July 2010 Issue | Pamela W. Smith, MD, MPH

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Welcome to *Functional Medicine Update*for July 2010. We're going to be focusing our interest and intention this issue on successful (or healthy) aging and its relationship to functional medicine. We have a marvelous discussant interview this month"Dr. Pamela Smith"who will be sharing some of her extraordinary contributions, both as a clinician and as a curriculum developer and post-graduate educator in this whole area of successful aging and the implication to functional medicine.
I returned, a month ago, from the Institute for Functional Medicine's 17th International Symposium, which was at the La Costa Resort in Carlsbad, California. What a remarkable meeting of people/excitement/innovation/adrenaline those four days were, under the title "Confronting Cancer as a Chronic Disease." This was a very interesting topic with extraordinary contributors looking at ways of managing malignant oncogenic disease successfully.

This follows very nicely from last month's *Functional Medicine Update*and the extraordinary discussion we had with Dr. Halsted Holman about chronic disease. We talked about the need for a new clinical education, and how we need to look at various aspects of biomarkers to assess the soil of a person's physiology, so to speak, as to the appearance of a disease, or the progression of a disease. I talked a lot about biomarkers last month.

We recognize that biomarkers can come in many different flavors and be used in many different ways. Cancer biomarkers may differ slightly from those of what we might call cardiovascular biomarkers, or diabetes biomarkers, or arthritis biomarkers. But in some senses the biomarkers that reflect distorted physiological function have some confluence and convergence and they tend to overlap at principal fundamentals of distorted physiology that are shared among these different disease types"things like inflammation, and altered serum lipids, altered insulin and insulin signaling, changes in cell mitotic activity, changes in autoantibody levels. These are representative of alterations that occur across many different disease entities that share a common soil in their mechanisms (so-called systems biology).

We might think of a biomarker as having a single disease focus, but sometimes it may have multiple comorbidities to which it is attached. For instance, rheumatoid arthritis can be connected to cardiovascular disease, which can be connected to osteoporosis, because they share common mechanisms that are associated with altered cellular signaling and proinflammatory mediators. We also see inflammation connected to type 2 diabetes. This web of interaction makes biomarker analysis very, very important as we start to try to understand how we can assist individuals to lower the risk to disease and improve their function (i.e. engage in successful healthy aging).

What type of data would we like to assemble in patients to start to evaluate serially, or longitudinally,

how they are changing over time at the physiological level? This could include things like cognitive tests. This could include memory tests. It could include things like peripheral neurological tests, reaction times, gait disturbances, balance, visual acuity, hearing acuity, skin elasticity, and cardio/respiratory parameters, including things like pulmonary testing like FEv1, pulse rate, blood pressure. All of these become part of a collection of observables that tell us something about the functional capacity of an individual.

Those observables can then be coupled with genetic markers. We're now looking at various SNPs that cluster themselves together as relative risk factor markers for the susceptibility to certain conditions. Or more importantly (maybe), we're even looking at how these genes are expressed into genetic expression patterns in RNA, or through the transcriptome ultimately into the proteome. We measure, then, the connection between altered gene expression patterns that ties to gene susceptibility patterns. That then ties to altered proteomics. The presence of certain proteins like hsCRP (high sensitivity C reactive protein in the blood) are a connection to gene expression associated by TNFalpha-modulated inflammatory gene expression, which then may tie back to certain susceptibility SNPs that pertain to increased or heightened sensitivity to inflammatory initiation.

We are asking, "What are the inflammatory initiators?" Are they things like substances in food, air, and water; chronic infection; bacterial cell wall debris? What are the precipitants? Are they heavy metals, toxic xenobiotics? This conceptual framework--to understand at the earliest level possible where the confluence of these various distorted parameters arise, both symptomatologically and biochemically--becomes the kind of teaching system, or evaluation system, of functional medicine. It is ultimately incorporated into what is called the functional medicine matrix. It is requesting or querying these various areas within the patient's physiologic function that cut across different diseases to correlate with poor outcome and unsuccessful or unhealthy aging.

All of these questions really become part of collecting information using tools likemolecular imaging or whole-body imaging. Radiology has now become part of functional assessment: using CAT scans and MRIs, and using various types of NMR data to evaluate functional capacity of various organs. We look at things like stress testing--going from the exercise EKG test into thallium scans and into electron beam, looking at calcium foci in the arterial wall, and looking at heart wall motion studies, and looking at insulin clamp, or things like vascular endothelial function using flow-mediated dilation or carotid intimal media thickness as a measure of potential atherosclerotic progression. All of these become a new arsenal of tools that the physician can use to assess aspects of this trajectory towards disease. We were talking about in this June issue of *Functional Medicine Update*.

What about inflammatory biomarkers that seem to be related to so many chronic diseases? These would include the use of blood cytokines as biomarkers, which are now undergoing preclinical safety assessment and sensitivity evaluation to see if, in fact, these things--IL-1, IL-6, interferon gamma, and tumor necrosis factor alpha--can be used as effective assessment biomarkers for evaluating onboard inflammation along with things like C-reactive protein or fibrinogen.

C-reactive protein is considered a late-phase reactant. It is produced by the liver in response to a message that occurs upstream from activation of cytokines, particularly IL-6. By understanding more about the upstream mediators that are the initiators of the downstream effects, we can get an earlier warning understanding of the general shift in physiology towards an inflammatory state. We can look at things like metalloproteinases and MCP1, or the difference between IL-4 and IL-6 as a contrast between

activation of the thymus-dependent-1 and thymus-dependent-2 trees of the immune system. It gives us much more differential assessment opportunity in understanding where the distortion is occurring in that individual patient's physiology. This is all fairly sophisticated discussion. We are probably still a few years away from completely nailing down how, for instance, serology of cytokines could be used.

There is one reactive molecule that is getting a lot of attention recently, myeloperoxidase (MPO), which is produced by white cells in response to an inflammatory insult and is also activated within the HDL particles to produce oxidant response. The activation of MPO is part of the microbiocidal killing response of the body in immune defense. But myeloperoxidase, when overactivated, also increases oxidant stress, and it associates itself with hypochlorite formation and oxidation. Once again--as is so often the case--we have this U-shaped curve (this parabolic dose response curve): too little is not good, too much is not good, in the middle of activity is where we want to be. Can MPO, myeloperoxidase, be used in serum or in red cells as a surrogate marker for looking at inflammatory status and function? These are the kinds of questions that are now being discussed and evaluated.[1,2] There are some laboratories doing studies on yet-to-be-fully-validated biomarkers and indicating a need for more presumptive testing.

Use A Variety of Biomarkers to Compile Information

We shouldn't put all of our eggs in any one biomarker basket. An example would be phospholipase A2 , which has been used for evaluating endothelial inflammation and unstable plaque inflammation. It's a very useful serological tool. Apo B and apo A-1 are apolipoproteins that we also associate with vascular function. We say too much of apo B and too little of apo A-1 is a shift towards atherogenesis. All of these become an extended group of biomarkers that have been used in some ways for compiling relative understanding of a person's functional status.

Again I emphasize that no one biomarker in and of itself answers all of the questions. It is really compiling these biomarkers as a pattern"a system"to look at interrelationships. Homocysteine would be a good example of this. We know that elevated homocysteine can be sometimes seen just as a consequence of inflammatory disorders, in which altered methyl group physiology occurs and you start to get an activation of the folate cycle at an increasing level of homocysteine, and when that person has managed their inflammation their homocysteine comes down, independent of their need for folate B6, or B12 supplementation.

These are complex relationships to physiology. How we use these tests "again" shouldn't be an all-the-eggs-in-one-basket approach. One test cannot provide a complete understanding of the patient's physiological status. Rather, we need to compile multiple snapshots that we weave together to form a total picture of the patient and their trajectory toward health or disease. That's what I think the more advanced functional medicine practitioners are doing: assembling this complex data set of information, doing pattern recognition, focusing this through the functional medicine lens to understand the individual status of that patient and develop a personalized program for their intervention. I think I'm speaking to a very different model than using a single analyte (biomarker) for a single diagnosis for a single drug for a single outcome. This is a very, very different model.

We learned about this model, very eloquently, at the 17th International Symposium from Dr. Dean Ornish, who was a keynote speaker and actually won the Ava Helen and Linus Pauling Award in 2010. As you probably recognize, Dr. Ornish's contributions have been multi-fold. He is one of the first people to really do the heavy lifting to demonstrate that lifestyle intervention with an appropriate and minimally

processed diet with exercise and stress reduction programs done in cooperation with one another has a tremendous impact on outcome of gene expression, of proteomics, and of metabolomics, and actually can result in the regression of existing things like atherosclerotic plaque, and can have a positive effect on prostate cancer and on insulin signaling.[3,4,5] Dr. Ornish has done the hard studies, with humans, to really demonstrate that what Pritikin talked about many years ago, which was more anecdotal and observational, when put to the more rigorous test of study and proof of concept can be demonstrated to be true.

Lifestyle medicine, as we are seeing it emerge, is becoming an extraordinary "re-found" tool. It's like learning old things in new ways, and is probably the most effective and certainly the safest way of managing many of these chronic disease entities. In fact, Dr. Ornish announced at the Symposium that after 16 years of developing the literature and the studies to prove the concept, the Office of Medicare Reimbursement has now agreed to reimburse for these lifestyle medicine intervention trials or programs/therapies for individuals with cardiovascular disease.

I think we are really starting to see very, very significant progress being made in understanding how to promote healthy or successful aging by asking the right questions and then intervening with the right personalized therapy, much of which may be at first initiated through modified lifestyle, diet, exercise, and stress management programs. Dr. Ornish said a series of very profound takeaways. One is that "diet" is a four-letter word, and if you talk to people about putting them on a diet there's going to be a pushback and almost a reflex reaction towards noncompliance. If you talk about an eating plan, a food plan, about eating healthy, about eating in abundance, eating with joy, and eating from this list of good stuff, it is amazing how much better the compliance and how much the attitudinal adjustment of the patient improves. They become part of their own program rather than feeling it has been forced upon them because they are being punished. I think those are very interesting things that we learned from Dr. Ornish's presentation.

He also made the very important point that awareness really is the first step in healing. If you don't have a self-aware patient, if they are not conscious of the fact that they are in control of their own physiology to some great degree, it's going to be a real uphill grind to get them to truly subscribe to healthy aging. They may still be looking for the proof in the bottle"what pill will be the answer to all these problems, make it simple, and they can continue to do whatever they have been doing that is self-destructive and anti-evolutionary? Awareness that they are the master of their own universe is actually the first step in their own healing process.

He also made a very, very interesting"I think"visual contribution to our sense as to how this field works. He said, "Let's look at the difference between illness medicine and wellness medicine." Looking at the spelling of illness medicine-"i-l-l-n-e-s-s""as contrasted to the spelling of wellness medicine""w-e-l-l-n-e-s-s""he said, "Illness medicine is "I-ness" medicine, and wellness medicine is "we-ness" medicine. Wellness involves the group support. It involves collaboration. It involves a different environment. It involves normative behavior patterns within your peer support group"your family and friends. That's a "we-based" medicine"wellness medicine"as contrasted to "I-based" medicine, where it is treating disease, fighting the battle, you against the onslaught of this disease in isolation. I think that's a very, very interesting metaphorical differentiation between illness, or disease-based medicine, and wellness, which is the functional approach towards improving outcome (not just treating a biomarker, but really enhancing the functional quality of life of the individual; that's so-called healthy aging).

Genotypic Stratification and Individualized Risk
In the course of these discussions, we recognize that the whole field of health risks is changing, as Dr. Nancy Emenaker talked about in her presentation at the Symposium. Epidemiology, which has been kind of the guiding force to look at variables in our life that create potential relative risk to disease, is giving rise to things like genotypic stratification, where we are looking at individualized relative risk, or individualized risk, based upon the genes and their interrelationship with the environment of that patient. This concept gets away from the 70 kg human"one size fits all, everything is about averages"to actually looking at this cohort stratification around individuals that share common genetic propensities or susceptibilities. I think that's a very, very important step.

Think about what Dr. Bernadette Healey gave us, through being the director of the NIH a number of years ago during the Women's Health Institute work, and really taking the Women's Health Initiative and moving it forward to try to evaluate the gender differences between men and women. This was kind of the first big cut of stratification--seeing that men and women do differ physiologically and that women need to have different intervention. Women have a different type of heart disease than men. They have, obviously, more prevalence in endocrine-related dysfunction, especially with breast, endometrial, and ovarian function. They have different relative risk to osteoporosis and so forth. These are characteristics that relate to gender stratification, which then can be taken beyond that to stratification at levels of other specific genotypes.

Public Health versus Individual Risk
At the Symposium we also heard from Dr. Gina Solomon, who talked about the difference between public health and individual risk to diseases like cancer. We have these public health messages"seat belts, and pap smears, and immunization, and cholesterol screening, and blood pressure screening"but then we need to take it down to the individual relative risk. I talked a little bit about the fact that individuals are exposed to different things in their environment and they may have different relative susceptibilities based upon their genes. In fact, we are going hear from Dr. David Jacobs on *Functional Medicine Update* in the August issue, next month, who will be talking about the pioneering work that he has done with Dr. Duk Lee, looking at the relationship between environmental xenobiotics and type 2 diabetes in susceptible individuals, which I think is a very fascinating story that really talks about individualization of relative risk.

Vitamin D as an Example of Balance and Consideration of Complex Variables
At the Symposium there was a discussion of vitamin D, this very interesting, complex, regulator of gene expression and cellular function. Once again, too little is not good, but too much may not be good either. I think we need to keep these things in balance"there is always this nature of the push and pull, yin and yang.

What do we know about vitamin D? We know that vitamin D is converted ultimately into its active hormone form, 1,25-dihydroxyvitamin D3, and it interacts with the vitamin D receptor (VDR) to heterodimerize, ultimately, with nuclear orphan receptors at the nuclear envelope to then regulate promoter regions of genes (probably more than 50 genes). Vitamin D, in its hormonal form, regulates gene expression that ultimately alters cellular function. Some of these activities are involved with immune function and cellular proliferation.

High levels of 1,25-dihydroxyvitamin D3 might be considered an immunosuppressant in terms of certain

arms or components of the immune system This is why it might lower relative inflammatory disorders. But too much suppression of the immune system by excessive 1,25-dihydroxyvitamin D signaling, as we heard from Trevor Marshall in *Functional Medicine Update* a number of months ago, could actually compromise immune integrity against viruses and bacterial infection, so you might have increasing risk to opportunistic infection. It might also increase risk to proliferative disorders like cancers. This is the yin and yang of vitamin D: taking it in the appropriate amount and converting it into the appropriate levels of 25- and 1,25-dihydroxyvitamin D3.[6]

What happens in cases of inflammation if that individual has a proliferative disorder or a proliferative situation? Probably the most common example of a proliferative situation is that of pregnancy. In pregnancy, there is obviously a growing tissue mass (a differentiated fetus). Because that fetus is a foreigner in the mother's body, there is an obvious alteration of the immune system to allow that fetus not to be rejected. Part of that process is to convert more 25-hydroxyvitamin D into 1,25-dihydroxy. So there is alteration in vitamin D chemistry that occurs in the case of pregnancy. Low levels of 25-hydroxy are associated with small for gestational age children, whereas adequate vitamin D levels are associated with gestational age births.[7,8] It has been suggested that there are some things about vitamin D deficiency or insufficiency that might be altering pregnancy. One needs to be in that mid-range and not assume that the more the merrier as it relates to these fat soluble hormonal stimulators.

You may have heard recently about this tragic situation with Gary Null, the well-known nutrition devotee who basically was in a life-threatening situation as a consequence of eating some of his own food that unfortunately had been inadvertently contaminated with excessive vitamin D. Rather than 2000 IUs they had 2 million units. He ended up with extraordinary hypercalcemia, and cardiac calcification, and immunological suppressive disorder, and was very seriously ill. He is recovering, but it is probably going to be a long time back from this acute vitamin D toxicity.[9]

I'm using an extreme example here just to try to remind us that these things have very profound effects. These are very biologically active molecules, these hormonal forms of vitamin D. It is not just low levels we should be concerned about, but excessive levels as well. In fact, there is a suggestion that 1,25-dihydroxyvitamin D3 could be very useful in mothers that are deficient to prevent spontaneous abortion because, as I said, it produces a modulation of the immune system that is desirable for patency of the fetus.[10] Too little not so good; too much obviously not so good either. That's kind of a watchword for all of the things that we use"intervention agents"when we are trying to promote improved health or healthy aging.

What about all of the biomarkers that are associated with vitamin D physiology? What would those be? Let me give you my opinion. Those include things like serum 25-hydroxyvitamin D (that's the analyte you normally measure to determine vitamin D status), but what about the hormonal form, serum 1,25-dihydroxy? It has been said, "That changes so rapidly that it might be not a very fixed number." But that's part of what we want to know: how vitamin D is being converted into its hormonal form. Making serial measurements at the same time of the day on a fasting blood sample of 1,25 along with 25-hydroxy might be very useful. We don't want the ratio of 1,25 to 25-hydroxyvitamin D3 to be greater than 1.5 to 2.0 to 1. If it gets above 2 to 1 then you start asking, "Is there inflammation onboard? What's promoting this increased conversion?" Often what might happen is the person would say, "Their vitamin D is low because their 25-hydroxy level is fairly low." They keep supplementing and the person's 25-hydroxy

vitamin D doesn't go up. You ought to be looking for the 1,25 level to see if it is being driven or converted into the 1,25 hormonal form due to agents on their physiologic function that increase or stimulate the conversion. Generally these are substances that activate cytochrome P450 27B1 in the kidney that is associated, then, with increasing conversion of 25 into 1,25-dihydroxy. There are many environmental factors and inflammatory factors that activate the expression of SIP27B1 and increase the conversion of 25 to 1,25.

We also look at things like parathyroid hormone levels. Is it possible that secondary hyperparathyroidism is a consequence of vitamin D insufficiency? Could we use PTH levels to evaluate relative functional need for vitamin D? The answer is yes and no. Studies have suggested only a moderate correlation between PTH (parathyroid hormone levels) and vitamin D levels, undoubtedly because PTH really varies as a consequence of a number of components, only one of which is related to vitamin D directly.[11,12,13]

There is also, of course, total serum calcium and ionized serum calcium. We recognize that calcium can elevate dramatically. In the cases of vitamin D toxicosis, calcium may be low. In cases of vitamin D insufficiency, the serum calcium-to-phosphorus ratio may increase as a consequence of vitamin D insufficiency. It may also increase as a consequence of vitamin D toxicity. I think that's the paradox. Are we on the deficiency side or are we on the insufficiency side?

And then lastly is the vitamin D receptor story. There are different polymorphisms of vitamin D receptors and some are much more sensitive to binding to 1,25-dihydroxy than others. There may be receptor genetics that would be helpful in understanding the relative sensitivity that that person has to their own vitamin D by transport by the VDR into physiological function.

Those are some thoughts about the vitamin D story. One of the things, clinically, you should probably be aware of as we talk about the vitamin D story is the hyperparathyroid/vitamin D/gastric bypass story. We recognize now, with obesity on the upswing as rapidly as it has become and with more and more people having gastric bypass surgery, that as they get into things like Roux-en-Y gastric resection there is very often found to be malabsorption of vitamin D and a low level of 25-hydroxyvitamin D, and this can present a negative outcome for the patient. I think in cases where there is a malabsorption syndrome present, as might be the case with Roux-en-Y or maybe even gastric banding, that we be very mindful of the vitamin D levels and make sure that adequacy is achieved.[14]

INTERVIEW TRANSCRIPT

Clinician of the Month
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I think I have been on a very, very remarkable roll over the last couple of years with the types of people that we've been able to interview, who are really the pacesetters, the leaders, the vision tenders of this new medicine. Certainly that is the case this issue with our interviewee, Dr. Pamela Smith.

The name "Pam Smith" probably is very familiar to many of you if you've been in this field for some time. She is a clinician's clinician, and has extraordinary accomplishment in building a practice in Michigan (actually several practices, several different offices). She was graduated from the Wayne State-affiliated hospital group, and became internal medicine board certified. She spent time first at Meharry Medical College, and later became committed to getting her Master's in Public Health at the Medical College of Wisconsin in the 90s while she was running her practice.

This is one of those universal energies that you find in some people. You wonder, how do they do all of these things? How do they form their life in such a way as to create this kind of driving continuity of growth, and development, and constant expansion of understanding? Pam is certainly that kind of person. She has most recently (over the last decade) been extraordinarily involved in the development of curriculum and teaching and training. You are going to hear much more about that. I don't want to steal her thunder, but she has really been instrumental in moving physician education into this whole area of functional and, I guess you'd call it, integrative and complementary and anti-aging medicine"the real tip of the spear"developing a very high quality education program/certification program to help people move their practices into what we think is right way to do medicine (good medicine) in the 21stcentury.

With that introduction, Pam, it is just such a treat to have you here today in our studio in Gig Harbor, Washington, coming all the way from Michigan and Florida, which I know you spread your time between. Tell us a little bit about your extraordinary run over the last 25 years. How did you get started in this field"I mean moving from maybe a very traditional medical view into now becoming really a leader in our field?

How Insomnia Led to a Change of Direction

PS: I was very happy being an ER physician at Detroit Receiving Hospital, which was a trauma center, until one day I could not sleep. I had never had any insomnia whatsoever, and for an ER doctor that's a problem because you have to change shifts between night and day. I went to 11 physicians, and they all said the same thing: "Take a sleeping pill." The last one was psychiatry. After two sessions the psychiatrist said, "This is not psychiatric. Please just take a sleeping pill." I was very lucky. Dr. Shelby-Lane, who was my ER partner, saw that there was going to be an interesting conference on anti-aging medicine featuring hormones. We thought we'd just go see what it was about. There I was. Second slide, second sentence saying, "Women without progesterone frequently have insomnia." I did the very first saliva test in the Midwest. I was very lucky that the pharmacist at the end of my block where I grew up was a compounding pharmacist. I had no progesterone at all on my saliva test, so what I did was I worked with my compounding pharmacist, started taking progesterone, and within 48 hours slept like a baby.

Of course this got me very interested in looking at the concept of why we never look at the cause of the problem. We just write out the golden prescription, which is fine, but it doesn't really answer a lot of questions. And fortunately, the science is now here to look at the cause.

JB: I think you have done something that is very complicated for most individuals, and that is bridge the gap between the mechanistic world and the clinical world (you know, where the tire meets the road"patient management). And this area of"I guess we call it functional endocrinology, or bioidentical hormones, or managing the web of physiology"is probably the most complicated place to jump in because you've got so many different components that are all interacting one with the other and with the patient's past (antecedents, triggers, mediators, signs and symptoms). Trying to figure that all out in this milieu is

not an easy job. How did you go about kind of teasing apart and gaining the mastery that you have? Was it through experience with patients, education, reading? For those who may be on their path, what was your path of discovery?

PS: It was a little bit of everything. I went to a second anti-aging conference and learned a lot more about hormones, but I discovered that wasn't the only answer. I was very fortunate at that time to become involved with IFM, and really learn that there was a whole other facet to what we did. It wasn't just prescribing hormones, because that would be just the golden prescription again. I really discovered that most people, honestly, don't need bioidentical hormones. If we are never stressed, then our body, after menopause or andropause, really does make an adequate amount of hormones to maintain function. However, I don't really know a lot of physicians that are never stressed. Because all of us do stress our adrenal glands probably to the max, many of us do need bioidentical hormones. But it was a fascinating road to go down with IFM and learn the web"everything is a web, including the hormones"and then go on to look at structure, spiritual health, and all the other facets.

JB: When you are in your practice...you know, we kind of self-select patients that affiliate with our world view. Have you watched your patient type or population change over the years as you have been on this path? How would you characterize, now, the types of people that seek out your care and your practice?

PS: When I first started this kind of medicine 14 years ago, I ended up mostly with patients looking for bioidentical hormones, I think because that was my area of expertise, plus my first book, HRT: The Answers, was on hormones.17 However, now my practice has really evolved. It's about 40{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} bioidentical hormones and 60{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} functional medicine. It has now changed from what was originally an all-female practice, because women seek health care more than men, to now being 45{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} male, 5{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} children, and 50{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} women.

Treating "Walking Wounded" Executives
JB: In that distribution"which, by the way, that's a whole textbook in and of itself, writing about the diversity of challenges for care"I would presume you probably are seeing people who might be considered executive health clients who are kind of in that walking wounded state (stooped shoulders and shuffling feet), saying, "When am I going to get sick enough that someone knows what's wrong with me?" kind of mentality. They are probably in the rat race of time compression, the picosecond we live in. Do you see these kinds of executive females and males coming to your practice asking, "What is going on with me?"

PS: All the time. And their universal statement is, "I feel like my body is divorcing myself." In fact, we took an attorney, and I always ask the patient, "What brings you in to see us?" His complaint, at 63, was, "I lost my first trial." I wasn't really sure what I was going to do with that, but what he really meant was he had never lost a trial, but now his memory was not as sharp, he couldn't smooze the jury, and so we worked with him and we got him nutritionally and hormonally sound, and he brought us into his law firm in Ann Arbor, Michigan. We worked with all of the attorneys, ages 50 and above, and increased all of their IQs at least 7 points.

JB: That's exciting. In your bag of tools...that's one of the nice things about this field, it seems to me: we don't have to give away any of our tools; we just can open up our bag and put more tools into it so it is expanding the number of opportunities that we have and diversity for intervention. What would be some of your "go to" areas? You've talked about hormone replacement. Are there other things you have found over the years that really seem to be little gems or pearls in managing some of these problems?

PS: I truly wish I had understood initially in the practice of medicine how important gut health was. I now really understand (I hope!) most of the ramifications, but early on I didn't realize that if the gut wasn't healthy, the patient wasn't healthy. I really encourage people to go back and look at the idea of gut health. When a patient had GERD, reflux, IBS, constipation, diarrhea, this really needs to be addressed. Obviously they are not going to make serotonin well. They are not going to make their nutrients well. The immune system is going to be compromised. But also they won't be able to take on any medications (or nutrients, as well) if their gut is not healthy.

JB: Now we are doing a very interesting little dance because it seems once we move into this arena we start crossing boundaries. There is this kind of siloed thinking in medicine, where you want to stay in your sandbox, and you don't want to go in anybody else's sandbox because you'll tread on their sacred territory. Now we are into gastroenterology. We could be in neurology. We could be in endocrinology. These "ologies" sometimes hold us rigid. Do you have challenges traveling across these boundaries from some of your colleagues, or does it happen fairly smoothly?

PS: Initially we did have some major challenges, particularly from endocrinology. Gastroenterology was a little more open. But the good news is, because we are so science-based in functional medicine, if you have the opportunity to present to the other clinician the science, most people will understand what we are doing.

JB: Let's talk about the lab, because for a lot of individuals, knowing something in a number helps them to understand the state of health they are in. They kind of deny their own feelings until they see a number. Or it might be useful for that person in tracking their performance because we are kind of a quantitative society; we like to see numbers improving. It could be a batting average if you're a baseball player, or your average bowling score, or your cholesterol level. Where does lab play roles in the practice of your health care?

PS: Because I'm a physician, it's really important that we can document what we're looking at in the patient, that they do have a process that needs augmenting or fixing, and it's also important to document that they are doing better (that they are improving), not just for the legal aspect, but the patient likes to see that they are improving as well; it's good encouragement. I always tell my patients, I'm there for 10{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36}. I'm there for information. They're really 90{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of this, and my goal is to guide them, but they have to really do what they need to do to be healthy and stay healthy.

JB: Is there a standard kind of portfolio of evaluative tools that you use, or do you tailor the individual test that you might select (the panels of tests) based on the history and physical and your acumen as you look at the patient and talk with them?

Delivering Individualized Treatment in Practice

PS: Really every one of the patients in my personal practice has totally individualized and personalized care. I don't go in with a preconceived notion. You've read the book, as have I, about how doctors think. I think a lot of us have a preconceived notion and I've turned that part of my brain off. I literally listen to the patient, and I think that's the most important thing that most clinicians have forgotten about. Fortunately, in functional medicine, we do listen to the patient. The patient will tell you what needs to be done. You have to address why they are there, but in addressing their key component"for example, depression or insomnia"you do go through the entire functional medicine matrix, and before that person is really healthy, you will have fixed all of those modalities; it just varies on which one you start with first.

Dialogue: A Lost Art in Medicine

JB: Let's talk about that extraordinary kind of dialogue, hearing the patient's story, which I think is, as you are indicating, kind of a lost art in medicine. If you go back to the turn of the last century and read some of the great medical figures, you'll find that they were great story listeners and great kind of "synthesizers" of information. But one of the things they had was time, which seems to be the most lacking part of our world right now (adequate time). How do you find enough time in your practice? How do you structure the way that the office visits go to get the amount of time to have this dialogue and to hear the story?

PS: Probably the most important thing is we don't take insurance in our practice. Insurance is a contract between the patient and the insurance company, and so we give them a super bill and they bill the insurance company, and the insurance company sends them a check. What that does is it stops me from worrying about the fact that I'm not being paid to see them. My goal is the healthy patient. And the insurance company pays me 5.2 minutes to see the patient. I cannot do individualized care in 5.2 minutes. So we have removed that issue from seeing the patient. Many times my initial office visit will be an hour, even not having done the physical yet, in just talking with the patient and taking a really good history, listening to the patient. Most patients want to talk; they want to tell their story.

JB: It is very interesting. There are themes that probably reoccur as I have the privilege of talking with leaders like yourself. I am reminded of last month when I had the privilege of talking with Dr. Halsted Holman from Stanford. We were talking a little bit about the same theme"about listening and spending the time to really be present with a patient's story. I brought up Lewis Thomas, who was at one time one of the editors for The New England Journal of Medicine and has written a number of best-selling books (one is The Medusa and the Snail), and was very, very much into describing medicine in a very allegorical way. One of his books that was not as well read as others I found fascinating. It is called Medicine: The Youngest Science, in which he really talked about the fact that his father, who was a physician at the turn of the last century, didn't have nearly the tools that we have today"the science-based pharmacopeia"but yet his patients got a lot better.18 He wasn't constrained by insurance, he wasn't constrained by Medicare, he wasn't constrained by a lot of the kinds of institutional things. What he had was a black bag. He would travel to homes and he would sit with people and he would listen to them. Through that process of engagement of dialogue often came solutions.

As you were indicating before, maybe people often really know the solutions; maybe they just need to have them reinforced. They need to have a guide. They need to have a wisdom authenticity factor. As you structured your practices (being spread across the multiple clinics), you obviously brought in other people into your practice to assist you. How do you train them? How do you communicate to them the

importance of what you have learned over the years so there is a consistent theme of quality? Because it seems like that's a central feature to this success.

An Angel Donor Leads to Functional Medicine Training Programs

PS: What we discovered is that a lot of times we would all learn the science, and we would come to very interesting conferences. But we didn't know how to apply everything on Monday morning. We really had to develop a system"a curriculum"for everyone to learn and be able to reproduce the information. We still had to provide customized and individualized care, but have the same core basis of knowledge.

Ten years ago I was very fortunate. I had a patient that we helped, and the patient was very wealthy and wanted to know what she could do to help us. She became an angel donor to us, and we started looking at how we would develop curricula. We did focus groups, etc. And we developed the Fellowship in Anti-Aging, Metabolic, and Functional Medicine, which has now become a Master's program in Metabolic and Nutritional and Functional Medicine at the University of South Florida College of Medicine. The good news is that it is open to all kinds of practitioners. This is the exciting part: Yes, we have MDs and DOs, but in the program we have 1700 people who are also pharmacists, chiropractors, naturopaths, PhDs, exercise physiologists, PAs, nurse clinicians. It's been a lot of fun because we all learn, and we all have new ways to help the patient, and we are able to put all those areas of knowledge together. So people can now literally get a master's degree in this field from a major medical school.

JB: I hope the people who are listening to this are really...I mean, you say this so easily"it flows off of your tongue as if it is something we can all do simply, just stepping off the curb and here you go, we produce a curriculum, and we produce a degree, and we get an affiliation with an accredited medical school, and, voila, it all happens. But having been in medical education myself for my first 13 years as a professor, I recognize that what is said easily is not so easy behind the scenes to accomplish. There are all sorts of barriers, and there are obstacles, and there are belief systems, and there is a long-standing sense of self-importance. You've got to kind of rise above all of this and find a common thread that ties people together to a bigger vision. Obviously this would be a conversation that could go on for hours, but can you kind of give us a succinct sense of how you traveled this terrain to be successful? This is quite an accomplishment.

How the Master's Program in Metabolic, Nutritional, and Functional Medicine is Structured

PS: I do really believe, honestly, that there was some divine intervention that was involved. Because there are a lot of talented people, we are the only accredited program right now for a master's degree. We are able to have the professors who literally are the leaders in their particular area of expertise. Because all the professors really want the patient to be healthy"that is their goal, we all have different ego structures"we were able to take that one core thought about a healthy patient and bring it together to provide a master's program for people who are out of their training. It's done in a fashion where it is three days at a time so that you can leave your practice and come back without having a big issue. You also have webinars every Monday evening, which are archived in case you can't be present for the webinars. There are eight core courses and there are two electives, and then the eleventh course is an online ethics course that the state of Florida requires for anyone getting any degree from any medical school in the state of Florida.

The eight core courses are endocrinology; the second course looks at hypercholesterolemia, hypertension, diabetes; the third course looks at gut health, neurotransmitters, neurology; the fourth is amino acids, fatty acids, spiritual health, and looking at nutritional depletions caused by medicines. What a key component

that we have not looked at that is just really turning out to be very major. The fifth course is what we call clinical intensives, where we go over hundreds of case histories. The sixth is introduction to functional medicine and neurology. The seventh looks at brain fitness, autoimmune diseases, chronic fatigue, and fibromyalgia. And number eight looks at psychiatry, an integrative approach to cancer therapies, sleep modalities, etc.

JB: Wow! That's an omnibus. That's intense. How many hours, in total, does this represent when a person goes through this curriculum?

PS: There are 24 hours of actual basic core course that you learn, plus you have to do (for each course) 10 webinars. Then in the master's program there are 2 quizzes, which are open book (we don't want to stress the adrenals), but they are timed, so you don't have 30 years to take them. And then you write case histories; you write 3 of them. That's really where the professors that are grading material understand whether you connect the dots or not. We can all learn material, but in functional medicine it is important to connect the dots.

JB: I think that is really where the tire does meet the road: seeing how this all integrates in the system of patient management. I mean there are many, many things that are wonderful little...I call it cocktail talk. They are little vignettes of knowledge that you can use to stimulate conversation, but then how does it all integrate within a system that ultimately delivers value to the patient? That's where the real value arises. Tell us a little bit about what you learned, because often--I have found over the years as a teacher--you become the best student because your students become really great teachers. That reciprocity is what can really drive the vitality of programs. Have you experienced that?

PS: Absolutely. We have, twice a month, what we call "Professor Day," where one's professors (and usually one of the two times it is me)...I sit by my computer and for 12 hours people can email me any question in the world that they want. It has been amazing. The more I learn the more I realize I don't know anything and I need to learn a whole lot more.

JB: When you look at how this has been received, because obviously your have gotten visibility not only within our medical community but certainly probably within the education system, what have been the reviews so far?

PS: It's been fabulous. All of the clinicians"their comment is this has reignited their love for medicine. This is why they went to medical school, or any other professional school that they went to. And from the viewpoint of the public, I literally could spend every day going to a different city, being asked to speak to the public on functional anti-aging medicine. There is that much of a need. People really want to know this information.

JB: When we look at healthcare reform"I know this almost sounds like an oxymoron in the way that it has been discussed, here, the last few years (and particularly the last few months) because it doesn't seem so much as a healthcare reform discussion as a reimbursement reform discussion"have you found that there is, both within the health professional and the patient, a real interest in "health" reform, not just universal access and reimbursement reform?

PS: I do think more and more people are wanting to be healthy. The problem has been that (at least from a

physician viewpoint) we've never spent the time to help the patient be healthy. Part of that is we never learned how to be healthy ourselves first. That's the most important part: you work on yourself first (you get yourself healthy) and then you can help others.

JB: Very well said. Example is the best teacher, isn't it? There is no question about it. As you've developed your curriculum, because this is such a remarkable changing field, how have you been able to kind of keep pace with changes that occur? It just seems like every week a new bit of understanding starts to develop. Let's use the vitamin D story. Five years ago, it was the outlier that talked about vitamin D beyond that of an anti-ricketic vitamin. Now, if you're not really up to speed with regard to all of the multiple activities that 1,25-dihydroxycholecalciferol has, you seem like you have been left behind. How do you keep pace in your curriculum with these rapidly changing events?

PS: Unlike most kinds of curricula, ours changes every time the course is given. Most of the courses are given twice a year. Next week we are about to give another course. I just went through all of the seminars. They are drastically different than they were even six months ago. The good news is our professors, because they are cutting edge and leading people in their fields, are able to impart that information and change it on a very rapid basis.

JB: Do you have to take your curriculum for annual review? Is there a curriculum committee? Is there somebody at the university that says, "We'd like to pass our eyes over what you are teaching," or have you become both a combination dean and curricular development person in one?

PS: Oh, no. I have had great amounts of help from the University of Florida College of Medicine. The Senior Dean, Dr. Klasko, is just phenomenal. He is almost 60 years of age. He's a gynecologist/obstetrician; he still delivers. He is very cutting edge and really allows you to be able to work on things without micromanaging. Dr. Michael Barber, who is my counterpart, is a PhD biochemist. He has been phenomenal to work with. He's the one that goes over the curriculum. I couldn't ask for a better team of people to work with, along with the other people at USF; they're great.

JB: Now let's talk a little bit about how you bridged this extraordinary gap. You talk about taking care of ourselves and being good examples, but it sound to me like you are stretched in time, stretched in distance, and stretched in responsibility. Tell us a little bit about how you manage the clinical world, the teaching world, the advocacy world, and all the other parts of the world in real life that connect to your being.

PS: I really do think I am stretched thin. The thing is, right now the time is here for a functional medicine approach. I really thought it would probably be 5 to 10 years from now, but medicine is moving so quickly that the time is here, so I don't mind being stretched a little bit thin. I do keep the things that help me stay not stressed. I like to hike and bike. I like to needlepoint and quilt. Those are the kinds of things that calm me and keep me centered. I'm also married to the nicest guy in the world, who also helps keep me centered, which is part of the phenomenal things that I think have to happen in life for you.

JB: Fantastic. This whole concept of a support system I think is, for all of us, critically important. It can be your office staff who can be a team that really provides nurture and support for one another. It can be your family. It can be your principal partner. It can be the community in which you live. I think we need to form those connections. When you read The Blue Zones you probably saw that one of the

characteristics that was associated with long and healthy life was being part of a tribe. We define our own tribe: people that understand us and give us that support. Obviously that's something you give back to your patients as well, as they are a member of your practice and your teaching. They are part of your tribe.

PS: I've learned as much from my patients as they will ever learn from me. I learned that, very fortunately, as an intern, so I've been very blessed in over 30 years of practice to really work with my patients on a one-on-one equal basis. It has been phenomenal. I'm also blessed to truly have a fabulous staff that I work with, from my receptionist, to my nutritionist, to my PA, to the people who work with me in the fellowship. They are all a key component as important as I"or more important"to make this all work.

JB: Let's talk a little bit to the person who is listening who may be new to this field and is either trying to transition into the field from where they have been in their medical practice previously, or maybe just starting out into their world. Is there some early guidance from your experience that you would provide or offer to people saying, "How do we make these first steps?" What are some of the things that you've learned that might be helpful to take this first step toward changing their practice to this style?

PS: The first thing is someone can come into this field from really any background. In the fellowship and master's program, we literally have clinicians from every field of expertise. In fact, we even have a pathologist, who, after 22 years in pathology, is now going to open a practice next month in Traverse City, Michigan, and see patients for the first time in her life. It is also a key component, when we look at all of this, not to take insurance in this kind of practice. What I usually suggest that people do is they keep their family practice (internal medicine practice, or OB/GYN, or whatever basis they have), and then set up a separate corporation, and on separate days they see their metabolic/functional/anti-aging patients. That way you don't mix the two. When people say, "Don't you feel extreme guilt if you don't offer functional medicine to your primary care patients that you've had before?" And my response is, "No." Because the initial practice for me was internal medicine. Internal medicine has certain guidelines, and that's the care that I provide to those patients. Yes, now that does include vitamin D, but it would not have 5 years ago. I don't, however, go through looking at nutritional depletions caused by every one of their medicines unless they are in my metabolic/functional/anti-aging practice. Now my practice is just anti-aging/metabolic/functional medicine, but initially people can have two practices"separate tax ID numbers"and then just don't mix the two. Just let people know that you have additional training in this field of expertise, and that on Thursdays, for example, you are going to see your functional medicine patients, and if they are interested in that kind of approach that you would be happy to see them on Thursdays.

JB: That's a real pearl. Thank you. That's real news-to-use"a very, very wise suggestion. Obviously over the years that you've been doing this, just from what you have said, you've built more and more interest in this other thing that used to have occupied maybe a part of your time, which now is occupying more than 100{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of your time. Have you done this through advertising? Have you done that through public speaking? Have you done that through radio shows? Have you done that through promotion of certain types? How have you built that reputation, or is it just word of mouth?

PS: The two best things that have brought us patients are, number one, word of mouth, which I think,

hands down, in medicine is always the best way, and number two is really public speaking. And you don't have to be a great public speaker. The first time I did a conference there were only four people there. But every Tuesday night we did a conference in our first office in Canton, Michigan, and it just grew and grew and grew. There are also other people that you can work with. For example, in my community, the compounding pharmacy helps promote our practice. We also work with other practitioners; we have a plastic surgeon that we do conferences with together. The chiropractor down the street from me"we do conferences together sometimes for patients.

My style is a little bit different. I don't do PowerPoint. I take open questions during the seminar that I give. It's a lot of fun. People really want to be able to talk to the clinician as opposed to necessarily looking at a PowerPoint presentation. We usually have about a 50{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} success rate: when we have a seminar, within a year 50{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of the people will want to see us. That part is very exciting. Again, it doesn't take a lot of people being there. One of my friends owns a quilting shop, and when one of my books came out she wanted me to do a book signing there because she was having a sale on her quilting material. It was the worst storm there has been in Detroit for years; it was an ice storm. Two people came. One person who came owned ten home healthcare stores, and that's all it took. So sometimes it's not about the numbers; it's really about how you are going to help people, because if you do it really does come back to you.

JB: That's a beautiful lesson, thank you. Let's turn it slightly here and talk about what you perceive as barriers. We've been very uplifting, I think, in this conversation, to this point, and very kind of high level, but obviously there is always a yin to a yang. What are barriers or what things that are obstacles"things that one should be aware of that make life a little bit more complicated?

PS: I think one thing that is really difficult for people to understand is that you never criticize someone else. Other practitioners will criticize me. I never criticize them back. My response is always, "I'm sure your other doctor is an excellent physician or you wouldn't be seeing them, but this area is my area of expertise. If your other clinician has a question, please have them call me, email me, fax me. I'll be glad to fax them a medical article that is a clinically controlled trial showing them why we are going down this pathway with you." And I think that's really the important aspect. I just keep giving back, to the other clinicians, the science. Then they realize that no one can read it all; we can't either. We really have--now--a pretty good interchange with most people.

JB: You've given us extraordinary news-to-use in this discussion. It is interesting how you've woven together philosophy and experience with real pragmatism. I guess that's what really separates high achievers from dreamers. We can all dream"and hopefully we all do"but then somehow translating that dream into a pragmatic action plan, and a list of achievables, and standards of internal control, where you say, "Okay, am I making progress along my list?" is probably what establishes performance. You have been very successful, I would imagine, throughout your whole life, being a person who establishes those milestones, benchmarks, measuring sticks for performance. Are there things that you would guide someone getting involved with this? Do you write a lesson plan? Do you have a business plan? Do you do journaling? Or is it just something that you have inherently developed in your daily routine?

PS: I think one of the things that makes good leaders is failure. I've not always been successful in

everything I have done. But everything that has been a failure, I've been able to have my glass be half full. I have turned it around to learning something, and then turning that into something that will progress into a better way to help patients. That has been a key component in my own life. We do encourage everybody to become involved in the fellowship and the master's. As we go forward as one group, we will be able to help people much more than if everybody kind of has their own little separate connections. We are all about the patient"all of us, all clinicians are, that's what we are here for. Even the PhD's that work in the labs"they are still there for the patients, they just do it in a different fashion. We hope people go forward in taking the master's. I'm sure other master's programs will develop, but if people are interested they are certainly welcome to email me. My personal email is pepper (just like the spice) @ sbcglobal.net, so that's pepper4@sbcglobal.net, and I'm happy to answer some questions and really look at other ideas, different ways of training. Right now we're involved with different medical centers and looking how we can impart this to residents and in medical schools.

JB: Anyone listening who is motivated is probably in awe of what you have been able to accomplish over your years of both practice and curricular development. This is really an amazing next step for the field. On behalf of the people that are listening I want to thank you for taking the time to be out here with us in Gig Harbor, and for sharing this and really motivating us. I think all of us need inspiration at times. Sometimes the daily routine of just getting up and making it through the day with all the compression of responsibilities seems overwhelming, so to have someone of your bright light giving guidance tends to lift us all up. Thank you, Dr. Smith, and we look forward to following your contributions and your program very, very closely as we move forward.

PS: Thank you, Jeff, and I've really been very privileged to have you as one of my mentors. That has been one of the nicest things in my life.

JB: Thank you, Pam. For those of you who are listening, this is a year in which we have had some very, very strong clinicians that have been speaking to us. Maybe those of you who have been long-standing Functional Medicine Update subscribers have recognized that we've drifted off into the esotericism of primary science. But I think over the last several months you can see that we've really tried to focus on bringing clinical acumen from people who have done this successfully into the body of understanding, because as Dr. Smith said, it is really through what we do with patients that makes this all real. The rest of it is kind of interesting intellectual fodder, but until we can really deliver better outcomes, it is pretty much just an intellectual enterprise.

Dr. Smith, once again, absolutely fantastic motivation for us to keep the vigilance and keep proceeding forward.

PS: Thank you.

It's my hope in having listened in this July issue to the really sage and insightful comments of Dr. Pam Smith concerning the curriculum, the study, and ultimately clinical implications related to successful aging, and coupling that together with what you learned in the June 2010 issue of Functional Medicine Update from Dr. Halsted Holman, that you started to emerge a fairly interesting way of approaching, in your own practice, the delivery of health care that will lead to healthy/successful aging. Obviously there are a lot of devils in the details and there are many more things we can and will be studying, but I hope that you got the general drift of how to use biomarkers: what kind of information to assemble, how that

gets put into a lifestyle medicine program, and what that might mean in terms of following the trajectory of the patient and using the patient as the center of their own universe and teaching them something about self-reliance and self-efficacy, and using orthomolecular substances where necessary to augment and support proper physiology. It's a whole new paradigm. It's the paradigm that we have been discussing for 20 years that we call functional medicine. See you next month.

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