tissue are all over the body. There are shallow and deeper sheets up the sides, front, and back of the body, as well as sheets spiraling around the trunk of the body.

The knots in the muscles and fascia draw and tighten these strings and sheets of fascia. They tighten the strings that go lengthwise through the body, and also the 360 degrees of other sheets that intersect within the muscle fibers. Consistent with this concept, when the knots are released, all relevant strings and sheets also immediately loosen. Loosening the knots in the upper shoulders will reduce neck stiffness and headache pain. In a similar fashion, loosening the knots in the lower back and buttocks will decrease lower back and radiating sciatic pain.

Understanding this anatomy of fascia, it is straight forward to understand the etiology of scoliosis. Scoliosis develops when there is an injury to fascia that makes some of the spiral sheets of fascia in the trunk of the body tighten and not lengthen as the spinal column grows longitudinally. The spine then grows along the path of least resistance--which happens to be a spiral. Releasing the tight fascia strings and sheets can slow or stop the progression of a scoliosis deformity (unpublished work from Blatman Pain Clinic).

Another more recent discovery is that fascia has contractile properties that are independent of muscle. Where muscle contracts voluntarily and immediately, fascia contracts slowly and over 1.5 hours. Similarly, where muscle can release immediately and voluntarily, fascia releases slowly and over 1.5 hours. Moreover it has been discovered that the triggers for fascial contraction are not voluntary. Research has yet to elucidate the triggers for fascia contraction.

The part of the nervous system that transmits pain signals from myofascial trigger points is the sympathetic component of the autonomic nervous system. The sympathetic nervous system also controls temperature, sweating, heart rate, respiratory rate, and other automatic functions in the body. Biological response to stress is also mediated by this part of the nervous system. In the 1990's, Hubbard and Gevirtz demonstrated that trigger points have spontaneous electrical activity[iii]. They further demonstrated that stress dramatically increases the activity of trigger points[iv]. Their work shows how stress increases pain throughout the body by increasing the activity of trigger points, tightening muscle and fascia. Similarly, they showed that relaxation reduces the electrical activity of trigger points[v]. There is other research that demonstrates effective relaxation and pain relief with meditation, yoga breathing, and heart rate variability biofeedback training (HRV).

Another mechanism of pain causation from fascia is also related to the level of tension and pressure in the area of injury. There are 10 times as many sensory nerve receptors in fascia as in muscle. These sensors include:

- Golgi tendon organs-measure stretch
- Paciniform endings-measure pressure
- Ruffini ending-inform CNS about shear forces

Pressure (from tight fascia) and inflammation (largely from food) between the sheets of fascia stimulates these receptors and results in transmission of pain signals and referred pain

along the lines of fascia in the body. This produces pain and radiating pain that cannot be measured by diagnostic testing, and the pain symptoms cannot be distinguished from those that are taught to doctors and nurses to come from pinched nerves and herniated discs.

Another common misconception is that muscles have memory. In actuality, muscles do not remember anything. If they did, people would not have so much difficulty relearning how to walk after a stroke. Fascia, on the other hand, remembers everything. It remembers every twist and trauma through life, as well as pain and sense of motion. What is called muscle memory of a golf swing is instead about fascia. The repetitive motion of a golf swing will cause a tightening of the fascia lines that support the swing motion so the muscles do not have to work so hard to reproduce it, and the brain can determine proprioception to reproduce it. If a person wants to change their swing, the previous fascia sheets and lines must relax and others need to tighten to support the new pattern of motion.

Proprioception of motion and knowing where the body is in space is also due to fascia and the nervous system sensors within the layers of fascia. These sensors in the fascia are more active in detecting and regulating body movement than the joint ligament receptors. Joints do not feed back information about position as much as the fascia in the tissue around and distant from the joint.

Treatment of pain from fascia is the common denominator for several types of therapy that include:

- Trigger point work
- Acupuncture
- Osteopathic manipulation
- Craniosacral therapy
- Rolfing
- Myofascial release

Degenerative joint disease also contributes to decreased joint motion and pain. In addition to healing ligaments and tendons, there are now very effective therapies to regrow cartilage in damaged joints. Joints wear out because the immune system attacks the cartilage or because the joint performs at a higher level than its physical capacity. This gradually causes the cartilage of the joint to wear out because it does not have the ability to repair itself from this higher level of wear and tear.

Glucosamine can change this equation and improve the body's ability to handle repair of joint cartilage. Glucosamine orally works well for knee joints. Success is often brand specific; MSM and chondroitin are not needed in the formulation. It also does not seem to matter whether the formulation contains glucosamine sulfate or glucosamine hydrochloride. Any studies that reportedly demonstrate glucosamine to be ineffective, used a brand of glucosamine that did not work. Success seems to be brand specific, and it is most interesting that all brands listing the same ingredients do not work equally. For glucosamine to work for other joints, it must be injected or applied transdermaly. In these cases, glucosamine cream and injections will work to restore jaw, neck, shoulder, elbow, wrist, finger, lower back, hip, knee, ankle, foot, and other joints.

While the glucosamine is often strong enough to change the equation of wear and tear so that the joint stops deteriorating, it may not be enough to regenerate the joint and dramatically improve function. The most effective protocol is to inject stem cells from bone marrow, platelet rich plasma, a fat cell graft, and other growth factors into the injured joint. This treatment restores cartilage to improve knee, hip, ankle, wrist, finger, toe, jaw, and other joints.

Nutrition and Pain

Food and nutrition are also major determinants of pain and healing. There are three rules that help with understanding the relationship of nutrition and pain.

- Do not eat or put poison into the body
- The body does not run well on low octane fuel

- The gut has to heal, and healthy flora are essential

The most important poisons that affect pain are artificial sweeteners and hydrogenated fats. Aspartame processes in the body to methanol and formaldehyde[vivii]. Sucralose is chlorinated sugar and ingestion leads to a change in intestinal flora[viii].

Ingested oils and fats are important because they are used by the body to synthesize cell membranes. Indeed, the ingested oils and fats are used to make or repair all cell types in the body--including the brain, muscles, and red blood cells. Cell membranes are much healthier if they are made of healthy omega-3 and omega-6 fats. Those that are made of hydrogenated fats do not function as well. Red blood cells, for example, do not deliver oxygen and nutrients to injured and tired muscles as well if they are made of hydrogenated fats. Since red blood cells live for 120 days, deep fried food and many prepared foods will increase pain and slow healing for 4 months. In addition, hydrogenated fats in cell membranes increase inflammation and pain signaling chemicals in the body.

With regard to octane, the lowest energy and most dangerous foods are wheat and sugar. Many pain patients are so sensitive to these foods that eating a small amount can increase pain for 3-4 weeks.

The DO NOT EAT list for pain patients includes

- Wheat
- Sugar
- Potato (not sweet potato)
- Juice
- Hydrogenated fat
- Artificial sweeteners

The third rule of nutrition is that food has to heal the gut and grow healthy flora. Foods on the "do not eat" list also encourage the growth of yeast and flora that cause harm to the body(dysbiosis). It is important to instead eat the vegetables that encourage the growth of healthy flora.

Healing

When the body is injured, a healing program is run to repair the injured tissues. In the case of an ankle sprain, the torn ligaments cause a release of inflammatory mediators that make the nearby blood vessels leak fluid and white blood cells. The fluid makes the ankle swell, and the white blood cells release enzymes that clean up and debride the injured ligament. Three days later, as a result of this process, fibroblast cells migrate to the ankle to repair and rebuild the injured ligament.

If anti-inflammatory medications are taken in the first few days after injury, this process is stopped and the area does not swell, hurt, or heal. Indeed, anti-inflammatory medications should not be taken after injury. Moreover, these medicines also stop glycosaminoglycan synthesis in the body[ix]. This action stops the body from rebuilding cartilage in joints. NSAIDs should also not be taken for arthritis. While they may decrease joint pain, they accelerate joint degeneration. Herbal anti-inflammatory medicines may be helpful for decreasing pain and inflammation, and these agents do not have the unfortunate side effects of decreasing cartilage growth[x].

There are three trigger point zones in any muscle (see diagram 1). These are the origin, muscle belly, and insertion. A weakness in the fascia or tendon at the origin or insertion of a muscle perpetuates the trigger point in the muscle belly, perhaps as a protective mechanism to discourage further stress on the tendon and additional damage. If the tendon is tender to palpation, it is damaged and the trigger points within it will continue to generate and radiate pain.

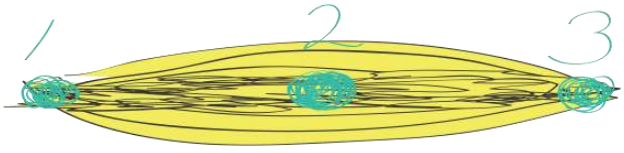


Figure 1 Three trigger point zones in a muscle. 1 and 3 are origin and insertion, 2 is muscle belly.

The best way to get the body to heal and strengthen an injured tendon is to trigger the body to rerun the healing program. Triggering the healing program requires reinjuring the tendon. The most efficient way to do this is to poke the tendon or ligament with a needle. An acupuncture needle can do this. The actual process of stimulating the healing is called "Prolotherapy" or "Regenerative Injection" therapy. To augment the healing response, prolotherapists will inject a mixture of dextrose and local anesthetic, and possibly add an additional irritating or inflammatory substance.

More recently, platelet rich plasma and stem cell injections have become available to inject as a procedure in the doctor's office. If either of these substances is injected into injured or degenerated tissue when the healing program is triggered by a needle, the healing reaction is greatly augmented and proceeds strongly for 4-6 weeks.

With the augmented nature of the healing response, significant improvement can be noted in just a few weeks. By this method of treatment, it has become evident that a weakness in the tendon causes referred pain along the fascia lines--and that pain goes away with tendon and fascia repair. Strengthening gluteal tendons at the upper part of the femur's greater trochanter will decrease and stop SI joint, lower back, and hip pain. In a similar fashion, strengthening quadriceps, tensor fascia lata and hamstring tendons at the proximal femur will stop radiating pain that goes down the leg. In addition, weakness associated with the injury can improve so much so that the injured extremity stops giving out and the patient stops falling.

Cervical trauma from a rear end motor vehicle accident can lead to chronic neck pain. One of the less known causes of this persistent pain is related to ligament damage in the neck. If the ligaments are injured so that neck flexion and extension results in anterior/posterior slipping of the vertebrae (see diagram 2), neck muscles will remain in spasm and spurs will grow on the joints as efforts by the body to minimize this slipping. This author has demonstrated in unpublished work that PRP injections into these ligaments can greatly reduce or stop the unwanted slipping and reduce neck and head pain.

Diagram 2. Notice the anterior slip in flexion of C4 on C5.

Summary

Pain is associated with tissue damage. Unfortunately our high technology testing and currently taught physical examination techniques miss detecting the damage that causes most of the pain in most people. The undetectable by testing and previously untreatable pain comes from fascia, muscle, and ligament damage and weakness. Doctors call these body parts "soft" tissues and think they cannot be a persistent problem and cause of pain. Juries tend to award victims who can demonstrate something wrong in a bone or joint, and not a "soft" tissue problem.

The way pain medicine is practiced needs change. Too many expensive procedures are performed that do not work as well as they would if they were really treating the actual injury or cause of pain. This dramatically increases healthcare cost, both by being suboptimally effective in reducing pain and by causing bodily harm from irreversible procedures. Learning more about physical examination and treatment of muscle and fascia should be part of medical curriculum, as well as the effects of nutrition on both causation and healing from pain.

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Multiple Chronic Infectious Disease Syndrome: Understanding Chronic Lyme Disease and Persistent Illness

Richard I. Horowitz, MD

We are presently experiencing a rise in chronic illness worldwide. Increasing numbers of individuals are now suffering the medical consequences of unchecked obesity, hypertension, diabetes, and cardiovascular disease. Significant numbers of individuals are being diagnosed with cancer, with rates approaching one out of every two men, and one of out of every three women in the United States. Medical journals report that the rates of Alzheimer's disease continue to climb, presenting a significant emotional and financial burden to families and the health care system. In March 2012, The New York Times[1] reported an alarming rate of autism where 1 in 88 children born in the US are now affected by this syndrome. Every day we are made aware of the burden of chronic diseases, either by reading about them or experiencing the consequences first hand as patients, caregivers, or healthcare providers.

Physicians often treat patients complaining of chronic fatigue, joint and muscle pains, headaches, with associated depression, anxiety, and memory and concentration problems. These patients usually seek answers from their primary care physician, who usually refers them for blood tests and for appointments with specialists to try and determine the etiology of their illnesses. They may go to 10-20 doctors, and are often told that nothing can be found despite the best laboratory testing and imaging techniques that modern medicine has to offer. The end result is that they are frequently diagnosed with Chronic Fatigue Syndrome or Fibromyalgia. If they have evidence of inflammation and elevated levels of autoimmune markers, they may be told that they have rheumatoid arthritis, lupus, a nonspecific collagen vascular disease, or they are diagnosed with multiple sclerosis if there is associated

demyelination. These patients are often placed on antidepressants, anti-anxiety medications, anti-inflammatory drugs, and immune modulators to deal with the clinical manifestations of their illnesses. We treat their symptoms, but fail to be able to find an underlying cause for their problem. Is this really the best that we can do? Are there no answers or common denominators that help to explain these patients' chronic illnesses?

I am a board certified internist who has been in practice for close to 30 years. I moved to the Hudson Valley of New York State in 1987 to open a medical practice after finishing my residency in internal medicine. I soon began seeing patients with a range of common ailments with uncommon regularity. In addition, my patients were exposed to a new problem in Dutchess County, N.Y. that I had only briefly heard about in medical school, which complicated their health issues even further. That problem was Lyme disease. Lyme disease is transmitted by the bite of the female deer tick, *Ixodes scapularis*. It sometimes produces a typical "bulls eye" rash, body aches and pains and flu- like symptoms. When I learned about Lyme disease in medical school, we were told that it is a relatively rare disease which was easy to diagnose and easy to treat. Nothing could be further from the truth.

Infectious diseases, like other medical illnesses, are spreading rapidly. Apart from newer threats like SARS and bird flu, we often hear about rising rates of TB, HIV/AIDS, malaria, HPV, and hepatitis that are affecting millions of people across the globe. Most people don't realize, however that Lyme disease is the number one vector- borne disease spreading worldwide[2]. I certainly didn't realize that the Hudson Valley was the number one hotspot for Lyme disease in the northeastern United States.[3] So I not only was seeing the usual high numbers of patients with cardiovascular diseases, cancer, and other chronic medical illnesses that are common in an internal medicine office. I was also seeing large numbers of patients with tick bites and an array of unusual symptoms. These patients would often complain of fevers, sweats, chills, severe fatigue, muscle and joint pain that would often come and go and migrate around the body, tingling and numbness, chest pain, shortness of breath, a stiff neck and headaches, light and sound sensitivity, dizziness, often with associated severe memory and concentration problems, as well as depression, anxiety and an inability to sleep. If they saw and removed the tick and then got the telltale rash, early treatment with doxycycline could eliminate their symptoms in 80 to 90% of the cases. The remainder of the patients however was not as fortunate. They would fail the antibiotic and go on to develop chronic symptoms that would severely impact their lives. Unfortunately the standard medical literature had no answers for me. I would retry antibiotics, and occasionally they were effective in relieving patient symptoms, but often once the antibiotics were stopped, the patients' symptoms would relapse. What was causing these patients to remain chronically ill?

I needed to better understand this disease, since so many of my patients were becoming disabled and were looking to me for answers. I therefore started out on a journey as a medical detective to understand an illness that was causing tremendous suffering. After several years in practice, I closed my office to new internal medicine patients and only accepted new patients with Chronic Lyme disease. I started scouring the medical literature for answers. I attended medical conferences on Lyme disease and tick-borne illnesses to better understand my patients' symptoms. I started conducting research in my medical office, and now after treating over 12,000 chronically ill individuals with tick-borne diseases over the past 28 years, I have found many of the answers that I had been searching for to help my patients. There are often not one, but many factors responsible for these patients' chronic symptoms.

Much of what we read in medical school textbooks is based on a paradigm established by Pasteur's postulate and the germ theory which was elaborated in the 1800's: if you can find the one cause and correctly name the one disease that causes it, you can then understand the underlying pathology and prescribe the right medications for the patient. However patients with chronic tick borne illnesses do not read those textbooks. Patients' illnesses can be much more complex than "one cause, one illness." The deeper that I searched for answers year after year, the more I discovered multifactorial causes for my patients' illnesses. From my research and clinical experience trying to uncover why Lyme disease patients remain chronically ill, I postulated that Lyme is better situated as being part of what I am calling **Multiple Chronic Infectious Disease Syndrome** (MCIDS)[4] and I believe that understanding this syndrome is the key to understanding most chronic illnesses.

Multiple Chronic Infectious Disease Syndrome (MCIDS) is a symptom complex of Lyme disease and multiple associated tick-borne co-infections which encompasses not only infections with *Borrelia burgdorferi*, the etiologic agent of Lyme disease, but also encompasses other bacterial infections, viral infections, parasitic infections and fungal infections. It also includes issues with immune dysfunction, inflammation, environmental toxicity, allergies, nutritional and enzyme deficiencies with functional medicine abnormalities in biochemical pathways, mitochondrial dysfunction, neuropsychological issues, autonomic nervous system dysfunction, endocrine abnormalities, sleep disorders, gastrointestinal abnormalities with abnormalities of liver function, and issues with pain, drug use, and physical deconditioning. The 15- point differential diagnostic map for chronic illness that I will elaborate in this chapter is the result of my work and research over the last 28 years of medical practice. Although this work started out as a way to understand chronic Lyme disease, it has now evolved into a map for all chronic illness. I believe this model has important implications for all patients suffering with both "explained" and unexplained chronic symptomatology.

Years ago many of the patients who initially saw me had been diagnosed with chronic fatigue syndrome, fibromyalgia, autoimmune diseases, or psychiatric abnormalities to explain their chronic symptoms. The problem that I discovered early on with Lyme disease is that like its cousin syphilis, it is a great imitator[5]. It can imitate many illnesses commonly seen in a modern day medical practice. The medical literature provides abundant evidence on this subject. For example, although patients were diagnosed with a primary psychiatric disorder when they first came to see me, Lyme disease has been known to cause a host of neuropsychiatric abnormalities. This is well-documented in the medical literature[6]. In fact, virtually every DSM psychiatric diagnosis can be caused by Lyme disease and associated co-infections! Similarly, Lyme disease can mimic a whole host of neurological syndromes. For example, Lyme disease can cause neurocognitive deficits in both children and adults[7] and has even been associated with Tourette's syndrome[8]. It also has been associated with neurological syndromes such as Alzheimer's disease.[9] *Borrelia burgdorferi* persists in the brain in chronic lyme neuroborreliosis and may be associated with Alzheimer's disease, and has been linked to ongoing inflammation in the brain affecting amyloid metabolism.[10] All health care providers need to be aware that any patient presenting with neurocognitive and psychiatric symptoms in fact might have Lyme disease.

The same problem exists with Chronic Fatigue Syndrome (CFS) and fibromyalgia (FM). These are common diagnoses given to patients who complain of chronic fatigue, muscle pains and joint pains, with associated depression and a sleep

disorder. These are the same symptoms that we see in chronic Lyme disease and MCIDS, and Lyme disease has been shown in the medical literature to imitate CFS and FM.[11] Lyme disease can mimic rheumatoid arthritis, lupus, and multiple sclerosis. Most medical providers are unaware that *Borrelia burgdorferi* can mimic rheumatoid arthritis (RA) and cause false positive rheumatoid factors with swelling and joint pain. Rheumatoid factor correlates with antibody titer against *Borrelia garinii*, a genospecies of *Borrelia burgdorferi* [12] and 57% of patients with RA showed reactivity to multiple borrelial antigens[13] *Borrelia burgdorferi* also has a similar pathology and immunology to Lupus [14]can lead to C3 deficiency like that found in lupus[15] and similarly can cause the production of anti-phospholipid and anticardiolipin antibodies. [16] It is not always easy to differentiate between true lupus and auto-immune diseases since Lyme disease can also cause an over stimulated immune system.

Lyme disease and tick-borne co-infections are now spreading rapidly worldwide, and are capable of mimicking many common symptoms and diseases seen in a physician's office. Why aren't more patients therefore being diagnosed with Lyme disease? Unfortunately the blood tests for Lyme disease are extremely unreliable. Doctors are taught that they should order an ELISA test to look for the presence of the spirochetes, as the first step in a two- tiered protocol to test for Lyme disease. If the ELISA is negative, they are instructed not to do a follow-up Western Blot. But the ELISA is a very insensitive test. An extensive review of the medical literature on the sensitivity and specificity of commercially available two-tiered testing for Lyme disease has shown that the sensitivity of the ELISA in numerous scientific peer review journals is only 56%.[17] This means on the average we will miss at least 44% of the patients who suffer from Chronic Lyme Disease. A 2005 study at John's Hopkins University confirmed the poor sensitivity of the ELISA, and their estimates of the sensitivity of testing were even worse. They found that the CDC two- tiered testing missed 75% of positive Lyme cases[18] This mirrors what I have found in my own practice. Many of my patients have seen 10-20 medical providers looking for answers before consulting with me. They do have Lyme disease but the testing protocols that were used were not sensitive enough to pick it up. This is understandable once you realize that many laboratories testing for Lyme disease have had difficulty reproducing their own results, and that the sensitivity of the ELISA test can vary widely, ranging from sensitivities of 37% to 70%.[19]

Apart from the problem of the poor sensitivity of the ELISA test, the other problem testing for Lyme disease is that there are over 100 strains of *Borrelia burgdorferi* (Bb) in the US, and most commercial Western Blots only test for the presence of one strain (B31). Laboratories like IgeneX laboratory in California have a much better chance of finding the spirochetal infection on the Western Blot because they test using the 297 and B31 strain, making it easier to see borrelial-specific bands on a Western Blot. IgeneX has passed all laboratory quality assurance standards in NY, California and in many other states, and I have reliably used their laboratory for over 20 years. If a patient has evidence of even one of 5 borelial-specific bands on a Western Blot (23, Osp C; 31, Osp A; 34, OspB; 39, and 83-93) this indicates that the patient has been exposed to Lyme disease. Why? These five bands are borrelial -specific bands, and should not otherwise be found in blood test results. The reason so many doctors miss the diagnosis is because they have adopted the CDC criteria for the diagnosis of Lyme disease: trying to find 5/10 positive bands on an IgG Western Blot, or two out of three specific bands on an IgM Western Blot (23, 39, 41). The CDC criteria however were only meant for health departments to screen large populations for epidemiological purposes and not

for other purposes. The CDC has clearly stated this on their web site: "This surveillance case definition was developed for national reporting of Lyme disease; it is not intended to be used in clinical diagnosis." [20]

The problem we therefore face is that even if a health- care provider suspects the presence of tick-borne diseases, and follow the two- tiered protocol recommended by certain infectious disease specialists and by insurance companies, they will find that the testing is often negative. This false seronegativity has been extensively documented in the medical literature. [21] Apart from the poor sensitivity of the ELISA, borrelial antibodies can also be sequestered in immune complexes, explaining the false negative test, and they have the ability to enter the intracellular compartments, where they can hide from the immune system.[22]

Borrelia spirochetes have also learned to adapt to their hosts, and can survive for long periods of time in the body despite seemingly adequate antibiotic therapy. This is due to their ability to transform into cystic forms [23] Multiple peer reviewed scientific studies have shown the ability of borrelia to persist. If a patient continues to have symptoms despite months of antibiotic regimens, there are at least three reasons for the persistence of that patient's poor health. It may be that not all of the different forms of the organisms have been properly treated[24], or that tick-born co-infections that are present were not sensitive to the antibiotics used, or because the organisms were also protected by biofilms in the body and sequestered deep in the tissues of the body where antibiotics do not penetrate well.[25]

However in addition to these issues, the primary reason that many patients with Chronic Lyme disease remain ill is because of Multiple Chronic Infectious Disease Syndrome (MCIDS). This syndrome encompasses a wide range of differential diagnoses, and the majority of my patients with chronic illness have multiple overlapping factors responsible for their ongoing symptoms. For example, patients that complain of fatigue with MCIDS usually have hormonal dysfunction with a combination of low adrenal function, low thyroid function and abnormal levels of sex hormones. They also usually have food allergies with overlapping reactive hypoglycemia, as well as environmental toxicities such as mercury and lead toxicity, detoxification problems, severe sleep disorders, and mitochondrial dysfunction. All of these can cause fatigue, and when they are combined with the multiple infectious agents they have been exposed to, such as Lyme disease, Ehrlichiosis/Anaplasmosis, Babesiosis, Bartonellosis, Mycoplasma infections, viral infections, other parasites, and Candida, the result is a patient with chronic resistant fatigue. It is as if they had 15 nails in their foot, and they went to the doctor complaining of foot pain. The physician might identify several of the nails, but if they are not all removed, the patient will still complain of ongoing foot pain. The patient's resistant symptoms are therefore not necessarily the result of failing to diagnose and treat the infections correctly, but rather from not having addressed enough of the abnormalities present in the MCIDS model. These abnormalities are summarized in the table below, with a brief explanation of some of the testing and treatment methods used to help patients with chronic persistent illness. More detailed information can be found in my forthcoming book (see reference #4).

Chronic Lyme Disease/MCIDS: Differential Diagnoses

1) Infections:

a) Bacterial: includes, but is not limited to infections with Lyme disease, Ehrlichiosis/Anaplasmosis, Bartonella, Mycoplasma, Chlamydia, RMSF, Typhus, Q-Fever, Brucella, Tularemia, Tick paralysis...

1) *Borrelia burgdorferi*: Combine drugs to address all three forms of Bb simultaneously due to the ability of the organism to shift between different forms, go dormant, and evade immune surveillance. Continue treatment until the patient is symptom- free for two months.

Treat the cell wall forms with drugs such as Amoxicillin, Augmentin, Ceftin ,Cedax, Omnicef, IM Bicillin, IV Rocephin, IV Claforan, IV Vancomycin, IV Primaxin...

Treat the cystic forms, L-forms, spheroplasts, CWD forms) with drugs such as Plaquenil (hydroxychloroquine), Flagyl (metronidazole), Tindamax (tinidazole) or nutritional supplements such as grape seed extract, which has been also shown to have some activity against cell wall deficient forms.[26]

Treat the intracellular forms with drugs such as tetracyclines (doxycycline, minocycline, tetracycline HCL), macrolides (azithromycin, clarithromycin), quinolones (Cipro, Levaquin, Avelox, Factive), and rifampin.

2) Ehrlichiosis/Anaplasmosis: Use tetracyclines (doxycycline, minocycline) or rifampin for allergic/intolerant patients

3) Bartonella, Mycoplasma, Chlamydia, RMSF, Typhus, Tularemia, Brucella, Q-fever

These are all intracellular co-infections, and are difficult to completely eradicate from the intracellular compartment. Consider two intracellular drugs simultaneously to improve clinical outcomes (doxycyline with a macrolide, a macrolide plus rifampin, a tetracycline plus a quinolone, a tetracycline with rifampin) and use Plaquenil to alkalize the intracellular compartment to achieve better intracellular killing. [27] If one regimen of an intracellular combo fails, one should rotate the regimen to another double intracellular regimen, and consider treating other co-infections not addressed (such as Babesiosis, and other parasites, viruses).

b) Parasites: Babesiosis and other piroplasms, filiariasis, amebiasis, giardiasis, strongyloides, pinworm, etc. Testing is unreliable, as with Lyme disease. Do not rely on Giemsa stains, but consider a Babesia panel through IgeneX laboratories with a Babesia IFA, Babesia WA-1 (duncani), Babesia FISH test and or PCR to properly test for the presence of this piroplasm. Babesiosis is treated with antiparasitic regimens such as Mepron (atovaquone) plus a macrolide, or Clindamycin plus a macrolide or quinine. Due to evidence of Mepron resistance in the medical literature[28], also consider treating with medications such as malarone (atovaquone/proguanil), mefloquine (Lariam), and Coartem, or herbs such as artemesinin or cryptolepis depending on the clinical response.

c) Viruses: EBV, HHV-6, HHV-8, CMV, St Louis Encephalitis, W Nile, Powassan encephalitis and other viral encephalopathies,?XMRV

d) Candida and other fungi: Use of Nystatin, Diflucan (fluconazole) and other antifungal drugs may be useful with high dose probiotics for the bowel, with a strict sugar-free, yeast- free diet.

2) Immune dysfunction: Patients with MCIDS often present with a history of a positive ANA's (Antinuclear antibody), RF (rheumatoid factor) and other autoimmune markers. Increased severity of symptoms is often seen if the patient has certain genetic HLA markers such as HLA DR2, or DR 4. A positive ANA or Rheumatoid factor does not necessarily imply that the patient has Lupus or Rheumatoid Arthritis. Patients with Lyme disease and MCIDS have overstimulated immune systems, due in part to the production of blebs from the organism's surface. These autoimmune markers often return to normal once the underlying infections are properly treated. It is therefore important to differentiate between a true

autoimmune disorder, and a patient with MCIDS who has infections and environmental toxins such as mercury driving the production of inflammatory cytokines.

3) Inflammation: Patients with MCIDS have increased production of inflammatory cytokines, such as TNF-α, IL-1 and IL-6. These are, in part, responsible for the "sickness syndrome" of fatigue, nausea, muscle and joint pains, headaches, memory and concentration problems, and mood swings present in these chronically ill patients.[29] Classical therapy involves the use of immune modulators (Plaquenil, DMARD's), drugs with anti-inflammatory effects (macrolides, tetracyclines), and occasionally require the use of IVIG, especially in patients with small fiber neuropathy and decreased levels of immunoglobulins. Integrative therapies can help with the down-regulation of the nitric oxide (NO/ONOO) cycle biochemistry with subsequent decreased production of inflammatory markers. This involves the use of antioxidants, CoQ10, B vitamins, α-lipoic acid, Mag++, Zn++, omega- 3 fatty acids, glutathione precursors, as well as PO, and IV glutathione. Once the production of inflammatory cytokines is decreased and the detoxification pathways are opened to help remove the cytokines and neurotoxins, patients often will clinically improve.

4) Toxicity: Multiple Chemical Sensitivity, Environmental Illness, Heavy Metals, Mold and Neurotoxins (external and internal biotoxins). Minimal testing for MCIDS patients includes doing a six- hour urine DMSA challenge to test for heavy metal toxins. This is routinely sent to Doctors Data, in Chicago, Illinois. Use 30 mg/kg of DMSA 1x as a loading dose, and collect urine for six hours to test for mercury, lead, and other heavy metals. Other commonly used tests include an Organix test/Ion test through Metametrix laboratory to look for blockages in functional biochemical pathways used for detoxification, and testing for mold such as stachybotris, as it is an often overlooked factor in biotoxin -related illness.

Treatment for heavy metals involves different chelation protocols, using medications such as DMSA, (Dimercaptosuccinic acid), DMPS, or EDTA. DMSA may be given in low doses to the MCIDS patient if they have overlapping detoxification problems, since they may not tolerate standard doses of DMSA (5-10 mg/kg TID, three days on, 11 days off). The low dose DMSA protocol would involve administering 100-200 mg every 3rd night with Chlorella (split cell, seven tablets) with 600 mg of NAC (N acetyl cysteine), and 600 mg of α-lipoic acid (ALA). Other nutritional supplements such as Med Caps DPO (Xymogen, with B vitamins, NAC, α-lipoic acid) may also be useful to support and modulate the phase I and phase II liver detoxification pathways. For patients who do not tolerate oral DMSA, IV DMPS, +/-EDTA suppositories (Detoxamine) may be useful, especially if high levels of lead are also present. It is important to replace trace minerals the next day after chelation, since chelation will also pull out beneficial minerals along with the heavy metals. Use of a good multivitamin and mineral supplement which contains a minimum of 800-1000 mg of calcium, 400-600 mg of magnesium, and 30 mg of zinc with trace minerals (iodine, chromium, vanadium) are also important. Alternatively, DMSA 5-10 mg/kg TID, 1 hour before meals, three days on, 11 days off, or two days on, five days off may be used effectively in the MCIDS patient with overlapping heavy metal toxicity.

Glutathione (GSH), either oral (liposomal) or IV, has also been shown to be effective in a subset of resistant Lyme patients with symptoms of toxicity. Up to 70% of patients with some level of resistant fatigue, muscle and joint pains, mood disorders, and neurocognitive deficits improve with glutathione, implying a need to include a

detoxification regime in the treatment plan for the majority of these patients. Other detoxification protocols that can be added for patients with significant toxicity would include the use of oral or IV phosphatidylcholine exchanges to help remove toxins from the lipid layers of the body (the oral use of phosphatidylcholine is much easier, and can still be effective), with use of nutritional supplements such as magnesium, NAC, glycine, α- lipoic acid, DIM (Diindomethane), sulforaphane glucosinalate, combined with a diet high in protein and cruciferous vegetables.

5) Allergies: Foods, drugs, environmental, etc. Testing involves doing both IgE and IgG panels for food allergies (Bioreference laboratories, Metametrix 90 food allergy panel, ALCAT among others).Treatment involves avoidance of the allergic foods, rotation diets, and occasionally immunizations. Some integrative practitioners have found that treating an underlying Candida problem with leaky gut can be helpful, plus using desensitization techniques such as NAET, NMT and others.

6) Nutritional and Enzyme Deficiencies/Functional medicine abnormalities in biochemical pathways: Testing involves checking serum mineral levels, such as magnesium, zinc, and iodine, as well as checking red blood cell (RBC) minerals, especially the RBC magnesium level. This is important since magnesium is involved in over 300 detoxification enzymes in the body, and 99% of the magnesium is intracellular. In difficult patients, checking amino acid (AA) and fatty acid (FA) levels, as well as doing an ION test/ Organix test (from Metametrix labs) may help to discover abnormalities in functional biochemical pathways. Some of the most useful parameters to monitor are the lipid peroxides, (from Metametrix) to check for increased free radical exposure (important in CNS disease, ALS...), as well as checking sulfate levels to evaluate the phase II detoxification pathways, and nitrates to measure the NO pathway (indirect/inaccurate with urinary tract infections).Treatment involves replacing deficiencies in vitamins, minerals, amino acids (AA's), essential fatty acids (EFA's), and/or enzymes (plant or pancreatic w/amylase, lipase, proteases).

7) Mitochondrial dysfunction: Mitochondria are the energy powerhouses of the cell. They are vulnerable to free radical exposure. Mitochondrial disease can manifest as chronic fatigue, but can also be responsible for a wide range of neurological manifestations (neuropathy, myopathy, encephalopathy..). Testing: lipid peroxides, and the Organix test (Metametrix) may provide indirect evidence of mitochondrial dysfunction secondary to nutritional deficiencies, and increased free radical exposure. Treatment: NT factors (gycosylated phospholipids), CoQ10, NADH, L-carnitine, D-ribose.

8) Psychological: Stress, PTSD, abuse, depression, anxiety, OCD and other psychological manifestations

Many patients with MCIDS have been sick for a long time, and experience significant depression and anxiety. The most severely ill patients may have suffered some form of abuse and can often demonstrate overlapping PTSD. Health care providers should ask about the patient's previous psychiatric history, and refer for counseling/psychiatric help when necessary. Treatment: Medications (SSRI's, buproprion, Remeron, anxiolytics,), Stress reduction (yoga, meditation, TaiChi). Integrative: Herbs (Saint John's Wort (SJW), Valerian, Kava Kava, L-theanine). Apart from psychotherapy and cognitive behavioral therapy (CBT), Cognitive processing therapy may also be useful (PTSD), as well as techniques such as the Journey work (developed by Brandon Bays), or the Emotional Freedom Technique (EFT). Once patients have worked

through the emotional issues surrounding their illness, greater levels of healing can take place.

9) Endocrine abnormalities: This often involves the thyroid and adrenal glands, and can also affect the sex hormones and other pituitary hormones. In MCIDS and Chronic Lyme disease, the hypothalamic-pituitary axis (HPA) may be affected. Check FSH, LH, IGF1 levels, TSH, T3 & T4, Free T3/4, as well as DHEA/Cortisol levels for adrenal function, and check sex hormone levels (testosterone, free testosterone, SHBG, estradiol, progesterone, DHT, and DHEA-S). It is also important to check Vitamin D levels, with 1:25 and 25 OH levels. Balancing, supporting, and replacing deficient hormones are important factors in recovering health.

10) Sleep disorders: Acute and Chronic

The chronically ill Lyme patient with MCIDS often suffers from severe insomnia. Apart from the effect of Bb and co-infections on sleep, other etiologies include, but are not limited to: Obstructive Sleep apnea (OSA), Medications, Caffeine, Nocturia, Pain, Depression/Anxiety, and Restless Leg Syndrome (RLS). Evaluations include doing a sleep study if the patient is unresponsive to standard treatment regimens. Treatment may include activating agents in the a.m. (such as Provigil, Nuvigil..), and sleep promoting agents in the p.m., especially those that encourage stage 3/stage 4 non-REM sleep (Lyrica, Trazadone, Gabitril, Seroquel, Xyrem...). Integrative protocols include checking neurotransmitter levels. Balancing neurotransmitters with 5-HTP to increase serotonin and other brain chemicals such as melatonin, increasing GABA, and the use of phosphatidylserine at bedtime if the patient has elevated cortisol levels can also help with sleep. Herbs such as Valerian root, extracts of green tea such as L-theanine, and supplements such as melatonin may similarly be useful. Getting the patient back to sleep is essential in having them recover from MCIDS. Sleep deprivation increases levels of inflammatory cytokines such as IL-6 and interferes with production of growth hormones,[30] which furthers the underlying inflammation and delays healing.

11) Autonomic Nervous System (ANS) Dysfunction/POTS (Postural Orthostatic Tachycardia Syndrome)

Many Chronic Lyme disease/MCIDS patients will complain of fatigue, dizziness, and concentration problems despite classical therapies. The blood pressure (BP) will be low on exam, usually equal to, or less than 90/60, with associated tachycardia, greater than 100 BPM at rest. Standing the patient up and testing serial blood pressure and pulse readings in both positions may help to determine the likelihood of POTS. Definitive testing involves doing a Tilt table test. The patient should keep a blood pressure log with home readings to determine the severity of the autonomic nervous system dysfunction, and to evaluate the efficacy of therapy. Treatment involves the use of salt (minimum 3-4 grams/day), drinking increased fluids (3 liters +), and considering medications such as Florinef, Midodrine, Cortef, and/or B blockers. Occasionally clonidine and SSRI's like sertraline (Zoloft) can be helpful if there is an inadequate response.

12) Gastrointestinal: Leaky Gut, Candida, Dysbiosis, Celiac Disease, Colitis, Cancer...

MCIDS patients may have varying levels of gluten intolerance or true Celiac disease, along with overlapping food allergies. Celiac disease is one of several malabsorption syndromes due to gluten sensitivity. Look for laboratory evidence of malabsorption such as decreased levels of albumin, low levels of cholesterol, calcium, magnesium, and B12 deficiency with a macrocytic anemia. The patient may also have low levels of iron and potassium. Testing involves checking Antigliadin antibodies, and a TTG (tissue

transglutaminase) level. Patients should avoid gluten as a therapeutic trial. Other overlapping GI problems may include undiagnosed Crohn's disease, Ulcerative Colitis (UC), parasites, Candida/Leaky gut/dysbiosis, or other malabsorption syndromes.

13) Elevated Liver functions (LFT's): These may be due to tick-borne diseases, antibiotic use, ETOH, Hepatitis, Hemochromatosis, and Wilson's disease, as well as α-1AT deficiency, chemicals (carbon tetrachloride, drugs) and many systemic and endocrine diseases. Testing: ANA, AMA, Hepatitis B and C screen, Fe-TIBC/Ferritin levels, Ceruloplasmin levels, α-antitrypsin levels, tick-borne panel, lipid levels..Treatment: Treat symptomatically if the above etiologies have been ruled out. Integrative: Use milk thistle (silymarin), Hepa #2 (TCM), NAC, and α-lipoic acid.

14) Drug use/Addiction. This may interfere with endocrine function, interfere with sleep, and cause a rebound phenomenon. Use of narcotics also interferes with the use of LDN (low dose naltrexone), an effective medication for pain and overlapping fibromyalgia symptoms. Referral to a pain/addiction specialist may be necessary.

15) Deconditioning: Many patients with an extended illness are deconditioned, and may need to participate in a physical therapy and medically supervised exercise program to regain previous levels of functioning.

This 15- point differential diagnostic category for Multiple Chronic Infectious Disease Syndrome (MCIDS) is applicable to most chronic disease states. It serves as a map for the clinician when they are evaluating not just a patient with Lyme disease and co-infections, but for assessing any patient with a chronic unexplained illness. The majority of the chronically ill patients I have seen over the last 28 years with symptoms of unexplained fatigue, muscle and joint pains, neuropathy, memory and concentration problems with an associated sleep and mood disorders had usually received a diagnosis of chronic fatigue syndrome, fibromyalgia, rheumatoid arthritis or a non-specific autoimmune disorder, multiple sclerosis from other physicians, or were told that their complaints were from a primary psychiatric disorder such as depression or anxiety. Yet the majority of these patients in fact suffered with MCIDS. Their symptoms were due to not one problem, but to a host of overlapping factors on the MCIDS map. These factors included Lyme disease and associated tick-borne infections, viral, fungal and parasitic infections, autoimmune phenomenon, increased levels of cytokines secondary to inflammation in the body, heavy metal toxicity with other environmental toxins with associated detoxification problems, mineral and vitamin deficiencies, hormonal imbalances, autonomic nervous system dysfunction, mitochondrial dysfunction, sleep disorders, and psychiatric symptoms such as depression and anxiety. All of these factors simultaneously interfered with the patient getting well and regaining their previous state of health. Moreover patients with disseminated, multi-system infections face a host of potential stressors: one or more infections, reduced psychosocial functioning, severe pain, sleep disorders, cognitive and neurological impairment, and difficulty in finding appropriate care from an often skeptical medical and insurance community. What can health providers do? We can institute the regular use of a 39-item screening questionnaire for Lyme and other tick-borne diseases (www.ilads.org), combined with a detailed history and physical and appropriate testing along with this 15- point MCIDS map for chronic diseases. These are the keys to solving the underlying mysteries of patients' chronic symptoms.

I hope that that in the years to come the concepts behind MCIDS will bring about a paradigm shift in how we think about chronic

diseases. I have been able to help the majority of the 12,000 ill patients who have come to see me after they have failed previous traditional medical evaluations and treatments. It is no longer acceptable to just label an illness, and then to give a drug to treat the symptoms. We can do better. Lyme disease and associated co-infections are occurring in epidemic numbers in the world, as are exposures to environmental toxins. We should suspect that the chronically ill patient may have an undiscovered tick-borne illness and be suffering from environmental toxicity with detoxification problems. The 39- item questionnaire and the 15- point differential of MCIDS give healthcare providers a framework with which to unravel the etiologies of a patient's complex illness. The strength of using this system is that healthcare providers can be overwhelmed by an endless list of what seem to be unrelated symptoms that a chronically ill patient will report during their office visits.

It is an enormously gratifying experience to help suffering, chronically ill patients regain their health. Look to MCIDS for diagnostic answers in your patients with chronic diseases.

You will not be disappointed.

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What is Biological Dentistry? Dentists as Physicians of the Mouth

George Keanna, DDS

" ...Dental and oral conditions can be understood only in relation to the whole body. Just as your foot bone's connected to your anklebone, your oral tissues are physically and energetically connected to every other part of your body. Biological practitioners know that the body reflects what goes on in the mouth—and that the mouth reflects what goes on in the body. Dysfunction or disturbance in one area will invariably show up as illness in related areas of the body.

A biological approach is holistic. It is a blend of clinical practice, sound scientific knowledge, and the traditions of natural healing. It does not automatically equate symptoms with illness. What we call "symptoms" often indicate important signs of healing. To suppress these symptoms and then call this suppression a "cure" would be superficial and shortsighted. By ignoring the actual causes of illness, this allopathic practice leaves the patient vulnerable to even more dysfunction and future disease.

In contrast, biological practitioners try to find the systemic causes of illness. To remove the root cause is to take a major step towards healing. As a rule, they opt for the least invasive, least traumatic, and least toxic means of diagnosis and treatment. True biological care supports the body's natural abilities of self-healing and regeneration.

Biological practice is socially, spiritually, ecologically, and environmentally aware. Its practitioners honor the right to informed consent. They know that the human body is more than a collection of parts that can be mechanically worked on in isolation. Seeing us as whole, unified beings, biological practitioners respect each person's individual uniqueness and dignity. They are committed to providing the patient with the knowledge, tools, and power to take charge of his or her health...." (1)

"Discovery consists in seeing what everyone else has seen and thinking what no one has thought."

—Albert Szent-Gyorgyi MD, PhD; Awarded the 1937 Nobel Prize in Medicine for the discovery of vitamin C, in connection with biological combustion.

Perhaps the greatest driving forces in creating the changes that are taking place in dentistry are today's more highly inquisitive and educated patients. Gone forever are the days when the dentist was the lone source of information for a patient trying to learn about these issues. Dentists, when confronted on a regular basis by these highly informed patients, may initially feel threatened, but dentists are eventually forced to take notice and address these issues.

Dentists as Physicians of the Mouth

The evolution of dentistry in this country changed abruptly in 1833. Until then, there were two types of practicing dentists. The first was a physician-dentist. Dentistry was viewed as a subspecialty of medicine. Upon graduating from an accredited medical university, a physician would do an apprenticeship under a practicing physician-dentist and learn the craft of dentistry. This was truly comprehensive health care. The second type of dentist was the barber-dentist. The barber-dentist came from the nonmedical trades, such as barbering, blacksmithing, and carpentering. Indeed, anyone who thought that working on teeth might be profitable could become a barber-dentist. These barber-dentists had no formal training or education in dentistry or its relationship to medicinal health care. These barber-dentists would fill teeth with whatever was at hand: with molten lead, pine resin, stone, woodchips, corks, tin foil, gold foil, etc. or just pull the troubled teeth for their clients. There were no dental schools, no licenses, no drills, no anesthesia, and no checks or balance in the profession of dentistry. The dental field therefore was wide open to swindlers, con artists, and snake-oil peddlers.

The practice of dentistry in this country was forever changed by the introduction of mercury-amalgam filling materials or "Royal Mineral Succedum" in 1833 by the Crawcours brothers. This started the Amalgam Wars between the craftsmen-dentists' ideal of ease of manipulating amalgam and the medical-dentists' ideal of avoiding the dangers of systemic mercurial poisoning.

Chaplin Harris, MD, the cofounder of the first dental school, said in 1833:

> "...Some have endeavored to [overcome] the objection to this amalgam by using silver perfectly purified, but it matters not how pure the silver may be; the material will be equally deleterious in it effects. . . . It is the mercury that does the injury, and it matters not, therefore, how pure or what the other metal may be that is employed with it for the formation of the amalgam...." (2)

The first dental society was formed in New York in 1834. The first dental school was charted in 1840 in Baltimore to educate craftsmen and future dentists. Months later, the world's first national dental organization was formed in 1840: the American Society of Dental Surgeons (ASDS). (3)

In 1843, the ASDS declared the use of mercury amalgams by any of its members to be malpractice and grounds for expulsion. All members were required to sign a declaration that they would not use the poisonous mercury filling material. This declaration against mercury amalgam led to the ultimate disbandment of the ASDA in 1856. (4) The financial gain was too great for the barber-dentists, and they left the ASDA and ultimately formed the American Dental Association (ADA) in 1859. This was the beginning of the first of three Amalgam Wars in this country.

Ironically, while it was the medical dentists who recognized mercury as a health hazard, and it was the medical profession [who] declared it unethical to use mercury fillings, it was the nonmedical barber-dentists who held the winning hand. This was the issue upon which the practice

of dentistry and the practice of medicine parted ways. In essence, the fracturing of dentistry from medicine occurred over a medical health issue, not a dental one; tragically, the fundamental reason for the split was not to improve the practice of dentistry or to provide better treatment to the patient, but for the pursuit of profit. (5)

At this same time, the medical establishment turned its back on dentistry. Then dental schools dropped courses in physiology, pathology, medical matters, and ceased teaching anything about anatomy except for the head and neck.

"...The atmosphere at most private dental colleges was more like the one prevailing in trade schools, and this attitude naturally permeated to the student body. Dental students gave scant attention to any subjects excepting those pertaining to the technical side of dentistry. Knowledge of anatomy, chemistry, or histology was considered useless and a sheer waste of time...." (6)

The use of mercury-amalgam fillings caused the divorce of dentistry from the medical profession. All parties involved suffered, especially the patients. Now it is over 175 years later, and the medical profession is poised to give dentistry another chance to be part of it again. This has been necessitated by the continued growth of chronic and degenerative diseases in the U.S. No competent doctor or health-care provider can overlook the oral-systemic correlation of the disease processes any longer. The days of the tooth-mechanic dentist who blindly fills holes in teeth without any understanding of what caused the problem in the first place or what systemic problems could arise from their treatment are over. (7)

As a result of research-based proof that an association exists between oral infection and systemic diseases (8,9,10), dentists have the opportunity—and some say obligation—to elevate their roles in their patients' care from that of " tooth technician" to "oral health physician."

What was previously an intuitive hypothesis has now been substantiated with research-based proof. An association was found to exist between oral infection and systemic diseases, particularly heart disease (11, 12, 13, 14, 15) and stroke (16), diabetes (11,17), and preterm low birth-weight babies (18,19,20), among others. High correlations have also been made to pneumonia (21), respiratory diseases (22), and osteoporosis. (8,9,10)

According to Associate Professor of Dentistry, Evanthia Lalla, DDS, MS, of Columbia University School of Dental and Oral Surgery:

"...In light of the oral-systemic association, . . . dental clinicians can play a significant part in promoting the general health of their patients. . . . We—as dentists—are sometimes so focused on individual teeth and the mouth that we forget that they are part of a person who needs to be systemically managed. We can do our part in that . . . making dentists aware that they truly are health-care providers; that by improving clinical outcomes—by helping a patient . . . better managing his or her diabetes—they are promoting the general health of their patients. We have to forget about being isolated to the mouth because we now know that the mouth mirrors the body...." (23)

"Half of what we have taught you is wrong. Unfortunately, we do not know which half."

—Dean Burnell, MD, addressing medical students at Harvard University

While biological dentists are made out to be quacks, it is interesting to note that the German term for mercury is "quecksilber," and the German pronunciation for queck is "quack." For this reason, dentists who placed mercury amalgams, at that time, came to be known as

"quacks." The term has now come to mean anyone who is an "ignorant pretender of medical skill". (24) It is in fact the biological dentists who are attempting to initiate a scientific debate on this subject of the medical, social, and economical ramifications of using mercury in amalgam fillings for over 175 years.

George Keanna was born in 1961 when Queens, New York was a brighter place. After completing high school, George attended Trinity College in Hartford, Connecticut where he earned a Bachelor of Science Degree in Psychology. The awareness that he enjoyed working with his hands, combined with his love of science, healthcare and psychology motivated George to seek a career in dentistry instead of psychology. Thus, he attended Georgetown University School of Dentistry from 1984 to 1988 and was awarded his degree in dentistry.

Even though his dental training was comprehensive and encompassed every facet of the practice of dentistry, George felt the need for further training. He applied and was accepted into a residency program at Castle Point Veteran's Hospital in upstate New York. This experience was the turning point in his perception and understanding of health care in this country. This veterans' hospital was a spinal cord injury facility. The horrors that George saw at that veterans' hospital have stayed with him for twenty years and have served to motivate him to seek "a better approach" to health care.

In his quest to provide improved health care to his patients, George began researching the issue of mercury amalgam fillings. After ten years of conducting research and reading volumes of peer reviewed articles and books from all over the world, George was lead to the realization that he had closed his mind to the issue of mercury based fillings, and he could no longer practice dentistry as he had been taught. He decided he needed to become a biological dentist. His quest led him to Albuquerque, New Mexico where he purchased an existing Biological Dental practice. After a quick review of the needs of his new environment, it was immediately evident to him that his dental education was woefully lacking in the ability to allow him to service his new patients.

Thus, the next steps of his journey began. During the next nine years, George traveled all over the country taking innumerable hours of continuing education in nutrition, physiology, and alternative medicine to mention a few. His greatest pleasure and accomplishment was that of graduating as the valedictorian of his class from Capital University of Integrative Medicine in Washington, D.C. His title of Doctor of Integrative Medicine is just as cherished as his degree from Georgetown University.

George and his wonderful wife, Erica, currently reside at the base of the majestic Rocky Mountains called the Sandia Mountains in Albuquerque, New Mexico. George and Erica stand shoulder to shoulder and support each other to practice and live the philosophy of Biological Dentistry.

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Pelvicology: A Neuro Muscular Skeletal Approach to the Treatment of Pelvic Conditions

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Introduction: Traditionally the care of patients who have symptoms related to pelvic organs has been divided between different medical practitioners. Gynecologists and Obstetricians treat women during their life cycles of reproduction and beyond, with a focus on female organs of reproduction. Patients with urological symptoms, or males with reproductive organ disease are seen by Urologists, while dysfunction of the gastrointestinal tract are treated by Gastro-enterologists, General and Colo-rectal surgeons. More recently the addition of Uro-gynecologists has been an attempt to bridge the specialties of Gynecology and Urology. In all these specialties treatment is mostly symptom driven and treated by dispensing medication or doing surgery. Although Physical Therapists in most parts of the world have been involved with patient care in all of the above fields for many years, their unique role in treatment of the neuro musculo-skeletal system as it relates to all pelvic conditions has only recently been acknowledged. Physical Therapists are the "Pelvicologists" who bridge the uro-gynecological, colo-rectal fields, and as such are beginning to become more mainstreamed as adjuncts to those specialties.

Physical therapists are neuro-muscular skeletal specialists, and the role this system plays in creating a healing environment for pelvic system health is well documented. In order to understand this role our approach in this article is to divide conditions into two main types of pelvic floor dysfunction. These can be classified as hypotonicity and hypertonicity of the pelvic floor muscles. Hypotonicity implies weakness of the

pelvic floor muscles which interferes with the muscles performing several of their crucial roles. Some important functions of the pelvic floor muscles are: to support the pelvic floor organs (bladder, uterus, rectum) which rest atop the sling like pelvic floor muscles; to maintain bowel and bladder continence; sexual function and an important core support of the body. As women age and hormone related changes occur, pelvic floor muscles and the surrounding ligaments become weaker. In addition, each pregnancy and vaginal delivery increases a patient's likelihood of developing pelvic floor muscle weakness. Furthermore, research has shown that there is an increase in joint laxity during pregnancy which may result in altered pelvic floor biomechanical alignment[i]. In addition, birthing position may adversely affect the positioning of the pelvic floor, especially if previous medical conditions exist. Therefore, women with sacroiliac dysfunction should deliver in in semi-reclining position (with hips supported, flexed abducted, and externally rotated), and women with coccyx (tail-bone) pain should deliver in squatting, side-lying, or upright kneeling position.[ii] Also, facilitated delivery with forceps causes more trauma to the pelvic floor compared to vacuum extraction assistance.[iii] In addition, in 2002, approximately 25% vaginal deliveries are still performed with episiotomies despite the fact that this procedure increases the risk of sustaining anal damage.[iv] The resulting scar may not heal properly or may restrict underlying tissue mobility.

Furthermore, prolonged repetitive straining and stress to the pelvic floor such as jobs that involve heavy lifting or chronic constipation increase the likelihood of developing weakened pelvic floor muscles. Several other factors that may contribute to hypotonicity of the pelvic floor muscles are trauma, infection, radiation, chemotherapy, and other co-morbidities that affect and weaken muscle and/or soft tissue (ex. Muscular Dystrophy, Multiple Sclerosis, Parkinson's disease).

Just like a weak biceps or deltoid muscle will interfere with the ability to lift or carry objects normally, so too a weakened pelvic floor will interfere not only with general activities of daily living, but more specifically with the ability to postpone the elimination of bowel and bladder, until arriving at a restroom at an appropriate time and fashion. The bowel and/or bladder related issues that this creates may affect daily activities in a very significant way. For example, a woman who fears that she might "have an accident" if she attempts to participate in a tennis match with her friend may choose to remain at home, within a short distance to a restroom, watching a movie alone. This may negatively affect her socialization as well as her productivity at work. In addition, another symptom that women may experience is a "dropping" sensation in the pelvic floor, as if something inside feels like it is descending. This is referred to as pelvic organ prolapse, and it may involve descent of the uterus, the urethra, bladder or even bowel descending onto the anterior aspect (front) of the vaginal wall (cystocele) or the rectum descending onto the posterior aspect (back) of the vaginal wall (rectocele)[v].

Fortunately, there are conservative treatment methods of the aforementioned conditions. The common denominator between all of these approaches is management of the symptoms through Physical Therapy without requiring invasive procedures or surgeries. Like any weak muscle, the key to improving core strength, incontinence and prolapse related symptoms is by strengthening the weak pelvic floor muscles. One way to accomplish this is by regularly performing two types of pelvic floor exercises, phasic or "quick flick" muscle contractions to strengthen the fast twitch muscle fibers, and prolonged tonic "holding" muscle contractions to strengthen the slow twitch

endurance muscle fibers. Laycock developed a four point grading scale called the P/E/R/F model. This scale measures Power (0-5 maximum voluntary strength measurement), Endurance (how long can maximum voluntary contraction be held?), Repetitions (how many repetitions can be performed prior to exhaustion?) and Fast Twitch (how many quick contractions can be performed prior to exhaustion?).[vi] The strengthening can be enhanced by using vaginal or anal weights, and gradually increasing the amount of resistance as the pelvic floor muscles get stronger. Sometimes, individuals do not know how to properly use their pelvic floor muscles, and they may think they are performing a pelvic floor muscle contraction when, in fact, they are mistakenly contracting their abdominal or gluteal muscles instead. This type of substitution is actually counterproductive, because using the more superficial prime movers (rectus abdominus and internal and external obliques) of the abdominal muscles will enhance the opposite role of pelvic floor muscles. Contraction of these substitute muscles cause the pelvic muscles to relax and pelvic contents to descend even further. Contraction of the pelvic floor muscles, muscles on the other hand will help support the pelvic organs and maintain continence. Oftentimes pelvic floor exercises are handed out to a patient in their Doctor's office, with little or no guidance on correct form and execution. Research has shown that abysmally few patients are able to do the exercises correctly, most patients bearing down with their muscles instead of contracting them. When the patient's symptoms do not improve or even worsen, leading to the misconception is that this conservative method was not effective and that the patient requires a more invasive therapy.

To ensure correct exercise technique, a practitioner needs to give adequate biofeedback by inserting a finger vaginally or rectally in order to digitally palpate the muscle contraction. Ultrasonography is another excellent educational biofeedback tool, as is surface electromyography (sEMG). It may even be necessary to use alternating electric current to simulate a pelvic muscle contraction if the above is not enough. Helping a patient make the correct neuromuscular connection is essential to improve their ability to learn how to contract and release their muscles effectively. Biofeedback has been proven to be an effective approach to treating anorectal disorders.[vii] It is sometimes also necessary to dispense a home electrical stimulating device, or biofeedback unit for use on a daily basis until the patient is able to carry out the required exercise independently.

Diet is also an important factor to be considered when treating pelvic floor muscle dysfunction. Some foods, especially highly caffeinated, highly acidic or spicy foods, act as bladder irritants, which make it more challenging for a patient to control bowel and bladder function. Treatment needs to include education about proper foods and beverages as well as tracking toileting habits with bowel and bladder diaries. This helps the individual keep track of the frequency and amount of leaks, and it helps them connect particular triggers in their diet to the incontinent episodes in order to prevent future occurrences. Toileting posture and technique play an important auxiliary role in all conditions. In case of organ prolapse, physical therapists can help guide the individual in the proper selection of a pessary, a device that may be inserted to support the descending pelvic organ during selected activities (ex. exercise) or throughout the day. There are many different types of pessaries, including platform, gellhorn, inflatable, cube, and Smith-Hodge pessaries.[viii] Most importantly these patients need to learn how to use their deep core muscles (levator ani, transverse abdominal and multifidus) during all activities of daily living. Core muscle activity needs to vary with the intensity of activity, for example using stronger muscle contraction when climbing stairs than walking on a floor. Muscles

need to learn how to relax appropriately during activities like sitting or lying down; too much contraction without appropriate relaxation can create a problem of hypertonicity.

Hypertonicity implies that the pelvic floor muscles are tight or overactive, which often is associated with pelvic floor pain. There are several factors that are associated with hypertonicity of the pelvic floor muscles including prior trauma or a genetic pre-disposition. Prior sexual or emotional abuse may sometimes contribute to pelvic floor hypertonicity. Van Der Velde and Everaerd performed a study with 45 women who presented with vaginismus, a condition making vaginal penetration difficult or impossible. Pelvic floor muscle and upper trapezius muscle activity was measured while the women were exposed to four different types of stimuli: neutral, threatening, erotic, and sexual threatening. Their research revealed that the women demonstrated increased pelvic floor muscle and upper trapezius muscle activity during film excerpts that were threatening and sexually threatening. In other words, these women tightened and "held" their pelvic floor muscles when exposed to traumatic stimuli, demonstrating that sexual and emotional trauma can contribute to hypertonicity of the pelvic floor muscles (2001).[ix] Stress can be a trigger for pelvic floor muscle hypertonicity: in the same way that some individuals store stress and tension in their upper trapezius muscle, at the top of their "core", so too, others store stress and tension in their pelvic floor muscles, at the bottom of their "core". Finally, there can be an insidious onset of pelvic floor muscle tightness, without any apparent reason for the hypertonicity.

The symptoms of pelvic floor hypertonicity differ from hypotonicity, and they include pain, tightness of the pelvic floor, sexual dysfunction and dyspareunia (pain with penetration during sexual activity in women). Urinary hesitancy, increased post void residual and frequent urinary tract infections and constipation can also be the result of increased pelvic muscle tone. The aforementioned symptoms are often accompanied by emotional issues such as anxiety and/or depression.

Pelvic floor physical therapy can be very beneficial in treating symptoms of hypertonicity as well. Following the aforementioned analogy of the tight and painful upper trapezius muscle, which requires manual therapy, massage, and soft tissue release to relax and stretch the tight muscle, so too, tight pelvic floor muscles benefit from manual therapy as well. Specially trained pelvic floor therapists are skilled in performing internal vaginal, anal and external muscle massage, stretching and manual trigger point release to tender localized spots. This approach has been demonstrated to be beneficial in decreasing pelvic floor muscle spasm and pain.[x] It is only when patients are taught how to administer this treatment themselves, that they do not become dependent on the therapist to treat their symptoms, but are able to treat themselves on a daily basis in the comfort and security of their own homes. In addition, any of the methods of biofeedback discussed above can also be utilized to help teach individuals with tight pelvic floor muscles how to relax their pelvic floor muscles. It is imperative to stretch and diffuse tender trigger points first, as sEMG administered on its own will only train the muscle to relax in its shortened, painful state. This "down training" helps people who clench the pelvic floor muscles involuntarily learn how to "let go" and lower the resting tone of the pelvic floor muscles from moment to moment in order to facilitate healing of the tissue. Use of vaginal dilators, anal dilators or wands can help patients perform self massage and stretching, especially if it is difficult for them to use self digital manipulation for same. At first, smaller sized dilators are used, and the individual gradually increases the size as their tolerance increases and the tightness decreases.

An additional key to managing pelvic floor hypertonicity is relaxation training. This includes learning how to perform proper diaphragmatic breathing. When used correctly this pattern is the most efficient and effective way to provide oxygen to cells throughout the body; it also promotes overall physiological relaxation of the neuro-musculoskeletal system. An additional approach to relaxation training is Jacobson's relaxation series, where the individual systematically contracts and then relaxes various muscles throughout the body in a specific order. This provides a contrast for the individual to learn how to "turn on" and then "turn off" muscles, with the ultimate goal of eventually "turning off" the overactive pelvic floor muscles at will. Dr. Anderson and Dr. Wise describe a more finely tuned relaxation concept, also developed by Dr. Jacobsen, and known as paradoxical relaxation. The paradox is that by learning to acknowledge and accept bodily discomfort and tension, the tension and discomfort stop fighting back, and so release more easily. At times, pelvic pain may be due to underlying soft tissue and organ restriction. In this case physical therapists can perform visceral mobilization techniques to facilitate proper movement of the internal organs and underlying fascia. This is especially important in conditions like endometriosis, where there can be diffuse scarring, sometimes even after surgery to remove the scar tissue. Even years after abdominal or pelvic surgery, scar tissue massage can release bowel adhesions, improve circulation and reduce tension around involved nerve tissue. Conditions like painful episiotomy or surgical scarring may limit mobility of tissue and or organs and contributing to pain. By teaching the patient how to perform a self-technique at home, it is possible to avoid the kind of symptoms associated with scarring, like repetitive bowel obstruction. Proper toileting posture and colonic transport self-massage is especially beneficial to those who experience irritable bowel syndrome, especially of the constipation type. This technique is an external massage along the direction of the colon to help promote peristalsis and normal passage of stool through the large intestine. Bowel stimulating exercises, usually involving some type of low impact activity, core strengthening and abdominal exercise are an important addition to the program.

It has been well documented in evidence based practice that there is a strong correlation between pelvic floor related problems, respiratory conditions and back pain. It is rare to find an adult patient who has cystic fibrosis who has remained continent. There is a higher correlation between patients who have incontinence (hypotonicity of pelvic floor muscles) and low back pain than patients who have a high body mass index (BMI) and back pain. All musculo-skeletal systems in our bodies are related, and as the pelvis, its contents and structure are supported by a substantial musculo-skeletal system, it is imperative to take this system into account when treating any of the conditions or symptoms related to the pelvis.

Marilyn Freedman has her clinical doctorate in physical therapy. She is certified in pelvic muscle dysfunction biofeedback and has completed a certificate of achievement in pelvic physical therapy through the women's health section of the American Physical Therapy Association (APTA). Marilyn has over thirty years of experience in helping people resolve complex pelvic conditions. She has worked with men, women and children with pelvic pain, urological, obstetrical, gynecological and colorectal conditions. She is an adjunct instructor at area physical therapy schools. She lectures to professional colleagues and has contributed to several publications in her field of expertise. Her research interests include

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Activating Our Healing Potential by Using Our Innate Faith

Vernon C. Barksdale, MD, MPH, CPI

When asked to contribute a chapter on medicine, healing and spirituality, I initially agreed, then realized I would be walking the line where science and spirituality oft share an uncomfortable border. We have traveled far in the science of Medicine but have yet to come full circle in acknowledging the power of the healing process each of us carries, except in the most significant health challenges, such as cancer treatment. Similarly, the faithful in so many religious disciplines and spiritual paths often are passive travelers, only living the faith when confronted with overwhelming challenges that they no longer can 'will' to resolution or rely on what science has to offer.

Consider however, that many people got better in the days of bloodletting and use of leaches despite having active disease. Was it placebo effect or the faith that healed? Are placebo effect and "faith" in healing closely related? Jerome Frank, MD, one of my supervisors during training in Psychiatry at The Johns Hopkins University, discussed his writings, theories and beliefs on the power of persuasion and healing, believing that even psychotherapy was somehow a process that helped change belief to initiate healing. These connections emotionally, and, as I eventually learned, spiritually, were powerful stimulants to the healing process. There are numerous examples in the medical and research literature on positive thinking, prayer and placebo effect helping patients overcome numerous health challenges. There is also personal clinical experience of those sad cases where demoralization promotes the reverse of healing, often leading to negative outcomes or hastening the patient's succumbing to the disease. Even in clinical trials we have seen placebo effect improving the patient and thwarting our data!

Current research also documents the conversion of emotional states into neurotransmitter substrates

that signal the immune system into action. We understand that we have this innate ability to convert an emotion into biological changes. Are positive emotion and cognition close enough to the concept of faith to satisfy our need for scientific evidence of the healing power of faith? Is there anything else that can be activated by our faith to further the healing process or improve the way our patients manage their health concerns? These are the challenges we face as clinicians as we strive to promote health as a part of overall well-being. Our patients are seeking ways to have a holistic experience of life that includes their health. We should be champions of their cause, as we know how powerful a role lifestyle plays in the health of our patients. Genetics may be the bullet but lifestyle pulls the trigger that often "wounds" us with chronic disease, stress and shortened lifespan. To exacerbate the issue, many of our chronic diseases have stress-related drivers that can foil remission or antagonize symptoms.

When our patients face health challenges, they look for meaning of the event as it relates to their life and belief. Often it's "gut check" time at the altar, where now they must seriously apply their faith. For many, fear fertilizes the weeds of demoralization, causing faith to falter. Negative attitudes or beliefs circle about and darken the sky of hope. Can we play a role to help overcome these obstacles? Often, despite our privilege to ask intimate details of a person's life, we rarely explore the details of this struggle, leaving the patient to go it alone. We miss this opportunity to be an ally and additional source of validation of their faith building to assist the healing process. We are not unwelcome visitors into their personal sanctum if we allow ourselves to become comfortable with asking to enter, honoring their avocation.

In his presentation on Spirituality and Healing, Herbert Benson, MD of Harvard Medical School and Director of the Hypertension Section of Beth Israel Hospital reports that many patients believe the God of their faith plays a role in their treatment response. Most interesting is the finding that many believe God is working through their doctor to bring them the best that Medicine has for their particular challenge. A National Institutes of Health-Centers for Disease Control (NIH-CDC) study in 2002 found that ~50% of patients used some form of religious or spiritual activity to promote their health. This included praying for themselves to God. Dr. Benson's experiments with the Relaxation Response meditation training revealed patients describing it as a "Spirituality experience," regardless of religious beliefs. I was also very impressed with the consistent finding over more than four years of lecturing patients in our Intensive Outpatient Program for substances of abuse. Patients described "Spirituality" as a personal relationship and experience of God, different from rules and conventions of "religion." These findings spanned different ethnic groups and faiths. Even those not participating in a religion agreed with this understanding. I believe many of our patients are already "ready" to have some form of spiritual activity or belief as part of the healing process.

Over years of studying with Eastern and Western schools of metaphysical and spiritual sciences, it has become clear to me that we have an underpinning to our existence that is based on the belief in a "Great Architect" of our universe, creating and sustaining all that we know as well as the things we are not aware of yet. The simple axiom, to use a mathematics term, is that all matter and life are "created" by God without need of primordial substance, as It supersedes the need for any existing substance to "work" with to make reality. All of reality as we know it, seen, unseen, is made of God's Substance. This brings an interesting observation: If all particles of matter are at their foundation God substance, then the infinite intelligence/capabilities of God are an innate part of all matter. How can we access it

more efficiently? Do we sometimes access by chance when in unique situations where faith and belief are optimal and persistent to transcend the connection? This God substance is the elusive "quantum" particle we are looking for. It is the primordial template of living things replete with Divine Intelligence even in the most minute particle. Thus, we are in essence spiritual beings having a human experience.

The great Yogis and acupuncture healing practitioners of the East point to the interface of the spiritual and physical beings at the neuroendocrine axis and central nervous system. The acupuncture meridians are also superimposed on this primordial "body." Perhaps this is why so many agnostics and people of faith in our substance abuse program all came to the same conclusion on spirituality: something they experienced independent of the structure of their religion, that was personal, a special internal connection that made them feel whole and at peace.

We may insist that it is not our role to support a belief we may not agree with or understand. However, the patient believes anyway and may be looking for validation or support that could be adding to activating the healing process and enhancing it by increasing connection to their spiritual side. We can walk a supportive and respectful path with our patients who entrust us with their well-being.

We also have good literature on the benefits of biofeedback on managing stress and promoting a sense of influence over how we respond to stress. We can also draw on the success of rehearsal by visualization and positive emotion on performance. Both support the impact of mental processes coupled with positive emotion on outcomes. Prayer and meditation can evoke a similar experience for the individual. Before belief slips too far, they both have strong emotional components—not just expressed emotion, but also internal feelings of peace, joy, calm, or well-being. The mental discipline of focusing on a thought, especially one that affirms the presence of God as part of us and helping us, found in prayer, chanting and meditation, also evokes the positive emotions noted above. When we access this source it helps to promote the healing process, reduces stress-related drivers of illness pathology and improves coping skills. Small studies on prayer for a patient by people not in their presence also showed concurrent changes in the brain activity even when the patient was unaware of the prayer times. Faith in the process and what one believes in are paramount to the chance for the best outcome. Even use of simple word chants as part of Transcendental Meditation in Benson's double-blind studies made a difference in changing vital signs with patients also reporting a "spiritual experience".

We can validate the faith of our patients as a tool to help healing by "normalizing" that it may exist with them. I learned these questioning techniques during my work with substance abuse patients and when attempting to clarify patient medication adherence. When we inform patients that an event is often seen with the patients we care for, we "normalize" it for them. This makes it easier for them to report their similar experience or behaviors, instead of feeling like an outlier, not doing the right thing.

After giving a patient a difficult diagnosis I may ask: Many of my patients are upset, frustrated or fearful about a diagnosis like this and need a way to cope with it. How do you cope with stressful or frightening situations where you are not sure you are in control of your life? Do you use spiritual supports? Do you have family or friends you trust with whom you can talk? Then, we do what we do best. Listen and the patient will

guide you to the place they are comfortable. More about this in the FAQ section at the end. This normalizing questioning also works when gathering substance abuse history. If patients get the impression that you often see patients who use marijuana to relax or reduce pain, it's easier for them to talk about their use. In these situations, patients may disclose that they used to go to church, temple or mosque and need to consider returning. Well, that may be easier than getting them to a disease-specific support group. However, if they are turned off by spiritual or religious programs, then illness-specific support groups, meditation or yoga for stress management can be appropriate. You don't have to be an expert but do have some contact information for local resources. Alternatively, give them a homework assignment to visit such a group to see if it fits their needs. Patients rarely ask about your faith but often benefit from feeling their health provider validates/supports the use of their beliefs. If patients ask for a strategy they can use for their illness, stress management is always a safe bet that can be used for general life issues, which then adds to overall health.

As with any advice and material given to a patient concerning these matters, one must proceed with a nonjudgmental approach respectfully honoring the patient's belief system. This works best if we understand that, at the end of the day, we are all made from God substance and the palette of different faiths/beliefs may just be the Creator's way of ensuring that there was freedom of choice on method of access: "each according to his need and faith." I also instruct patients that the use of spiritual or meditation resources serves to enhance the healing interventions prescribed. They work together, not against each other. You as the provider must also reconcile any personal belief/faith issues so that they don't interfere with those of your patient. If these can't be reconciled then this approach may not be for you.

FAQS:

- "What if the patient says: "Why do you ask?" This question may have a few different origins. If you have not explored or discussed these issues before with the patient they may be wondering what's different with you. Now would be a good time to discuss your interest in helping them to consider a holistic approach to care for their health challenge, to marshal any and all resources that they may find or consider helpful. If their question is not hostile, you can drill down a little to ask about their experience with meditation or prayer or if they have a formal spiritual program or faith and encourage them to consider it a helpful coping skill.
- "What if the patient asks: "What would you do?" Honestly, what would you do? Read the latest literature, consult colleagues, seek support from family, read a book on living with the illness, or pray. Be prepared to have a sincere answer besides "follow doctors' orders". Honesty is a lot better than being too professional. If you don't practice a stress reducing program or faith or don't have a belief system, consider referral to support groups for their illness. Clarify with them that belief is a personal process and what works for one may not work for the other, but research has shown it can help coping and attitude, which is important to increase the chance for the best outcome.
- "Is there any tool you use in your practice?" If the patient has a belief in God, even generically/agnostically, I recommend they practice the Golden Key by Emmet Fox. I have and do use this regularly for stress management, and as a scientific prayer to manage challenges. You have to try the exercise yourself to see if it resonates with you. This is a difficult exercise but pays great dividends. Alternatively, as a strong supporter of self-care, I often put the responsibility on the patient to look for inspirational scriptures, quotes, invocations, or other

inspiring words they find, as a mantra to focus on by repetition to "crowd out" the fears/ruminations about their health challenge. You may be surprised at their creativity, as long as it works for them. This can become a practical tool they can use for any challenge. Keep a collection of these works with their permission to help others in the future. The Golden Key is generic enough that I have had Muslim and Christian alike find it helpful. It also may be applied to daily stressors. A link is provided at the end of this FAQ section.

- "My patient only wants to use their faith or natural means of healing and not take medication or surgery." There are certain faiths, such as Jehovah's Witnesses, for example, that won't take a transfusion due to their beliefs. Sometimes family in a particular faith will extend prohibitions to medications in general. I have requested a meeting with the local leader or pastor to review with the patient my recommendations and clarify if they are against their faith. Generally, I have received the support of the leader for the treatment and their prayers that it shall be successful. If this is not possible or does not support treatment, then you are back to discussing the risks/benefits of their decision, referral to get a second opinion or discharge the patient. I also ask them to seek help from a provider who practices their faith for a better understanding of their needs.

Vernon Barksdale is Board Certified in Psychiatry and is ASAM (American Society of Addiction Medicine) Certified in Addiction Medicine. He attended Harvard University, majoring in Economics and Premedical Science. He matriculated from The Johns Hopkins University School of Medicine in Baltimore, Maryland with both a Medicine Degree and a Master's Degree in Public Health. He has completed fellowships in Psychiatry and Forensic Psychiatry. He is a Certified Acupuncture Detoxification Specialist, using acupuncture for drug detox. He has also taught meditation techniques for stress management, conflict resolution, relationship enrichment and assistance in spiritual development. He is a Certified Physician Investigator, having served as Principal Investigator for clinical trials of new medications in Psychiatry and Internal Medicine. Dr. Barksdale is most excited about his parallel and ongoing training in metaphysical sciences as they relate to healing and attainment of optimal health and wellbeing. His training began during medical school and spans eastern and western spiritual sciences. It has allowed him to understand and utilize the interface between the spiritual and physical aspects of being for optimal health and success. He has worked with shamans and completed trainings at schools dedicated to spiritual advancement.

Dr. Barksdale has presented at international conferences on topics of medical meditation, the convergence of spirituality and medicine to synergize the healing process, and techniques to increase one's wellbeing. He has published CDs for practical application of meditation techniques in daily life for busy people and trainings for advanced meditation skills.

Dr. Barksdale hosted "My Mind, My Health", 13-week series on spirituality, mental health and wellbeing on VoiceAmerica.com's Variety Channel.

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Link to Golden Key via Useful Links page at www.mymindmyhealth.com