Chapter 2
What is Functional Medicine?

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Introduction to Functional Medicine

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A 2003 article in the *British Medical Journal*[1] generated the following editorial comment: "It is almost a daily occurrence for primary care doctors to encounter patients whose symptoms are probably not due to discernible organic cause." Many of these symptoms appear to be related to chronic inflammatory complaints of unknown origin. Because no specific disease can unequivocally be attached to these complaints, the following question arises: What physiological processes/mechanisms result in the expression of these signs and symptoms? Could their underlying "organic cause" be related to altered function in the absence of observed pathology?

A major challenge for medicine in the 21st century will be to move toward a thorough understanding of physiological mechanisms that underlie disease rather than simply labeling later-stage effects with the names of diseases. "What should we say to patients with symptoms unexplained by disease?" asks the article associated with the editorial comment quoted above. The authors suggest that, for most patients, using the term "functional," as in "functional illness," would be more socially acceptable than "medically unexplained symptoms."

Historically, the term "functional" has been used pejoratively in medicine. It has implied either a disability associated with geriatric medicine or a psychiatric problem. Now, the term "functional" is being used to describe a manifestation of changes in basic physiological processes that produce symptoms of increasing duration, intensity, and frequency. These symptoms often represent the first signs of a later-stage, pathophysiologically definable disease. So, the term becomes applicable not only to diseases of unknown origin, but to early alterations in function that clearly move a patient toward chronic disease over the course of a lifetime.

A new model of medicine is emerging to describe these altered physiological processes that presage the onset of histopathologically defined disease. This model takes the term "functional" beyond psychosomatic illness to define a state of chronic dysfunction associated with altered physiological processes that create a physiological alarm state.

What is Functional Medicine?

Functional medicine is a dynamic approach to assessing, preventing, and treating complex chronic disease. Functional medicine helps clinicians identify and ameliorate dysfunctions in the physiology and biochemistry of the human body as a primary method of improving patient health. Functional medicine acknowledges that chronic disease is almost always preceded by a lengthy 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.

The Functional Medicine Domain

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 a patient care model for complex, chronic disease, functional medicine encompasses the whole domain represented by the graphic shown in Figure 2.1, but concentrates on the section below Organ System Diagnosis, which differentiates it from the conventional medical model. Assessment and treatment *first* address the patient's core clinical imbalances, fundamental physiological processes, environmental inputs, and genetic predispositions, rather than heading straight for the diagnosis. (These elements are explored in detail and thoroughly documented in separate sections of this book. Here in the *Introduction*, we provide an overview of the content and concepts.) Diagnosis is not excluded from 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 practitioners reason that scientific evidence strongly indicates that impaired physiological processes, if not corrected, lead to significant clinical imbalances in essential body systems. If left in a dysfunctional state, those clinical imbalances often progress to more significant signs and symptoms that may be the precursors or actual indicators of a disease state that can be diagnosed. Improving balance and functionality in these basic processes creates momentum toward health.

Conventional medicine normally acts either when a diagnosis can be made, or when signs and symptoms are severe enough (or the patient is persistent enough) to demand a clinical intervention. Functional medicine practitioners certainly do intervene when a diagnosis has already been made, but they also evaluate functionality at a much earlier stage, often averting (or deferring for a substantial period of time) the disease outcome or its secondary effects. And, in all cases, 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 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.

Functional medicine could be characterized, therefore, as "upstream medicine" or "back to basics"—back to the patient's life story, back to the processes wherein disease originates, and definitely back to the desire of healthcare practitioners to make people well, not just manage symptoms.

Principles

These basic principles characterize the functional medicine paradigm:

- An understanding of the *biochemical individuality* of each human being, based on the concepts of genetic and environmental uniqueness;
- Awareness of the evidence that supports a *patient-centered* rather than a disease-centered approach to treatment;
- The search for a *dynamic balance* among the internal and external factors in a patient's body, mind, and spirit;
- Familiarity with the *web-like interconnections* of internal physiological factors;
- Identification of *health as a positive vitality*—not merely the absence of disease—emphasizing those factors that encourage the enhancement of a vigorous physiology; and
- *Promotion of organ reserve* as the means to enhance the health span, not just the life span, of each patient.

Each of these principles is discussed in depth in the *Principles* section, and the evidence supporting their inclusion is presented there.

Environmental Inputs

Environmental inputs (at the base of the medicine tree graphic) include the basic 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. Many environmental factors that affect genetic expression are (or appear to be) a matter of choice (such as diet and exercise), but 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 through travel). 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.

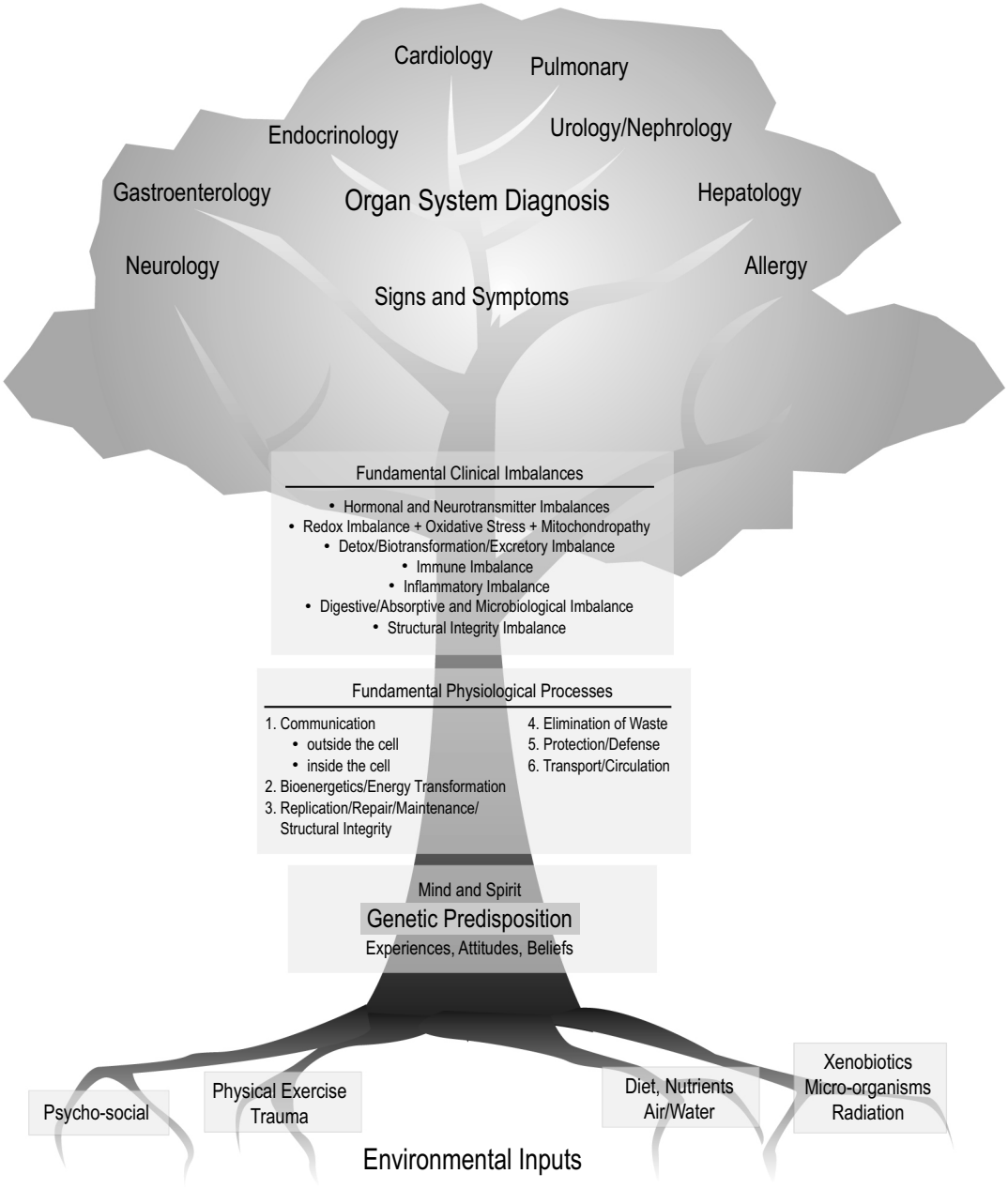

Figure 2.1 **The continuum of health and health care**

Whatever the nature of these "inputs," their influence on the human organism is indisputable, and they are often powerful agents in the search 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. The functional medicine practitioner takes the elements listed below into consideration when working with a patient 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
- Psycho-social factors (including family, work, community, economic status, stress)
- Xenobiotics
- Radiation

Environmental inputs are intimately connected with the functional medicine principle of *dynamic balance* mentioned above. The importance of this critical interweaving between internal and external factors in a patient's body, mind and spirit is fully explored later in the book.

Fundamental Physiological Processes

The fundamental physiological processes that ultimately determine health or disease include:

- communication, both outside and inside the cell;
- bioenergetics, or the transformation of food, air, and water into energy;
- replication, repair, and maintenance of structural integrity, from the cellular to the whole body level;
- elimination of waste;
- protection and defense; and
- transport and circulation.

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 medical care. However, subsequent training in the clinical sciences often fails to fully integrate this rich understanding of the underlying functional mechanisms of disease with therapeutics and prevention. In the second two years, conventional clinical training heavily emphasizes teaching/learning based on organ system diagnosis.[2] This approach—aggregating the patient's signs and symptoms into groupings that follow organ system declensions—has given us both the power and the weakness of specialization (e.g., the breakdown of medicine into cardiology, neurology, gastroenterology, pulmonology, nephrology, dermatology, hematology, hepatology, endocrinology, the surgical specialties, and so forth). Specialists become exceedingly knowledgeable in a well-defined subset of the human organism, but they often evaluate and treat diseases within their specialty area as though the inevitable cross-talk among all organ systems does not occur.

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 cookbook exercise in finding the right "recipe"—the drug or procedure that best fits the diagnosis (not necessarily the patient). Every medical problem thus becomes a personal health issue in search of a pharmacological agent or surgical procedure[3] and that leads to a significant curtailment of the critical thinking pathways: "Medicine, it seems, has little regard for a complete description of how a myriad of pathways result in any clinical state."[4]

Even more important, the pharmacologic treatments specific to each specialty are often implemented without careful consideration of the physiological effects across all organ systems and physiological processes (and genetic variations).[5] Pharmaceutical companies have exploited this weakness. Did you ever see a drug ad that urges 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.[6,7]

Pharmacological and medical hardware interests also strongly influence the research that is done and the

information that reaches physicians about new drugs and procedures.[8,9,10] Our national research establishment—both private and governmental—is heavily focused on drug development and medical devices technology, rather than multifactorial, individualized, lifestyle-focused interventions. Physicians (and now patients as well) are subjected to the disproportionate impact the drug industry's ad campaigns have on information about treatment approaches for disease—everything is centered on taking a drug,[11] rather than helping patients change behavior. By controlling research topics,[12] selecting what data will be published,[13,14] and dominating continuing medical education programs,[15,16,17] the pharmaceutical industry often replaces complex thinking with more simplistic approaches relying on pharmaceuticals.[18] Even our less commercial research models (at NIH, for example) all too often concentrate on "single disease—single agent—single outcome" methodologies. Examination of lifestyle and the attendant physiological and health consequences seldom receive needed research support because the medical-industrial complex that surrounds conventional training and practice is driven by these powerful commercial interests. (Lifestyle approaches are also more difficult to study prospectively, but the work certainly can be done with the will and the resources.)

Fortunately, a stronger voice from within the ranks of medical educators and practitioners is emerging on behalf of re-evaluating the influence of commercial interests on our healthcare system—from education to research to clinical practice.[19,20] Many mainstream publications are including articles by leading medical thinkers that patient-centered health care requires a broader focus than simply labeling the problem (diagnosis) and selecting the right drug.[21]

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 (information from the patient's story, signs, symptoms, and laboratory assessment) through a matrix focused on functionality requires critical thinking that is quite different than matching diagnosis with drug and hardware interventions. A deeper understanding of biochemistry and physiology is required of a functional medicine practitioner. 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 delineating 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. (Re-examine the medicine tree graphic to appreciate how the core clinical imbalances fit within the total framework of health care.)

Core Clinical Imbalances

The practice of functional medicine is characterized by an examination of the core clinical imbalances that underlie the expression of disease. Those imbalances arise as *environmental inputs* such as diet, nutrients (including air and water), exercise, toxins, and trauma *are processed* (see above list of the fundamental processes involved) through a unique set of *genetic predispositions*, attitudes, and beliefs. The *core clinical imbalances* that arise from malfunctions within this complex system include:

- *Hormonal and neurotransmitter imbalances*
- *Oxidation-reduction imbalances and mitochondropathy*
- *Detoxification and biotransformational imbalances*
- *Immune and inflammatory imbalances*
- *Digestive, absorptive, and microbiological imbalances*
- *Structural imbalances* from cellular membrane function to the musculoskeletal system

Imbalances such as these are the precursors to the signs and symptoms by which we detect and label (diagnose) organ system disease. These imbalances arise from dysfunction or defect within the fundamental physiological processes that cut across all organ systems, and they alert the healthcare provider to pay attention to the full expression of disease and dysfunction. Each of these imbalances is explored in considerable detail later in the book, and the underlying evidence supporting this approach to patient care is thoroughly discussed.

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—can be both a precursor and a concomitant activity to evaluating and treating chronic illness, and to improving health. It involves much more than treating symptoms.

Short Description of Functional Medicine

Functional medicine is dedicated to prevention, early assessment, and improved management of complex, chronic disease by intervening at multiple levels to correct core clinical imbalances and thereby restore each patient's functionality and health to the greatest extent possible.

History of Functional Medicine

David S. Jones, MD and Jeffrey S. Bland, PhD

If contrast is the essence of vision, then clearly delineating the differences between present day conventional medicine and functional medicine will help improve our understanding of the road being pioneered by functional medicine.

In his commentary in 2003, *The Medicine We Are Evolving*,[22] Sidney MacDonald Baker, MD, postulates that current conventional medicine rests on two primary principles:

1. The fundamental subject of medical concern is disease;
2. The inquiry as to health rests first on the naming of the patient's disease.

He points out that treatment is then prescribed for the disease without rigorous consideration of the patient's unique individual needs, which may include the need to be rid of something toxic, allergenic or infectious, or the need to add something vital that is missing, or both.

Dr. Baker describes the difference between the acute-illness legacy of conventional medicine and today's functional medicine model that is focused on prevention and treatment of chronic, complex illnesses (the dominant medical problems experienced in our modern, industrialized, hygienic society):

> How do we think differently? The emerging school of thought [*functional medicine*] does not deny the usefulness to the patient and physician of diagnostic groups that allow us the comfort of knowing "what you've got." We are careful to keep in mind that a diagnosis is an idea we form about groups of people and properly belongs to the group, not an individual. Making a diagnosis in the realm of chronic illness—such as the many conditions of chronic inflammation whose proud names end in "-itis," and autism, schizophrenia, depression, anxiety, cardiovascular disease, and a host of otherwise eponymous, classical, and respectable diseases—is for us not the end of a diagnostic road, but the first step, to be followed by the … [*consideration of unique individual needs*]. These questions are <u>not</u> applied to "curing the disease" but to healing the person.
>
> This approach is based on the recognition that individuality … [*has*] a spiritual as well as a biological foundation in the sense that each of us is a unique creature. Hence our patients are denied dignity when given a group identity (diagnosis) and a group treatment (the "treatment of choice" for that diagnosis).[23]

Functional medicine evolved from a medical paradigm that, instead of emphasizing the primacy of diagnosis and pathology, focuses on the antecedent events that precede the onset of diagnosis (*cf*. the notion of "upstream medicine," discussed above under *The Functional Medicine Domain*). Leo Galland, MD, elaborated this principle first in the early 1990s in his unpublished, but widely disseminated paper, *Patient-Centered Diagnosis: A Guide to the Rational Treatment of Patients as Individuals*,[24] later expanded and published in 1997 as *The Four Pillars of Healing*.[25] Patient-centered diagnosis depends on knowledge of the mediators, triggers, and antecedents of the patient's specific disease (discussed in detail in Chapter 8). According to Dr. Galland, arriving at an accurate, detailed, structured assessment of the patient requires a collaborative context within which the patient's story includes:

> aspects of the patient that had previously been ignored. We were interested in the effects of the common components of life: a patient's thoughts and beliefs, home or work environment, exposure to potential toxins, and allergens, food and drink, stressful life events, social interactions, patterns of physical activity.

The evaluation investigates past history, including family history and clues regarding genetic and social inheritance, the environmental/emotional conditions affecting the patient's health, and those factors that continue to mediate the dysfunction and/or disease. The patient's narrative always includes clues that will eventually inform the physician about the underlying mechanisms of dysfunction, without "segregation of biological and psychosocial dimensions."[26] This model derives from the integration of research in molecular biology and behavioral psychology about the influences that lead to the clinical manifestation of disease. One approach of this kind has been labeled the "biopsychosocial model,"

and it helps clinicians understand "how suffering, disease, and illness are affected by multiple levels of organization, from the societal to the molecular."[27]

Starting in the early 1980s, Jeffrey Bland, PhD, first developed the fully elaborated model of functional medicine that now includes both the *six principles* and the *fundamental clinical imbalances* that underlie the dysfunctional devolution of health into disease. Writing in the preface of his 2004 seminar series syllabus,[28] Dr. Bland states:

> It amazes me that this accumulated body of information … now comprises more than 2000 pages and 5000 referenced articles demonstrating the importance of diet, nutritional intervention, lifestyle and environment on both the prevention and management of virtually every chronic disease … . We are involved in what Thomas Kuhn termed a "paradigm shift" in our understanding of the origin and treatment of age-related chronic diseases. The discovery of the code of the human genome and the recognition that our function is determined by much more than just our genome is a revolution in thinking. Our health and disease patterns after infancy are not "hardwired" deterministically by our genes, but rather a consequence of the interaction of genetic uniqueness with environmental factors. Our experiences wash over our genes to give rise over time to how we look, act, feel and our disease pattern. This is truly a change in thinking about the origin of disease that requires a similarly bold change in how we treat disease.

This model emerges from the groundwork of six great innovators who carved out from the domain of molecular medicine the foundational concepts underpinning functional medicine. The six pioneers of this new medical paradigm are Archibald Garrod (1902), Linus Pauling (1949), Roger Williams (1956), Abram Hoffer (1957), Hans Selye (1979), and Bruce Ames (2002). Let us pause and reflect on the contributions of these six pioneers who have improved our understanding of the human organism and the factors that contribute either to ongoing health or to the progression toward chronic, degenerative diseases.

Archibald Garrod, MD

Dr. Garrod was first to discover the diseases of genetic metabolism in the early 20th century. (He investigated the genetic metabolism diseases of infancy.) Although those diseases originated in the genes, he said, the ultimate expression of the diseases depended on the exposure of those genes to factors in the environment. He discovered alkaptonuria, which led to the understanding of phenylketonuria and the role of the phenylalanine-restricted diet in its management. In 1902, Dr. Garrod wrote, "It might be claimed that what used to be spoken of as a diathesis of a disease is nothing else but chemical individuality. It is nearly true to say that the factors which confer upon us our predisposition and immunities from disease are inherent in our very chemical structure, and even in the molecular groupings which went to the making of the chromosomes from which we sprang."[29]

Linus Pauling, PhD

Dr. Pauling made extraordinary contributions to the way we view the origin of disease. His article in *Science* magazine in 1949 on the origin of sickle cell anemia taught us that single gene mutations could contribute to disorders that cut across organ systems and produce multiple symptoms. In this article he introduced the term "molecular medicine."[30] Dr. Pauling explained that in sickle cell anemia, a single point gene mutation on the heavy chain of the globin molecule of hemoglobin could contribute to a conformational change in the way the hemoglobin molecule was structured in three dimensions. That conformational change affected the way oxygen bound to the heme portion of the hemoglobin molecule and changed the relationship between the molecule and its oxygen absorption/desorption. The change in shape of that molecule changed the shape of the red cell, because hemoglobin made up about three-quarters of the volume of a red cell. The red cell then became sickle-shaped, and this sickle would "cut" its way through the vasculature, creating the pain and disability of sickle cell crisis.[31]

Dr. Pauling predicted in 1949 that the molecular origin of disease would have extraordinary implications. As we learned more about the origin of these diseases, he believed, we would find ways to modify the expression and function of these genes to prevent the expression of disease. In 1997, 48 years after Dr. Pauling proposed this model of the potential power of molecular medicine, a paper in *The New England Journal of Medicine* validated his thesis. That article explained that administering hydroxy urea intravenously to patients who carried the genetic trait of sickle cell anemia could prevent the hemoglobinopathies associated with this genetic disorder.[32] Hydroxy urea upregulated the

expression of fetal hemoglobin in these patients and "diluted" the amount of sickle cell hemoglobin, resulting in a reduction of sickle cell crisis.

Roger Williams, PhD

Dr. Roger Williams, a professor of biochemistry at University of Texas at Austin and past President of the American Chemical Society, discovered members of the B-complex vitamin family, including pantothenic acid. Dr. Williams's book, *Biochemical Individuality*, published in 1956, proposed a role of various nutrients in preventing what he called "genetotrophic diseases."[33] Genetotrophic diseases are those for which genetic uniqueness creates demands for specific nutrients beyond the average to facilitate optimal function and prevent premature disease. Dr. Williams theorized that when those specific needs are not met in a given individual, disease results.

Dr. Williams believed the major chronic degenerative diseases of aging—heart disease, stroke, cancer, diabetes, and arthritis—were related to genetotrophic imperfections. In his model, the unique genes of each individual require different levels of nutrition and a specific lifestyle for optimal health. The consequences of not meeting the specific needs of the individual are expressed, over several decades, as degenerative disease "of unknown origin." In the category of what he called genetotrophic diseases, Dr. Williams even included diseases of mental illness, childhood diseases, behavior disorders, and alcoholism. He believed they all were related to the mismatch of genes and environment. At a genetic level, the individual needed a different level of nutrients to promote proper phenotypic expression. If that need was not met, the resulting undernutrition would manifest as chronic disease in midlife. This very powerful concept revolutionized our thinking about the origin of age-related diseases.[34]

In defending his concept of biochemical individuality, Dr. Roger Williams said, "Nutrition is for real people. Statistical humans are of little interest. People are unique. We must treat real people with respect to their biochemical uniqueness."

Abram Hoffer, MD, PhD

As a psychiatrist who also held a doctorate in organic chemistry, Dr. Hoffer in the 1950s provided a unique perspective on mental illness. He discovered in the urine of schizophrenics unique chemicals that represented the oxidative byproducts of adrenaline.[35] He found that these substances produced central nervous system toxicity. As a result of these discoveries, Dr. Hoffer proposed that certain forms of mental illness resulted not from bad early childhood experiences, but as a consequence of altered brain chemistry.[36] He found that increased doses of the common B vitamins, niacin and pyridoxine, could treat these conditions in some schizophrenic patients.[37] Dr. Hoffer, with the synthesis of a new idea that incorporated biochemical genetic individuality, nutritional modulation of gene expression, and functional physiology, provided the bridge that allowed psychiatry to enter the field of biologically based, functional therapy.

Hans Selye, MD, PhD

As the father of the physiological definition of the word "stress," Dr. Selye introduced to both medical professionals and healthcare consumers the role of the mind in the function of the body.[38] Dr. Selye's tremendous insight gave birth to the rapidly evolving field of psychoneuroimmunology, which is redefining the way health practitioners view the impact of lifestyle and behavior on health. The combination of the physiology of stress and the understanding of the influence of perceived stress on genetic expression served as a powerful driver for the evolution of functional medicine.

Although Dr. Selye was never awarded a Nobel Prize for his contributions, many historians of 20th century medicine believe his insights on the role of behavior and environment in health represent one of the most important factors shaping the new medicine.

Bruce Ames, PhD

Dr. Bruce Ames, Professor of Biochemistry and Molecular Biology, and Director of the National Institute of Environmental Health Science Center, University of California, Berkeley, published his landmark paper in 2001.[39] His team's research provides the bench science to substantiate Williams's postulates on genetotrophic diseases. Ames shows in his encyclopedic review paper that "as many as one-third of mutations in a gene result in the corresponding enzyme having an increased Michaelis constant, or *K*m (decreased binding affinity), for a coenzyme, resulting in a lower rate of reaction." Some

people carry polymorphisms[i] that are more critical in determining the outcome of their health history. He goes on to argue that studies have shown that administration of higher than dietary reference intake (DRI) levels of cofactors (specific vitamins and minerals) to these polymorphic genes restores activity to near-normal and even normal levels. He concludes, "Nutritional interventions to improve health are likely to be a major benefit of the genomics era."

The functional medicine model rests on the stout shoulders of these worthy researchers and clinicians. They pioneered the concepts that postulated that many agents modify gene expression in such a way as to create different phenotypes. They provided the breakthrough science that demonstrates that significant influences in this process include diet, exercise, stress, environmental, and lifestyle factors.

Molecules of functional importance transmit messages and receptors receive them. The transmitters are the molecules we call the mediators. The receivers are the membrane receptor binding and soluble receptor sites that translate the messages into altered gene expression and altered function. It is possible to manipulate both the messages and their reception on the basis of things we do every day, by the way we think, act, eat, and feel, by where we live, the nature of our relationships and our spiritual belief systems. All these factors influence the mediating molecules and can lead to an expanding health paradigm. An informational rubric encompasses communicating and receiving the right messages to be in synchrony with our genes to give rise to healthy function.

These six individuals pioneered the new medicine for the 21st century by establishing the scientific basis for recognizing that our genes generally do not determine our disease. The awareness that our environments are powerful agents influencing the genetic expression of both health and disease represents a major shift in medical thinking.[40] The utility of this model within the medical paradigm is no longer in question. It is just a question of how long it will take for this model to be fully integrated within the standard practice of medicine.

[i] A polymorphic gene is an alternate form of a *wild* gene present in >1% of the population. The most common polymorphic genes are single nucleotide polymorphisms (SNPs) that result in translational proteins and enzymes with decreased functionality. We all share at least 99.9% of the nucleotide code of our species' genome. The SNPs are what make us unique within our species. The translation of our genome message that includes our SNPs results in our individual phenotype. [Burghes, et al. Science. 2001;293: 2213–14.]

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