

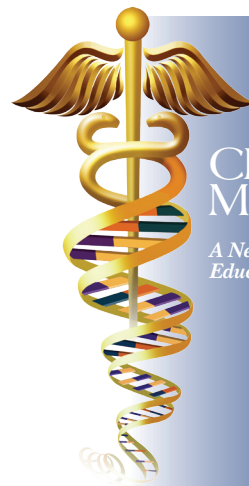
21ST CENTURY MEDICINE:

*A New Model for Medical
Education and Practice*



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Chapter 5

FUNCTIONAL MEDICINE: A 21ST CENTURY MODEL OF PATIENT CARE AND MEDICAL EDUCATION

It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has. The good physician treats the disease; the great physician treats the patient who has the disease.

—WILLIAM OSLER

Treat the patient, not the diagnosis.

—THE INSTITUTE FOR FUNCTIONAL MEDICINE

In this chapter, we will review the basic principles, constructs, and methodology of functional medicine. It is not the purpose of this paper to recapitulate the range and depth and science of functional medicine; books and monographs covering that material in great detail are already available for the interested clinician and for use in health professions schools. Our purpose in the first part of this chapter is to describe how functional medicine is organized to deliver personalized, systems medicine and, as such, is equipped to respond to the challenge of treating complex, chronic disease more effectively. In the second part of the chapter, we will discuss how clinicians can be helped to re-integrate the art and science of medicine to create a healing partnership.

Part I: What is Functional Medicine?

Functional medicine conceptualizes health and illness as part of a continuum in which all components of the human biological system interact dynamically with the environment. These interactions produce patterns that change over time in individuals. To manage the complexity inherent in this approach, functional medicine has adopted practical models for obtaining and evaluating clinical information that leads to individualized, patient-centered therapies.

Functional medicine encompasses a dynamic approach to assessing, preventing, and treating complex, chronic disease. It helps clinicians identify and ameliorate dysfunctions in the physiology and biochemistry of the human body as a primary method of improving patient health. In this model of practice, we emphasize that chronic disease is almost always preceded by a period of declining function in one or more of the body's systems. Returning patients to health requires reversing (or substantially improving) the specific dysfunctions that have contributed to the disease state. Those dysfunctions are, for each of us, the result of lifelong interactions among our environment, our lifestyle, and our genetic predispositions. Each patient, therefore, represents a unique, complex, and interwoven set of influences on intrinsic functionality that have set the stage for the development of disease or the maintenance of health.

Historically, the word “functional” has been used somewhat pejoratively in medicine. It has implied a disability associated with either a geriatric or psychiatric problem. We suggest, however, that this is a very limited definition of an extremely useful word. Medicine has not really produced an efficient method for identifying and assessing changes in basic physiological processes that produce symptoms of increasing duration, intensity, and frequency, even though we know that such alterations in function often represent the first signs of conditions that, at a later stage, become pathophysiologically definable diseases. If we broaden the use of functional to encompass this view, *functional medicine* becomes the science and art of detecting and reversing alterations in function that clearly move a patient toward chronic disease over the course of a lifetime. Thus, with functional medicine, we begin to define a model of patient care that seeks to identify underlying chronic dysfunctions associated with altered physiological processes and to maximize functionality at all levels of body, mind, and spirit.

One way to conceptualize where functional medicine falls in the continuum of health and health care is to examine the functional medicine “tree.” In its approach to complex, chronic disease, functional medicine encompasses the whole domain represented by the graphic shown in Figure 11, but *first* addresses the patient's core clinical imbalances, fundamental physiological processes, environmental inputs, and genetic predispositions. Diagnosis, of course, is part of the functional medicine model, but the emphasis is on understanding and improving the functional core of the human being as the starting point for intervention.

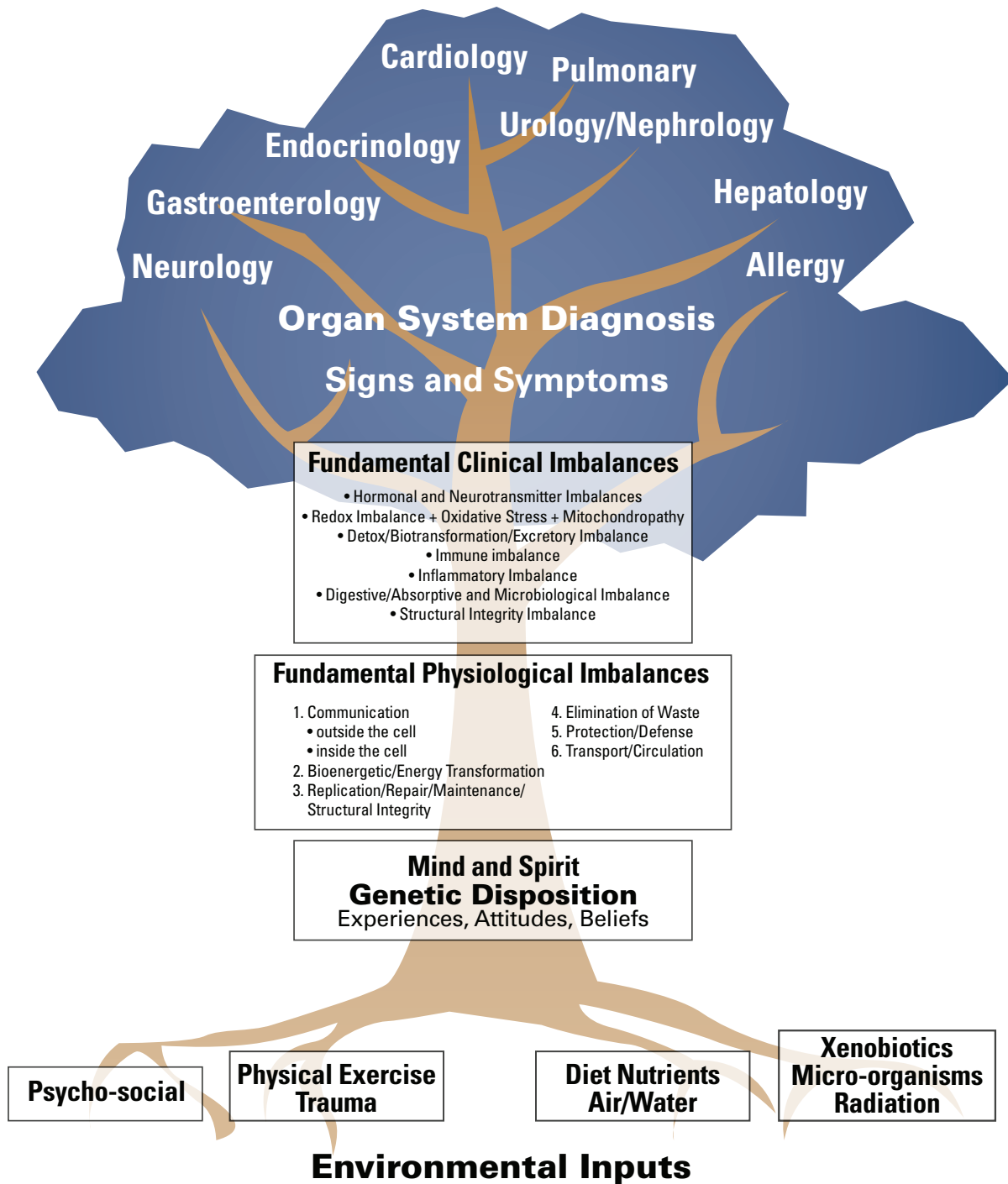


Figure 11:
 The Continuum of Health and Health Care

Functional medicine clinicians focus on restoring balance to the dysfunctional systems by strengthening the fundamental physiological processes that underlie them, and by adjusting the environmental and lifestyle inputs that nurture or impair them. This approach leads to therapies that focus on restoring health and function, rather than simply controlling signs and symptoms.

Principles

Seven basic principles characterize the functional medicine paradigm:

- ⊗ Acknowledging the **biochemical individuality** of each human being, based on the concepts of genetic and environmental uniqueness
- ⊗ Incorporating a **patient-centered** rather than a disease-centered approach to treatment
- ⊗ Seeking a dynamic balance among the internal and external factors in a patient's body, mind, and spirit
- ⊗ Addressing the **web-like interconnections** of internal physiological factors
- ⊗ Identifying **health as a positive vitality**—not merely the absence of disease—and emphasizing those factors that encourage a vigorous physiology
- ⊗ **Promoting organ reserve** as a means of enhancing the health span, not just the life span, of each patient
- ⊗ Functional medicine is a **science-using profession**

Environmental Inputs

At the base of the medicine tree graphic are found the building blocks of life, as well as the primary influences on them. When we talk about influencing gene expression, we are interested in the interaction between environment in the broadest sense and any genetic predispositions with which a person may have been born—including the epi genome^{xvi}. Many environmental factors that affect genetic expression are (or appear to be) a matter of choice (such as diet and exercise); others are very difficult for the individual patient to alter or escape (air and water quality, toxic exposures); and still others may be the result of unavoidable accidents (trauma, exposure to harmful microorganisms in the food supply). Some factors that may appear modifiable are heavily influenced by the patient's economic status—if you are poor, for example, it may be impossible to choose more healthful food, decrease stress in the workplace and at home, or take the time to exercise and rest properly. Existing health status is also a powerful influence on the patient's ability to alter environmental input. If you have chronic pain, exercise may be extremely difficult; if you are depressed, self-activation is a huge challenge.

^{xvi}Epigenetics—the study of how environmental factors can affect gene expression without altering the actual DNA sequence, and how these changes can be inherited through generations.

The influence of these inputs on the human organism is indisputable and they are often powerful agents in the battle for health. Ignoring them in favor of the quick fix of writing a prescription means the cause of the underlying dysfunction may be obscured, but is usually not eliminated. In general terms, the environmental inputs listed below should be considered when working to reverse dysfunction or disease and restore health:

- ⊗ Diet (type and quantity of food, food preparation, calories, fats, proteins, carbohydrates)
- ⊗ Nutrients (both dietary and supplemental)
- ⊗ Air
- ⊗ Water
- ⊗ Microorganisms (and the general condition of the soil in which food is grown)
- ⊗ Physical exercise
- ⊗ Trauma
- ⊗ Psychosocial and spiritual factors (including family, work, community, economic status, stress, and belief systems)
- ⊗ Xenobiotics
- ⊗ Radiation

Fundamental Physiological Processes

There are certain physiological processes that are necessary to life. These are the “upstream” processes that can go awry and create “downstream” dysfunctions that eventually become disease entities. Functional medicine requires that clinicians consider these in evaluating patients, so that intervention can occur at the most fundamental level possible. They are:

1. Communication
 - outside the cell
 - inside the cell
2. Bioenergetics/Energy Transformation
3. Replication/Repair/Maintenance/Structural Integrity
4. Elimination of Waste
5. Protection/Defense
6. Transport/Circulation

Although these fundamental physiological processes are usually taught in the first two years of medical training, where they are appropriately presented as the foundation of modern, scientific patient care, subsequent training in the clinical sciences often fails to fully integrate knowledge of the functional mechanisms of disease with therapeutics and prevention, emphasizing instead teaching/learning based

on organ system diagnosis.³⁰⁴ Focusing predominantly on organ system diagnosis without examining the underlying physiology that produced the patient's signs, symptoms, and disease often leads to managing patient care by matching diagnosis to pharmacology. The job of the healthcare provider then becomes a technical exercise in finding the drug or procedure that best fits the diagnosis (not necessarily the patient), leading to a significant curtailment of critical thinking pathways: "Medicine, it seems, has little regard for a complete description of how a myriad of pathways result in any clinical state."³⁰⁵

Even more important, pharmacologic treatments are often prescribed without careful consideration of their physiological effects across all organ systems and physiological processes (and genetic variations).³⁰⁶ Pharmaceutical companies have exploited this weakness. Did you ever see a drug ad that urged the practitioner to carefully consider the impact of all other drugs being taken by the patient before prescribing a new one? The marketing of drugs to specific specialty niches, and the use of sound bite sales pitches that suggest discrete effects, skews healthcare thinking toward this narrow, linear logic, as notably exemplified by the COX-2 inhibitor drugs that were so wildly successful on their introduction, only to be subsequently withdrawn or substantially narrowed in use due to collateral damage.^{307, 308}

Core Clinical Imbalances

The functional medicine approach to assessment, both before and after diagnosis, charts a course using different navigational assumptions. Every health condition instigates a quest for information centered on understanding when and how the specific biological system(s) under examination spun out of control to begin manifesting dysfunction and/or disease. Analyzing all the elements of the patient's story, the signs and symptoms, and the laboratory assessment through a matrix focused on functionality requires analytic thinking and a willingness on the part of the clinician to reflect deeply on underlying biochemistry and physiology. The foundational principles of how the human organism functions—and how its systems communicate and interact—are essential to the process of linking ideas about multifactorial causation with the perceptible effects we call disease or dysfunction.

To assist clinicians in this process, functional medicine has adapted and organized a set of core clinical imbalances that function as the intellectual bridge between the rich basic science literature concerning physiological mechanisms of disease (first two years of medical training) and the clinical studies, clinical experience, and clinical diagnoses of the second two years of medical training. The core clinical imbalances serve to marry the mechanisms of disease with the manifestations and diagnoses of disease. Many common underlying pathways of disease are reflected in a few basic clinical imbalances:

- ⊗ Immune/inflammatory imbalance
- ⊗ Energy imbalance/mitochondrial dysfunction
- ⊗ Digestive/absorptive and microbiological imbalance
- ⊗ Detoxification/biotransformation/excretory imbalance
- ⊗ Imbalance in structural, boundary, and membrane integrity
- ⊗ Hormonal and neurotransmitter imbalances
- ⊗ Imbalance in mind-body-spirit integration

Using this construct, it becomes much clearer that one disease/condition may have multiple causes (i.e., multiple clinical imbalances), just as one fundamental imbalance may be at the root of many seemingly disparate conditions (see Figure 12).

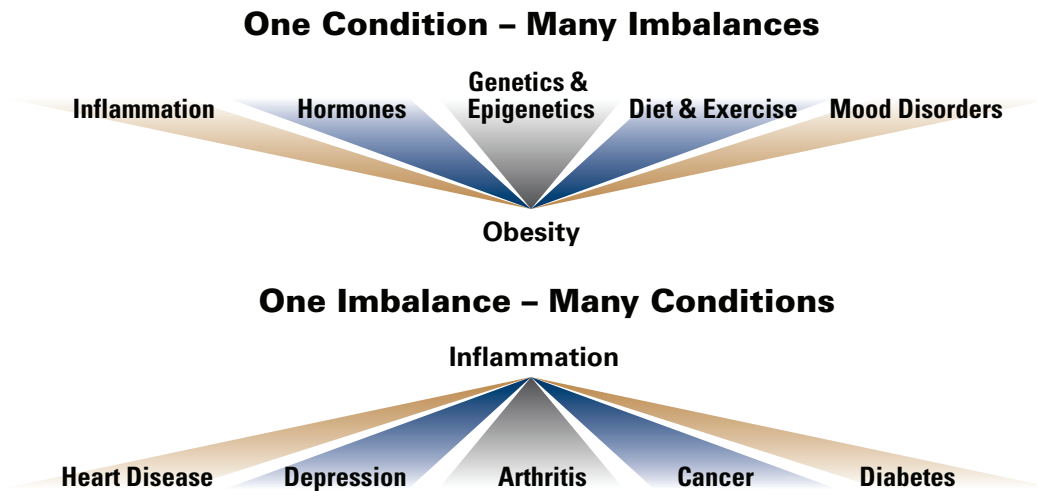


Figure 12:
Core Clinical Imbalances—Multiple Influences

The most important precept to remember about functional medicine is that restoring balance—in the patient’s environmental inputs and in the body’s fundamental physiological processes—is the key to restoring health.

Constructing the Model

Combining the principles, environmental inputs, fundamental physiological processes, and core clinical imbalances creates a new information-gathering-and-sorting architecture for clinical practice. This new model includes an explicit emphasis on principles and mechanisms that weld meaning and mechanistic explanations to the diagnosis and deepen the clinician’s understanding of the often overlapping ways things go wrong. Any methodology for constructing a coherent story and an effective therapeutic plan in the context of complex, chronic illness must be flexible and adaptive. Like an accordion file that can compress and expand upon demand, the amount and kind of data needed will necessarily change in accordance with the patient’s situation and the clinician’s time and ability to piece together the underlying threads of dysfunction. There are many pathways to illness; therefore, the accordion file must expand to incorporate a much larger database of relevant information. For example, the Chief Complaint, History of Present Illness, and Past Medical History sections must expand to include a thorough investigation of antecedents, triggers, and mediators. Personalized medical care without this expanded investigation will fall short.

Distilling the data from the expanded history, physical exam, and laboratory into a narrative story line that includes antecedents, triggers, and mediators can be challenging. Key to developing a thorough narrative

is organizing the story according to the seven common underlying mechanisms that influence health (the core clinical imbalances), as shown on the Functional Medicine Matrix Model™ form (see Figure 13).

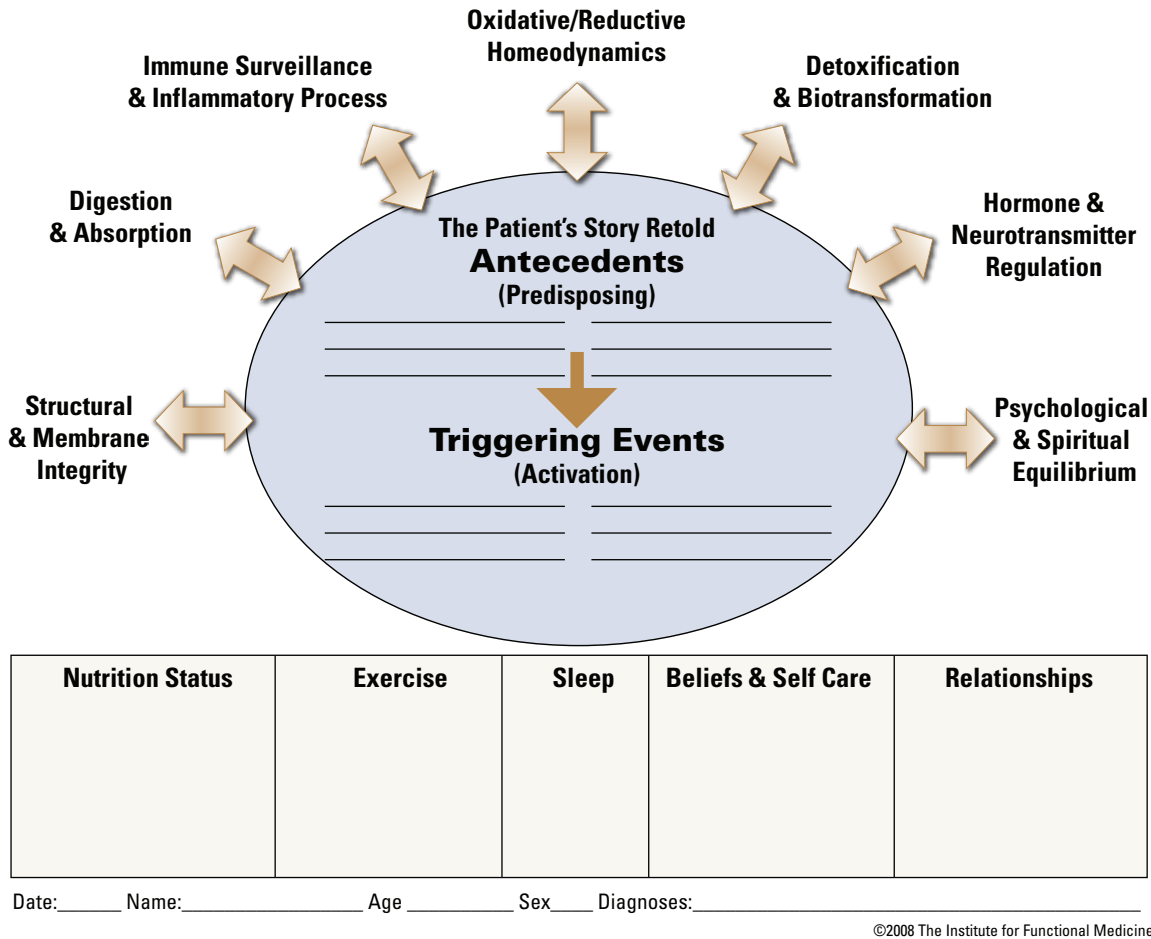


Figure 13:
The Functional Medicine Matrix Model™ Form

The matrix form helps organize and prioritize information, and also clarifies the level of present understanding, thus illuminating where further investigation is needed. For example, indicators of inflammation on the matrix might lead the clinician to request tests for specific inflammatory markers (such as hsCRP, interleukin levels, and/or homocysteine). Essential fatty acid levels, methylation pathway abnormalities, and organic acid metabolites help determine adequacy of dietary and nutrient intakes. Markers of detoxification (glucuronidation and sulfation, cytochrome P450 enzyme heterogeneity) can determine functional capacity for molecular biotransformation. Neurotransmitters and their metabolites (vanilmandelate, homo vanillate, 5-hydroxyindoleacetate, quinolinate) and hormone cascades (gonadal and adrenal) have obvious utility in exploring messenger molecule balance. CT scans, MRIs, or plain x-rays extend our view of the patient’s structural dysfunctions. The use of bone scans, DEXA scans, or bone resorption markers^{309, 310} can be useful in further exploring the web-like interactions of the matrix.

Newer, useful technologies such as functional MRIs, SPECT or PET scans offer more comprehensive assessment of metabolic function within organ systems. It is the process of completing a comprehensive history and physical and then charting these findings on the matrix that best directs the choice of laboratory work and successful treatment.

A completed matrix form facilitates the review of common pathways, mechanisms, and mediators of disease, and helps clinicians select points of leverage for treatment strategies. However, even with the matrix as an aid to synthesizing and prioritizing information, it can be very useful to consider the impact of each variable at five different levels:

1. Whole body (the “macro” level)
2. Organ system
3. Metabolic or cellular
4. Subcellular/mitochondrial
5. Subcellular/gene expression

Therapies should be chosen for their potential impact on the most central imbalances of the particular patient. Evaluating interventions that are available at each of the five levels can help to identify a reasonably comprehensive set of options from which to choose. The following lists incorporate only a few examples of various types of interventions within these five different levels.

1. **Whole body interventions:** Because the human organism is a complex adaptive system, with countless points of access, interventions at one level will affect points of activity in other areas as well. For example, improving the patient’s sleep will beneficially influence the immune response, melatonin levels, T cell lymphocyte levels, and will help to decrease oxidative stress. Exercise reduces stress, improves insulin sensitivity, and improves detoxification. Reducing stress (and/or improving stress management) can reduce cortisol levels, improve sleep, improve emotional well being, and reduce the risk of heart disease. Changing the diet can have myriad effects on health, from reducing inflammation to reversing coronary artery disease.
2. **Organ system interventions:** These interventions are used more frequently in the acute presentation of illness. Examples include splinting; draining lesions; repairing lacerations; reducing fractures, pneumothoraxes, hernias or obstructions; or removing a stone to re-establish whole organ function. There are many interventions that improve organ function. For example, bronchodilators improve air exchange, thereby decreasing hypoxia, reducing oxidative stress, and improving metabolic function and oxygenation in a patient with reactive airway disease.

3. **Metabolic or cellular interventions:** Cellular health can be addressed by insuring the adequacy of macronutrients, essential amino acids, vitamins, and cofactor minerals in the diet (or, if necessary, from supplementation). An individual's metabolic enzyme polymorphisms can profoundly affect his or her nutrient requirements. For example, adding conjugated linoleic acid (CLA) to the diet can alter the PPAR system, affect body weight, and modulate the inflammatory response.^{311, 312, 313} However, in a person who is diabetic or insulin resistant, adding CLA may induce hyperinsulinemia, which is detrimental.^{314, 315} Altering the types and proportions of carbohydrates in the diet may increase insulin sensitivity, reduce insulin secretion, and fundamentally alter metabolism in the insulin-resistant patient. Supporting liver detoxification pathways with supplemental glycine and N-acetylcysteine improves the endogenous production of adequate glutathione, an essential antioxidant in the central nervous system and GI tract.
4. **Subcellular/mitochondrial interventions:** There are many examples of mitochondrial nutrient support interventions.^{316, 317} Inadequate iron intake causes oxidants to leak from mitochondria, damaging mitochondrial function and mitochondrial DNA. Making sure there is sufficient iron helps alleviate this problem. Inadequate zinc intake (found in >10% of the U.S. population) causes oxidation and DNA damage in human cells.³¹⁸ Insuring the adequacy of antioxidants and cofactors for the at-risk individual must be considered in each part of the matrix. Carnitine, for example, is required as a carrier for the transport of fatty acids from the cytosol into the mitochondria, improving the efficiency of beta oxidation of fatty acids and resultant ATP production. In patients who have lost significant weight, carnitine undernutrition can result in fatty acids undergoing omega oxidation, a far less efficient form of metabolism.³¹⁹ Patients with low carnitine may also respond to riboflavin supplementation.³²⁰
5. **Subcellular/gene expression interventions:** Many compounds interact at the gene level to alter cellular response, thereby affecting health and healing. Any intervention that alters NFκB entering the nucleus, binding to DNA, and activating genes that encode inflammatory modulators such as IL-6 (and thus CRP), cyclooxygenase 2, IL-1, lipoxygenase, inducible nitric oxide synthase, TNF-α, or a number of adhesion molecules will impact many disease conditions.^{321, 322} There are many ways to alter the environmental triggers for NFκB, including lowering oxidative stress, altering emotional stress, and consuming adequate phytonutrients, antioxidants, alpha-lipoic acid, EPA, DHA, and GLA.³²³ Adequate vitamin A allows the appropriate interaction of vitamin A-retinoic acid with over 370 genes.³²⁴ Vitamin D in its most active form intercalates with a retinol protein and the DNA exon and modulates many aspects of metabolism including cell division in both healthy and cancerous breast, colon, prostate, and skin tissue.³²⁵ Vitamin D has key roles in controlling inflammation, calcium homeostasis, bone metabolism, cardiovascular and endocrine physiology, and healing.³²⁶

Experience using this model, along with improved pattern-recognition skills, will often lessen the need for extensive laboratory assessments. There will always be, however, certain clinical conundrums that simply cannot be assessed without objective data and, for most patients, there may be an irreducible minimum of laboratory assessments required to accumulate information. For example, in the clinical workup of autistic spectrum disorders in children, heavy metal exposure and toxicity may play an important role. Heavy metal body burden cannot be sensibly assessed without laboratory studies. Another example is

in the context of the progressive, ongoing workup. When clinical acumen and educated steps in both assessments and therapeutic trials do not yield expected improvement, lab testing often provides rewarding information when focused on the unexpected outcomes in the progressive workup. This is frequently the context for focused genomic testing. In most initial workups, lab and imaging technologies can be reserved for those complex cases where the initial interventions prove insufficient to the task of functional explication.

Even using the functional medicine model that has been reviewed here, no single practitioner—and no single discipline—can cover all the viable therapeutic options. Interventions will differ by training, licensure, specialty focus, and even by beliefs and ethnic heritage. However, all healthcare disciplines (and all medical specialties) can—to the degree allowed by their training and licensure—use a functional medicine approach, including integrating the matrix as a basic template for organizing and coupling knowledge and data. So, functional medicine can provide a common language and a unified model to facilitate integrated care. Regardless of what discipline the primary care provider has been trained in, developing a network of capable, collaborative clinicians with whom to co-manage challenging patients and to whom referrals can be made for therapies outside the primary clinician’s own expertise will enrich patient care and strengthen the clinician-patient relationship.

Part II: The Healing Partnership— A Synthesis of the Art and Science of Medical Practice

We form partnerships to achieve an objective. For example, a business partnership forms to engage in commercial transactions for financial gain; a marriage partnership forms to build a caring, supportive home-centered environment. A *healing partnership* forms to heal the patient through the integrated application of both the art of medicine (insight driven) and the science of medicine (evidence driven). An effective partnership requires that trust and rapport be established. Patients must feel comfortable telling their stories and revealing intimate information and significant events.

The characteristics of a *therapeutic encounter* are fundamentally different from a *healing partnership*, and each emerges from specific emphases in training. In the therapeutic encounter, the relationship forms to assess and treat a medical problem using (usually) an organ system structure, a differential diagnosis process, and a treatment toolbox focused on pharmacology and medical procedures. The therapeutic encounter pares down the information flow between physician and patient to the minimum needed to identify the organ system domain of most probable dysfunction, followed by a sorting system search (the *differential diagnosis heuristic*). The purpose of this relationship is to arrive at the most probable diagnosis as quickly as possible and select an intervention based on probable efficacy. The relationship is a left brain-guided conversation controlled by the clinician, steeped in Bayesian statistics (EBM), and characterized by algorithmic processing and statistical thinking.^{327, 328}

The functional medicine *healing partnership* forms with a related but broader purpose: to help the patient heal by identifying the underlying mechanisms and influences that initiated and continue to mediate the patient’s illness(es). This type of relationship emphasizes a shared responsibility for both identifying the causes of the patient’s condition and achieving insight about enduring solutions. The healing partnership is critical to the delivery of *personalized, systems medicine*, and to manage the uncertainty (choices under risk)

inherent in clinical practice. Here, in the healing partnership, we find the appropriate utilization and integration of left-brain and right-brain functions.

Germane to this discussion, Dr. Jerome Groopman—quoted previously in Chapter 4—states:

So a thinking doctor returns to language: “Tell me the story again as if I’d never heard it—what you felt, how it happened, when it happened.”³²⁹

In language, we have the fullest expression of the integration of left- and right-brain function. Language is so complex that the brain has to process it in different ways simultaneously—both denotatively and connotatively. For complexity and nuance to emerge in language, we need the left brain to see the trees, the right brain to help us see and understand the forest.^{330, 331}

To grasp the profound importance of the *healing partnership* to the creation of a system of medicine adequate to the demands of the 21st century, we need to briefly address the nature of healing and its role in the therapeutic relationship. We have noted an emerging body of research in this area.^{332, 333, 334} As Louise Acheson, MD, MS, Associate Editor for the *Annals of Family Practice*, articulated recently in that journal³³⁵:

It is challenging to research this ineffable process called healing.... Hsu and colleagues asked focus groups of nurses, physicians, medical assistants, and randomly selected patients to define healing and describe what facilitates or impedes it.³³⁶ The groups arrived at surprisingly convergent definitions: “Healing is a dynamic process of recovering from a trauma or illness by working toward realistic goals, restoring function, and regaining a personal sense of balance and peace.” They heard from diverse participants that “healing is a journey” and “relationships are essential to healing.”

In the 20th century, contemporary medicine, traditionally considered a healing profession, evolved away from the role of *healer of the sick* to that of *curing disease through modern science*. Research into this transition reveals that healing was/is associated with themes of wholeness, narrative, and spirituality. Professionals and patients alike report healing as an intensely personal, subjective experience involving a reconciliation of meaning for an individual and a perception of wholeness. The biomedical model as currently configured no longer encompasses these traditional characteristics for practitioners. Healing in a holistic sense has faded from medical attention and is rarely discussed in biomedical research reports. Contemporary medicine considers the wholeness of healing to be beyond its orthodoxy—the domain of the nonscientific and nonmedical.³³⁷

Research into the role of healing in the medical environment has recently generated some thoughtful and robust investigations. John Scott and his co-investigators’ research into the healing relationship found very similar descriptions to those of Hsu’s group, mentioned above. The participants in the study³³⁸ articulated aspects of the healing partnership as:

1. Valuing and creating a nonjudgmental emotional bond
2. Appreciating power and consciously managing clinician power in ways that would most benefit the patient
3. Abiding and displaying a commitment to caring for patients over time

Three relational outcomes result from these processes: trust, hope, and a sense of being known. Clinician competencies that facilitate these processes are self-confidence, emotional self-management, mindfulness, and knowledge.³³⁹ In this rich soil, the healing partnership flourishes.

The starting point for creating a healing partnership is the patient’s experience: *People, not diseases, can heal.* The integration of brain science research discussed in Chapter 4—to frame and apply right- and left-brain functions to create a *mindful, insightful* context—enhances the healing partnership during the therapeutic encounter. Mindful integration of brain function is at the heart of a healing partnership. Some of the basic steps for establishing a healing partnership include:

1. Allow patients to express, without interruption,^{xvii} their story about why they have come to see you. (This is an elaboration of the Chief Complaint and Present Illness.) The manner in which the patient frames the initial complaints often presages later insight into the root causes. Any interruption in this early stage of narrative moves the patient back into left-brain processing and away from insight.³⁴⁰
2. After focusing on the main complaint, encourage the patient’s narrative regarding their present illness(es). Clarifications can be elicited by further open-ended questioning (e.g., “tell me more about that”; “what else do you think might be going on?”). During this portion of the interview, there is a switching back and forth between right- and left-brain functions.
 - During this conversation, signs and symptoms of the present illness are distributed by the practitioner into the Functional Medicine Matrix Model form, according to the functional medicine heuristic sorting system described in Chapter 4.
 - The parsing is determined by an assessment of probable underlying causes—based on the robust research evidence base about common underlying mechanisms of disease—and ongoing mediators of the disease.
3. Next, convey to the patient in the simplest terms possible that to achieve lasting solutions to the problem(s) for which he/she has come seeking help, a few fundamental questions must be asked and answered in order to understand the problem in the context of the patient’s personal life. This framing of the interview process moves the endeavor from a left-brain compilation to a narrative that encourages insight—based on complex pattern recognition—about the root causes of the problem.
4. Explaining the structure of the next step helps the patient participate in a journey of exploration about their illness—and their search for health. At this stage, partial control is handed over to the patient with the statement: “*Without your help, we cannot understand your medical problem in the depth and breadth you deserve.*” Leo Galland, MD originally articulated the structure for the patient’s part of the investigation in his antecedents/triggers/mediators schema (ATM model).³⁴¹ (An excerpt from his outstanding chapter on this topic in the *Textbook of Functional Medicine* is included in the Appendix.)

^{xvii}Research focused on the therapeutic encounter has repeatedly found that clinicians interrupt the patient’s flow of conversation within the first 18 seconds or less, often denying the patient an opportunity to finish. (Beckman DB, et al. The effect of physician behavior on the collection of data. *Ann Intern Med.* 1984;101:692-96.)

- a) For determining **antecedent conditions**, the following questions are very useful:
 - When was the present problem not a problem? When were you free of this problem?
 - What were the circumstances surrounding the appearance of the problem?
 - Have similar problems appeared in family members?
- b) For **triggers**, the following question is critical:
 - What conditions, activities, or events seemed to initiate the problem? (Microbes and stressful personal events are examples, but illustrate quite different categories of triggers. Triggers by themselves are usually insufficient for disease formation, so triggers must be viewed within the context of the antecedent conditions.)
- c) **Mediators** of the problem are influences that help perpetuate it.
 - There can be specific mediators of diseases in the patient’s activities, lifestyle, and environment. Many diverse factors can affect the host’s response to stressors.
 - Any of the core clinical imbalances, discussed above and shown on the Functional Medicine Matrix Model, can transform what might have been a temporary change in homeostasis into a chronic allostatic condition.

It helps at this juncture to emphasize again that the following issues are elemental in forming a healing partnership:

- ⊗ Only the patient can inform the partnership about the conditions that provided the soil from which the problem(s) under examination emerge(s). The patient literally owns the keys to the joint deliberation that can provide insight about the process of achieving a healing outcome.
- ⊗ The professional brings experience, wisdom, tools, and techniques that can be applied to the journey of healing. The professional also works to create the context for a healing insight to emerge.
- ⊗ The patient’s information, input, mindful pursuit of insight, and engagement become “the horse before the cart.” The cart carries the clinician—the person who guides the journey using evidence, experience, and judgment, and who contributes the potential for expert insight.

The crux of the healing partnership is an equal investment of focus by both clinician and patient. They work together to identify the right places to apply leverage for change. Patients must commit to engage both their left-brain skills and their right-brain function to inform and guide the exploration to the next steps in assessment, therapy, understanding, and insight. Clinicians must also engage both the left-brain computational skills and the right-brain pattern-recognition functions that, when used together, can generate insight about the patient’s story.

Two patient case studies (presented below) provide a glimpse into a functional medicine practice and the healing partnership that is necessary for success. The Appendix contains a form developed by IFM faculty for enhancing the pattern-recognition process in ulcerative colitis.

Patient #1: Kikuchi syndrome in an 18 year old female—insight from the healing partnership

Lila was an 18-year-old female transitioning from high school to college, who during the intervening summer experienced rapid onset of unexplained fever, profound fatigue, and lymphadenitis, especially pronounced in the cervical region. Her extended family included physicians, one who lived locally and led the initial investigation. The differential included lymphoma; because of the seriousness of this possible diagnosis, a biopsy of the enlarged cervical lymph nodes was completed expeditiously. Fortunately, the biopsy was more consistent with Kikuchi syndrome than lymphoma. The pathology of Kikuchi is a histiocytic necrotizing lymphadenitis. Her ANA was positive at 1:320, speckled. Kikuchi syndrome is presumed to be an immune response of T cells and histiocytes to an infectious agent, probably viral. At this point, I was asked to consult with the patient and her parents.

The patient was articulate, intelligent (she had been accepted to Harvard), and appeared recovered from the acute phase of her illness. Her father and mother were both present during the consultation. Lila was asked to narrate her story. During the telling of her story, I sorted her symptoms and signs using the FM Heuristic (Chapter 4) and the Functional Medicine Matrix Model (discussed above). At the end of recounting of her story, I explained to her and her parents the functional medicine sorting system, postulating that what we now knew from the history, lab results, and the biopsy was that Lila's immune system had probably been activated by a triggering agent (e.g., microbe, toxicant). I explained that our job now required forming a partnership, using Lila's and her parents' experiences through this episode of illness and my experience with immune-mediated illnesses to build a hypothetical story together.

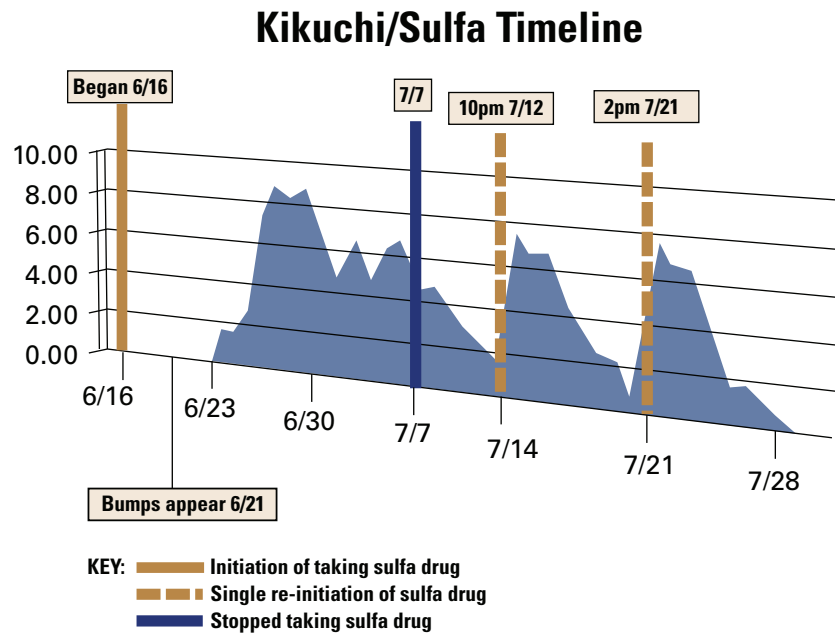
I further explained that we would need to consider the conditions in Lila's family and "habits of living" history that could be antecedent to her illness. I explained that we would then move to the possible triggers in her recent past that might be causal or correlative in the acute expression of her illness. I explained that once an acceptable model emerged from our joint inquiry into the antecedents and triggers of her present illness, we would evaluate the possible probes that might elicit further information or generate treatment plans. They agreed to work together with me using this partnering model.

They were not aware of any exceptional family history of autoimmune or other immune dys-regulatory illnesses. The family's lifestyle, including eating and exercise habits, was laudable. We next addressed the issues of triggers. We knew from reading research sources on Kikuchi syndrome that the most common cause of the lymphadenitis associated with the syndrome was a microbe trigger. The parents were hopeful that we could perform lab analyses for a host of potential viral agents. Lila interrupted her parents at this point to advocate for quite a different possible cause.

Lila recounted that she had been seen in the regional dermatologic referral center for her worsening *acne vulgaris*. The treatment recommended by the consulting dermatologist was a sulfa-containing antibiotic. Before coming for consultation in my clinic, Lila had posited to her dermatologist and her primary care physician that her lymphadenitis was an adverse drug reaction. She and her parents had been told that the severity of her illness, if caused by a drug reaction, would necessarily be accompanied by a rash; she, however, was absent a rash. She had been advised to continue her antibiotic. Her parents retreated from this inquiry in the face of the authoritative disclaimer by both the specialist and the family doctor.

However, Lila did not retreat from her insight. We discussed her intuition (insight) and her reasoning. On the basis of her hypothesis, we jointly finalized a plan that included abstinence from her antibiotic. I advised against a planned back-packing trip to Mexico because of possible toxicant exposures in that environment that might confound her clinical story. We chose to call this a therapeutic probe with my added advice regarding follow-up. (We planned a low allergy diet and detoxification program IF the simple step of removing the triggering agent proved to be an insufficient intervention.)

That evening, I received an email from Lila with the following graph of her illness:



Outcome: Lila has been asymptomatic following continued abstinence from the sulfa-containing antibiotic. She has started her first semester at Harvard. The student health center physician became very interested in her story and has provided regular follow up, including lab. Her ANA titer has slowly returned to normal. No further interventions have been required. She has sought non-pharmacologic treatment interventions for her acne.

**Patient #2: Ulcerative Colitis in a 45 year old female—
providing a context for insight**

The next case illustrates the use of this same model: the pursuit of an antecedent and/or initial trigger for illness (these categories often overlap considerably)—that is, we looked for causes underneath the surface explanations for her condition. This 45-year-old female presented at my office for IBS and diverticulitis with a recent history of hemicolectomy for infectious colitis. The patient's primary residual postsurgical complaints were diffuse abdominal pain and loose stooling alternating with constipation. The review of her present illness revealed a history since her mid-twenties of "gut problems" (her words), including intermittent loose stools with alternating constipation. She had also over the years become intolerant of a plethora of foods. As a result, she had received thorough work-ups for food allergies and intolerances and was trying to follow a rather patchwork diet plan in response to these previous lab evaluations. She had received imaging and endoscopic procedures. However, she had not had follow-up colonoscopy since her surgery. We discussed the need to do follow-up endoscopy to evaluate her present symptoms (to rule out possible post-surgical adhesions complicating stool passage).

The conversation soon shifted into the ATM (antecedents, triggers, and mediators) portion of the investigation. After describing the joint responsibilities for a deeper understanding (insight) regarding her GI maladies, we moved to the questions regarding antecedents for her condition. She denied any family history of similar GI illnesses in her siblings. I then asked the question: *"When was the present problem not a problem? That is, when were you free of the problem and what were the circumstances of the problem's first appearance?"*

At this point, our conversation stopped. She looked a bit flummoxed and asked to consider the question further and more fully answer it when she next returned. At her next appointment, she returned to the question, stating that she wanted to share an experience that preceded her first episode of GI irritability. She said that she had not shared this story with any physician before in the context of the clinical workups for her GI problems. She then told the following story:

I left home at an early age to escape my father. He sexually abused me and my sisters. There did not seem to be any way to stop him; my mother seemed powerless, even when she walked into an abusive episode. In desperation, I left my sisters and my family, married and moved away.

My mother called me one afternoon, years after my leaving home. By that time I was a mother myself, having married and started my own family. My mother was quite upset and related that one of my sisters had arrived at her door, confronting her with the accusation of my father's sexual abuse of her in childhood and the lack of protection by our mother. My mother was adamant in her denial of knowledge of such wrongdoing by my father (my father had died in the intervening years since my leaving home).

I was silent for a moment on the phone with my mother. I then made a choice to placate my mother; I responded to her distress with a lie: "Mother, you know how my sister is; she is so hysterical."

My response seemed to settle my mother down. However, now that you have asked, this was the beginning of my gut problems. I stuffed that lie about our childhood with our father deep down into my gut and my gut has not been normal since.

Outcome: My patient’s therapy for her GI problems has been guided by both this insight regarding the origins of her illness as well as by my professional expertise in the area of both mind-body connections and GI physiology. Her therapeutic interventions focused on the 4R functional medicine approach to GI dysfunctions³⁴² and EMDR psychotherapeutic modalities developed for PTSD³⁴³ (an approach that has emerged from work with returning GIs from the Gulf War and the Afghanistan and Iraq conflicts). She now reports no further problems referable to her GI tract.

Our healing partnership helped elicit the insights that focused our attention on a fundamental issue that was critical to her healing. Without the supportive, mindful context that encouraged her insight to emerge, we would not have had the comprehensive patient story that was necessary for resolution of her problems. In this journey together, both left-brain computation (clinical and scientific evidence about the importance of the 4R GI dysfunction program and EMDR therapy in the context of PTSD) and right-brain functionality (a context for insight) were necessary.

As described in Chapter 4, insight researchers call this “aha” experience the *moment of categorical insight*. The epiphany registers as a new pattern of neural activity in the prefrontal cortex. The brain cells have been altered by the breakthrough. An insight is a restructuring of information—it’s seeing something in a completely new way. Once that restructuring occurs, you never go back.³⁴⁴

Summary

At The Institute for Functional Medicine (IFM) we believe that functional medicine exemplifies a systems-oriented, personalized medicine that recognizes the common underlying mechanisms of complex and chronic diseases that cut across multiple organ systems to shape a patient’s trajectory toward health or disease. IFM’s model of comprehensive care and primary prevention for complex, chronic illnesses is grounded in both science (the Functional Medicine Matrix Model™; evidence about common underlying mechanisms and pathways of disease; evidence about effective approaches to the environmental and lifestyle sources of disease) and art (the *healing partnership* and the search for insight in the therapeutic encounter). We have shown how this approach offers both a conceptual model and pragmatic tools that help to integrate the best of emerging models in both conventional and integrative medicine. When practiced with an explicit emphasis on the importance of pattern-recognition and heuristic competencies inherent to right-brain function, a healing partnership can flourish, insight can be achieved, and a broad array of assessment and therapeutic tools can be utilized. We can produce a *mindful* medical practice paradigm shift that can encompass the uniqueness of each person, deriving probabilities that are clinically meaningful.

As articulated in Gerd Gigerenzer's thoughtful book, *Rationality for Mortals: How People Cope with Uncertainty*, heuristic processing (right brain) and statistical thinking (left brain) are "complementary mental tools, not mutually exclusive strategies; our minds need both."³⁴⁵ Through this uniting of competencies, we can incorporate the strengths of both science and art to craft an effective, personalized, and integrative approach to patient care. Without both elements steadily at work, we will find it exceptionally difficult to address successfully the epidemic of chronic disease that is the challenge of 21st century medicine.

What's Ahead?

Over the past few years, at least 17 of the schools with membership in the Consortium for Academic Health Centers in Integrative Medicine (CAHCIM) have sent attendees for training with IFM. These faculty, residents, fellows, and students have returned to their home institutions as strong advocates for functional medicine (see Appendix for a compilation of relevant comments). They have helped to guide us toward key decision makers and have coached us on useful strategies.

Thanks to these relationships, IFM has already initiated collaborative work on integrating functional medicine into medical education. Two different medical school courses on functional medicine nutrition and genomics were offered in 2008-2009, and six institutions have indicated strong interest in participating in a pilot project program for 2009-2010. Early funding has been secured and strategies, timelines, delivery formats (grand rounds, guest lectures, Webinars, print/online course materials), faculty training, and other issues are now being worked out. We anticipate that these early pilot projects will involve at least one allopathic medical school, one osteopathic medical school, a graduate nutrition program, a residency program in family medicine, and a naturopathic medical school. In addition, at least one online elective in functional medicine for medical students is in the planning stages.

A summary of these pilot projects and their short-term outcomes will be written up and added to this paper as an update following the end of the 2009-2010 academic year. As we bring the current discussion to a close, we'd like to reiterate that the ultimate goal of this entire project is to inspire system-wide change. We look forward to a transformation in health professions education and clinical practice that will help us conquer the 21st century challenge of chronic disease with as much efficacy as the 20th century brought to acute care. The change is imminent, it is urgently needed, and it is entirely possible.