March 2011 Issue | Steven Gundry, MD The International Heart and Lung Institute

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Welcome to Functional Medicine Update for March 2011. Why "Functional Medicine"? The definition of functional medicine, as it now is used within the Institute for Functional Medicine, is built around the 'omics' revolution that includes nutrigenomics, genomics, proteomics, metabolomics, lipomics—all these various new things that we're learning about cellular biology, cellular physiology, and intercellular signaling.

As we got into discussing this concept in greater and greater detail and seeing how it spread out to have so many implications in medicine, it became more and more clear that alteration in the functional status of cells precedes the onset of pathology: functional changes in signaling, functional changes in gene expression, functional changes in the way proteins are manufactured, how they are post-translationally modified, how they interact with substrates, how those are activated by co-factors, and how ultimately the expression of all these is influenced in their cellular organization to give rise to this dance of life that is called the phenotype of the cell. Looking at how the collection of cells to make tissues, tissues to make organs, organs to make organ systems, and organ systems to make the whole body then starts to demonstrate how individual changes at a cellular level could ultimately influence function of the whole organism.

The Whole is Greater Than the Sum of Its Parts

I think it's important to recall that the whole is greater than the sum of its parts. I don't want to sound reductionistic to the point of saying that if we understand each cell in the body that we would understand the organism as a whole; there is something greater than the sum of the individual piece parts. I think if we were to look at the emerging understanding of the origin of disease, we would recognize that the genes interact with the environment to give rise to the changing architecture of function, which ultimately gives rise (over some period of time, generally) to what we call a diagnosed disease. Understanding this dynamic systems biology process is very different than just driving for the diagnosis, which is the sine qua non for medicine (from the diagnosis comes the 'treatment').

The functional medicine model that has emerged over the last 20 years looks at antecedents as encoded within genetic pluripotentiality. This means the genetic background of the person, their family history, their individual genetic history, the things that wash over them as it relates to their lifestyle, the ecology that they're living in, their home (ecos—the home), their diet, exercise patterns, workplace, and relationships—all of these things are antecedents which then are worked upon by various triggers. Triggers are things that come up in the environment. It could be a motor accident, a problem with your employer, a change in the world economy, being laid off from your job, a serious infection. These things trigger the production, at the cellular level, of mediators.

Mediators reflect the status of the function of the organism. Mediators could be things like proinflammatory molecules, such as cytokines or chemokines that regulate the function of cells at a distance. It's a cross-talk situation. Now the body is under alarm. It is responding to an apparent offender or an onslaught; it perceives it needs to mobilize its defenses. Sometimes the body recognizes that the best defense is a good offense. It goes on an active seek-and-destroy-type mission to find the origin of these invaders and to try and do them in. Sometimes, however, what the body is doing in are its own host cells--the kind of auto-suicide types of situations that occur with apoptosis, oxidative stress, and activation of caspase genes that then cause the cell to be extinguished.

This leads to senescence: loss of biological reserve, increased frailty, loss of metabolic degrees of freedom, and sarcopenia (muscle loss in the aged). All of these things are ultimate manifestations from years of living with this alarm process that the body has been shifted into. From that will ultimately occur a pathology--maybe a a dementia of Alzheimer's, or it might be a motor dysfunction like Parkinson's disease, or it might be a metabolic disturbance that we call type 2 diabetes, or it might be a cellular proliferative disorder that we call a cancer, or perhaps an atheroma (a benign tumor on the interior of the arterial wall that restricts blood flow). All of these are outward manifestations of this inward alteration of function from the gene-environment interaction.

That is how we differentiate the functional medicine model from the histopathology model. They both have a place, obviously. It's not that one necessarily replaces the other. There is a place for each. Certainly in the emergency room--in the hospital environment where there is a need for immediate intervention--the histopathology model may be very primary in managing that patient quickly and rescuing them. In the chronically ill patient, however, it may require a different model and that's what we've been talking about in Functional Medicine Update over these many years.

We interviewed Dr. Halsted Holman last year, from the University of California at San Francisco, who is a professor emeritus of medicine. He talked about a patient-centered model that we need to implement for the chronic disease patient, the ambulatory patient, the one who never really completely gets rid of their disorder but rather it has to be managed. There is an element of the patient managing their own situation and teaching them how to do that and giving them the right tools. This is the place where functional medicine has its biggest role to play and its biggest opportunity to provide value to improve patient outcome and to reduce unnecessary expensive medical services.

Why "functional medicine"? I hope this summary I have give distinguishes the point of differentiation from a traditional pathology-based model. Functional medicine can be applied to the dominant patterns of dysfunction today in our society--these chronic disease areas that now constitute over 70{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of our healthcare expenditures.

This month in Functional Medicine Update I'm very pleased to interview a person who has taken this concept I'm describing and woven it into a very effective management program. Interestingly enough, this individual, Dr. Steven Gundry, has come through the histopathology model of medicine very, very skillfully as the head of adepartment of a medical school. In the department of cardiothoracic surgery, he has refined his skills and developed his expertise in the interventional model of medicine. It has only been in the latter part of his career (now) that he has transitioned to what we might call the functional part of medicine: the management of the chronically ill patient. He's going to tell us his story and give us news

to use in a way that I think makes very, very powerful sense.

With that in mind, let's move to our Clinician of the Month, Dr. Steven Gundry.

INTERVIEW TRANSCRIPT

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This is the time we always look forward to; it's our future, pace-leading clinician or researcher of the month. I'm very fortunate this month to introduce to you a person I think fills both of those bills. He is a master clinician, and he also has a research mind that is obviously very unique and very effective in assembling data in a complex area. I'm talking about Dr. Steven Gundry. Dr. Gundry is an MD. He has a very interesting background. He was a cum laude graduate at Yale, where he was a special honors student in a very interesting degree: human biology and social evolution.

After graduation he went on to the medical college at Georgia and completed a general surgery and thoracic and cardiac surgery program. He was at the University of Michigan as an academic, both looking at the research side of surgery and the clinical side. He ended up at Loma Linda University in southern California. Loma Linda is a very interesting medical school and medical institution that focuses on the interface between lifestyle, environment, and high-technology medicine. Dr. Gundry was department chairman there, and he did remarkable things in developing new surgical techniques.

I'm going to let him tell you his own story of how he made the transition from being one of the leaders in the technology of interventional medicine, and coupling that with lifestyle medicine and nutritional intervention.

It's a robust journey that Dr. Gundry has been on. He's written a book that I would call mandatory reading for all of us, Dr. Gundry's Diet Evolution, which is available on Amazon and elsewhere and in bookstores.[1] It has become mandatory reading among all of the members of our research staff and our clinical group here. I think it is a news-to-use, "aha"-type of book because it talks about the evolutionary approach—kind of a molecular anthropological/genetic anthropological approach towards understanding what type of diet, what type of foods, what type of nutrition might be best for beating back the chronic disease epidemic that we're starting to see right now.

With that in mind, Steven, it is wonderful to have you here at the Functional Medicine Update audio studio.

SG: Thanks for having me, Jeff. Great to be here.

JB: I've given, I know, a very cursory snapshot of your background. Maybe you can fill in the gaps with your personal experience, which I think will help to set the context for what you are going to tell us.

One Patient Led to a Change in Perspective

SG: Sure. I'm a researcher (primarily a bench and a clinical researcher). Most of my research interests were in the lab, in preserving heart tissue from ischemia or from resurrecting dead hearts. Believe it or not, we developed a technique where you could take a heart out of a baboon that had been dead for 30 minutes—literally lifeless—and resuscitate it, and give it a bunch of cute little chemicals through its blood supply, and put it into another baboon and it would start right up as if nothing had happened. I've got a nice little Lazarus poster in my office from my colleagues.

I'm interested in taking things that would seem to be irretrievably damaged and figuring out how to stop that damage from happening or reversing it. That wasn't so much the case in my own life. I was pretty much a big fat guy most of my life, particularly when I was at Loma Linda. I ate a standard Seventh Day Adventist low-fat vegetarian diet, and yet my weight had spiraled out of control. I weighed about 228 lbs at my top and I'm only 5'9" or 10". My cholesterol profile was terrible. I had pre-diabetes, I had hypertension, I had arthritis, and I tried every diet in the world and was very successful at them for a couple of months. You name the diet, I was good at it.

All that changed about ten years ago. A guy came into my office. I call him "Big Ed" in the book. He's from Miami. Big Ed had inoperable coronary artery disease. Every one of his blood vessels was clogged up; so clogged up that you couldn't put stents in, and you couldn't do bypasses because there wasn't any place to land the blood vessels.

Ed had been going around the country looking for a surgeon who was crazy enough to operate him. I fit that bill. I'm famous for operating on people nobody else wants to touch. I looked at Big Ed, and I looked at the angiogram (the movie of his heart), and I said, "You know, everybody who has seen you is right. I'd love to help you, but I just don't see how I'm going to do you any good." Big Ed lets out a sigh and he says, "Well, that's what everybody else says, but, look, here's what I've done. It's been six months since that angiogram was made, and I've gone on a diet, and I've lost 45 lbs."

Now, Big Ed was still a big guy; he weighed 265 when I saw him. He says, "I went to a health food store. I bought all these supplements." He brings in, actually, a big huge shopping bag of supplements. He says, "I've been taking these supplements every day. Maybe I did something with my weight loss and these supplements." So I'm kind of scratching my professor beard and patting my big belly, and I said, "Good for you for losing weight, but that's not going to change anything in your blood vessels. And I know what you did with all those supplements; you made expensive urine." And I really truly believed that at that time. I said, "At the most you've just wasted all your money." He said, "Well, I've come all this way. What do you say we get another angiogram? What would it hurt?" So I said, "Okay." We got another angiogram and then the next day I did a five-vessel bypass, because in six months' time he had cleaned out fifty percent of the blockages in his coronary arteries. He still had blockages, but now there were places to actually land blood vessels.

If I had known then what I know now, the last thing I would have done is operate on him, but I didn't know. After I operated I said, "Big Ed, give me that bag of supplements." I started looking through these supplements and a lot of them that he was taking I was using down in the laboratory in the form of intravenous solutions to protect hearts for heart transplant or to resuscitate hearts that had been dead. I was giving them through the veins of the heart; it never occurred to me to swallow them.

The other thing was I started talking to him about how he'd constructed his diet (because I loved diets). As he is describing it, light bulbs were flashing off in my head because, as you mentioned, I had a very fascinating major at Yale. For four years I investigated, basically, how we evolved from a great ape into a human based on social pressures and environmental pressures; basically, how our genes interacted with our environment and the foods we ate, and how that could turn a great ape into a human. I had a thesis that I got an honors for, and of course my mother had my thesis, so I called her and said, "Still got it?" And she said, "Oh yeah, absolutely." She sent it up to me and I'm looking through my thesis and I said, "Son of a gun, this is what I should have been doing for the last 20 years."

Self-Experimentation Leads to Healthy Results, a New Practice, Better Patient Outcomes, and a Book

I put myself on this diet, which is pretty well described in Dr. Gundry's Diet Evolution, and I started taking a ton of supplements. Not just willy-nilly—I actually started reading about them, which really, for me, would be the last thing I thought I'd be doing. I started sending my blood work up to Berkeley Heart Lab in northern California (it wasn't called that then). Lo' and behold, within a couple of months, my good cholesterol of 32 (which was terrible, my HDL) went up to 80 mg/dl, and my total cholesterol went from about 266 to 166 mg/dl, and my LDL went from 166 down to about 70 mg/dl. I said, "Son of a gun. I was told that this is impossible." Then several of my staff members started doing it, and the same thing happened on their blood.

So whoever I operated on at Loma Linda I would kind of enroll them into this program—teach them what they should eat and start giving them supplements—and the same thing started happening to them. Not only did their lipid profile get better, but a lot of these folks would call in a week or so and say, "What supplement are you giving me that is making me dizzy?" I'd kind of look at my nurse (I didn't know much about supplements at this time) and I'd go, "There's nothing in this that would make you dizzy. Get back into the clinic and let's see what's going on."

Of course their blood pressure was like 80 over 50, and they were on two or three blood pressure medications, and I said, "Well, son of a gun. I guess we better stop your blood pressure medicines." "Are you sure that's okay?" "Well, look. It doesn't look like you need them anymore." And then another patient would call and say, "Gee whiz, I think my blood sugars are getting really low. What are you giving me that's making my blood sugar low?" "Get back in here." And sure enough, we have to start backing off on their insulin, or backing off on their metformin, or their glyburide.

This kept happening, so much so that after about a year of doing this at Loma Linda I looked at myself in the mirror one day and basically told myself I was in the wrong business. So I made a leap of faith. I moved to Palm Springs to set up an institute, which I called the Center for Restorative Medicine, where I basically teach people how to restore their health. If they have heart disease, we basically teach them how to get rid of it. If they have diabetes or hypertension, we teach them how to get rid of it. And through the years it has expanded. I have a real interest in Parkinson's and Alzheimer's, which I actually think is the same disease (just a variation), and in autoimmune diseases, and more recently I've gotten into stage IV cancer patients. I've been actually surprised—maybe I shouldn't have been—with the effect everybody can have on seemingly dire problems.

So that's basically what I do, and being a researcher I decided that I was going to continue this as a research project, so everyone who comes in my office gets labs drawn that we send to a national lab every three months. We have an incredible database that we use to track what is happening to people. One of

the first things that appeared (very, very consistently) was I noted that the more people's triglycerides went down on their blood work, the healthier they got in almost anything I cared to look at. I said, "Isn't that odd?" That actually took me back further into my book (my thesis) and I said, "Son of a gun, I could have predicted this based on millions of years of evolution."

And that's how most of my thought processes have evolved.

JB: It's an unbelievably interesting story. There are so many levels of this to me when I hear your story. I've heard it now three times and each time there's another nuance that I catch. People who are real seekers are exploring all sorts of domains that are not necessarily within the midline of what they were trained to do. You find that as a characteristic in all innovative people—that somehow they were willing or inclined to go way outside the boundaries of what they were told they should be focusing their energy on. And that's how discoveries are made: by putting all that stuff together in a new perspective, which you've done so beautifully. Obviously the proof of the pudding is the outcome with your patients.

So this transition you made from academic medicine into private practice—that's a huge cultural change in its own right: the whole concept of billing, and office management, and procedures that used to be maybe handled by somebody at the institution now get handled by you, and how you make known your services, and all those things. Those are kind of the nuts and bolts part of it, but then the big issue is, of course, the transformation that's occurring both in you and your patients through this new advocacy.

Tell us about this 565-patient retrospective. I guess it is really more of an ongoing clinical observational trial or study. It's really very interesting.

Data From An Observational Study of Cardiac Patients Using Nutritional Therapy

SG: We started with a few of these patients, and then we started really enrolling them. One of our most recent studies has been to look at 500 patients that we've tracked now for almost six years. At the five-year mark (last year) we gave a paper at the American Heart Association. These were patients who had known coronary artery disease. They either had an MI, or they had a positive angiogram with lesions, or they had stents, or coronary artery bypass, or they had positive stress tests and didn't want a cardiac or surgical intervention like a stent or a bypass but wanted to try nutritional therapy.

We enrolled these people in my dietary program. The dietary program is actually fairly simple. We have fun little rules (they're rhymes). The first principle is, "If it's white, you keep it out of sight." We basically take away everybody's ground up grain products. The corollary to that is, "If it's beige, behave." Most beige foods are ground up grain products masquerading in some form. The third rule is, "If it's green, you'll become lean." We actually made our patients—and still do—consume a bag (or the equivalent) of dark green lettuce a day (however they want to get it into their system). If they want to cook a bag of spinach down into creamed spinach that's fine with me. If they want to eat a spinach salad that's fine with me. But dark greens: Romaine lettuce (Iceberg lettuce is banned), arugula, some of the really dark greens like kale, and Swiss chard, things like that. Those are the fundamental principles. We ask them to use only olive oil or canola oil for their salad dressings (to not buy any commercial salad dressings if at all possible). We ask them to eat—hopefully—grass-fed animals (that's pretty impractical, but it's getting easier and easier every year—eat animals that ate what they were supposed to eat): omega-3 eggs, grass-fed beef, lamb—the last lamb that is grass-fed now comes from New Zealand (almost all lamb is grain-fed), wild fish (get your good old Northwestern salmon that is out doing what it is

supposed to do). These are our main principles.

We then started them on some supplement programs that we would actually tailor based on the results of the Berkeley Heart Lab tests, which told us whether they had insulin resistance or what sort of other genetic profiles they had. Obviously we would have a completely different dietary program for someone who carries an ApoE 3,4 or 4,4 gene (the so-called Alzheimer's genes). We might have a totally different statin recommendation based on whether or not they carry a mutation of a gene called KIF6. I think actually any practitioner who deals in heart disease should get a KIF6 on their patients. It really can guide who should have statins and who shouldn't. Fifty percent of us probably have no business taking a statin drug because it will be totally ineffective, even though your LDL cholesterol comes down.

We enrolled these people in the trial. Every three months they had to have a complete set of Berkeley Heart Labs. We would check compliance by actually looking at how people's triglycerides were going. If I was going to get one blood test, that's the blood test I'd get on someone to predict their problems with heart disease. The lower the triglycerides the better. Most people will soon learn that the ratio of HDL to triglycerides is the best predictor of avoidance of heart disease or getting heart disease. That ratio should be at least 1:1, and the higher the ratio of HDL to triglycerides the better off you are. And yet most people walking around this country with normal levels of triglycerides and normal levels of HDL actually have a terrible HDL-to-triglyceride ratio. I think that's a huge cause of why we see so much heart disease in healthy living people.

At the end of five years, these people would be predicted, on the basis of very large (10,000 people) studies, to have somewhere in the range of 25 to 50 percent recurrence rates of heart disease (in other words, a new event—a new heart attack, a new bypass, a new stent, a new stroke, a new death). That's the standard of most tests, even on statins. Even on statins, the best statin trials still show an around 25{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} recurrence rate in 2 ½ years of a new event. So clearly this is not acceptable.

In our patients, in five years, 2 out of the 500 patients had a new stent put in, which is 0.4{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36}. One other patient had a carotid artery endarterectomy, which I did (because he didn't listen to me), and one patient had a stroke who was in atrial fibrillation and refused to take Coumadin. So our overall cardiac event rate in five years in 500 patients was 4 out of 500 or 0.8{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36}, so virtually nothing. This is 500 people with known coronary artery disease following a very simple diet and supplement program. This is not an irreversible process. This is not something that is going to happen to you. This is something that can be stopped. And the really exciting thing is we now have angiograms of people who have volunteered that show that the process is reversible, and it is reversible very, very quickly. I had the pleasure of showing you one of our more recent patients, who, in basically nine months, did a remarkable job of cleaning out his coronary arteries. The proof is in the pudding.

JB: I hope everybody is taking a deep cerebral breath to oxygenate those frontal lobes as they are hearing you speak. Let me, if I can, for those of you who don't have the privilege of seeing Dr. Gundry because you are listening to him, just mention—he would not say this himself—he's an extraordinarily fit, lean and mean as they say (in the best sense of the term), highly capable, good looking, fit, and raring-to-go professional. He showed us pictures of what he looked like a mere 10 to 15 years ago. I'm sure he was

intellectually lean and mean back then, but I think his physical frame and his physiology demonstrates a remarkable transformation in the 10-plus years.

We can talk a lot conjecturally and theoretically. There is lots of stuff we can theorize on, but where the tire meets the road is the real outcome. When we talk about 500 patients and a 0.8{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} secondary event in high-risk individuals, even if it's not double-blind, randomized, placebo-controlled and structured in biostatistical perfect language at Harvard Med, this can't be just dismissed as cocktail talk. There's something really serious here that we need to pay attention to. Just think of the cost savings, not to mention the potential human lives saved. It's just amazing.

Let's trace back briefly to a couple of things you said that I think are real ahas. I believe these would be considered "new" information for a lot of people. The first is the use of particle count versus normal lipid panels and your belief that routine use of these can make forecasting or trajectory assessments possible. And secondly, this triglyceride thing that falls off your lips very easily because you're very familiar with it, but for the average person who may be "Framingham-ized," triglycerides doesn't even end up on the Framingham Risk Factor trials. To say this is really a major determinant is an aha. Maybe you could speak a little bit more in-depth about those two.

The Use of Particle Count Versus Normal Lipid Panels

SG: Sure. Let's talk about particle size first. I really don't look at people's total cholesterol counts. I really don't look at their LDL counts. In fact, it may amuse your listeners to realize that there are major international lipid meetings that occur on a yearly basis. At these international lipid meetings, we vote once a year as to whether we should eliminate LDL from our nomenclature in talking about people's risk factors. Most lipidologists will absolutely tell you that LDL has really no meaning because there are seven particles of LDL (that are at least known now). They are generously described as either big and fluffy or hard and dense.

I actually use for my patients the idea that LDL carries fat around your body. These are mainly moving vans that carry fat. And if you have big moving vans—big professional moving companies—these are actually good for you. They carry fat around safely. They deposit it safely and so much the better. On the other hand, these little hard particles are what I call little pickup trucks. These are guys who put three rooms of furniture on the back with bungee cords and have mattresses flying off down the freeway. In fact I think the analogy is actually really good because these little guys are the ones that get activated, get oxidized, they're the ones that burrow into the endothelium that cause the foam cells, that bring the macrophages, and start this whole process. So the big guys are doing their job; it's the little guys that we have to worry about.

The nice thing is that in general, triglycerides are a very, very good indication of what kind of particle size you are going to make. Triglycerides are the first form of fat that we manufacture from sugars and starches, A long time ago in our evolution, the only time we ever saw sugars and starches was when fruit ripened on a tree, and that happened to be once a year in the summer, and we needed to store fat for the winter. If we're making lots of triglycerides, we actually kind of overwhelm this moving van system and we tend to make quite a few of these little pickup trucks. On the other hand, if we're not making very many triglycerides, we don't overwhelm any of these systems and we actually don't make very many of these little guys. That's simplistic, but it's amazing how accurate this is.

The corollary to that is that HDL, the so-called good cholesterol, is actually five different particles. There are little ones and big ones, and you might guess that the big one is good for you and you're right. The big one, called HDL-2B, is nicknamed "Pacman" because it literally goes around and gobbles up fat off of blood vessels where ever it can find it. It is produced by the liver and it goes out as kind of an empty sac. As it goes around it literally fills up. You can actually watch these particles fill up with lipids. It's really kind of exciting to watch.

If it is winter time you need to go pick up fat, so you make a lot of HDL in the winter when you need it. But if you are trying to store fat for the winter, the last thing you want to do is make HDL, because if you are trying to store fat for the winter you wouldn't want to pick it up. That's how I could go from 32 HDL to an 80 HDL by changing my triglycerides. The really fun thing I get to watch is that people can actually control, by their sugar and starch intake, what their lipid panel can look like. I don't really care if a patient has a very high LDL if 70 {56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of his or her LDL is these big fat moving vans. That is the vast majority of us—about 75{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of us carry a normal gene called the ApoE 3,3 gene. All bets are off when you carry an ApoE 3,4 or 4,4 gene (the so-called Alzheimer's gene), and unfortunately those individuals: 1) need to know they have that gene, and 2) need to know because there is something they can do about it. They are somebody who we would manipulate much differently than the average human being.

JB: I think that's another very extraordinary part of your program. As I've heard you describe it, I can imagine the extraordinary reaction your patients have when you are talking about personalization. Often we have these generic thoughts of, "Okay, you've got elevated lipids, we see a high cholesterol and LDL, so you need this statin, and if that one doesn't work for you we'll try another one." It's not personalized to that person's own specific genotype, and it also doesn't serially measure how what they're taking is influencing their overall dynamics. Maybe you can describe how you tie your Yale experience into this personalization. I think it's a very important part of what you are doing.

Genes: As Any Gambler Knows, It's Not the Hand You're Dealt, It's How You Play the Cards
SG: Our genes are, in the scheme of things, not very important. You and I have almost the identical genes. We have a few different ones. You have blue eyes and I have brown eyes, but in general most of our genes are exactly the same. What is different in each individual is the information that we give those genes via the food we eat, the nutrients we ingest, and the environment that we live in. It's now becoming clear that epigenomics--the information that these materials, these particles, these compounds have on turning genes off or turning genes on--makes all the difference in the world.

I like to say genes are just like little mini computer programs—they're either off or they're on. It's the switch that throws things off or on that makes all the difference. The gene just tells things what to manufacture. It's telling the gene to get activated or not to activate that makes all the difference. That's the incredible power that people don't realize they have.

There are bad genes. They actually aren't bad genes; they actually served an incredibly useful purpose, and most people don't seem to realize that. Bad genes got weeded out a long time ago. The genes we have had a very useful purpose. It may not seem very useful to the individual who has them, but I can guarantee you that they had a very good role, and that's one of the exciting things about looking at the

interaction of genes and the environment. A person who carries thalassemia minor—it's a wonderful gene to have if you live in the Mediterranean or live where malaria is because malaria can't reproduce in these little cells because they are abnormal. On the other hand, if you have a double copy of that gene and you have thalasseniaminor, that's a big problem, but that's weeded out usually. It's the same with sickle cell trait. Sickle cell trait is a great thing to have if you're in Africa where there is malaria. If you have full-blown sickle cell it's a terrible thing to have. And it is the same with these genes in cardiac disease.

The neat thing about genes is, as any gambler knows, it's not the hand you're dealt, it's how you play your hand. The wonderful thing about genetic testing is that as long as you know the hand you're holding, and know what you can do about that hand, it actually—to me—is incredibly empowering. I think it's a far better thing to have a patient know that they carry the Alzheimer's gene than not know.

Just yesterday I met a new patient who was from Los Angeles. She is in her early 70s and we did her testing. She's a very thin woman, and she is ApoE 3,4. I start going through the diet that she should eat, which is primarily a green-based diet (almost a vegan diet without the grain products). She said, "Isn't that funny? Since I was a little girl the only thing I like to eat is greens. I don't like animal products. I don't like grains. All I eat is greens. My favorite food is a big pot of collard greens or mustard greens and my husband thinks I'm crazy." And the interesting thing is (this was her first test that I had), she had the most perfect lipid panel for someone who has ApoE 3,4 gene, and she had designed her diet herself. Whether her genes told her "this is the food you ought to eat so I won't kill you" I don't know, but it was so great to hear, "Doctor, this is the diet I designed for myself," and lo and behold, she couldn't have done better in designing this diet for that gene.

JB: That's fascinating. One of the things you talk about in your book is an extension of this model. It's more than a model really, it's a fundamental paradigm that you've developed related to this interface between our outside environment and the antennae (the way I envision it) of the body—the immune system—that's picking up information all the time. We have an increasing tide of nonspecific autoimmune disease in our culture: thyroiditis, SLE-like, rheumatoid arthritis-like, multiple sclerosis-like symptomatologies. You have a very remarkable and, I think, clear distinction and explanation for this that relates to this gene-environment connection. Could you talk through that with us?

The Immune System Doesn't Make Mistakes

SG: Sure. I like genes. It turns out that we—in our intestines—have about 5 lbs of bugs. There are probably about 500 different species of bacteria, protozoa, and viruses that live in our intestines. There is 1000 times more genetic material in that 5 lbs than in the entire 150 lbs in our body. It's actually staggering to think about. We have about a trillion genes in each of our bodies, and yet there are a thousand trillion genes in that 5 lbs of crap.

Most people have really forgotten their basic biology course. Our alimentary tract, starting at our mouth and ending in our anus, is actually the outside of us. All the contents that flow through are the outside world. We now realize that those bacteria have been with us through evolution for as long as we've been evolving.

We inherit our colonic bacteria from our mother. As we pass through the birth canal, her fecal material actually inoculates us. So for each one of us, our colonic bacteria are maternal (our father gives none of our colonic bacteria). It's fascinating that babies who are born by caesarian section take a full six months

to establish a normal colonic bacteria because they never get inoculated.

The “old friends” theory says if we’ve got that much stuff in there they are obviously doing important things, and we really ought to find out what they are doing. We now know that for most animals, the bacteria in our colon, in one way or another, contribute to most of the food we actually absorb. Herbivores have to have bacteria to break food down into absorbable fats. A gorilla gets 58{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} percent of his diet from the fat the bacteria ferment, so a gorilla—believe it or not—eats a high fat diet. The fascinating thing is that we get about 500 calories of fat from bacterial fermentation in our colon. We now know that that fat, which is primarily butyric acid, carries a lot of information.

The old friends theory says that these bacteria are doing another job: they are the outside world. They have so much more genetic material and if they are going to have a free ride inside of us they ought to contribute something. And the contribution we now think they do is to tell our immune system what’s going on in the outside world as an early warning system.

They do this in a number of ways. The first is butyric acid, a fascinating compound that lets our immune system—our gut—know how happy the bacteria are. If they are busy making a lot of fat, they’re actually very happy. It’s no surprise to anyone looking at the gut—and I was a general surgeon before I was a heart surgeon—that the vast majority of our lymphatic system lines our alimentary canal, from our mouth all the way through our intestines. We’ve always thought of these guys as the first line of defense. Well, we’re beginning to think that it’s actually more than that. These bacteria may be the first messengers of information from the outside world.

The second thing that is fascinating is that our intestinal wall is one of the most impervious barriers there is. The tight junctions are incredible. Literally—as with our skin—we don’t want the outside world inside. And we’re realizing that it is the bacterial happiness that contributes to the integrity of that wall. The compounds that the bacteria make actually make that wall good or bad. Why is that important? Well, if a bunch of rogue bacteria were to come in, or if you take a bunch of antibiotics and kill off all your good guys, and you feed those bacteria things that you shouldn’t eat, all of a sudden you have a peaceful neighborhood that is being invaded by a gang war.

The walls of our intestines get little breaks in them. A large molecule like gluten could easily get through a break. Like with any splinter, when our body sees a molecule that’s not supposed to be there it makes antibodies in an attempt to signal to killer cells to kill it, and that’s a wonderful thing. But these molecules bear very striking resemblances to other protein structures in our body. When you look at the ladies who develop Hashimoto’s thyroiditis, they, to the person, are generally skinny, grain-eating women. There is a fascinating correlation between gluten and Hashimoto’s thyroiditis. Multiple sclerosis has incredible predilection for wheat-eating countries. Hard-wheat areas have much higher incidence of multiple sclerosis than soft-wheat eating areas. And you don’t even need that. All you need is a mixture of a problem in your intestinal flora—maybe a viral illness, maybe food poisoning—to just for a few brief moments break that intestinal barrier and let these compounds in, and then the whole cascade starts.

I don’t think the immune system makes mistakes. This whole idea that all of sudden we’ve got this epidemic of our immune system making mistakes just doesn’t make any sense to me. The immune system has been around a lot longer than the last 100 years. We never saw these problems before the

advent of antibiotics, and that's because in general our gut flora was there and did what it was supposed to do and was being fed proper things. It turns out that gut flora in humans actually loves two-leafed plants. They actually like cruciferous vegetables the best. On the other hand, they actually hate one-leafed plants (grains). By eating grain products, you will totally change the gut flora in any human being. It's how happy your gut flora are that actually determines how happy you are.

The prevailing theory now is that the gut bacteria actually tell your brain what they want you to do. For people who find that so hard to believe, we have more neurons (more nerve tissue) in our gut than we have in our entire brain. Truly this is the second brain, and in fact it may actually be more important than this thinking thing up above. Each of these neurons is capable of thinking, and each of these neurons gets information from its surrounding environment, which just happens to be the one thousand trillion bits of genes that are pumping out material to tell us what's going on.

JB: This is really, really fascinating. I interviewed--it must have been nearly 15 years ago--Michael Gershon, the author of The Second Brain, about this topic that you are describing.[2] I also had the privilege about a year ago to interview Dr. Nathalie Delzenne and Patrice Cani at Louvain University in Belgium, who were the first to discover this connection between gut bacteria and obesity.[3][4] That was another aha. I think what you've layered on, here, is a systems biology interaction of how all this ecology contributes to gene expression and modulation of function. ,

I want to go back and pick up one last topic before we finish this more than stimulating discussion, and that relates to the personalized supplement program. I know you probably have a whole array of different things that you use for different patients, but are there some that that you find that are extraordinarily helpful to fill in some of the gaps that should be in everybody's thought process as they are evaluating patients?

Recommendations and Rationale for Certain Supplements

SG: Yes, I personally like the idea of using the anthocyanins, the procyanins, and the polyphenols as a large packet of individual supplementation. Ancient hunter/gatherers used to interact with about 250 different plant species on a rotating basis (on a yearly basis). And the animals that they ate also interacted with those 250 different plant species. I don't care if you're the best organic food eater in the world, I would dare say that none of us interacts with 250 different plant species today, nor do I think those 250 different plant species were grown in six feet of loam soil with all the ecology of the root system that we now know exists between the bacterial interplay with plants.

Having said that, I think even the best possible human diet right now can't possibly duplicate what we used to encounter. I used to be one of the biggest anti-supplement persons there was, but now I think a person who doesn't supplement is not going to achieve the ultimate health that they could. Certainly the berry extracts are important. I am a big fan of tree bark extracts of all kinds, particularly in my cancer patients (pycnogenol, just to name one, Pau D'Argo, cat's claw).

The other thing that I think is very important to look at is mitochondrial health. I'm a big fan of L-carnosine as another generator of mitochondrial health. As you know, there are a number of "longevity experts" who have gone so far as to put themselves on metformin (glucophage). I haven't made that step yet. I can understand the logic. I would much rather use something like L-carnosine to break the glycolytic pathway down a little bit. I think the next area of my interest is getting the mitochondria to

function as well as it can.

JB: I know you have spoken also very eloquently about magnesium, which is a soil-depleted nutrient. Maybe you can just say a word about that as well.

SG: I think every practitioner ought to ensure that their patients take supplemental magnesium. Magnesium is so important for so many things. It is one of the major membrane stabilizers of all cells, and certainly of nerve cells and of cardiac muscle cells. I study (obviously) patients with heart disease, and if someone is coming in for a coronary artery bypass, we have to give them two grams of magnesium sulfate intravenously every six hours for 48 hours to replete their magnesium stores. Potassium is kept in serum at all costs. You will completely, totally, utterly get rid of your potassium from every cell to keep your serum level normal. For instance, if you have a patient who has a low potassium, you can say that that patient absolutely is probably 400 milliequivalents deleted just off the bat. Same way with magnesium. Most people walk around with a "normal" magnesium level, but they are so depleted of magnesium that it is startling how much we have to give them.

Magnesium stabilizes the brain. Magnesium may be one of the best sleep aids there is. Magnesium is an incredible antidepressant. It's amazing how many people who are depressed, if I can get them swallowing 500 milligrams or 1000 milligrams of magnesium (you build their tolerance to it), that helps with depression. People who walk around with restless legs, get your magnesium levels up.

One interesting sideline of my diet: magnesium is actually stored with glycogen in muscles, and one of the effects of an initial sort of low carb diet is obviously to deplete liver and muscle glycogen stores. When we first started doing this patients would call in and say, "I've got muscle cramps. What's the deal with that?" I didn't know it at the time, but I said, "Well, take magnesium and that will solve it," and of course it did. Then I started investigating why they would they get muscle cramps. It turns out it is because the magnesium is pulled out with glycogen, and so your muscles are depleted of magnesium and they go into spasm.

JB: That's a nice segue to maybe the last part of this discussion. Again, I really recommend listeners obviously should follow up with Dr. Gundry's Diet Evolution book. I think it will give a lot more of the details. One of the things you describe in that book is the power of a ketogenic diet and how that could be considered kind of a therapeutic diet. Can you tell us a little bit about your experience and why you feel that's a desirable therapeutic approach?

Discussion of a Ketogenic Diet

SG: We're certainly designed, as an animal, to go through prolonged periods of starvation. Those of us who are walking now are the result of our ancestors being able to tolerate long periods of starvation. Starvation in and of itself, and a calorie restricted diet, puts animals (or ourselves) into a period of ketosis. The really interesting thing about us, as an animal, is that we have absolutely no need for carbohydrate as a fuel source. Just ask an Eskimo. Eskimos don't eat fruit and they don't eat plants; they eat blubber (they eat fat and protein). We, of course, have the ability to convert fat into ketone bodies, and actually free fatty acids are incredibly good fuel. These fats live on phosphate backbone. When fats are broken down, the phosphate it is a phenomenal fuel for ATP. We're designed to be able to not only survive on a ketogenic diet, but actually to run quite well on a ketogenic diet. The heart prefers fatty acids as a fuel far more than glucose. This is well known.

The interest in ketogenic diets as a therapeutic diet probably first started in the treatment of epilepsy. A very, very high fat diet (particularly a high fat diet with medium chain triglycerides, which generate ketones) was very therapeutic for seizure disorders. The brain clearly loves glucose. In fact, the brain is the major consumer of glucose in our body, but the brain will run on fat. It doesn't particularly like it, that's why you get a headache when you go on an Atkin's diet for a couple days as your brain switches over to burning ketones. Your brain says, "No, no no. I want sugar. Give it to me now." That's why we get a headache.

We are now beginning to realize that Alzheimer's, and Parkinson's, and a lot of the neurodegenerative diseases, are the brain cells actually starving from insulin being unable to deliver sugar into cells. We've not really appreciated how important insulin is as a hormone in delivering sugar into brain. For many years we thought it really wasn't necessary, that the brain didn't need insulin to use sugar. In fact, we now know it does. Brain cells develop insulin resistance just as the rest of our body does. There is now an increasing theory of type 3 diabetes, where literally we have insulin resistant brain cells. One theory is, "Okay, let's give those brain cells insulin," and interestingly enough you can spray insulin into the noses of Alzheimer's patients and for a couple of hours they'll get smarter. It's not a long term practicality. The alternative is that brain cells don't need insulin to use fat. And so you can actually use a ketogenic diet to feed brain cells.

Where I first started using a ketogenic diet is in patients with Parkinson's and Alzheimer's. One of my best examples is my father. My father, five years ago, was on three Parkinson's medications. He could walk maybe across the living room and that was about it. I took my mother aside—my father was 80 at that time—and I said, "Look, you're going to have to intervene here and I want you to try my diet on him." My father now walks five miles a day. He's on no Parkinson's meds. He looks, unfortunately, like me a great deal. He lost about 45 lbs. We were in a winery the other day and the fellow serving us said, "So are you two brothers?" It pissed me off. This is a classic example. We totally changed what we're feeding his brain. We took away his starches. We took away his fruits. We took away his grain products. He eats quite a high fat diet. He gets cheeses. He takes coconut oil. But it totally changed the fuel that his brain was capable of using.

That experience led me into using a ketogenic diet for cancer patients. I think cancer cells are fascinating because they have an Achilles' heel. Cancer cells have to have glucose because they can't do glycolysis properly; they can't do oxidative glycolysis. They have to use huge amounts of glucose. I tell my patients, "Guess how we found your cancer cells? We took some sugar. We attached radioactive isotopes to it. We injected it into you. And we put you under a scanner. And guess what? The hotspots, where the sugar is being eaten most quickly, is where the cancer cells are and that's how we found them, because they're eating the sugar." This is such a simple concept: If that's what they eat, starve the little devils. You and I do not need sugar. Our cells will run perfectly fine on fat and will run perfectly fine on protein. We don't need sugar. The really interesting thing is that if cancer cells try to use fat as a fuel, they actually explode; they produce hydrogen peroxide. They kill themselves.

I use a very extreme form of my diet, in which basically people don't get any fruit. They get no seeded vegetables. Seeded vegetables are fruits: cucumbers, squash, tomatoes, zucchini, peppers, eggplant. These are all fruits. And I take away all their grain products because ground up grain products are just sugars. We give them quite a bit of coconut oil (extra virgin coconut oil). It turns out there are polyphenols in extra virgin coconut oil, and that's actually probably where the benefit is; it's about one-tenth of what's

in olive oil.

I think there are a whole host of reasons why a ketogenic diet is useful. The last reason is that during starvation, our system (our body) is designed to go around and look for cells that aren't pulling their weight. There is only so much food to go around, and we have an incredible system to create apoptosis in cells that aren't doing their thing because they're dead weight and they ought to be disposed of. There is periodic fasting in every great religion. This is not hocus pocus. Every religion has some form of fasting built in. You look at people who practice calorie restriction, or you look at animals. We've now done it in Rhesus monkeys. The University of Wisconsin published, in 2009, a 20-year study.[5] You can have two littermate monkeys and one 40-year-old looks like a grizzly old arthritic animal and the other one looks like a teenager bouncing around in the cage next to him. This is ketogenesis. These guys are on a slightly ketogenic diet.

I'm a big believer in it. I see patients whose cancer "miraculously" goes away, I see Parkinson's people like my father pick up their cot and start walking. This is not placebo effect. This is real.

JB: That's about the most extraordinary advocacy that we could probably have to end this discussion. Obviously all of you who are listening I think want to look at Dr. Gundry's Diet Evolution book and fill in some of the gaps here.

Steve, I really want to thank you. This has just been extraordinarily uplifting. Also, clinically, news to use, for the people who are looking for where the tire meets the road and how you speak to your patient in the exam room. You are a master of the metaphor, which is always the best teaching tool. I just want to compliment you. You're very courageous. It's a very complicated thing to make a career change as you have and to do it with grace and provide value to your patients. All we can say is be very, very successful. We really appreciate your leadership.

SG: Thanks for having me here. You've been a real beacon for all these years and keep up the good work.

JB: Thank you so much.

I hope you enjoyed Dr. Gundry's comments as much as I did. There was some really interesting and important information captured by Dr. Gundry. Again, I think his book is really worth looking at because it brings this whole concept he described to life: modifying the environment of the individual to quell some of the genes that are expressing alarm and inflammation.

I want to say a few things in close about that because this theme that Dr. Gundry has been speaking about so eloquently is not just a side bar of minor importance. We're seeing more and more--in peer-reviewed top-tier journals--discussion of this concept of genes and environment and how to modulate the function of an individual who is in a state of distress (distress meaning proinflammatory, or pro-oxidative, or in an apoptotic model where they are losing cell mass prematurely and losing biological reserve, increasing their biological aging). This concept is really at the forefront of molecular and cellular biology, physiology, and even at the etiology of tertiary diseases. For the first time we are starting to see emergence of a mechanistic understanding of the origin of so many of these age-related diseases. They derive from this concept of gene-environment interaction, as Dr. Gundry was speaking to us about.

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