April 2009 Issue | Victor Sierpina, MD Professor

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Welcome to *Functional Medicine Update* for the April 2009 edition. In this issue, we are going to be focusing on what has been termed "integrative functional medicine," a concept that may be coming into its own as we move through this extraordinary period of healthcare revolution that we are in as we witness the opening up of the next chapter in the history of health sciences and healthcare delivery.

In 2005, in the *Textbook of Functional Medicine*, I wrote a preface, which I think--as I look back now--embodies much of the conceptual framework that we are now describing and discussing pertaining to how the future might look for health care.[1] I said clinicians who focus on the management of complex chronic disease have not chosen an easy path and we all know that. It is a complex field that requires diligent work and it is not easy.

In the *Textbook of Functional Medicine*, we describe an approach to improving patient outcomes across a wide range of chronic health conditions through careful analysis of common underlying pathways that interact to produce disease and dysfunction or health and vitality. Outstanding is the content that has been contributed by many experts in the development of this concept-this systems biology approach towards health care. The approach to disease management and health promotion described within the concepts of functional medicine represents the evolution of this model over the past, now, nearly 18 years, through the voices of its leaders. In this preface I wrote, "Functional medicine reflects a systems biology approach to health care: a comprehensive analysis of the manner in which all components of human biological system interact functionally with the environment over time. Over the past century, biology and medicine have focused heavily upon understanding the physiology and biochemistry of individual organs, cells, and molecules. Traditionally, researchers and clinicians have explored one component of various biological systems at a time. In clinical practice, this process usually leads to the differential diagnosis [the driving force for much of our medical education to become a better diagnostician]. In drug discovery, it helps us to understand how individual, new-to-nature molecules, or new compounds, interact with a specific drug target to modify human physiology. From these investigations has emerged an exceptional knowledge base [that we call the medicine of our past--certainly the patent medicines of the past 70 years]. We are now poised to comprehend the common underlying pathways of health and disease as never before."

The new tools of molecular biology, and molecular science, and ultimately cell physiology examine what we call energy and medicine. Looking at things like nuclear magnetic resonance and various types of very sophisticated imaging has given us a new view of the body.

In the *Textbook of Functional Medicine*, I continue, "We can acknowledge that most diseases that we

diagnose are rarely the result of a single physiological problem localized to a single organ. Rather, most chronic disease results from the complex interactions of multiple organ systems and multiple physiological and biochemical pathways with the environmental influences and genetic predispositions." This knowledge demands a new clinical approach to prevention and treatment that is framing where we are going in 2009 and beyond.

Two challenging questions have stimulated the development of functional medicine: How are the body's physiological systems linked together and how is their function influenced by both environment and genes (the interfacing of those two)? The recognition that these two questions are inextricably linked to each other has become much clearer with the discovery that the human genome contains far fewer genes than expected, and that much of our biological uniqueness is related to the "non-coding" region of the genome-the region that controls systems of gene expression. In essence, we've learned that our complex phenotype cannot be adequately understood by exploring one gene at a time (although we recognize, now, that exploiting one gene at a time can lead to a drug development process for remediation of a specific endpoint, but it doesn't apply to a systems biology understanding of the dysfunction). Systems of genetic expression give rise to our biological complexity, and they need to be understood from an integrated perspective, hence integrative functional medicine, as a term.

Health care is an enterprise focused on the alleviation of human suffering caused by disease and dysfunction. Disease, at the start, is a functional impairment (we call it a dysfunction) that, if left untreated, becomes a diagnosable disease that later can become the cause of death. Each disease has a past, a present, and a future tied to the progressive loss of function and vitality. In 1980, Dr. James Fries, professor of medicine at Stanford, authored his landmark article that appeared in the *New England Journal of Medicine* titled "Aging, Morbidity, and Natural Death," and the loss of function was what he called the loss of organ reserve.[2] This functional systems biology approach to understanding the origin of disease is now being encouraged by the National Institutes of Health under a program that was started by Dr. Zerhouni, the NIH Roadmap, as a route to accelerate discoveries that will improve health.[3]

We are now starting to see cross-disciplinary work recognizing that the only answers that will really be meaningful in solving these complex chronic diseases are those of a systems approach that integrate different knowledge bases and different experiences. Three characteristics define the systems biology approach to medicine: emergence, robustness, and modularity. Emergence represents the specific characteristics that are displayed in a complex system that are not demonstrated by its individual parts. In functional medicine, we call this web-like interconnections of physiological processes and biochemical pathways that give rise to networks. Robustness is the ability that complex biological systems have to maintain homeostasis in the face of changing environmental conditions; in functional medicine, we call this homeodynamics: the greater the degree of physiological freedom within an individual, the more robust their health and the more ability they have to accommodate change. Modularity refers to a system that is comprised of functional units working together to produce an outcome that cannot be produced by any of the units working independently. An example of this concept of functional medicine is a view of the immune, endocrine, and nervous system as one super system: the neuroendocrineimmune system. Only by working at the system level as a whole, and not at each of its units in isolation, can the practitioner fully understand the complex presentation of multiple signs and symptoms that a patient often exhibits upon presentation.

We now recognize in excess of

75{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of healthcare expenditures are for the treatment of chronic disease and most physicians are not adequately trained to deal with these complex problems.[4] In functional medicine, it is the conviction that developing a healthcare system that effectively manages and prevents chronic disease will depend upon our ability to apply this systems biology approach to medicine. Functional medicine incorporates many aspects of this approach, each of which plays a vital role. Identifying and following biomarkers of function that can be used as indicators of the onset of disease and also as markers for the success of intervention is an extremely important activity in functional medicine. Using a patient-centered rather than a disease-centered model emphasizes the importance of eliciting the patient's story and incorporates mindfulness in the narrative tradition. Recognizing that the extent and severity of chronic conditions in middle to late life are, to a large extent, the outcome of environmental insults received at any point from conception forward, allows for a focus on long-term prevention to be integrated into clinical practice. Harnessing the healing power of the mind-body interaction is also important to functional medicine clinicians, as developed from scientific progress in the field of psychoneuroimmunology.

The Origins of Functional Medicine

In looking back at the history of medicine in the 20th century, the origin of the concept of function can be credited, in a large degree, to people that we have talked about over the years in *Functional Medicine Update*, such as Dr. Hans Selye. His pioneering work related to the functional endocrinology of what he termed stress and its relationship to chronic disease as diverse as peptic ulcer, hypertension, and heart disease, carried a new medical model for a disease arising out of dysfunction, rather than from infectious organisms or inborn errors of metabolism. He put a physiological mechanism behind the concept that "it is more important to know what kind of a person has a disease than what disease a person has," as was so really beautifully stated by William Osler.[5]

Voices from all aspects of our society are now merging into a unified call for this new model to address chronic health conditions. In a 2005 article in the *New England Journal of Medicine*, it was pointed out that children being born today may be the first generation in the history of the United States with a lower life expectancy than that of their parents. This prediction comes at a time when the United States spends nearly 40{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} more per capita on health care than any country in the world, but is now seen-as a World Health Organization outcomes measure-as 37th in the world in terms of health outcomes.[6]

Functional Medicine is an Effective Response to Call for a New Model: An Epic Week of Healthcare Policy Meetings

We are living in a very interesting time. Functional medicine is an effective response to this call for a new model of care. It was born out of collaboration among clinicians of many disciplines and specialties-clinical laboratory specialists, health science researchers, health educators, health policy professionals, and healthcare administrators-to address the rising incidence and cost of chronic disease.

Over the past 15 years, functional medicine has become an experienced voice in these discussions. As we move into this issue of *Functional Medicine Update*, we have just completed, in late February of 2009, an epic week of healthcare policy meetings on Capitol Hill in Congress, and at the executive branch of our government. Reforming the United States healthcare system--implementing an effective approach to chronic disease--has become a very, very big call to action. One of the meetings in Washington, DC the

Summit on Integrative Medicine and the Health of the Public, was sponsored by the Institute of Medicine, a branch of the National Academy of Sciences, and co-sponsored by the Bravewell Collaborative. This summit took place February 25-27, 2009, and was chaired by Dr. Ralph Snyderman, President Emeritus from the Duke University Medical School.[7]

At this three-day colloquium and summit, extraordinary discussions were held among people from a whole variety of backgrounds. The singular mission of the meeting was to find more effective ways of delivering health to the country. The keynote address by Senator Tom Harkin from Iowa, the third-ranking member of the health committee in the Senate, gave us a call to action in which he quoted from a speech given by Dr. Mark Hyman earlier in the week at the Senate Committee hearing Dr. Hyman said, "It is time to change not only the way we do medicine, but the medicine we do," which is a wonderful quote that Senator Harkin picked up on and incorporated within his talk, with appropriate attribution to Dr. Hyman.

We are at that interesting cornerstone-that nexus, that inflection point, that opportunity point-when great things can happen. Some people say these things occur only once in a century (these moments of great opportunities for change) when everything is poised for a tipping point. It is certainly the case right now, given all the various events that we have seen in our world community over the past year, and certainly it focuses on healthcare reform as well.

Many years ago, Lewis Thomas, ex-editor of the *New England Journal of Medicine* who was a wonderful medical writer as well as a clinician/doctor, as you probably recall, authored a Pulitzer Prize-winning book that talked about the nature of medicine and the nature of biological sciences: *The Medusa and the Snail*.[8] Another book that he wrote in 1983 didn't receive quite as much attention, but I though was an extraordinarily important book and was titled *The Youngest Science*, in which Dr. Thomas described how medicine was evolving from a descriptive science where a disease diagnosis was the most important feature of medicine, to a preventive science based upon understanding the etiology of disease.[9] He predicted in this book that by the end of the 20th century or the start of the 21st century, biomedical sciences would have discovered enough about the origin of chronic disease to treat early causes of the disease and not just its late-stage effects, based on understanding the mechanism of disease.

Dr. Thomas' prediction has proven to be largely correct. Over the past 30 years, the underlying physiological dysfunctions that give rise to later disease have been discovered and we are witnessing a transition in medical thinking from that which is reactive (i.e. pathology-based medicine) to that which is proactive (i.e. prognostic-based medicine) and based on an understanding of the early alterations in physiological function. The emerging understanding of the origin of chronic diseases is that they result from a complex interaction, as I have said, between the genetic uniqueness of the individual and their lifestyle and environment. Chronic disease is, therefore, the translation of an alteration in physiological function in the individual that reflects the translation of genetic susceptibilities through exposure to specific lifestyle and environmental factors.

Statement by Senator Edward Kennedy

We are really at a very interesting time of change. Senator Edward Kennedy, who is the chairman of the committee of the senate that looked at the relationship of health for the future of the country (this is the United States Health, Education, Labor, and Pensions Committee) issued a statement about integrative

medicine as a vital part of the new healthcare system.[10] His statement covered much of what we have just been talking about. The American healthcare system urgently needs repair and reform. As a nation we are spending 16{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of our gross domestic product on health care (more per capita than any other country in the world), yet health outcomes of Americans, as Senator Kennedy points out, are ranked 37th in the world.

Our system is often called a sick care system, not a healthcare system because it is designed to treat disease and illness instead of promoting good health. Paraphrasing from Senator Kennedy's statement, he said, "Genuine health reform, therefore, requires a major transformation in our national mindset of how we care for ourselves and others. It must incorporate and encourage disease prevention activities and lifestyle changes that promote long-term health and well-being. The current incentives in our health system that lead to overtreatment and mistreatment must be changed to promote high quality, appropriate, and coordinated health care. The nation's alarmingly high and growing rates of obesity and chronic disease today are a clear call to action. By preventing diseases before they start and adopting a broader approach to medicine we will actually reduce costs in the long run, and will extend and improve the quality of life as we do so. To achieve this fundamental shift in the nation's healthcare mindset, it will be necessary to reform how medicine is practiced. Low cost or even free health screenings and vaccinations will encourage individuals to take part in preventive medicine. Patient-centered and coordinated care that addresses the whole person, from genetic predisposition, to lifestyle choices, to potentially harmful conditions is essential for treating acute diseases and managing chronic conditions. We must adopt a more integrated approach to medicine through health care that addresses the mental, emotional, and physical aspects of the healing process."

This is just a small part of Senator Kennedy's statement. We are at that extraordinary time where these great changes can occur, it is necessary they occur, and integrative functional medicine may take its seat at the table and make contributions to this healthcare change. Our clinician of the month this month on *Functional Medicine Update* could not be a better choice for carrying this message. You'll hear, from his own voice, about his years of experience in developing what I consider a true integrative functional medical practice, and about his advocacy as an academic medical person in charge of a department that is delivering this at the University of Texas Medical System.

The concept of genetic polymorphisms (or the diversity that Roger Williams talked about in the late 1940s and early 1950s) is now starting to gain a foothold in not only pharmacogenomics and how different people respond to drugs, but also relative to how people with differing genotypes respond to environmental exposures and to diet. In fact, there are so many papers being published in the area of nutrigenomics now that it is virtually impossible to keep up each month with the expanding body of literature.

As an example, a paper was recently published looking at the role of various genetic variants in how methylenetetrahydrofolate, or a form of folic acid, and choline are metabolized as it relates to their impact on blood homocysteine levels.[11] In this paper that appeared in the*Journal of the American Dietetic Association* in 2009, it was reported that certain single nucleotide polymorphisms (SNPs) in the phosphatidylethanolamine N-methyltransferase enzyme (the genes that control the production of that enzyme), and also methylenetetrahydrofolate dehydrogenase SNPs, influence the biomarkers of choline metabolism, and particularly are seen when folate intake is restricted, with much more significant increases in the blood levels of homocysteine. This is not simply treated by giving folic acid supplements;

one needs to also give higher levels of choline, as well, in order to overcome these metabolic, I guess you would call it, "tight spots" that relate to these single nucleotide polymorphisms of the phosphatidylethanolamine N-methyltransferase genes.

I think we are starting to witness that one size doesn't fit all in nutrition any more than it does in drugs. When we start to really look at various patterns of response and susceptibilities, we have to take into account these families of genetic uniquenesses. The so-called genome-wide association studies (or GWAS) studies that are being used now for evaluating SNPs that might be associated with increasing susceptibility to disease are starting to help us understand that it's not that genes in and of themselves cause disease, it is that the genes in and of themselves determine the response that we might have to our environment and how genes are expressed that give rise to their phenotype. We can't change the genes, but we certainly can change the environment that the genes pick up the message from

Let me, if I can, take this to another step of clinical application, and that has to do with statin therapy and one of the adverse effects that is seen of statin therapy, which has to do with muscular signs and symptoms, neurological issues, and, in the extreme case, severe problems of muscle atrophy (rhabdomyolysis). As we recognize, the extreme case is very infrequent, but there are much more mild cases of adverse response to statins that are seen. They are not seen in all individuals, and, in fact, by changing from one statin drug to another, you often are able to modify response in that patient with the adverse symptoms. This suggests that the concept of a class effect of a drug may be a little bit of a misunderstanding--that different molecules have different effects of gene expression, and therefore we can't say that because it is a member of a class called statins that it has the same exact physiological response in the body, depending upon that person's own genetic uniqueness. However, we do know that one of the potential adverse effects that statins (as a family of HMG-CoA-reductase inhibitor molecules) has, is lowering the sterile biosynthesis that goes through isoprenoid polymerization and biosynthesis that has, ultimately, to do with other molecules that are being built by that same pathway, such as coenzyme Q10 (or ubiquinone).

Low Levels of Coenzyme Q10 as a Contributing Factor to Statin Myopathy

There have been longstanding questions as to whether the low intracellular and plasma levels of coenzyme Q10 that are seen in patients who take statins are, in fact, the contributing factors in some of the musculoskeletal problems that are associated with adverse response to statins. A number of papers have been published over the years trying to make some kind of a correlation between statin use, coenzyme Q10 levels in plasma, and the clinical adverse effects of statins. Recently there have been many more studies published on this that help to enlighten us as to this relative interrelationship. I'd like to take you through some that I think are quite fascinating.

Genetic Predisposition to Statin Myopathy

The first paper has to do with genetic predisposition to statin myopathies. It now appears that these conditions of adverse effects to statins are not seen in all people, but rather there may be certain genotypes that are more susceptible than others. In a recent paper that was published in *Current Opinions in Rheumatology* titled "Genetic Predisposition to Statin Myopathies," the authors say that technological advances have now made it possible to identify genetic variations in the human genome through GWAS (genome-wide association studies) that reveal disease-related mutations in single nucleotide polymorphisms that are associated with more risk to specific diseases.[12] More than 30,000 individuals in the United States, this article goes on to say, suffer from severe life-threatening symptoms of statin-

induced myopathy that may, in some cases, persist long after the secession of therapy. That was a number that was quite surprising to me-30,000 individuals suffering from severe life-threatening symptoms of statin-induced myopathy. Genes of interest include those involved in the pharmacokinetics of statin response (muscle atrophy, exercise intolerance, pain perception, and mitochondrial energy metabolism). These researchers have just completed a genetic analysis for variants that relate to this station myopathy that provides some understanding of predispositions that might then lead to individuals being at higher risk to adverse effects to statin medication application. This has to do with things like carnitine palmitoyltransferase 2 deficiences and a range of other SNPs (single nucleotide polymorphisms) that go on to potentially define individuals that may have increasing risk to myopathic outcomes.

Is it one gene or is it a family of genes? The answer is obviously the latter. The genes that they have defined in this particular paper that seemed to come out with higher prevalence include various types of cytochrome P450 polymorphorisms of cytochrome P4502C8, 2D6, and 3A5, as well as metabolic muscle-related genes like CPT2 and AMPD1. And then other things like nitric oxide synthase 3 and APOE4. So there are a whole series of genes that appear to be associated with the increasing risk to statin myopathies; these are the various SNPs (the single nucleotide polymorphisms). In screening for patients who might be at risk to myopathies as a result of statin therapies, one would then form a cluster of gene SNPs that you would analyze to determine a relative risk factor. I think this is the way we are starting to see pharmacogenetics infiltrate its knowledge base into that of clinical practice and clinical medicine.

The Issue of the High Cost of Screening

At this point, one would ask, what is the relative prevalence of these SNPs that are associated with increasing susceptibility to adverse effects to statins? Is it very miniscule prevalence, or is it prevalence of high enough impact that we would be concerned across the board and want to do screening? In other words, is it cost effective to do screening? (Because it is an expense, obviously, to do SNP testing.) Or do we just take it as an outlier that is such a small frequency of individuals that we can't really justify the expense? These are very, very complicated questions in medical decision-making, aren't they, when we start asking how much expense is a system willing to bear to screen for those individuals who might have an adverse response in or to protect those individuals?

We don't really have hard and fast rules as to how to make those decisions, and that's part of the uncertainty as we start developing this understanding of genetic variation and individual response as to what is justified in terms of cost for doing screening. Once we ask that question, then the next question (which further complicates the issue) is, does coenzyme Q10 intervention play any useful role in either preventing or even managing myopathy in statin users? Of course, this is another controversial area for which no hard and fast rule has emerged either. There is, however, some interesting recent research that has been published in this area that I think is noteworthy for consideration. One of these papers appeared in the *Current Opinions in Lipidology* journal in 2008.[13] This paper looked at the effects of coenzyme Q10 therapy on myopathy in statin users. This was a review summarizing the current evidence on coenzyme Q10 supplementation. The conclusion was that present evidence did not support supplementation in statin-induced myopathy because they could not find statistically significant meta-analysis justification for Co-Q10 oral supplementation to ameliorate statin-induced myopathies.

One can be a little bit-I would say-confused in how to interpret this data because the question is did doing a meta-analysis stratify for the appropriate people who might be most sensitive to Co-Q10 supplementation? Did it look at the right levels of Co-Q10 supplementation, knowing that these studies

have a variety of different dosage levels, from 100 to as much as 600 milligrams a day? We know that in patients who have various types of mitochondrial encephalopathies, like MELAS (Mitochondrial Encephalopathy Lactic Acid Syndrome), that these individuals have low muscle Co-Q10 concentrations. Supplementation with 250 milligrams per day of Co-Q10 was found to have some positive influence on clinical symptoms in these patients with this metabolic inborn error of metabolism that we call mitochondrial encephalopathy.

These patients can end up with various types of myopathies that resemble rhabdomyolysis, although they have slightly different etiology. One might say, "Well, gee whiz, then giving doses of 200 milligrams a day of Co-Q10 with a patient on statins should be adequate." Studies did not seem to show a positive effect when patients were given simvastatin and got 80 milligrams of Co-Q10 a day; there wasn't a clinically significant improvement in reduction in myopathies. Maybe 80 milligrams is the wrong dose, maybe we need a higher dose, or maybe we need to look at individuals with unique types of sensitivity because maybe myopathies come from a variety of different mechanisms, only some of which are related to the statin issue.

Let me go to another review paper. This is titled "Coenzyme Q10: Is There a Clinical Role and Case for Measurement?"[14] The question is: how low is the serum or plasma level of Co-Q10 that would be correlated with the therapeutic dose required to modulate myopathy? This appeared in *Clinical Biochemistry Reviews* in 2008. I think this is another interesting contribution to our advancing knowledge in this area. We consider coenzyme-Q10 to be an essential cofactor in mitochondrial electron transport that has to do with establishing proper redox control (reduction-oxidation control) within the mitochondria. It is also known to be an intermediate that is biosynthesized in the body. Coenzyme Q10 is not considered an "essential nutrient," but might be considered a conditionally essential nutrient, meaning that if a person has insufficient biosynthesis to meet their needs, that they might need augmented levels from the diet in order to make up the gap (fill in the gap). That is the justification, then, for Co-Q10 supplementation in times where a person is consuming statins and inhibiting Co-Q10 biosynthesis.

Being endogenously synthesized via the mevonalate pathway, we now recognize that although some is obtained from the diet, most Co-Q10 in people is synthesized directly in situ from the same pathway that goes on to produce squaline lanosterol and ultimately into cholesterol itself. If an individual, then, has a low plasma level (or serum level) of Co-Q10, does it then indicate that they have a poor synthesis of Co-Q10? This paper really looked at that correlation between serum levels of Co-Q10 and whether that is an indicator of low intracellular Co-Q10 levels, meaning it is a surrogate marker for a reduced mitochondrial sufficiency of Co-Q10.

The authors of this article went on to say that it appears as if (from the data accumulated to date) that there is a correlation of some reasonable significance between low serum Co-Q10 levels and that of insufficient Co-Q10 in mitochondrial functional states to regulate redox potential within the mitochondrion. These can be further aggravated, obviously, through specific polymorphisms of genes that have to do with the electron transport chain, like Factor 2, where Co-Q10 plays a very important role, or cytochrome oxidase, in the mitochondrial oxidative chemistry. So some individuals may be at much higher risk than others, and a number-a plasma level or serum level of Co-Q10-may not give the full story, depending upon that individual's own sensitivity and how that reflects oxidative stress at the cellular level.

With all of this in mind, what it leads us to recognize is that Co-Q10 certainly seems to have a suggested benefit when orally taken as a supplement during times of statin therapy, somewhere between, say, 100 milligrams or 200 milligrams a day. One needs to be concerned a little bit about the bioavailability of the Co-Q10 formula. Some formulas have been found to be much more bioavailable than others. Clearly it has to get into the body in order to do some good. If it is a non-absorbable form, it won't promote the appropriate improvement in plasma and cellular levels. Co-Q10 can be measured in the body, so bioavailability studies can be done and should be done to demonstrate the increase in plasma levels after oral consumption. The better brands of the product have this kind of data associated with it.

I found it interesting that in the question and answer section of the *Harvard Health Letter* in 2008 (the September issue), a question was posed: "Why don't you tell readers that everyone who takes a statin should be taking coenzyme Q10 as well?"[15] The response says that taking a statin lowers coenzyme Q10 because it is carried through the bloodstream in LDL. Lowering LDL-the main job of statins-means less Co-Q10 in circulation.

It has been hypothesized that statin effects of Co-Q10 might account for muscle aches and pains from these drugs, however statins don't appear to affect Co-Q10 inside cells or mitochondria. Taking a supplement increases blood levels of Co-Q10, but the effect inside muscles is inconsistent, with one study showing an increase in Co-Q10 after supplementation, and another a decrease. More to the point, the only two trials of Co-Q10 for statin-induced muscle problems contradict each other. It is possible that Co-Q10 supplements may prevent statin-associated muscle problems in people who don't take enough Co-Q10, or who are at risk for muscle damage due to hypothyroidism or pre-existing muscle disorders It is hoped that clinical trials will be conducted to explore this. For now, though, there is no credible evidence that everyone who takes a statin should also take Co-Q10. That's the position that the *Harvard Health Letter* has taken and I think it probably summarizes my point.

There is one other fat soluble vitamin that I think we should also be thoughtful about that relates to this heart healthy connection, and that's vitamin K (menaquinone and phylloquinone) . A very interesting series of papers has been published over the years about vitamin K and its relationship to cardiovascular disease. The most recent paper I am aware of appeared in *Nutrition Metabolism and Cardiovascular Disease* in 2008 and is titled, "A High Menaquinone Intake Reduces the Incidence of Coronary Heart Disease."[16] We often think of vitamin K as a blood clotting nutrient helping to regulate blood clotting factors, but it also seems to have impact on other aspects that relate to vascular calcification and heart health thereof. I would put vitamin K as an important part of our assessment of nutrients and cardiovascular risk. Obviously, I would also still continue to put vitamin E on that list, knowing that vitamin E (as an antioxidant) does have effects on mitochondrial oxidative chemistry. It (along with Co-Q10) helps to protect against free radical injury, and there are studies that have at least suggested that a combination of vitamin E and Co-Q10 might produce benefit in protection against myopathies of statins beyond that of Co-Q10 itself. I think we are starting to see some very, very interesting clinical clarity being brought to this question about the pharmacological effect of statins on Co-Q10 biosynthesis and that influence on myopathies. Again, the concept of genetic uniqueness, and polymorphism starts to play a role.

Let me, if I can, summarize what I've tried to give you here in this rapid-fire introduction. What I have tried to say is that we are undergoing a transition in basic biological sciences and our understanding of how it relates to medicine, health, and disease, that is second (probably) to the revolution that occurred at

the turn of the last century. This paradigm shift is really a remarkable sea change as it pertains to how we understand physiological function as a network of differing interacting variables that give rise to cross-organ changes in function, ultimately expressing signs and symptoms that we categorize as diseases that are all interconnected through similar mechanisms.

I went on to say that genetic polymorphisms (or a variety of these kinds of SNPs) may determine relative risk to certain types of conditions, either both gain in function or loss in function types of responses. We often think of SNPs as only being harmful, but actually the maintenance of single nucleotide polymorphisms in our genome may reflect the legacies that we have within our genetic diversity that have helped certain populations to protect themselves against certain conditions in the changing of their environment, like starvation or infection, where certain SNPs were selected for in times gone by. So what we might consider today to be a disadvantageous SNP, might (at one time) have been actually advantageous for survival for the people carrying it. We recognize that SNPs can impart either gain in function or loss in function depending upon the environment to which they are being exposed, and we start to see that SNPs express themselves in families (it is generally not one SNP at a time, but it is rather these nucleotide polymorphisms that cluster themselves together to give increasing risk).

I also talked about the homocysteine connection. Maybe homocysteine is just a marker for a whole family of different uniquenesses that relate B6, B12, choline, phosphatidylcholine, and folic acid and its conjugers that, then relate to regulation of vascular dynamics and immune function.

Lastly, I've kind of finished this up by talking about what happens if you pharmacologically modulate or modify normal function (like the statin examples with myopathy), and can you then use a conditionally essential nutrient to back fill in the area of function, knowing that different genotypes may respond differently with different relative susceptibilities? This medicine that we are seeing emerge today is much more complex than that which we probably learned as a memorized list of diseases and presenting signs and symptoms, with a specific drug to treat each of those diseases. What we are really being given is a chance to look at a variety and how it influences the function of organisms in a positive way-this is a new functional medicine model. With that, we are going to have one of the pioneers in functional integrative medicine talk about their clinical reality, Dr. Victor Sierpina

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INTERVIEW TRANSCRIPT

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Many of you ask me about this section of FMU, which is our clinician/researcher of the month section. You've made comments like, "Wow, we've been so fortunate to get these opinion-leading, pace-setting, visionary researchers who are really charting the new biology that is underpinning medicine." But then the parenthetical question is: why can't we have a little bit more of the clinical how-to, or the people who have their fingers in the exam room more, who really are the people doing the work? It is a balance

between the biology of the new medicine as well as the practice of the new medicine. I'm honoring that by having someone who I would consider, from my experience, probably the top of the class in this area of delivering the medicine in a humanistic, compassionate, intelligent, wise, and balanced way, and that is Dr. Victor Sierpina.

Let me give you a quick introduction to Victor. If you are in our field, you probably already know the name or even know him personally; he is very noteworthy. Quickly, to just review his background: Dr. Sierpina has a BS in biology from Arizona State and then later an MD from the University of Illinois. He went into a family practice residency, and then ultimately went on to do all sorts of postgraduate work, including body/mind training and acupuncture training. He went through many years of work, academic study, scholarship, contribution, and clinical work, and now is at the Department of Family Medicine at the University of Texas Medical Branch at Galveston. He is a professor-the WD and Laura Nell Nicholson Family Professorship in Integrative Medicine. He is one of the leaders and has just come off the Chairmanship of the consortium of medical colleges that are dealing with integrative medicine in some fashion in their curriculum. More than that, I would say Vic is just a doctor's doctor. He is really very, very balanced and very capable of doing what we call integrative medicine and finding the right tool for the right application.

With that introduction, Dr. Sierpina, it is wonderful to have you as a guest on Functional Medicine Update. Let me ask, I guess, the question that always starts any one of these interviews: what is the path that ultimately led you to your integrative medicine interest from family practice?

VS: Thanks, Jeff, for that kind introduction. Early on my family was always interested in nutrition and home remedies and such. As a child of the 60s, and growing up in that era (I was in high school and college during that period of time), there was a lot more focus on natural remedies and things that were kind of outside of the mainstream. As my friend, Mark Blumenthal, said, "We went through the 60s and never exhaled," which is one of the ways that we changed our minds about how the world looks. During that period I started to become more interested in realms such as mind-body and spirituality, as well as more natural approaches to health care that I had kind of been exposed to as a child.

JB: As this happened, and knowing that your path has been really not only clinical but also academic medicine, I'm sure you probably raised the eyebrows (or looks) of some of your colleagues. When was your first sense that you were going to be put under a different level of scrutiny, or maybe you haven't had that experience and it's been a smooth transition?

VS: Well, it has had its rocky points, that's for sure, but it hasn't been nearly as bad as people might have expected. I was in private practice for about 15 years prior to coming to academia. I worked as a medical director at an urgent care center in the Chicago area, did home births, worked at a holistic center there, and then ultimately started a solo practice in the mountains of Colorado. During this time I did acupuncture, mind/body work, and herbs/supplements/nutrition as part of my practice. When I came to the university and decided to go into the teaching field it was because I enjoyed teaching so much (in Colorado I taught the ambulance crew and the ski patrol crew, both of which I was medical director of, and I realized how much I liked that). So when I came to Texas I thought, "Well, I'm going to just keep practicing like I did, and this is what they hired me to do." And nothing was too exciting until people started noticing that I was doing acupuncture; all the rest of my armamentarium of treatments wasn't nearly as exciting, apparently, to people as acupuncture. That seemed to be a marker that let a lot of

people here in Galveston (which is actually a very liberal community) kind of come out of the closet about their interest in everything from Reiki, therapeutic touch, traditional Chinese medicine, botanical medicine, etc. The fact that a physician was doing these practices... people that were researchers, nurses, other physicians, felt like they had somebody kind of as their point person to talk to and say, "Well, he's doing this and we want to hear more about it." So that was back, gosh, in '97, '98, and so I kept getting invitations to talk about the range of things, so although there were certainly some skeptical faculty, by and large people recognized this was a trend among the public and there was some validity in some of the services that I was offering that they weren't doing yet.

JB: So as you have moved forward, obviously you have been very successful in building a team and also in getting funding. I know that you have been a recipient of at least two NIH grants supporting what is going on there in integrative medicine at the University of Texas Medical Branch in Galveston, and I think you've got a couple of very fine colleagues, Susan Gerik and Julie McKee, who are part of your integrative healthcare center. Tell us a little bit how you built this.

Funding for Integrative Medicine Research

VS: Well, the first thing was an intramural grant (the President's Cabinet Grant, here, which is a grant that is meant to seed small projects that might not get funding otherwise). I applied for that to set up a website at UTMB-this is back in the late '90s-that would serve as kind of a clearing house for information about complementary medicine. We had faculty, peer-reviewed websites; anything that we posted on there went through our process of vetting the websites that were on our websites, so that people linked to quality materials. We licensed some databases, such as Health Notes Online, natural medicine's comprehensive database that students would use. So that was a small grant (like $25,000), and that was kind of a nice crystal, I suppose, around which other activities were built-a journal club, a course on spirituality and healing (we got another $50,000 grant from the George Washington Institute of Spirituality and Healing-it was a Templeton Fund grant at that time). So several of those kinds of activities started to move, and then when the National Center for Complementary and Alternative Medicine said, "We've got to start developing curriculum in medical schools in this area," we had a track record of several years, so we were awarded, in the first round, 1.6 million dollars over a 5 year period to initiate curriculum across not only medicine, but nursing and our allied health schools here.

JB: The question that I think a lot of people have always raised is, in a very crowded medical curriculum (when people are in medical school everyone is vying for another moment of mind space of the student), how have the students responded to your opportunities?

Including Integrative Medicine into Medical School Curriculum

VS: The students are very open in this area. In fact, I'm kind of in a situation right now where I'm having to retool the curriculum because it is a constant maintenance project, so curriculum changes all the time. What we were able to do (you mentioned our team, like Dr. Gerik, Dr. McKee, Kara Geary, others that we have had over the years-Dr. Frenkel), that we were on various curriculum committees. When you're on the curriculum committee, you can't be a one-focus, one-issue person; you pitch in, but you see the opportunities. Rather than adding a whole additional course, we would take, for example, the clinical reasoning course and add cases on integrative medicine/alternative medicine topics. We'd bring in the librarian and have her drive the students in a lecture hall demonstration on how to get to websites that they could look things up if a patient came in on a number of supplements, where they could find reliable science-based information about that. We added cases (web-based cases) that the students could go

through. We had some demonstrations, as well as electives and selectives later in their third and fourth years. We haven't done as much, obviously, as I'd liked to have done, but it is that hydraulic effect, and the best approach to it, I think, and the greatest compliments we have, is that the students feel like they get enough material, but not too much, and sometimes they don't even recognize that it is integrative because we've integrated it.

JB: You've authored two recent papers, and I think just the titles alone kind of describe your skill in putting these things together and making them stand up and be valid. One is titled (from Academic Medicine last year), "Integration of the Biopsychosocial Model: Perspectives of Medical Students in Residence," and the other was from 2007 titled "Barrier Strategy and Lessons Learned from Complementary and Alternative Medicine Curricular Initiatives."17,18 Both of those kind of define a domain, so if we kind of take an away point, here, looking at the academic side, would you say that curriculum has shaped up enough now that it is starting to stand up and be looked at by people who may not understand it, saying "Wow, there's really something here that we should pay more attention to?"

VS: I think so. It is somewhat institutionally based. We try, through the LCME, which is the Licensing Commission for Medical Education, and our Consortium of Academic Health Centers for Integrative Medicine, to create some standards in which all medical schools would have to incorporate certain integrative medicine content into their curriculum. We were partially successful in that; they listed this area as one of the areas that medical schools now have to catalog and describe what they are doing in that area.

In reference to those two articles, for example, that you referenced, the mind/body area is really an area of non-evidenced-based practice and teaching, which is to say that there is plenty of evidence for mind/body therapies, but we don't act as if they are evidenced; they don't fit into the medical culture. If someone comes in and they are depressed or anxious we give them a pharmacological treatment rather than some self-actuated self-care strategy that they can do (deep breathing, or meditation, or visualization). It is still outside of the culture of medicine, although when you expose students to it, particularly through personal practice, they get it and they will start using it with their patients.

Some of the strategies, like I say, are just embedding curriculum within courses rather than having it as separate courses. For example, we just started (this year) a pilot program for our family medicine residency with seven other residency programs. This is hosted through the University of Arizona as a distance learning program. Residents are even busier than medical students because they take care of patients in the hospital and clinic, but we have been able to integrate 200 hours of training in integrative medicine, which includes prevention, self-care, chronic disease and acute disease management, motivational interviewing, behavioral science objectives, botanicals, nutrition, physical fitness, and so forth, across the board in the residency, relatively painlessly through online modules and short lectures, and it fits with their need to learn what they need to learn for their board exams and in training exams. So that is a strategy, and certainly the time barrier/resource barrier is always there, but if you are persistent you kind of get things done.

I'll add, too, Jeff, that we are doing a survey right now of the 42 centers that are part of our Consortium of Academic Health Centers for Integrative Medicine, of what curriculum they are all doing as far as medical school and residency. So that survey should be out sometime within the next month or so, and we are going to really have, then, a very comprehensive catalog of what people actually have been able to

implement at their various schools.

The Consortium of Academic Medical Centers

JB: That's a really interesting segue, Vic, because I wanted to get your, kind of, insight. I know a number of people have heard of the Consortium of Academic Medical Centers, but probably don't know the root origin of it, or what its principles are, or what its objectives are. Could you tell us a little bit about it?

VS: Back in, I think it was '99, eight schools decided that they had some interest in this area and they had a retreat. Jon Cabot Zinn, the founder of mindfulness-based stress reduction; Andy Weil from Arizona; Jim Dolan, who was the Dean (I think) at Massachusetts at that time (although it could have been Arizona); Ralph Snyderman; and some other folks from these different schools sat around with deans of their schools and had a discussion on how this area might proceed. And during the discussion (according to the folklore, at least) the lights went out, so they had to sit around with candles and Jon said, "Well, let's just have a meditation session." So they left with that idea that they would try to build a sufficient number of schools with projects and interest in research, clinical, and educational areas in integrative medicine so that we would have a voice within the medical establishment. Arbitrarily, they picked somewhere around 25{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of the schools (there are 130 medical schools now--17 in Canada, 130 in the US, plus the DO schools). We have exceeded, now, over the years, that 25{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} metric, so we've got a substantial voice in the academic setting. The schools are not only in Texas and Arizona-we have many of the Ivy League schools, such as Harvard and Yale, Duke, Stanford, and really some of the top schools in the country are part of our Consortium, as well as four in Canada. It gives us a chance to look at policy, we look at educational initiatives to research collaborations, clinical models, as a larger group, and not feel like we're out there rowing upstream in a single boat, but it is really a rowing team.

JB: I know you just finished up a tenure as...you know, probably you give the new jobs to the person that is most busy...so you got the job of being the Director of this Consortium over the year. What was the learning curve for you?

VS: I'm still in that position until the end of this year, and then Adam Perlman, who is my vice-chair is going to take over; it was a two-year term. The learning curve for me is somewhat personal. When you are working with people in a very large context like this it is very important to be inclusive. I have always been a bit of an impatient, non-procrastinating person. When I see something that needs to get done I just like to charge ahead and do it. But when you are leading a large group like this, it is very important to get input from the largest number of people; to get buy-in and cooperation, otherwise you end up do everything yourself and it doesn't go very far.

JB: I notice that you've got some support from the Bravewell Collaborative, which is another interesting, really, I think, innovative group. Maybe you can tell us a little bit about Bravewell and the connection to the Consortium and this whole evolving movement.

The Bravewell Collaborative

VS: This group started, as I said, with 8 schools and then maybe grew to about 10 or 12 by 2001. At that time it was called the Bravewell Philanthropic Collaborative for Integrative Medicine; now it is just called the Bravewell Collaborative. This was a group of wealthy people who were highly committed to

integrative medicine: Ken George and Bill George, who was the founder of Medtronics; Christie Mack and John Mack (he's the CEO of Morgan Stanley; and I think about 20 other philanthropists, similarly placed across business and industry, with wealth that they really wanted to commit towards integrative medicine's development. So among their projects-and they have a number of projects, including seeding some clinical sites, and helping, actually, with the recent Institute of Medicine Summit-was a project to support this Consortium of Academic Health Centers, which at that time was 12 schools. With their support for infrastructure (for maintenance of an office, a website, some travel, and so forth), we've been able to grow very quickly, now (over the last 8 years), to 42 schools from 12 schools. They have been enormously supportive-very, very beautiful people that have just strong hearts about the need to change medicine, and they really want to use the Consortium as a tool to really change the educational culture, and the content, and the process of delivery, and the way that doctors are trained at pre-doctoral and residency levels. They are most concerned about the medical school curriculum. They continue to be our partners, and we are so grateful for the Bravewell Collaborative.

The Institute of Medicine

JB: You've done a beautiful job of taking us down this path because you mentioned the Institute of Medicine Summit, which I believe is, by all accounts, kind of an epic meeting that was just completed in February of 2009, in that we were told it was the largest Institute of Medicine meeting ever held at the National Academy of Sciences. You were one of the principals in developing the curriculum and organization of the meeting. Tell us a little bit about how that connected to Consortium, Bravewell, and this whole evolving movement, and this time of great change.

VS: Sure. That definitely was a capstone meeting. As you know, Jeff, there has been a series, over the years, of symposia. The original conference in this zone was the Chantilly Conference in Virginia back in the early '90s. That seemed to be one of the things that led up to the formation of the Office of Alternative Medicine. Under the Clinton administration, the White House Commission on Complementary Medicine Policy worked to develop a report. The Institute of Medicine also published a report on complementary medicine in the United States about 4 or 5 years ago. So there has been a number of these kinds of major, state-of-the-field initiatives. It was felt to be necessary now (given the current change in political opportunities) that in changing health care, there could be some kind of a major focus that not only looked at integrative medicine from an educational standpoint and practice standpoint, but really from a potential policy change standpoint. So this was a brainstorm of the Bravewell group; they approached the Institute of Medicine-I think it has been, Jeff, a couple of years in the making-and said, "If we put together a summit on integrative medicine and public health, can we partner with the Institute of Medicine?"

The Institute of Medicine, for those who aren't familiar with it, it is a part of the National Academy of Sciences. It is not part of the government. It is purely a scholarly group. It is highly prestigious; if you are a member of that academy, you are respected by your peers throughout the world (lots of Nobel Laureates and top scientists and so forth). So the Institute of Medicine is a subgroup of that, which just focuses on medicine. Other academies, like engineering, and so forth, are there.

The Bravewell folks funded (or co-funded) this with the Institute of Medicine, planned it over this period of time, and actually still has a lot of planning and outreach media follow-up in process. But the general idea was to bring people together from all areas of health care (stakeholders). They included physicians, people like us from academia (we had over 50 attendees from the Consortium, for example), people like you, Jeff, that are in the research and education realm, certainly people from insurance, from business,

researchers, and we tackled about 5 major areas of health care with panels and white papers. They had kind of a vision for what health care might look like: issues of research and the science behind integrative medicine, clinical models, workforce and education, and, finally, economics. So over the two-and-a-half days, we had people from all over the world. Over 600 people attended; it was free to attend, but you had to register in advance, and they had over 200 people on the wait list because they were just oversubscribed.

It was extremely well organized. I was on the planning committee. I say it was organized not because I was on the planning committee, but I saw it start from ground zero and it was just amazing how it became very interactive. The audience had a chance to participate. There were a number of breakout groups. And there will be a proceedings published in November. For people that have an interest, if you go to the Institute of Medicine website (just dial up the Institute of Medicine on Google and put in "integrative medicine"), there is a list of the commissioned papers there, the agenda, and, as of tomorrow, there are video tapes that will be posted of all of the sessions, so you can watch any of the sessions. So the Consortium played a very important role with that. Like I said, we had over 50 people, and all of the commission papers had some member of the consortium on them. We had 7 or 8 of our folks on panels or as keynotes. The summit came during the same time that President Obama is talking about the need for prevention and lifestyle change as part of the basis of good health care in this country, and on what health reform might look like. This group really brought a tremendous amount of experience and practicality to the table, and I think we'll, hopefully, have a major influence to bring more focus on integrative medicine into the health care reform scenario now.

JB: I really want to support and second your acknowledgement as to what a watershed meeting it was. You know, I'm kind of a consummate meeting-goer for many, many years, and I think it was one of the best organized and also visionary meetings that really developed collaboration among people of disparate fields in ways that I hadn't seen in other meetings. I think what will come out of that in the monograph should be very remarkable. Simultaneously, as you know, there were the Senate hearings on integrative health care for a healthier America. Senator Harkin, who spoke at the IOM meeting on Friday was, I think, one of the most visionary...you know, kind of "integrative thinking" in his own presentation. He was one of the principals in the Senate hearing. I found it interesting and I'm sure you have as well, Vic, this point-counterpoint that we have in society, which I think is good because it kind of distills some of the debates down into a central theme. What we see is, on the other side of the house, people saying that nothing has really ever happened that is good out of NCCAM other than to prove that alternative and complementary therapies don't work and that Harkin has been a handmaiden for unscientific medicine, and that these things are really all just taking us in the wrong direction; we should stay where we really know what we are doing and not wander off into voodoo medicine. You've probably seen the websites that are now propounding that this week. Do you have any thoughts about that point-counterpoint, or do you think that's just all part of the healthy argument?

Senate Support for Integrative Medicine

VS: You bet. First of all, I'm enormously impressed with Senator Harkin's vision. Just a couple of simple examples of things that he has done, besides starting the Office of Alternative Medicine: he started a program (he is from Iowa, as you), and he looked at Iowa and a few surrounding states and looked at underprivileged schools, and put together a free fruits and vegetables program for 100 schools. He had a little hassle doing that. People thought the kids would throw apple cores at each other, which, of course, I never did when I was a kid. It was so successful. Many of these children had never eaten a fresh orange or

apple; it was always other kinds of food. He was able to improve the attitudes and the nutrition of those kids, and now he has expanded that program to a billion dollar program across the country to get fresh nutrition into these schools.

He has also taken on the vending machine companies that are in schools selling junk food, and has been able to replace high-fructose-corn-syrup-based drinks, which fuel childhood obesity, and all these high-carbohydrate sugar snacks. So the man...he's the third-ranking member of the Senate's Health Affairs Committee, and he has a vision and a passion for this work like no other.

The other thing that I believe that Senator Harkin really gets, and this kind of replays a conversation I've had several times in the last week with the media and at the IOM, is that moving around how we reimburse health care right now is like moving deck chairs on the Titanic. Unless we do some fundamental change in the way that medical care is delivered, we are simply feeding an ever-increasing beast that is unsustainable in terms of cost and indefensible in terms of patient outcomes. The problems that we have are based primarily on our avoidance of basic lifestyle changes that are necessary to support good health and prevent disease with the kind of Pollyanna-ish expectation that when we get our heart attack there will be a technological cure for it, and when we get cancer we'll be able to fix that. So we end up disproportionately rewarding specialty care. Over 60{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of physicians in this country are specialists; less that 40{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} are primary care; less than 5{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of students now (medical students) are going into primary care because it is not adequately reimbursed, and the lifestyle of the primary care doctor is very strenuous, trying to manage in the face of the fact that you can council a patient for 30 minutes on their diabetes and maybe make a $100, but if the hospital cuts the person's foot off for diabetic gangrene, they make $10,000. It is just a disproportionate share going into secondary tertiary care that could have been prevented. So I think Harkin really gets it. Unless we change our workforce and our policies of reimbursement, no matter how we rearrange how we are paying things at the top, it is going to be unsustainable. That's a piece where this counterpoint, I think, needs to come out and people need to understand that you have to change the paradigm. I think patients understand that now. It is not just those of us in medicine and academia that realize that the model is not working.

JB: That leads, obviously, to maybe a final question on this path that we're on (not to say that the journey's over, it is still continuing), but operating system. How do we encode all of these things into a system that respects and really has reverence for the body/mind connection and the environment and still recognizes the biology, physiology, and some of those things? I know you have been evaluating looking at the functional medicine model. Do you have any thoughts as to whether that's a part of a bridge that builds the structure among these different things?

VS: I think it is essential and I addressed it in my keynote vision statement when I was at the IOM. In a sense, it is part of the solution to the primary care quandary. If we broaden the base of primary care practitioners to nurse practitioners, physician's assistants, complementary practitioners (naturopaths, chiropractors, etc.), and physicians who have a different level of training then end up addressing more complex problems. This ends up often being this poly-factorial systems biology approach that functional medicine does so well.

I had a patient this morning, Jeff, who came in. She was a 40-ish year-old lady from Germany and South Africa (both places), had three kids, and just had a diffuse number of symptoms that were disposed of by her preceding doctors by a recommendation that she take an antidepressant. She had fatigue, brain fog, emotional lability, constipation, easily cold, decreased libido, some depression, poor sleep, and everything seemed to start 10 years ago, when she had some change in her hormonal therapy. We took a careful dietary and lifestyle history. This was a great opportunity for my student to learn a systems approach to biology. I talked to this lady for probably 90 minutes (fortunately I had that today), but was able to kind of create a story for her that she understood that her problem wasn't a single thing; it wasn't her hormones, and it wasn't mood, and it wasn't her structural problems with her back surgery, but it was a combination of things. I think that is where she could have gone to 10 different specialists. She could have gone back to orthopedic clinic and the pain clinic, and the endocrine and the gynecologist. We are generalists, by disposition, to step back and look at it from the high altitude of instead of 8 different organ systems we have 8 potential windows into the body's function or dysfunction. And you can keep people like that from overusing healthcare resources, having adverse events from too much testing or too much medication, so that's where this systems biology is the cutting edge that links that high-touch with high-tech medicine.

JB: That's beautiful. I'd like to close with one last question (I could go on, I know). This is an open-ended-probably colloquial-question, but maybe you could give me a sound bite. You alluded to the patient's story. I'd like to go down to the reason for being for medicine, which is the patient, ultimately. Not for the doctor, not for the technology, not for the reimbursement company. We go to the primacy of the patient at the center of their own healing opportunity and then we talk about the therapeutic encounter. How does all of this-from your experience, Vic-really translate down into that seminal moment of healing? How does the patient relate differently from your experience to that which would be more related to disease diagnosis and treatment of traditional kind of approach?

VS: You bet. Just let me follow-up with this example that I was just talking about. This lady looked at me and she said, "I've been to so many doctors and they don't hear me. I tell them things and they don't listen to what I'm saying." So I looked her in the eye, and I said, "Okay, you tell me what it is that you feel these other doctors are not hearing you say." Then she kind of went down her list of things. You could visibly see she was relieved. So I take the next step, and I say, "What do you think is wrong and what will it take for you to heal?" So that involves the patient at the sensor-the nexus-of the healing event. It is not something that is done to them, it is something that is done in collaboration with a trusted advisor who can be a primary care doctor, or a specialist doctor, or a non-physician that has other healing tradition.

JB: We are really talking about collaboration versus judgment, I guess. Or it is some kind of a different nature of the relationship from which the context of healing can occur. I guess that's really applicable to almost any center. It could be in surgery as well as an outpatient clinic, it seems.

VS: You bet. But one of the things I've learned from the functional medicine training is that that patient's story is nodal. Sir William Osler said it takes at least 30 minutes for the patient to really tell their story, and that was over 100 years ago. I don't think it is anything less than that now, and probably is later and if you get on their side of the table and listen to their story, they'll tell you their diagnosis.

JB: Dr, Sierpina, I want to thank you. What an insight; I can see that your patients love you. You bring that quality that everyone looks for when they define a good doctor. And your constant quest, and

willingness to continue to learn, and push at the edge, and refine, interpretively, the model...it's a model for all of us. Thanks for all of your work. Thanks for your leadership. And thanks for your friendship.

VS: Jeff, thank you for everything you've done over the years to bring this whole idea of systems biology into health and healing that helps bridge the sciences of biochemistry, molecular biology, genetics, genomics into a cutting edge of really helping people manage chronic disease and complex disease that otherwise people throw that hands up at and just otherwise shop from one doc to the next in an ever decreasing spiral of happiness (or unhappiness).

JB: Thanks a million and we'll be checking in with you, and the best of luck in everything you are doing.

VS: Thanks, Jeff. Be well.

I'm sure that you have the same thought after hearing Dr. Sierpina as I, and that is this field that we call integrative functional medicine draws from some of the most remarkable minds. These are people who have had experience in the field and continue to question and answer the problem of why people get sick and what to do about it and are willing to have a non-judgmental view of that which works. They keep their minds open, and-I would call it-have neuronal plasticity, or the willingness to accept new information, and look at actually what does work-not what is presumed to work, but actually what does work.

It is really extraordinarily heart-warming to hear someone like Dr. Sierpina talk about his experiences as a family physician, working through his experience with patients, learning from his patients, and ultimately seeing how this system of healing fits together, and that the context of healing is more than just the absence of disease. And it is more than just treating the diagnosis. It is setting up the healing environment. I think that is a unifying theme that seems to tie together so many of the leaders in this field. We recently heard from Dr. Berman about his work at the integrative medical program at the University of Maryland School of Medicine, and now Dr. Sierpina. We've had the opportunity to hear from Dr. Wayne Jonas, past director of the National Center for Complementary and Alternative Medicine and now the director of the Samueli Institute. The characteristics that tie these individuals together seem to be kind of common threads in the field of looking at the context of healing, the context of disease, the context of ill health and finding the appropriate ecology for the patient, personalized to their need that draws together diet, lifestyle, environment, past histories, antecedents. This is the underpinning, really, of the functional medicine model. As much as we can take away specifics, I think we can take away the more general theme that seems to embody and characterize this field of good medicine. We thank Dr. Sierpina for once again guiding us in that direction.

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