May 2010 Issue | Jeanne Drisko, MD Director, Program in Integrative Medicine

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Welcome to *Functional Medicine Update* for May 2010. We're very privileged this month to have Dr. Jeanne Drisko, from the Kansas University Medical Center, who has been a true pioneer in our field for the last 20 or so years, during the evolution of what we might call the functional medicine model or the integrative medical model. In setting the tone for her interview, I thought we might talk about this confluence or convergence of different medical perspectives that is occurring right now. Hopefully we are going to create a catalytic event, which will transform medicine as we move into the later part of the 21st century.

One of the common themes that you see among all disciplines--be it environmental medicine, or functional medicine, or the complementary/alternative/integrative medicine, or holistic medicine, or naturopathic medicine--is the recognition that by modulating aspects of the environment of the individual, the phenotype of that individual can be changed through this gene/environment interaction transduction process. All of us in these fields are trying to find ways to improve the tools in our toolkit to be better able to personalize a program to the needs of each individual. That translates into a form of medicine that is more participatory, more preventive-focused, more personalized, and more proactive or prospective.

Modulating Environment Means Personalizing Therapy
Therapies can be delivered that cut across all types of diseases, and can range from early stage prevention, into the various aspects of the wellness model, and ultimately into early stage chronic disease. Using just diabetes as an example, you could go from early stage insulin resistance/metabolic syndrome into pre-diabetes, and then right into type 2 diabetes, and into the more severe sequence of events related to type 2 diabetes. All of the stages that manifest as distorted physiology would be amenable to the model that I'm describing which involves trying to modulate the interaction of the environment with the individual to create a positive outcome.

Another example of this would be the individual who has a gluten sensitivity. You can personalize that person's environment by putting him or her on a gluten-free diet. For an individual who has a very strong reaction to a certain class of chemical exposures because they have an altered cytochrome P450 and Phase II detoxification system, personalizing their environment means eliminating that exposure so they will be less likely to have an adverse response. It may also mean improving the functional capacity of their detoxification systems by using certain kinds of nutritional support that might upregulate or modulate the expression of those enzymes that we call the cytochrome P450s and the Phase II conjugase enzymes. Or it might be such things as improving musculoskeletal function, improving lymphatic

drainage with various types of physical medicine-body work, various types of movement therapies-that ultimately delivers better information and better release of toxic burden.

All of these things may ultimately allow physiology to perform at a higher level. These would be considered rational therapies based upon a different model, a model that is not compartmentalized or siloed. This model does not look at each organ as an individual or separate part of the body with each organ that is diseased having its own disease family, treated by its own kinds of drugs, with its own diagnostic criteria and treatment options within a different subspecialty of medicine. Rather, this model looks at how these are all connected together in the symphonic orchestration that we call life. It is called our physiology. It's called our body function. We are going to have the privilege of exploring this model in greater detail with Dr. Drisko. We will talk about how this model gets taught and how it gets implemented in clinical practice.

Basic science underpins much of what we teach medical students and ultimately practice. The whole nature of thinking about pathophysiology, cellular biology, and molecular biology is undergoing a dramatic change. Let me, if I can, give you my thought about how I think this dramatic change in thinking affects every day practice and translates into the exam room (the relationship of the practitioner with their patient).

It used to be that we thought these diseases were independent. If a person had heart disease, it was an independent disease from osteoporosis, and it was an independent disease from inflammatory bowel disease, which was an independent disease from rheumatoid arthritis. As people looked more significantly at the epidemiology of these different diseases, it was found that often they were linked. That there was a higher probability that a person who had heart disease might have diabetes and might also have osteoporosis.

People started to ask, "Why would this be?" We had a weigh station of our thinking. We called these conditions "comorbidities," meaning they shared commonalities in their origin somehow or they seemed to be interrelated, statistically, and we didn't know how. We scratched our heads, but called them comorbidities. A person seeing a cardiologist might also be seeing an orthopedist and a rheumatologist simultaneously, and using three different classes of drugs treating three different sets of pathologies.

As we move forward in our understanding of the mechanisms that underlie the appearance of these dysfunctions, we find that there are common immunological disturbances that relate to alterations in the balance of various types of immune cells, like the thymus-dependent 1 and the thymus-dependent 2 lymphocytes. These disturbances can influence regulatory functions at different tissue levels and lead to increased risk to a number of companion diseases. These comorbidities really are interconnected at the gene expression level and at the cellular physiological level. Treating the cause rather than the effect might help us to reduce the rather significant impact of more than one disorder simultaneously.

This model is at the root of functional medicine, as it has been redefined for the last 20 years. The functional medicine concept involves trying to look at the origin of these situations at the level of disturbances in the gene/environment interaction. These disturbances can spread through the individual in a unique way to express as either pre-clinical or later-stage clinical diseases that need management. We have to have different reference points--different weigh stations along the road--to understand this. These become biomarkers and signs and symptoms that become hallmarks for these different conditions.

Looking for the convergence of these signs and symptoms around central themes can help guide us as to the principal or primary treatment option to personalize therapy to that individual patient. That model-that functional medicine model-really differentiates itself quite significantly from the histopathology model of driving toward the disease that that patient has as the diagnosis and then treating it as an individual, unique, independent entity.

With that broad brush reminder of the conceptual framework, let me talk about some interesting recent examples that I think illustrate how this plays out in our evolving understanding of basic biology, and why biological sciences and physiology and molecular genetics are all really rapidly changing. I have recently said that I got together with a number of my fellow alumni who graduated from undergraduate school with me back in the middle 60s. All of us were reminiscing on our molecular biology class that we took. Now this was not too many years after Watson and Crick had discovered the structure of DNA in the middle 1950s, yet we thought, 10 years downstream when we took (in the middle 1960s) molecular biology, everything was known that needed to be known. We were feeling pretty sophomoric, meaning "wise fool," about the level of understanding of molecular genetics.

We all mused (at this 40-year reunion that we had) that if we would take the same tests today that we took back then, with the same answers that we provided for those tests back in the mid-60s (for which we got high marks in these classes), that we would get Fs and none of us would be considered professionals in our disciplines today because those answers that we got As for back in the mid-60s now would be considered wrong. The one-gene-one-enzyme concept, for instance, now is not totally wrong, but clearly has been modified to a whole new conceptual framework as to how protein regulation is controlled at the transcription and translational level, and then post-translational modification by various types of secondary processes to give rise to active protein that then modulates cellular functions.

These concepts--that genes and proteins are interrelated, and how they are acted, and how they are expressed, and how they function in cells--have undergone a tremendous change in the last 40 years. The very rigid system of the one-gene-one-enzyme concept now looks very ancient in terms of its conceptual framework. Now we see gene plasticity. Now we see epigenetics, which is the concept that genes are regulated in their expression by marks placed on the histone coats of the genome that then relate to how certain messages may be read, or how genes may be silenced. Some of these particular marks are labile; they can be put on and off as a consequence of different environmental exposures, including, as we have indicated in functional medicine, things like life experiences, traumatic stresses, and exposure to low levels of biocides. Things of this nature can modulate the epigenome in such a way as to change genetic expression and ultimately the phenotype of cells, tissues, organs, organ systems, and the whole body. These are dramatically changing landscapes as to how we view basic biology and the whole construct of what is known-what is factual-about biological sciences, from a rigid framework to this more plastic kind of interactive system, going from a deterministic model to an environmentally modulated model of biology is really a very profound change in our thinking over the last 40 years.

Abscisic acid is a chlorophyll-related derivative. If you know anything about the past history of alternative cancer therapy, you probably know the name of Virginia Livingston. Dr. Livingston, in San Diego, pioneered this concept of progenitor cryptocides, which she felt was a microorganism that had something to do with cancer initiation. It was a very primitive organism, and its growth process could be arrested by abscisic acid. Her treatment approach was to use a lot of abscisic acid-rich vegetable products as part of the therapy for her patients.

Since that time, which was back in the 50s and 60s, a lot has been studied on various phytochemicals, including abscisic acid. A report that appeared in 2010 in *Clinical Nutrition*talks about the role that abscisic acid has in synergizing PPAR-gamma that then modulates cellular signaling through the protein kinase A/PPAR-gamma axis into altered gene expression patterns.[8] If you go back to my previous discussion about how PPAR-gamma has a role to play in the CD36 nuclear receptor and how that, then, controls aspects of gene expression related to cellular proliferation and atherosclerosis, it might suggest that there is something interesting about this other phytochemical, abscisic acid, and its connection with diabetes, cancer, and heart disease. Clearly this is not exactly the same as what Dr. Livingston talked about as it relates to progenitor cryptocides, but it does suggest that there issome support for its activity.

What we are really doing is enhancing, significantly, the level of various types of phytochemicals that may modulate these processes that I am describing (these intercellular signal transduction processes) that spread out, when disturbed, into a variety of diseases: cancer, diabetes, and heart disease. hese long-forgotten phytochemicals, which we thought were not that important in the diet (we could take them out and make foods white and stable for long periods of time), we're now finding out may be very important in modulating cellular signaling and ultimately translation and trafficking of messages that relate to cellular function (cellular phenotypes).

I don't want to put too many eggs in one basket. There are many variables that can modulate these functions: environmental agents, radiation, stress, dehydration, ischemia, chemical exposures, alcohol, cigarette smoking. We know that all of these play roles in modulating reactive oxygen species, redox potential at the mitochondrial level, and intercellular signal transduction process. The point I am trying to make for our thinking as we move into our interview with Dr. Drisko is that there is a convergence from many historical lines of thinking, across many disciplines, as to how diseases in and of themselves are not the sine qua non of health care. What is the sine qua non is understanding the distortion of physiological processes from the mismatch of genes with environment that creates an altered sense of trajectory of function that then produces a disturbed state-a new emergent state of the function of the cell that becomes the cell, tissue, organ, or organ system that is now what we call dysfunctional. I think that model leads one to ask, what tools does the therapist/physician/healer of the 21 st century need to be properly prepared for managing the diseases of chronic nature that we're now burdened with?

INTERVIEW TRANSCRIPT

Clinician/Researcher of the Month
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We're at that place in Functional Medicine Update -the clinician/researcher of the month portion of our commentary. We've been so privileged to have some of the most remarkable contributors to the emergence of the new medicine. We're moving in that same direction in this issue with Dr. Jeanne Drisko, who is the Riordan Endowed Professor of Orthomolecular Medicine at the Kansas University Medical

Center and a medical school professor.

Dr. Drisko is a woman who has been a leader in our field for many years, through medical education, clinical work, and her leadership in organizational development. She has been involved very significantly with the development of recent work on chelation therapy and an international clinical trial that is ongoing. She has also been a fundamental person in establishing, I think, academic respectability for the field of orthomolecular medicine. Last year I had the privilege of interviewing Dr. Abram Hoffer, who we would certainly say was one of the founding members of this concept of orthomolecular medicine. Jeanne is the next generation of the orthomolecular movement.

Dr. Hugh Riordan, the namesake of the Chair Dr. Drisko is occupying, was an interviewee on Functional Medicine Update some 20 years ago. He was one of the founding members of the field or orthomolecular medicine, through the work that he did in his extraordinary clinic in Wichita, Kansas.

Jeanne, it is really a privilege to have you representing the field, both as a leader in the field and also, I think, as a woman of influence in medicine, who is shaping what I think is going to be the medicine of our future. Welcome to Functional Medicine Update.

JD: Jeff, thank you for such a spectacular introduction. I just have a question, did my mother write that? I also want to thank you for these many, many years of updates that you have done. I tell you, it is a wonderful way to re-educate and to re-tool when we are moving from conventional medicine into real medicine.

JB: Thank you. That's a really wonderful segue into the body of this conversation. You have just stepped down as the president of the American College for the Advancement of Medicine, originally AMPS and later ACAM, an organization that has been kind of at the frontier of bringing many of these concepts into practice and certifying doctors through their fellowship program in this field. Tell us a little bit about your experience with ACAM and how you saw the organization evolve over your tenure as president.

The Four Pillars: Education, Clinic Care, Research, and Service

JD: It was a very interesting experience. It was a two-year tenure as president of ACAM. It gave me opportunity to reflect and to participate nationally in the reshaping of medicine. But that was just one of the ways that I was able to dovetail with this change in health care. In any academic program you have four pillars: education, clinic care, research, and service. I see my service as being able to sit on committees, both locally in the medical center and for the state board of healing arts, but also nationally for many organizations, like Alliance for Healthcare Freedom, the IFM Faculty, the Consortium of Academic Health Centers for Integrative Medicine, ACAM, and on and on. Another organization that I am very excited about is our International Medical Consortium. That is a group of organizations. There are six of us, including IFM, ACAM, the International College for Integrative Medicine, the American Association for Environmental Medicine (AAEM) (the naturopaths are part of that organization), and the American Holistic Medical Association. We have all climbed out of our silos, so to speak, and joined forces and become, really, one voice, and we respond as one voice, with some help from the Alliance for Health Freedom, to answer politically charged questions. Yes, I sat as immediate past-president of ACAM, but I see this as a much broader focus, more of an international focus.

JB: That is really a great platform from which to get your perspective on how you visualize where we are

in this change, going through this recent very vitriolic (at times) debate about healthcare reform, and seeing what's happened in the rising tide of chronic disease globally, and recognizing that in countries like China the increasing incidence of diseases that were considered Western diseases are now becoming absolutely pandemic. Tell us a little bit about where you think we are in this continuum of change.

Changing Medical School Curriculum: Acute Care Versus Chronic Care

JD: I'd like to back up at the very grassroots level of this, and that is in the medical school curriculum. There's been a change in the way that the curriculum has been addressed during the first two years. You and I both recall the days when, during the first two years of medical school, you took the basic science-focused classes: biochemistry, pharmacology, microbiology. But now, curriculum has been changed to a systems-based approach. You may have 15 or 16 modules that you complete in the first two years, let's say immunity, inflammation, genetics, neoplasia, GI tract, and nutrition (if you can believe that nutrition is now actually taught in medical schools). These are interwoven with these core foundational basic science underpinnings. And you have, woven through the modules, both clinical aspects as well as the basic science aspects. So those are the first two years, and the students are thriving in this model.

But the second two years continues to be largely a hospital-based experience and focused on the acute care model. I don't know if you recall, Jeff, but in 2004 you mentioned this wonderful commentary in your updates. It was in the Journal of the American Medical Association, and it was an editorial calling for change in the model, from the acute care model of education to more of a chronic care model.9 They discussed how chronic care has really become the main focus over the past 50 years, but our educational system still focuses on the acute care. So doctors are not being trained, really, in how to care for patients that have chronic, complex disease. We're really failing in preparing our medical students for the future. And the patients are dissatisfied. We really need to change this model.

JB: I think you are referring to the Halsted Holman article, "The Need for a New Clinical Education." I was down at Stanford, where he is a professor of medicine, recently, and had a chance to talk to some of their students about, "Okay, is this advocacy that Dr. Holman talked about in that paper in JAMA really starting to be seen as something happening within the curriculum at Stanford?" You know, you get kind of interesting mixed reviews from the students themselves. I talked to third- and fourth-year medical students and some will say, "Yes, we think we are starting to see more focus on management of chronic conditions," and then others will say, "No, really all of the drive is to go into specialty medicine and treat acute care-type problems because that is where the universal attractor for making a good living is." So only 5{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of students going to medical school now are really focusing on the family practice/generalist kind of approach toward prevention and management of chronic disease, with most people (95{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36}) heading out into the specialties. I'm not sure. I guess it is still kind of a mixed report card, it would seem.

Insights on the Healthcare Reform Debate: Is the Government Becoming Too Intrusive?

JD: It's a very mixed report card and it's because of the model. It is an apprentice-type of a model (apprenticeship), and that's the way our attendings have been taught, and that's the way they choose to continue to teach. It's going to take a revolution.

I want to tell you a little story about what's going on. It's on the internet, but it's a little bit in the background. We've had, as you mentioned, this debate on healthcare reform, but I think what we are

missing in this discussion is that we have moved into the era of government intrusion in healthcare freedoms. What has happened is...if you recall, in 2001, the Institute of Medicine report, Crossing the Quality Chasm.10 That really spurred change in Health and Human Services and in the Agency for Healthcare Research and Quality. Just for an example, the Agency for Healthcare Research and Quality received an enormous increase in their budget from this recent stimulus package. They received an almost 55{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} increase in their budget. Let me give you another example: the NIH only received a 2.4{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} increase. And preventive care only received a 1{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} increase. And education and health jobs received no increase in their budget. So this agency is now really the driving force in this change in health care.

What they do is they collect data on health care in the United States, and they also fund studies. This information that they collate is then handed off to the National Quality Forum, and that can be found at nationalqualityforum.org. Their job is to take and collate this information from the Agency for Healthcare Research and Quality and develop new measures. Okay. Currently, this year, we have 70 quality measures that we have to follow in hospital-based medicine, and I'll come back to that in a minute. They predict that by next year there is going to be 130 quality measures that hospitals have to follow. This is compared to 2006, when there were only 21 measures. This is an enormous growth in a very short period of time.

What these measures do is inform us around, let's say, hospital-acquired infection. If a nosocomial infection occurs while that patient is hospitalized, the Medicare funding, or even some insurance companies, will not be responsible for paying for that treatment. If that patient acquires that infection while hospitalized, it will be the responsibility of the hospital to pay for that treatment. This is a huge change, a huge shift. The National Quality Forum hands these measures off to the Hospital Quality Alliance. They receive electronic data from the hospitals around the country. What the Hospital Quality Alliance does-and this is part of Health and Human Services-is they compare hospitals on their performance, amongst themselves, one another, and by state. This is a very regulated experience, and we can only expect more from here.

As I mentioned, this is for hospitals only. Currently there are no regulations for ambulatory clinics or clinics that many of us have in integrative medicine. There are no rules and regs as of yet, but this is expected to occur. How does this translate into how we care for patients? We may be mandated to do certain things. For example, when someone is signed out of the hospital here at KU Medical Center, we go into the electronic medical record and discharge that patient. We have to document, in that electronic medical record, every event that occurred during that hospitalization: Did the patient have pneumonia? Did they have congestive heart failure? Did they have a myocardial infarction? That info is then transferred back to the Hospital Quality Alliance Network, and what is mandated are specific instructions for that patient. They have to receive certain medications if they have had certain illnesses. And if they have had pneumonia, they'll be required to get a vaccine before they leave, and they have to be given a specific set of instructions.

Currently, there are very few core measures that are mandated and regulated, and this is the evidence-based medicine model. But we can expect that these measures are going to come more and more-there are

going to be more and more of them for all of us, not just the hospital-based patients. I'm very concerned about this, and I think a lot of this-even though it's transparent (it's out there on the internet)-has been lost in the noise of the healthcare debate.

JB: You said so many interesting things in that discussion. At the Institute of Medicine conference recently held in 2009 on integrative medicine, Senator Tom Harkin from Iowa was talking about the way we language things and how all of the motivations are to really have a disease-based economy; we don't have a health-based philosophy in this country and then that determines the outcome. It is almost like a self-fulfilling prophecy. Just in the way these organizations are named I find interesting. "Hospital-based care" somehow fits under the rubric of "Health Quality Alliance." I think most would probably suggest that "hospital-based care" and "health" are not exactly synonymous words; "disease care" might be more the appropriate term. How do we fight to get out of these linguistic boxes that we have been built into? It seems like sometimes the perceptions that come from words already predetermine an outcome. We have kind of been painted into the corner when we talk about health care, which is really disease care reimbursement reform.

Integrative Medicine is Now More Accepted in a Hospital Setting
JD: That's exactly the problem. I don't know if you recall what you spoke about, but you were here at KU Medical Center about 7 years ago. You showed a slide that had a profound impact on me. It was the slide of the tree, with the diagnosis up in the branches, so you've got hepatitis, or you've got pneumonia,t or pulmonary disease, or cardiovascular disease, up in the branches. But you told us to forget the branches and go back down to the roots. Dig down in the roots to solve the problem. That was such a startling awakening for me. I loved that model and I have used it repeatedly since then. And I use that model with my conventional colleagues here in the medical center.

We have had a really revolutionary set of events happen here. I've been here 12 years. In the beginning I was shunned and a number of people tried to drive me out of the medical center, but with persistence and really knowing what I was doing was right, I hung on and grew and gained respect, and now work very, very closely with my conventional colleagues. So the students, the residents, and the attending staff all are very interested in what we are doing. In fact, we're starting to get consults in hospital patients-patients in the ICU, patients that are very, very ill. I always claimed that we are really the chronic care model and that Western medicine is the acute care model, but when you see that these patients in the ICU really have underlying, very chronic complex disorders, it seems that we do have a place in this entire healthcare picture.

Our conventional colleagues invited us into the ICU to see their patients. We almost don't care what the diagnosis is because we look down at that fundamental root. We are digging down in the roots. We are looking at vitamin and mineral levels, essential fatty acid levels, how is the GI tract working, how is immunity faring? We're looking for those fundamental abnormalities, and we make correction in a very straightforward, simple way. And those simple additions have such profound effects on these very, very sick patients. They are often better very quickly and discharged very quickly from the ICU as a result.

These are not complicated tests that we are doing. We've worked out a panel of laboratory tests with our laboratory here at KU Medical Center, and we simply order routine vitamin and mineral/essential fatty acid levels off of this lab req. The lab comes up, draws the blood, and it gets done and it is back on the patient's chart, just like a CBC or a metabolic profile. And then we can advise our colleagues. And we

also support this with papers; there are wonderful papers in the literature about supporting essential fatty acid levels, for example. In that way we are able to really teach and train on a very exciting level.

JB: Let's go back to the four pillars that you started this conversation with (education, clinical, research, and service). In that little discussion you really hit on all four of those. I want to note-and you probably would not state this yourself-at KU Medical Center you were acknowledged as one of the top 10 researchers of the year. That suggests that you are building-in the way that you have survived against the critics-an edifice that incorporates these four pillars very, very effectively. I guess the question is, do we have, in our field, enough research base, enough stuff in the literature (the peer-reviewed literature), to hold the critics at bay, or do you think that's still an area of deficiency?

JD: Oh, it's a horrible deficiency. I'm going to get on my soapbox here a little bit. We are on a merry-go-round that we can't off of. There is a bias against integrative medicine. They say, "Well, there's not enough research." But then our research arms are not really set up for the real-world integrative medicine practices. Because of this bias...let's use the NIH, for example. The NIH-the scientists at the NIH-really have bias against complementary and alternative medicine or integrative medicine, and they actually want to close the National Center for Complementary and Alternative Medicine. Periodically in the Journal of Science or somewhere you'll see an editorial saying that that needs to be closed.

In fairness to Steven Strauss, who was the previous director of NCAM, and currently Josie Briggs, they were intramural researchers at NIH; they're not integrative medicine devotees, so to speak. So they really had to learn from the ground up. They're really not interested (Steven wasn't, and Josie is definitely not) in investigating the real-world integrative medicine practices. Josie has stated that her interest is in looking at the basic science-the underpinnings-of integrative medicine. That's not going to answer the questions. And that's not going to provide the research needs that the doctors and the other healthcare practitioners are demanding. So we're really in a very bad state. For a number of us who do the real-world integrative medicine research, what we are dependent upon, then, is funding from private foundations. And I'm so thankful for these private foundations, because they see the need and they are willing to step up where the federal government hasn't.

JB: That's a beautiful additional segue into your endowed chair, the Riordan Endowed Professor of Orthomolecular Medicine. I think I was first actually introduced to you when he invited me to speak...I think it was at his first congress, or first conference in Wichita in 1976. He was a colleague of Linus Pauling. He really took on this whole concept of looking at the web of metabolism in a way that had not been usual and customary in medicine. He really put a tremendous amount of energy into understanding things like intravenous vitamin C, had work published in the literature. You obviously-with your fellowship, your endowed chair-are continuing to keep that model alive. I know that there has been continued work being done on the vitamin C and many other things that we feel are kind of still in need of better science to support what we have seen clinically. Can you tell us a little bit about the whole Riordan Professor of Orthomolecular Medicine and how that interrelates with this proof of concept model that we're describing?

Ongoing Studies on Intravenous Vitamin C

JD: Who would have thought that at a conventional medical center there would be a chair named after an integrative medicine doctor with the word "orthomolecular" appended to it? No one would have believed it. But, anyway, it has happened, and it was because of grateful patients that have been helped. They

really pulled together the funds to establish the endowed chair. And I was so fortunate to have been trained by Hugh. I went back and forth between Kansas City and Wichita for over a year to sit with him and learn from him in his clinic practice. It was like nothing I had ever seen before, but it resonated with me. Hugh was a great teacher; he has taught a lot of people. And his son, Neil Riordan, continues on with research in his place, and the center in Wichita continues as well. I'm very, very grateful to Hugh and to the center.
From Hugh, I learned about I.V. vitamin C. I also knew that very minimal research had been done. In fact, in my first trial that I wrote on ovarian cancer, I called intravenous vitamin C an "antioxidant." Well, along came Mark Levine at the NIH, and Qi Chen, his post-doc, and the other members of his lab at the NIH and NIDDK. They started looking at intravenous vitamin C, both in a number of normal cell lines and cancer cell lines, and then translated that into basic science research in animal models, both healthy rat models and then a new mouse model of cancer (a number of different cancer types).11

I've been very fortunate to attract Qi Chen, after she'd finished her post-doc with Mark Levine, to come here to KU Medical Center, and she's now an independent investigator set up in her own lab here, and continuing this research on the basic science of IV vitamin C. In fact, we are having our basic science research meeting today at noon. I'm always so excited. Once a month we do this and I get to hear the latest and greatest that Qi is finding in her basic science research.

They've been able to advise us (all of us out in the clinical world) that indeed vitamin C is not an antioxidant when it is given in the veins; it is a pro-oxidant. It becomes hydrogen peroxide in the extracellular space (not in the blood space, but in the extracellular space), and that hydrogen peroxide diffuses, then, or crosses the cell wall, into the intercellular environment, where it impacts multiple pathways. We're not even sure of all the pathways at this time. We also believe that besides its pro-oxidative effects, it has some immunoregulatory effects.

I'm also doing a small clinical trial with a brain imaging investigator here at KU Medical Center, where we are giving I.V. vitamin C both to healthy adults and to adults with type 2 diabetes. We are imaging the brain after I.V. vitamin C infusion by MR spectroscopy to look at the peaks of the vitamin C in the brain and the differences between an oxidative environment brain (the diabetic patients) and the patients that are considered to be normal. Very, very exciting days for vitamin C research.

JB: That is exciting. Are you collaborating at all (or have communication with) John Hoffer? Because I know that John published that very nice clinical trial recently looking at intravenous vitamin C in a number of patients in Montreal.12

JD: Yes. I'm very good friends with John. I do miss Abram. I would receive these emails from Abram Hoffer in the middle of the night and it was always fun to hear from him. John and I are colleagues. We had the opportunity about 18 months ago or so to meet at the National Cancer Institute with Jeff White who runs the Office of Cancer, Complementary and Alternative Medicine, under NCI. Mark was there, and Qi Chen, and Mike Espy. We were able to have a really nice roundtable discussion with Jeff White about the future of vitamin C research and cancer care, so we are very close colleagues.

An Important Clinical Trial on Chelation Therapy
JB: I know you are involved in a very important additional large clinical trial on chelation therapy, and that is another kind of step along the path toward putting some scientific explanation/proof on things that

people have observed, clinically, to be beneficial for some time. Can you tell us about the status of that trial?

JD: Yes. You know, that's a very interesting trial. That's really, I think, the model of how integrative medicine should be structured. This is a partnership between conventional cardiology researchers. Tony Lamas is not an integrative medicine doctor. He's the principal investigator. He is a conventional cardiology trialist, and he is connected nationally. What he did...he realized that there might be something to this chelation therapy. He approached the practitioners of this, so we were able to work with Tony in setting up how this trial might run. We had multiple phone conferences, and he had his statistical team from Duke on the phone calls. All of the events for the trial-whether patients had congestive heart failure or myocardial infarction-those events are being adjudicated at Harvard. This is really a partnership, nationally and internationally, now, because these study patients are not being run through academic centers. Some of them are in academic centers, but the majority of these study participants are coming through integrative medicine doctors' clinics. So they are receiving chelation therapy as they would in a real-world setting.

This is startling. Why hasn't this model been replicated? It's really unfortunate that it hasn't. It's because there was a strong push from Congress, and Congress told the NIH National Heart, Lung, and Blood Institute that they had to do this trial, so they were forced to do it. But because they were forced to do it, they wanted to do it right. They had a call for proposals, and they did the usual vetting of proposals, and they selected Tony's trial. We're very excited about this.

I'm sure you heard about the bump in the road, where the trial was shut down temporarily. There was a group of...well, they're not all physicians, but there is the Quackbuster group, and they attempted to close this trial for good. What had happened was there were erroneous accusations about patient safety, and this went to the Office of Human Research Protection. So because they had to investigate it, the Office of Human Research Protection asked the NIH to stop the trial until the investigation could be done correctly, so the Data Safety Monitoring Board at the NIH and the Office of Human Research Protection delved into every data point available, and at the end of the day, they found that there were no concerns for safety or further enrollment of patients, so they allowed the trial to continue. I think this is a victory for science, because it is not a political movement. This is about science. Either the hypothesis is correct or it's not, and at the end of the day, we'll know.

JB: When is the study, you believe, likely to conclude?

JD: There's probably about another 150 or so participants that need to be enrolled. They are given their chelation therapy and then followed. So it's probably not going to be over for another 2 - 2 1/2 years. This is a very large trial. There are almost 2000 participants enrolled in this trial. They are enrolled in the United States, Canada, and South America, so it is a very large trial. It is a Phase 3-a good, solid Phase 3-trial.

JB: Obviously we are all waiting with bated breath. That sounds like a very, very exciting trial, and something that I'm sure we'll have data beaucoup, and probably cohort analysis will prove all sorts of interesting things out of the trial. Congratulations. I know that that has been a very big project that you and many others have been dedicating time and energy to. Again, it's a model for the kinds of things that need to be done in our field.

JD: Absolutely.

JB: I know that we've taken a lot of your time, but one of the questions that I'm sure is on the mind of the listener is, how does all this translate, in Dr. Drisko's mind, to the future of medicine? And how is the family doc who is delivering care every day and organizations like the American Academy of Family Practitioners, which is the largest subspecialty organization in medicine, going to be affected? What will medicine look like? I guess I'm asking the crystal ball question, which is always an impossible question to really answer. Given that you have a vantage point that most of us don't, maybe you could speculate a little as to how you see things moving forward.

JD: I reflect on this question, actually, quite a bit. And I want to back up just a minute to talk about why I would even be reflecting on this question, and that's because one of my four pillars is education. I have students that rotate through our clinic. I have a standalone, fourth-year medical student elective. I have nursing students visit. We have PhD students go through Qi Chen's lab. We have residents that are rotating; I have a resident from internal medicine working with me currently. And then we started a fellowship and really, I think, built a wonderful fellowship that is probably not replicated anywhere in the United States currently; it's really a fellowship that teaches real integrative medicine. The fellows come after primary care residency, so family medicine, or internal medicine, or pediatrics. I'm actually looking at possibly getting a pediatric fellow soon.

How do we really point them to the future of medicine? What we try and teach them is that we're here to serve our patients. If you think about that acute care model, there really isn't a lot of time to spend getting to know that patient. In the acute care model, you have a problem: you've got bleeding, and you stanch the blood flow, and the problem is corrected, and the patient walks out. So it is really largely driven by the physician. But in the chronic care model, you're now looking at a partnership, and this is one thing that Hugh Riordan taught me: that really you are learning as much about that patient as that patient is learning about themselves, so it is a partnership.

What do we do? We need to listen. We spend a lot of time listening. And then we get down into the roots. We live down in the roots of the tree for that patient. We try and teach them how to get down in those roots, and to listen to their bodies, and to understand that the foundation is sleep and good nutrition. Then we try and correct the core deficiencies, and really clean up the terrain. I've been fortunate to be able to participate in the functional medicine module for detoxification and really helping to teach cleaning the terrain.

What we are trying to do, then, is build a new model to show-to tell--the next generation of healthcare practitioners how they're going to be taking care of patients. What is beautiful is all of the people that have come before me and standing beside me in the integrative medicine world that have taught me so much and continue to teach me so much. This is what we have to do. We have to pass it on to the next generation and they are so hungry. And even the attending staff, now-the people that are old and crusty like me-are also becoming more open-minded. They are saying, "Wow, this is working. This might be okay. This isn't so wacky as we thought it was." It's this grassroots...just teaching in medical schools, I think that's so critical.

JB: Dr. Drisko, that's about the most inspiring, enlightening, and hopeful message that I think we've heard recently on Functional Medicine Update. I think your leadership shines through by example. You've done

the heavy lifting. You've gone through the appropriate academic training and credentialing. You've kept your search for knowledge and learning alive and well. You've inspired people by your enthusiasm and your sense that there is a better horizon that is in our future. All of things, to me, kind of focus on a central theme that seems to be true about all great social change, and that is the concept that truth wills out. It may take some time for truth to find its way through the tortuous path of selective interest and control, but eventually a truth will out. And it seems that there is a central truth to this field that you are describing. Maybe not all of the details are exactly i-dotted and t-crossed precisely, but the general construct...as my father would say, it fulfills a rule of reasonableness. There is something reasonable about what you are saying, and as we get more data, and more clinical information, and more young fresh minds that are really searching for the right answers, it seems that your model that you provided us here at the end, which is one of optimism and hope, is a very likely outcome. Thank you, you have given us all a big gift in your vision for our future.

JD: You've been very kind and I appreciate the opportunity to speak with you.

JB: Thanks and keep up the great work there. We are going to follow the studies and follow your work as part of the consortium very closely because these are the agents of change. Thank you very, very much.

I certainly hope you had that extraordinary kind of "aha" experience that I had talking with Dr. Drisko as you were listening to her. If you calculate a takeaway value of this whole issue of Functional Medicine Update, there would be several takeaways, one of which is optimistic: that we are really seeing a confluence/convergence of education, clinical research, and service moving into a new medical paradigm. We'll be speaking about that, actually, at some length in next month's Functional Medicine Update. You're going to get a two-part hit on this because next month we'll be speaking with Dr. Halsted Holman, the individual who authored the article in the Journal of the American Medical Association on the need for a new clinical education.

I think beyond there is also an implementation takeaway from this discussion, and it goes back to my introduction around antioxidants, and the CD36 receptors, and LDL oxidation, and the confluence or convergence among atherosclerosis and diabetes type 2, and cancer. When we look at things like vitamin C, should everybody be taking vitamin C? My answer would be yes. Clearly everybody should be taking it to prevent scurvy, but that's a minimum expectation. I think what we should take away is the recognition that there is a level of vitamin C intake beyond that required to prevent scurvy that is optimal for individuals in a normal, healthy function to support proper redox potential and to modulate oxidative chemistry. Here we are talking about intakes of something like 500 to 1000 milligrams...I guess you call it nominally. Then if we talked about in case of infection, or a chronic illness, or ischemic events would there be required higher levels of vitamin C? The answer appears to be absolutely yes from the work of Mark Levine and Qi Chen and others that have been really looking at the role that vitamin C plays in these processes.

What about vitamin E? Vitamin E, although it has been hit heavy in some of the negative press, certainly falls as an important member of this family of redox potential active nutrients. What about this rich array of phytochemicals that modulate along with minerals, like selenium, and zinc? Shouldn't they also be part of the antioxidant arsenal? My answer is yes, if we think of these all as signaling substances-as things that modulate intercellular signal transduction (berries, and grapes, and the whole vegetable family that has carotenoids, and has the nature of these pigmented substances that modulate cellular function).

What does it come down to? Again, almost the fundamental rules of logic that we've heard for so many years: diversity, minimally processed, high-plant-food-based diets, and things that we take in augmented levels that help regulate this complex interaction between our environment and our genes that gives rise to the expression of our health. A very interesting paradigm model that's a very big shift from the way most of us were taught either nutrition or medicine.

Thanks for being with us and look forward to Dr. Holman next month

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