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Functional Medicine: A 21st-Century Model of Patient Care and Medical Education

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OUTLINE

In this chapter, the basic principles, constructs, and methodology of functional medicine are reviewed. It is not the purpose of this chapter to recapitulate the range and depth of the science underlying functional medicine; books and monographs covering that material in great detail are already available for the interested clinician and for use in health professional schools (see Bibliography at the end of the chapter). The purpose is to describe how functional medicine is organized to deliver personalized systems medicine and is equipped to respond to the challenge of treating complex chronic disease more effectively.

WHAT IS FUNCTIONAL MEDICINE?

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

Historically, the word *functional* was used somewhat pejoratively in medicine. It implied a disability associated with either a geriatric or psychiatric problem. The authors suggest, however, that this is a very limited definition of an extremely useful word. The medical profession 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, although it is known that such alterations in function often represent the first signs of conditions that, at a later stage, become pathophysiologically definable diseases. By broadening 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.

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 Fig. 1.1, but it first addresses the patient's core clinical imbalances (found in the functional physiological organizing systems); the fundamental lifestyle factors that contribute to chronic disease; and the antecedents, triggers, and mediators that initiate and maintain the disease state. 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.

Functional medicine clinicians focus on restoring balance and improved function in the dysregulated 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

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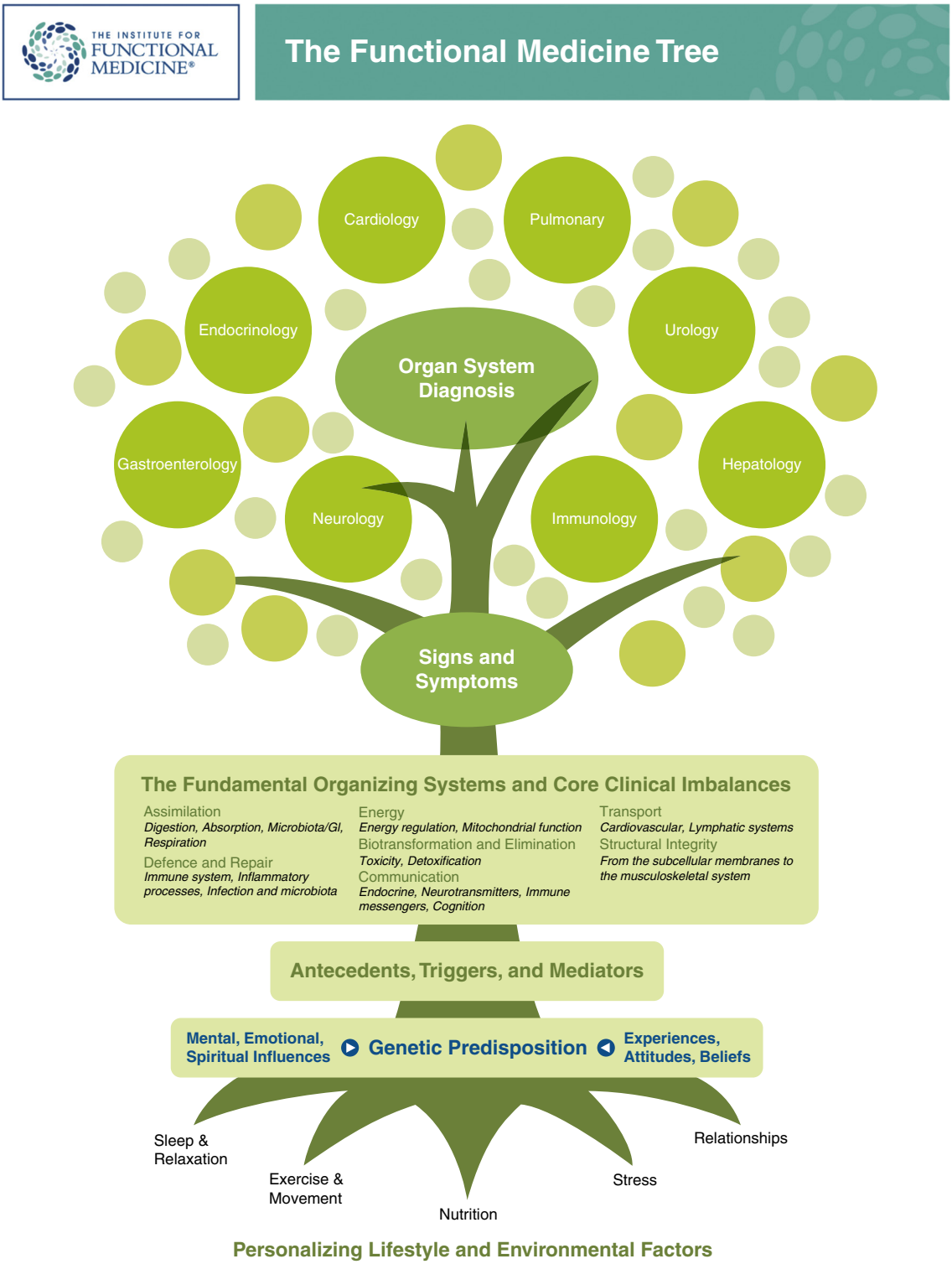

Fig. 1.1 The continuum of health and health care: the functional medicine tree. (Courtesy the Institute for Functional Medicine.)

- 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, cellular, and subcellular function as the means of enhancing the health span, not just the life span, of each patient
- Staying abreast of emerging research—a science- and evidence-based approach

LIFESTYLE AND ENVIRONMENTAL FACTORS

The building blocks of life, and the primary influences on them, are found at the base of the functional medicine tree graphic (see Fig. 1.1). When we talk about influencing gene expression, we are interested in the interaction between lifestyle and environment in the broadest sense and any genetic predispositions with which a person may have been born—in a word, the epigenome. (Epigenetics is 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.) Many environmental factors that affect gene 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). 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 nutritious 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 major challenge.

The influence of these lifestyle and environment factors on the human organism is indisputable,[1,2] and they are often powerful agents in the attempt to restore health. Neglecting to address them in favor of merely writing a prescription—whether for pharmaceutical agents, nutraceuticals, or botanicals—means the cause of the underlying dysfunction may itself remain unaddressed and further able to contribute to the genesis of other disease conditions. In general terms, the following factors should be considered when working to reverse dysfunction or disease and restore health:

- Diet (type, quality, and quantity of food; food preparation; calories, fats, proteins, carbohydrates)
- Nutrients (both dietary and supplemental)
- Air and water
- Microorganisms (and the general condition of the soil in which food is grown)
- Physical exercise
- Trauma
- Psychosocial and spiritual factors, such as meaning and purpose, relationships, 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 expressed as disease entities. Functional medicine requires that clinicians consider these in evaluating patients so that interventions can target the most fundamental level possible. These processes are as follows:

1. Communication
   - Intracellular
   - Intercellular
   - Extracellular
2. Bioenergetics/energy transformation
3. Assimilation
4. Structural integrity
5. Biotransformation/elimination
6. Defense and repair
7. Transport/circulation

These fundamental physiological processes are usually taught early in health professions curricula, where they are appropriately presented as the foundation of modern, scientific patient care. Unfortunately, subsequent training in the clinical sciences often fails to fully integrate knowledge of the functional mechanisms of disease with therapeutics and prevention, emphasizing organ system diagnosis instead.[3] 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 health care provider then becomes a technical exercise in finding the drug or procedure that best fits the diagnosis (not necessarily the patient or the underlying physiological dysfunction), leading to a significant curtailment of critical thinking pathways: "Medicine, it seems, has little regard for a complete description of how myriad pathways result in any clinical state."[4]

Even more important, pharmacological treatments (and even natural remedies) are often prescribed without careful consideration of their physiological effects across all organ systems, physiological processes, and genetic variations.[5] This was notably exemplified by the cyclooxygenase-2 inhibitor drugs that were so wildly successful on their introduction, only to be subsequently withdrawn or substantially narrowed in use because of collateral damage.[6,7]

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 became dysregulated and began 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 analytical thinking and a willingness on the part of the clinician to reflect deeply on the 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 called disease or dysfunction.

To assist clinicians in this process, functional medicine identified and organized a set of core clinical imbalances that are linked to the fundamental physiological processes (organizing systems). These serve to marry the mechanisms of disease with the manifestations and diagnoses of disease. Many common underlying pathways of disease are reflected in these clinical imbalances. The following list of imbalanced systems and processes is not definitive, but some of the most common examples are provided. We recommend that the organizing systems be considered in the order as shown in the following list:

- Digestion
- Absorption

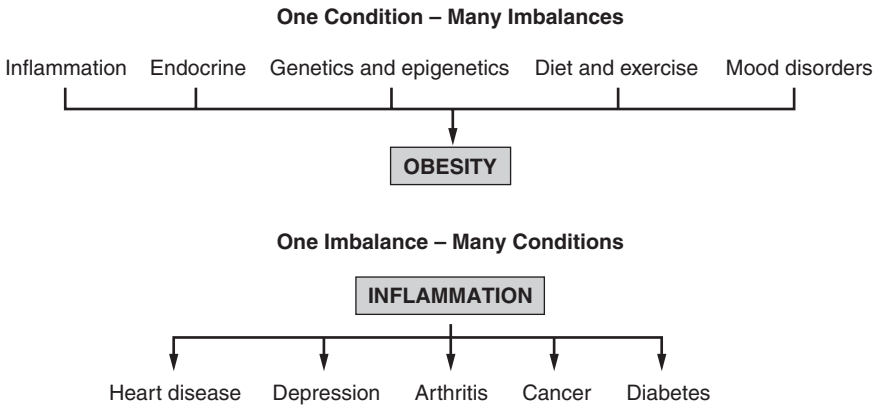

Fig. 1.2 Core clinical imbalances—multiple influences. (Courtesy the Institute for Functional Medicine.)

- Microbiome/gastrointestinal
- Respiration
- Immune system
- Inflammatory processes
- Infection and microbiome
- Energy regulation
- Mitochondrial function
- Toxicity
- Detoxification
- Endocrine
- Neurotransmitter
- Immune messengers
- Cognition
- From the subcellular membranes
- To the musculoskeletal system

Using this construct, it becomes much clearer that one disease and/or 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 (Fig. 1.2).

The most important precept to remember about functional medicine is that restoring balance—in the patient's lifestyle and/or environment and in the body's fundamental physiological processes—is the key to restoring health.

ANTECEDENTS, TRIGGERS, AND MEDIATORS[8]

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 19th 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.

It is, therefore, the functional medicine practitioner's job to know not just the patient's ailments or diagnoses but also the physical and social environment in which illness occurs, the dietary habits of the person (present diet and preillness diet), his or her beliefs about the illness, the effect 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 medicine treatment plan.

Identifying the biochemical mediators that underlie host responses was the most productive field of biomedical research during the second half of the 20th century. Mediators, as the word implies, do not cause disease. They are intermediaries that contribute to the manifestation and/or continuation of disease. Antecedents are factors that predispose to acute or chronic illness. For a person who is ill, antecedents form the illness diathesis. From the perspective of prevention, they are risk factors. Knowledge of antecedents provides 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 the 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 or her current health status. Antecedents may be thought of as congenital or developmental. The most important congenital factor is gender: women and men differ sharply 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.

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 N-methyl-d-aspartic acid receptors, induction of nitric oxide synthase, and liberation of free intraneuronal calcium

BOX 1.1 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 because of social isolation or poverty
The nature of the sick role and the doctor–patient relationship

determine the late effects. Intravenous magnesium at the time of trauma attenuates the severity by altering the mediator response.[9,10] 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.

Mediators and the Formation of Illness

A mediator is anything that produces or perpetuates symptoms or damages tissues of the body, including certain behaviors. Mediators vary in form and substance. They may be biochemical (e.g., prostanoids and cytokines), ionic (e.g., hydrogen ions), social (e.g., reinforcement for staying ill), psychological (e.g., fear), or cultural (e.g., beliefs about the nature of illness). A list of common mediators is presented in Box 1.1. Illness in any single person usually involves multiple interacting mediators. Biochemical, psychosocial, and cultural mediators interact continuously in the formation of illness.

CONSTRUCTING THE MODEL

Assessment

Combining the principles, lifestyle and environment factors, fundamental physiological processes, antecedents, triggers, mediators, and core clinical imbalances demands a new architecture for gathering and sorting information for clinical practice—in effect, a new heuristic to serve the practice of functional medicine. (Heuristics are rules of thumb—ways of thinking or acting—that develop through experimentation and enable more efficient and effective processing of data.) This new model includes an explicit emphasis on principles and mechanisms that infuse meaning into the diagnosis and deepen the clinician's understanding of the multivalent contributors to physiological dysfunction. 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 compresses and expands upon demand, the amount and kind of data collected 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.

The conventional assessment process involving the chief complaint, history of present illness, and past medical history sections must be expanded (Fig. 1.3) to include a thorough investigation of antecedents, triggers, and mediators and a systematic evaluation of any imbalances within the fundamental organizing systems. Personalized medical care without this expanded investigation falls short.

The Functional Medicine Matrix Model

Distilling the data from the expanded history, physical examination, and laboratory findings into a narrative storyline that includes antecedents, triggers, and mediators can be challenging. Key to developing a thorough narrative is organizing the story using the Functional Medicine Matrix Model form (Fig. 1.4).

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 highly sensitive C-reactive protein, interleukin levels, and/or homocysteine).
- Essential fatty acid levels, methylation pathway abnormalities, and organic acid metabolites help determine the adequacy of dietary and nutrient intakes.
- Markers of detoxification (glucuronidation and sulfation, cytochrome P450 enzyme heterogeneity) can determine the functional capacity for molecular biotransformation.
- Neurotransmitters and their metabolites (vanilmandelate, homovanillate, 5-hydroxyindoleacetate, quinolinate) and hormone cascades (gonadal and adrenal) have obvious utility in exploring messenger molecule balance.
- Computed tomographic scans, magnetic resonance imaging (MRI), or plain radiographs extend the view of the patient's structural dysfunctions. The use of bone scans, dual-energy x-ray absorptiometry scans, or bone resorption markers[11,12] can be useful in further exploring the web-like interactions of the matrix.
- Newer, useful technologies such as functional MRIs, single-photon emission computed tomography, and positron emission tomographic scans offer a more comprehensive assessment of metabolic function within organ systems.

It is the process of completing a comprehensive history and physical using the expanded functional medicine heuristic and then charting these findings on the matrix that best directs the choice of diagnostic evaluations and successful treatment.

Therapies should be chosen for their potential effect on the most significant imbalances of the particular patient. A completed matrix form facilitates 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 effect of each variable at 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 beneficially influences the immune response, melatonin levels, and T-cell lymphocyte levels and helps decrease oxidative stress. Exercise reduces stress, improves insulin sensitivity, and improves detoxification. Reducing stress (and/or improving stress management) reduces cortisol

Chief Complaint (CC)
History of Present Illness (HPI)
Past Medical History (PMH)
– Explore antecedents, triggers, and mediators of CC, HPI, and PMH
Family Medical History
– Genetic predispositions?
Review of Organ Systems (ROS)
Medication and Supplement History
Dietary History
Social, Lifestyle, Exercise History
Physical Examination (PE)
Laboratory and Imaging Evaluations
Explore Core Clinical Imbalances:
Assimilation Imbalances
Digestion
Absorption
Microbiota/GI
Respiration
Defense and Repair Imbalances
Immune system
Inflammatory processes
Infection and microbiota
Energy Imbalances
Energy regulation
Mitochondrial function
Biotransformation and Elimination Imbalances
Toxicity
Detoxification
Communication Imbalances
Endocrine
Neurotransmitter
Immune messengers
Cognition
Structural Integrity Imbalances
From the subcellular membranes to the musculoskeletal system
Initial Assessment:
– Enter data on Matrix form; look for common themes
– Review underlying mechanisms of disease
– Recapitulate patient's story
– Organ system-based diagnosis
– Functional medicine assessment: underlying mechanisms of disease; genetic and environmental influences
Treatment Plan:
– Individualized
– Dietary, lifestyle, environmental
– Nutritional, botanical, psychosocial, energetic, spiritual
– May include pharmaceuticals and/or procedures

Fig. 1.3 Expanding the accordion file: the functional medicine assessment heuristic. (Courtesy the Institute for Functional Medicine.)

levels, improves sleep, improves emotional well-being, and reduces the risk of heart disease. Changing the diet has 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 reestablish 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 ensuring 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 to the diet can alter the peroxisome proliferator–activated receptor system, affect body weight, and modulate the inflammatory response.[13–15] However, in a person who is diabetic or insulin resistant, adding conjugated linoleic acid may induce hyperproinsulinemia, which is detrimental.[16,17] 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 gastrointestinal tract.

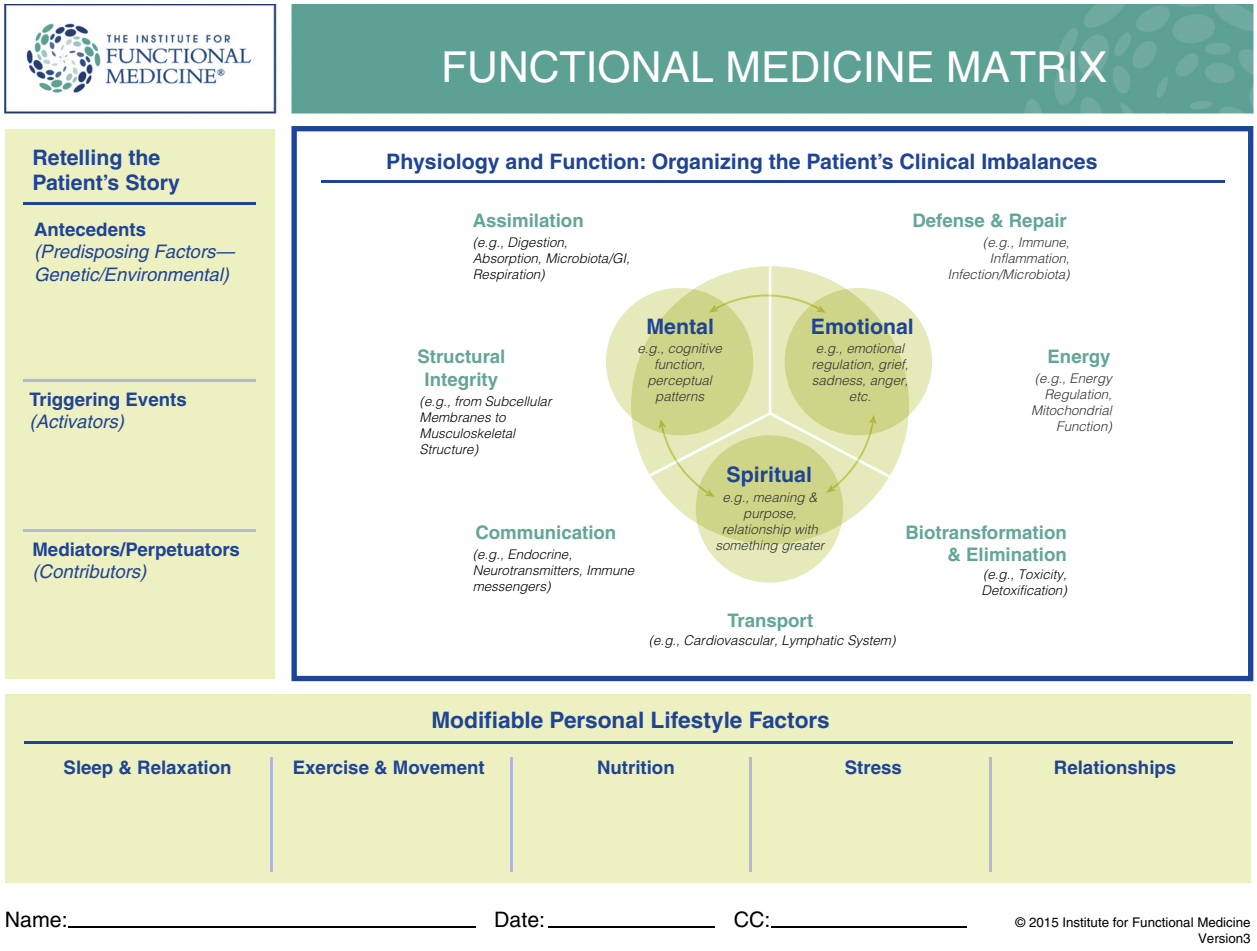

Fig. 1.4 The Functional Medicine Matrix Model. (Courtesy the Institute for Functional Medicine.)

4. Subcellular/mitochondrial interventions: There are many examples of nutrients that support mitochondrial function.[18,19] 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 more than 10% of the U.S. population) causes oxidation and DNA damage in human cells.[19] Ensuring 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 β-oxidation of fatty acids and resultant adenosine triphosphate production. In patients who have lost significant weight, carnitine undernutrition can result in fatty acids undergoing ω-oxidation, a far less efficient form of metabolism.[20] Patients with low carnitine may also respond to riboflavin supplementation.[20]
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 nuclear factor-κB entering the nucleus, binding to DNA, and activating genes that encode inflammatory modulators, such as interleukin-6 (and thus C-reactive protein), cyclooxygenase-2, interleukin-1, lipoxygenase, inducible nitric oxide synthase, tumor necrosis factor-α, or a number of adhesion molecules, will affect many disease conditions.[21,22] There are many ways to alter the environmental triggers for nuclear factor-κB, including lowering oxidative stress; altering emotional stress; and consuming adequate phytonutrients, antioxidants, alpha-lipoic acid, eicosapentaenoic acid, docosahexaenoic acid, and γ-linoleic acid.[21] Adequate vitamin A allows the appropriate interaction of vitamin A–retinoic acid with more than 370 genes.[23] 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.[24] Vitamin D has key roles in controlling inflammation, calcium homeostasis, bone metabolism, cardiovascular and endocrine physiology, and healing.[24]

Experience using this model, along with improved pattern-recognition skills, will often lessen the need for extensive laboratory assessments. However, there will always be 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 autism spectrum disorders in children, heavy-metal exposure and toxicity may play an important role. The heavy-metal body burden cannot be sensibly assessed without laboratory studies. In most initial workups, laboratory and imaging technologies can be reserved for those complex cases in which the initial interventions prove insufficient to the task of functional explication. When clinical acumen and educated steps in both assessments and therapeutic trials do not yield expected improvement, laboratory testing often provides rewarding information. This is frequently the context for focused genomic testing.

The Healing Partnership

No discussion of the functional medicine model would be complete without mention of the therapeutic relationship. Partnerships are

formed 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.

In the 20th century, contemporary medicine, traditionally considered a healing profession, evolved away from the role of healing the sick to that of curing disease through modern science. Research into this transition revealed that healing was traditionally 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 characteristics.

Contemporary medicine considers the wholeness of healing to be beyond its orthodoxy—the domain of the nonscientific and nonmedical.[25] We disagree. 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, an emerging body of relevant research was reviewed.[26–28] As Louise Acheson, MD, MS, associate editor of the *Annals of Family Practice,* articulated insightfully in that journal[29]: "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.[30] 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."

Research into the role of healing in the medical environment has generated some thoughtful and robust investigations. Scott et al.'s[26] research into the healing relationship found very similar descriptions to those of Hsu et al.[30] The participants in the study[27] articulated aspects of the healing partnership as follows:

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.[27] In this rich soil, the healing partnership flourishes.

The characteristics of a conventional 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 and characterized by algorithmic processing and statistical thinking.[31,32]

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 shared responsibility for 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 of medicine and to managing the uncertainty (choices under risk) inherent in clinical practice. In the healing partnership, the appropriate utilization and integration of left-brain and right-brain functions are found.

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, the left brain needs to see the trees, and the right brain helps us see and understand the forest.[33,34]

The starting point for creating a healing partnership is the patient's experience. People, not diseases, can heal. Mindful integration of brain function is at the heart of a healing partnership. Some of the basic steps for establishing a healing partnership include the following:

1. Allowing patients to express, without interruption, their story about why they have come to see you. (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.[35]) The manner in which the patient frames the initial concerns 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.[36]
2. After focusing on the chief concerns, encouraging the patient's narrative regarding the 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 as previously described.
   - Analysis of the data thus collected proceeds by assessing probable underlying causes—based on evidence about common underlying mechanisms of disease—and ongoing mediators of the disease.
3. Next, conveying to the patient in the simplest terms possible that to achieve lasting solutions to the problem(s) for which the patient has come seeking help, a few fundamental questions must be asked and answered 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. At this stage, control is shared with the patient: "Without your help, we cannot understand your medical problem in the depth and breadth you deserve." Implementing this shared investigation can be facilitated by certain approaches:
   a. For determining antecedent conditions, the following questions are useful:
      - When was the last time you felt well? When were you free of this problem?
      - What were the circumstances surrounding the appearance of the problem?
      - Have similar problems appeared in family members?

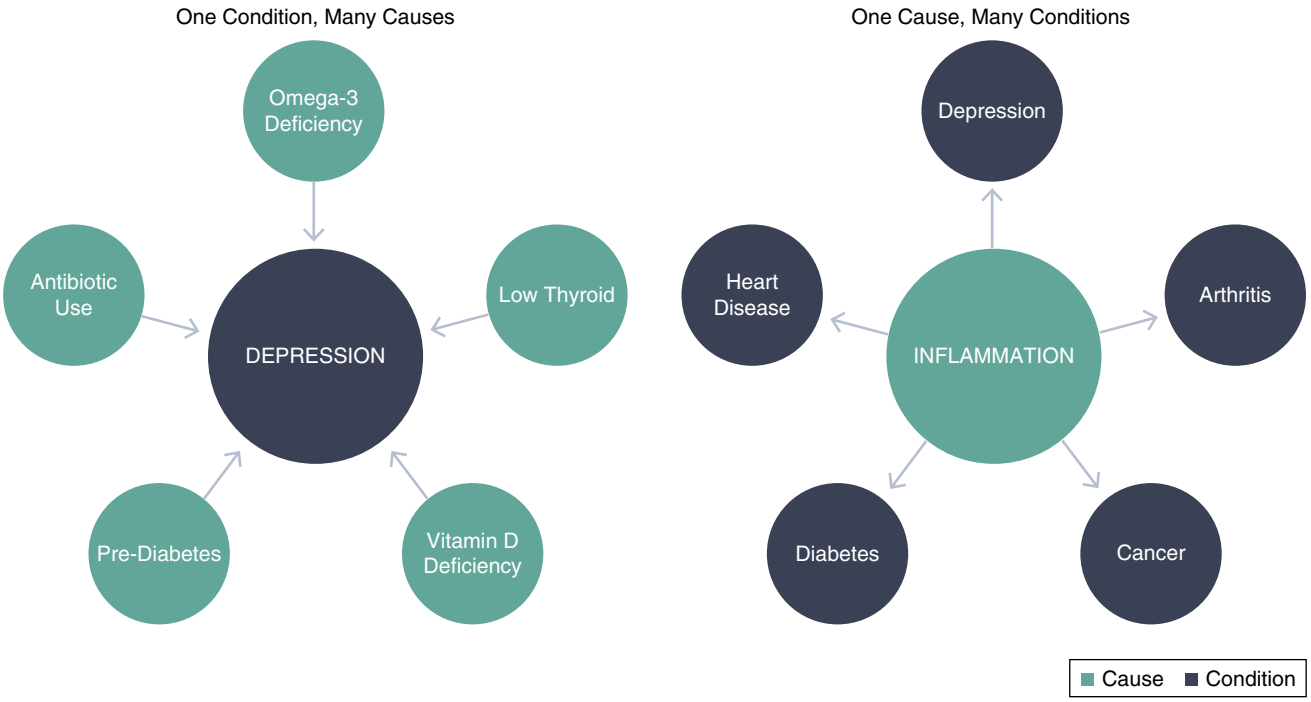

Fig. 1.5 Overview of the functional medicine (FM) model. (Courtesy the Institute for Functional Medicine.)

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 previously 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 emerged. The patient literally owns the keys to the joint deliberation that can provide insight into the process of achieving a healing outcome.
- The professional brings experience, wisdom, tools, and techniques and 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. An overview of the functional medicine model is given in Fig. 1.5.

INTEGRATION OF CARE

Functional medicine explicitly recognizes that no single profession can cover all the viable therapeutic options. Interventions and practitioners will differ by training, licensure, specialty focus, and even by beliefs and ethnic heritage. However, all health care disciplines (and all medical specialties) can—to the degree allowed by their training and licensure and assuming a good background in Western medical science—use a functional medicine approach, including integrating the matrix as a basic template for organizing and coupling knowledge and data. Consequently, functional medicine can provide a common language, a flexible architecture, and a unified model to facilitate integrated and integrative care. Regardless of the discipline in which the clinician has been trained, developing a network of capable, collaborative practitioners with whom to comanage 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.

REFERENCES

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REFERENCES

1. Goetzel RZ. Do prevention or treatment services save money? The wrong debate. *Health Aff*. 2009;28(1):37–41.
2. Probst-Hensch NM. Chronic age-related diseases share risk factors: do they share pathophysiological mechanisms and why does that matter? *Swiss Med Wkly*. 2010;140:w13072. Available at http://www.smw.ch/index.php?id=smw-2010-13072. Accessed October 11, 2010.
3. Magid CS. Developing tolerance for ambiguity. *JAMA*. 2001;285(1):88.
4. Rees J. Complex disease and the new clinical sciences. *Science*. 2002;296: 698–701.
5. Radford T. Top scientist warns of "sickness" in US health system. *BMJ*. 2003;326:416. https://doi.org/10.1136/bmj.326.7386.416/b.
6. Vioxx. Lessons for Health Canada and the FDA. *CMAJ*. 2005;172(11):5.
7. Juni P, Nartey L, Reichenbach S, et al. Risk of cardiovascular events and rofecoxib: cumulative meta-analysis. *Lancet*. 2004;364:2021–2029.
8. This section was excerpted and adapted from Galland L. Patient-centered care: antecedents triggers, and mediators. In: *Textbook of Functional Medicine*, Ch. 8.
9. Cernak I, Savic VJ, Kotur J, et al. Characterization of plasma magnesium concentration and oxidative stress following graded traumatic brain injury in humans. *J Neurotrauma*. 2000;17(1):53–68.
10. Vink R, Nimmo AJ, Cernak I. An overview of new and novel pharmacotherapies for use in traumatic brain injury. *Clin Exp Pharmacol Physiol*. 2001;28(11):919–921.
11. Yu SL, Ho LM, Lim BC, Sim ML. Urinary deoxypyridinoline is a useful biochemical bone marker for the management of postmenopausal osteoporosis. *Ann Acad Med Singapore*. 1998;27(4):527–529.
12. Palomba S, Orio F, Colao A, et al. Effect of estrogen replacement plus low-dose alendronate treatment on bone density in surgically postmenopausal women with osteoporosis. *J Clin Endocrinol Metab*. 1002;87(4): 1502–1508.
13. Moya-Camarena SY, Vanden Heuvel JP, Blanchard SG, et al. Conjugated linoleic acid is a potent naturally occurring ligand and activator of PPARa. *J Lipid Res*. 1999;40:1426–1433.
14. Gaullier JM, Halse J, Hoye K, et al. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. *Am J Clin Nutr*. 2004;79:1118–1125.
15. O'Shea M, Bassaganya-Riera J, Mohede IC. Immunomodulatory properties of conjugated linoleic acid. *Am J Clin Nutr*. 2004;79(S): 1199S–1206S.
16. Malloney F, Yeow TP, Mullen A, et al. Conjugated linoleic acid supplementation, insulin sensitivity, and lipoprotein metabolism in patients with type 2 DM. *Am J Clin Nutr*. 2004;80(4):887–895.
17. Riserus U, Vessby B, Arner P, Zethelius B. Supplementation with CLA induces hyperproinsulinaemia in obese men: close association with impaired insulin sensitivity. *Diabetalogia*. 2004;47(6):1016–1019.
18. Ames BN. The metabolic tune-up: metabolic harmony and disease prevention. *J Nutr*. 2003;133:1544S–1548S.
19. Ames BN, Elson-Schwab I, Silver EA. High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased Km): relevance to genetic disease and polymorphisms. *Am J Clin Nutr*. 2002;75(4):616–658.
20. Bralley JA, Lord RS. *Laboratory Evaluations in Molecular Medicine: Nutrients, Toxicants and Metabolic Controls*. Atlanta: Institute for Advances in Molecular Medicine; 2001.
21. Yamamoto Y, Gaynor RB. Therapeutic potential of inhibition of the NF-kB pathway in the treatment of inflammation and cancer. *J Clin Invest*. 2001;107(2):135–142.
22. Tak PP, Firestein GS. NF-kB: a key role in inflammatory disease. *J Clin Invest*. 2001;107(1):7–11.
23. Balmer JE, Blomhoff R. Gene expression regulation by retinoic acid. *J Lipid Res*. 2002;43:1773–1808.
24. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular diseases. *Am J Clin Nutr*. 2004;80(suppl 6). 1678S–1688S.
25. Egnew TR. The meaning of healing: transcending suffering. *Ann Fam Med*. 2005;3(3):255–262.
26. Scott JG, Cohen D, DiCicco-Bloom B, et al. Understanding healing relationships in primary care. *Ann Fam Med*. 2008;6(4):315–322.
27. Miller WL, Crabtree BF, Duffy MB, et al. Research guidelines for assessing the impact of healing relationships in clinical medicine. *Altern Ther Health Med*. 2003;9(suppl 3):A80–A95.
28. Jackson C. Healing ourselves, healing others? first in a series. *Holist Nurs Pract*. 2004;18(2):67–81.
29. Acheson L. Community care, healing, and excellence in research. *Ann Fam Med*. 2008;6:290–291.
30. Hsu C, Phillips WR, Sherman KJ, et al. Healing in primary care: a vision shared by patients, physicians, nurses, and clinical staff. *Ann Fam Med*. 2008;6(4):307–314.
31. Brown M, Brown G, Sharma S. *Evidence-Based to Value-Based Medicine*. Chicago, IL: AMA Press; 2005.
32. Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. *Evidence-Based Medicine: How to Practice and Teach EBM* (3rd ed.). New York: Churchill Livingstone.
33. Fiore S, Schooler J. Right hemisphere contributions to creative problem solving: converging evidence for divergent thinking. In: Beeman M, Chiarello C, eds. *Right hemisphere language comprehension: perspectives from cognitive neuroscience*. Philadelphia, PA: Erlbaum Publishing; 1998:255–284.
34. Seger CA, Desmond JE, Glover GH, et al. fMRI evidence for right hemisphere involvement in processing unusual semantic relationships. *Neuropsychology*. 2000;14:361–369.
35. Beckman DB, et al. The effect of physician behavior on the collection of data. *Ann Intern Med*. 1984;101:692–696.
36. Lehrer J. The annals of science: the eureka hunt. *The New Yorker*. 2008:s40–s45.

BIBLIOGRAPHY

Galland L, Lafferty H. *Gastrointestinal Dysregulation: Connections to Chronic Disease. (Functional Medicine Monograph)*. Gig Harbor, WA: The Institute for Functional Medicine; 2008.

Hedaya R, Quinn S. Depression: advancing the paradigm (Functional Medicine Monograph). Gig Harbor, WA: The Institute for Functional Medicine. In: Jones DS, ed. *Textbook of functional medicine*. Gig Harbor, WA: The Institute for Functional Medicine; 2008.

Jones DS, Hofmann L, Quinn S. *21st Century Medicine: a New Model for Medical Education and Practice (White Paper)*. Gig Harbor, WA: The Institute for Functional Medicine; 2009.

Lukaczer D, Jones DS, Lerman RH, et al. *Clinical Nutrition: A Functional Approach*. 2nd ed. Gig Harbor, WA: The Institute for Functional Medicine; 2004.

Vasquez A. *Musculoskeletal Pain: Expanded Clinical Strategies (Functional Medicine Monograph)*. Gig Harbor, WA: The Institute for Functional Medicine; 2008.