March 2013 Issue | Sara Gottfried, MD Gottfried Center for Integrative Medicine

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Welcome to *Functional Medicine Update* for March 2013. What a way to end our first quarter of 2013, by focusing this issue on women's health problems that we recognize are rising in prevalence—things related to perimenopause, things related to dysmenorrhea, things related to what I guess you would categorize as disturbances of hormone signaling as women go through different phases in their development process. We're very excited this month to speak with a noted clinical expert, a person who has really been studying this area in depth, way back from her early studies at MIT in bioengineering and later at Harvard Medical School, and that's Dr. Sara Gottfried, who you're going to be hearing from just in a moment.

I want to just set a couple of ground rules for our discussion that will follow. Those ground rules are related to how we view the symphony of information that comes into the body through different proprioreceptor systems that stimulate certain receptors that then activate certain downstream processes, and ultimately give rise to what is our function. That complex orchestration is obviously tied in part to how our genes respond to this information, so we have different genotypic responses (no two people are identical). We have epigenetic modulators, as you know, that have put different kinds of tags onto our gene code that say either "read here" or "don't read here" that relate to how certain expression patterns of our genes are realized under certain circumstances. We can say that we are hard-wired from our genes, but we're also soft-wired with our software called our epigenome. We've studied that extensively in Functional Medicine Update over the past 10 or more years. And then, there are the environmental modulators that influence the way that metabolism actually works, so these could be things like simple nutrients like the B-complex vitamins that are precursors to the co-enzymes that regulate enzymatic function at the metabolic level.

All of these things, when woven together, give rise to this control of the complex orchestration of our individual response to our environment. As our environment has continued to change in the 21st century, with even more time urgency, with even more digital connection, with even more environmental perturbation through the development of and environment contamination by new chemical species from which the human genome is only now getting its first information. All of these things are starting to create different signals that then translate through the genome and the epigenome into the phenotype that

then produce different kinds of health patterns, and those disease patterns or chronic illness patterns then become the dominant reflection of the gene-environment interaction of our time.

I think this is why many of the things that we're going to discuss in the women's health area have started to demonstrate shifting sands of prevalence because we're seeing different types of information being delivered to the genome through lifestyle and environment that is then translated into the phenotype with different types of outcomes as it relates to these messages and how they're translated into function.

I believe that Dr. Gottfried has a wonderful way of contextualizing this, of actually helping us to understand the complexity of these interrelationships at a level that people can actually deal with. Sometimes, the scientific, high level, mumbo jumbo is a little off-putting and you need to translate this down into news-to-use where it can actually be effective in people's own life process and how they'll manage their own challenges of environmental pressure. I think you'll find, in discussion with Dr. Gottfried, that she does a beautiful job of helping to assemble this information in a user-friendly way that can be dealt both at the clinical level and ultimately at the patient-management level.

It's all about self-management, isn't it? In the end, self-regulation has to engage the person in their own life in a different way. This is not all going to be a solution from a pill, or a solution from outside. It's going to be a solution from the inside, from the way that person constructs and ultimately delivers their own life experience through the environment in which they find themselves.

So this will be, I think, a very interesting conducted tour through a functional medicine perspective on women's health, taking what I think is a broader context of this post-genomic era that we're living right now, in how the genome, the epigenome, and the environment interact to give rise to function. I hope you'll enjoy this. You'll note that we are going to travel across some uncharted terrain. We'll talk about upstream and downstream modulators, we'll talk about various types of factors that engage women in altering physiology in response to environmental stress and pressure, and then we'll talk about how these can be remediated and modulated based upon sensible programs. So, a lot of stuff, here, ahead of us, but I think you'll find it very, very useful and fun to listen to Dr. Gottfried and the way she describes this. Let's move on into our interview with our clinician of the month, Dr. Sara Gottfried.

INTERVIEW TRANSCRIPT

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Once again I'm at the place in Functional Medicine Update where you and I both collaborate in wondering: who's going to be the clinician or researcher of the month? You know, we've not been disappointed, have we, over the last several years, in some of the most remarkable luminaries who have brought clinical news-to-use, or new conceptual frameworks to our thinking about health care, and you're not going to be disappointed this month. A long-standing colleague, friend, and person who I have tremendous respect for professionally in the way that she has chosen to orchestrate her practice, Dr. Sara Gottfried is an endocrinologist—well, actually, obstetrician/gynecologist, but you'll find that she also is an endocrinologist from the way that she has done her own training and her own work to apply some of the recent breakthroughs in understanding of the female endocrine system and how it interrelates with obstetrical and gynecological issues within the female of the species.

The Hormone Cure: Reclaim Balance, Sleep, Sex Drive, and Vitality Naturally with the Gottfried Protocol

She has a new book out, a book that I think is an extraordinary contribution to our literature and I'm sure we'll be speaking through, about, and around the book, and the book is titled, "The Hormone Cure: Reclaim Balance, Sleep, Sex Drive, and Vitality Naturally with the Gottfried Protocol," so that leads us, obviously, into the news-to-use part, because we're going to discuss some things that Dr. Gottfried, over the years, has discovered through really hard work and by understanding the complexity of the interaction of the female genome with the environment, and how that weaves its way through messenger molecules, called hormones, into function.

Let me give you a little bit of a background on Sara. She's quite a remarkable scholar, having been involved with both Harvard Medical School and MIT in her training. She completed her residency at the University of California at San Francisco, and she is still involved with teaching medical students and is board-certified in OB/GYN. As you probably recognize, California has a very interesting population of proactive, get-real, resist authority, female patients who are looking for the right answer, which keeps her sharp all the time. I think you'll find that she has obtained that balance between the left and the right hemispheres of the brain, between the seductive rational thinking and the emotional and—I would call it—intuitive thinking, to really weave together quite a remarkable approach to her practice. You will discover that she is very, very skilled in some of the body/mind components—what I call comprehensive or integrated delivery systems (kind of functional medicine systems). So, we have a very skilled, diverse, constant learner that we're going to be listening to. Dr. Gottfried, thanks so much for being with us. It's such a pleasure to have a chance to share your work with our functional medicine group.

SG: Thank you so much, Dr. Jeff Bland. I'm so delighted to be with you and with your tribe.

JB: It really is. I think it's a shared tribe, probably, between us, here, or among us. Let's talk a little bit about how someone with your extraordinary educational background might have, by some perspectives, ventured off the beaten path and ended up in the kind of practice that you have, which I think is a very broad-based comprehensive practice using complementary and functional concepts. How did this happen, because one might look at your resume and say, "Well, this must be a purveyor the most scientific,

rigorous, analytic, reductionist form of staying-in-the-lines practice."

How You Eat, Think, Move, and Supplement

SG: Well, I would definitely agree with the rigor, Jeff, and I think the reductionist part is where I want to make some changes. My story actually dates back to childhood. I'm 46 years young now, and I grew up with a great grandmother who really taught me about functional medicine 40 years ago. I was living in suburban Maryland, and she would show up at our house (she lived in Palo Alto, California). She would show up at our house not with Barbies and See's Candies like my friends' grandparents, but she would show up with kale, and omega-3s, and she really believed that you find the answer to health in how you craft your lifestyle, and how you eat, move, think, and supplement. She practiced yoga, she was a whole food-ist, and this was at the time of Pop-Tarts and Charlie's Angels. You know, it was quite radical at the time, but it wasn't really something that I understood completely, Jeff, until I was in my 30s. I had finished all of that medical training that you so nicely described, and I found myself as a working mother, two kids, married, working in McMedicine (I was working at the local health maintenance organization). I just was miserable. I felt chronically overwhelmed. I was burning the candle at both ends. I blamed my husband for much of this. I had PMS. My sex drive was low, and I know most doctors don't reveal these kinds of things, but I actually think it's important to speak the truth. And I did what many folks do in that situation. I went to my primary care physician, and I was offered vitamin P, so he really thought that Prozac was a good idea for me, and that was a defining moment, Jeff, because I really felt that it was wrong—that it was exactly the wrong treatment for me—because I wasn't depressed; I was chronically stressed out, and yet, I didn't have the sort of training (conventional training) to address it. But I was able to take my medical training, at that point, and apply it to myself because I had a hunch that it could be that my hormones were off. Ultimately, it turns out, that's exactly what it was. I started testing myself—doing something that here in California we call 'biohacking'. I started testing myself, and I found that my serum cortisol in the morning was 30. So it was about three times the ideal level, and this was not Cushing's syndrome; it was stressed out mom in her 30s. Once I started to correct my cortisol and stared to apply what I later figured out was functional medicine, systems-based thinking, that's when I started to really feel better. It took me about four to eight weeks to really get my hormones back in balance again, and I realized that this was a gigantic gap in conventional medicine, so that's what ultimately led to me bringing these functional medicine tenets to the next 10,000 people that I took care of, and to develop what I now call the Gottfried Protocol, and to write the book "The Hormone Cure."

JB: First of all, thank you so much for your direct honesty. I think that sets a really great tone for the conversation we're going to have. It makes this very authentic, and I think we can all identify and tap into the pico-second, time-compressed society in which we live, and sometimes the last thing on our list is us; everything else comes first and then we wonder, where are we in this this whole equation? So I think you've laid that out beautifully. You just crossed an interesting line with me, however, that I want to come back and pick up, and I'm sure there are other listeners that are thinking the same thing. In my introduction to you, you notice I made a Freudian slip, and that is I talked about you as an endocrinologist, when you're really a board-certified obstetrictian/gynecologist. I think that was my subconscious mind kind of at play because your work is very, very skilled—what I would call functional endocrinology—applied to the female, and it crosses disciplinary boundaries. You know, we're in this interesting world where we know more and more about less and less until we know everything about nothing kind of model, so how does this work that you can cross this boundary and remain intact in your medical community, because that's one of the challenges in functional medicine we all have, are these

boundaries?

Reproductive Endocrinology

SG: Sure. Well, those boundaries, I think, are often artificial and unnecessary, right? I think many of them were developed at a time when we were very disease-based, and we know that the healthcare system is failing, so first of all, let's just question the dogma of the boundaries to begin with. But you raise an important point, and also hat's off to you, Jeff, because you similarly are a totally genre-bending thinker when it comes to these issues. But dialing back to the whole question of endocrinology, I'm board-certified in gynecology, and it's definitely true that most women, I believe, start with their gynecologist when it comes to the most common endocrine problems that come up. So, if they're feeling premenstrual, or their sex drive is low, or they just feel tapped out, like their energy is not where they want it to be or it's inconsistent, I think they often will start with their gynecologist. As part of my training, one of the subspecialties in OB/GYN is reproductive endocrinology, so I definitely learned a ton of reproductive endocrinology when I was in my medical training at UCSF. In fact, at the time the chairman was a foremost authority on reproductive endocrinology, and that definitely influenced our training, and that's Robert Jaffe. His focus is actually on the fetal adrenal, but that's maybe a conversation for another time. Anyway, I learned a lot of endocrinology in my training, but you're right that I'm not board-certified in endocrinology and yet I really found that women, especially, come up against this gap between what they want to solve: being overwhelmed, their sense of being stressed out, their sense of being hormonally out of whack, and certainly what is offered by traditional endocrinologists. I think endocrinologists are great when you have a crisis. So if you have Cushing's, or if you have Addison's, which as you know, are the only two extremes of adrenal function that are really recognized by conventional medicine, there's definitely a time and a place for endocrinologists, and I would say that's a good example, but for the rest of us that are in that middle road between Addison's and Cushing's, and we have what I would call dysregulated glucocorticoids such as cortisol, then I think we've got to look at other solutions. When I saw that gap, when I came up against it myself, I had that "a-ha" moment of just realizing, "Okay, endocrinologists are just going to dismiss anyone who goes to them with a problem related to cortisol, so why don't I start addressing that?" And what I found, ultimately, is that most of the hormone problems women face trace back to stress hormones, especially cortisol. So that's like the longest answer ever to your simple question.

JB: No, that was a brilliant answer. Thank you. As you are speaking, you're giving me an "a-ha" here, so thank you. The "a-ha" I'm having is when I think about your both professional training and then your after-traditional professional training, things like becoming a yoga expert and yoga instructor, I'm thinking that often in our downstream training—let's call it our professional training—we learn about things that are specific to that discipline, whatever we call it (let's say, in this case, gynecology), and so the vocabulary that we have for that field, and the topics that we discuss, and our expertise are designed around that body of information that specifically relates to those target organs. And often those are maybe downstream messenger molecules, so let's talk about steroid hormones. Cortisol is one of those. Aldosterone is one of those. Testosterone is one of those. Estrogen is one of those (the estrogen family of molecules). DHEA is another one of those. So we have a family of these downstream modulators we call steroid sex hormones, or let's just call them steroid hormones, that are all related to tissue-specific effects that occur as a consequence of the upstream things that are going on in our life. You might ask, then, "Well, what controls the downstream effects? What are the upstream players?" And so we get things that are not hormones from a traditional steroid hormone sense; we get releasing peptides, like luteinizing

peptide, or like corticotropic-releasing peptides, or like hypothalamic-releasing peptides, thyrotopic-releasing peptides. So these are proteins that are upstream from these hormones that come from specific tissues that regulate tissue activity. And then we think, "Well there are other peptides that are upstream that also weave into this symphony, like the peptides that we call cytokines, these inflammatory immune modulators, and there are endorphins that are peptides that are produced by the central nervous system that interface with these downstream mediators." And then I think of your training in yoga, and I think, "Well, hold it. Training like that often has an effect upstream. It influences the releasing substances that control the downstream regulators of these steroid hormones." And often we spend all of our time talking about the downstream things, and maybe we forget a little bit about the upstream things. It seems like your approach—your 3-step protocol—really deals with both up- and downstream relationships. Am I on the right track, here, or is this taking us in a funny place?

Start Upstream: Focus on the Brain and Steroid Hormones

SG: You're exactly on track, and this is why I love having conversations with you, Jeff. It just makes me do the happy dance. You're exactly right. If we look at that upstream control system…I'm an MIT bioengineer, so I always like to think about, "Okay, what's the control system? How do we modulate this?" And I completely agree with you that you want to look at, really, the brain, and I would say starting with the amygdala, where we perceive stress and we perceive threats. I like to think about, for instance, the HPA axis (the hypothalamic-pituitary-adrenal axis) and all of those peptides that you described (the corticotropin-releasing hormones), as well as those other mediators that you're describing (the endorphins, the cytokines), and you're correct in that I'm not a big fan of just addressing the downstream modulators. You know, if I were just trying to focus on cortisol and maybe creating a better balance between estrogen and progesterone for a woman who is in perimenopause, or if we're just focused on trying to improve T3 levels (free T3 levels) in someone who is suffering from thyropause, I don't find that you're as likely to get a cure if you approach it that way. I really believe you've got to go as upstream as possible. There are many ways to do that. I've tried to address that in my book through a number of strategies. In fact, I've got about 97 ways that you can do it. And then another upstream piece that I want to bring in that was a topic of conversation the last time I was seated next to you at dinner, Jeff, was the gene-environment interface. Right? I remember…can I put you on the spot for a moment, because I asked you a very direct question. You had just come from some big meeting, I think in Colorado, maybe it was in Aspen, where you were having the latest immersion in the gene-environment interface, and I asked you, "So, Jeff, what about epigenetics? Where are we with understanding the opportunity of epigenetics? What percentage of our DNA can be modulated with epigenetic effects, or as my great grandmother would say, how you eat, move, think, and supplement?" I don't know if you remember your response. Should I say what I recall you response was?

JB: Yes, please. You're doing a beautiful job. I love it.

SG: Okay, good. You said that you really felt that 50 to 80 percent of our DNA, and the way it is expressed (the expression of our DNA), could be modulated by epigenetic effects. Does that still feel accurate to you, because this was a few months ago that we talked?

JB: Yes, yes. I think that is what is emerging to be seen, that the big, maybe, regulators—these things that we call the promoter regions of genes that control whole systems of gene expressions—are very heavily impacted by epigenetic triggering. So, yes, I agree.

Glucocorticoid Resistance: An Example of Upstream Thinking

SG: Yes, and I've gotten super interested mostly because I'm a board-certified gynecologist, although I also work with men. I've gotten very interested in what is that epigenetic opportunity for women? So as we talk about this upstream control system…maybe I'll just give an example, here, so it feels a little less abstract. Maybe what we can do is just talk for a moment about the serotonin transporter gene (SLC684). What stymies me is that somewhere around 40 to 45 percent of Caucasians have one or two copies of the short serotonin transporter gene (the normal version is to be long-long). What we know is that folks who have one or two copies of the short genes, and especially two copies (who are homozygous), they have an increased susceptibility to depression. They don't move serotonin around the brain in an ideal way, so the communication system is faulty. They also are much more likely to have what I would call a hot amygdala. So they are more likely to perceive danger, especially of the emotional type. Another piece that I think is interesting—and this has mostly been shown in monkeys (I like to be really clear about the evidence that we have)—what we know is that women who have a normal amount of estrogen (well, female monkeys, in this case) behave as if they have the long-long, or the normal version, of this gene, and once their estradiol starts to drop, they behave as if they have the variance (one or two copies of the short gene). So to me this is really interesting and it sort of was another "a-ha" moment for me when I thought, "Okay, this is why so many women who are of a certain age—let's just call it maybe 45 to 55—perhaps this is why they feel like they suddenly go into survival mode where they're perceiving threats and we also know that they have something called cortisol resistance, or glucocorticoid resistance, meaning that they become bathed in cortisol at a high level, and feel this chronic stress that keeps getting reinforced, and they are unable to respond to glucocorticoids the way that they normally would." So, similar to insulin resistance, there's this phenomenon of glucocorticoid resistance. How is that as an example? I was trying to keep it ridiculously simple. I'm not sure I succeeded.

JB: No, you did, and I think that raises a couple of really important points. First of all, you know, often in our society what we would do when we look at that kind of information of the short-short versus the short-long and the long-long versions of that serotonin transporter gene is we might say that those individuals born with the short-short homozygous are people that have flawed genes—that they've got some disease propensity because they got this inheritance factor that made them more susceptible, or made them more vulnerable or brittle in our society. And so we put a stigma on them—and we do this continuously as it relates to these genetic characteristics. It's really a form of discrimination in some sense because what we start doing is saying, "Oh, well, you didn't really get good genes." What really we should be saying is, "Those genes that you have are genes that maybe at a certain time in history were selected for, in your distant ancestors, that gave them survivability in the environment in which they found themselves, so in a certain set of circumstances those genes would be considered advantageous, not flawed." Like the thrifty genes of the Pima Indians, you know, that make them more at risk to obesity and diabetes, aren't flawed genes; those are genes that are really selected for the biggest threat that they had in their history, which was survival against starvation. So in a certain environment of low calories, these are really desirable characteristics, just as maybe a hyper-responsive/hyper-vigilant/perceived-danger gene might be very good in an environment where you're worried about your survival every day and you're a mother trying to protect your young. I think these constructs that we often use as labels end up being off-putting and stigmatizing, and sometimes keep a person from really recognizing that what might be perceived as a weakness may be a strength if we were just to put them in the right environment. So that's point number one that I would make from your discussion. And secondly, is this concept of, "Okay, are these modifiable factors?" Once you recognize that you have this genetic characteristic, can you change its

expression or the pattern by which it—in the phenotype—produces an adverse outcome? In other words, it doesn't allow the person to properly manage daily living in a way that gives them great pleasure and joy, and I think that's what your program really does. Your three-step Gottfried Protocol—is it is a way of designing an environment for those individuals whose genetic uniqueness, not necessarily genetic flaws, to be successful, to be victors? Am I on the right track, here, as to what I heard?

SG: You're totally on the right track. You've just described precisely what I love the most about you, Jeff. I mean, I just think you're such an incredible integrationist when it comes to thinking about these things, and I also really appreciate how you're talking about these genes, not in a stigmatizing, but rather in what I would call a glass-half-full way. So you're absolutely right that this propensity to be hyper-vigilant if you are homozygous for the short serotonin transporter gene, the propensity to have depression, to not shuttle serotonin around very well, to have glucocorticoid resistance and a hot amygdala, what I have found is exactly the point that you're making. Yes, there must have been a time where this was advantageous from an evolutionary point of view, and I would also add that anecdotally, in the people that I have tested, I've only gotten short results (homozygous short) in my female patients. In the people that I've tested, I would even say that they have some mystical qualities to them. I don't want to get too woo-woo; I'm going to stay with the data, here, but you've got to remember I'm also trained as a yoga teacher. These folks have really found a way, I think as they've been challenged by this short serotonin transporter gene (maybe there are other genes that we don't know about that relate to this). They made their mess their message, and they've become really world experts at how to reverse the effect of this particular gene. So, I really love where you're going with this in terms of understanding not from an either/or dualistic way of looking at genes, but first of all to say, "There might be an evolutionary benefit to this," and then to say, "Okay, and here's what we know about how to influence those genes." As I mentioned, what we know in monkeys when it comes to the short serotonin transporter gene is that estradiol seems to help. It seems to help folks with the short variance behave more like they are long-long. We need to collect that data in humans, but it might become one of those really important decision points, especially as women hit perimenopause, that second phase of perimenopause where estradiol starts to drop. You know, it may be one of those important decision points on their dashboard when they are making decisions about whether to take hormones or not. And then the other one that I wanted to mention—another epigenetic influence—is P5P (pyridoxil-5-phosphate). That's another one that has animal data showing a benefit in terms of the effect of the short serotonin transporter gene and how it's expressed. It seems to help with the cortisol resistance.

JB: You know, I'm absolutely fascinated with where we're going in this conversation. For those that are listening, this wasn't premeditated and rehearsed. I think this is the magic of what happens when you have conversation and true communication with people that are experts like Dr. Gottfried, and that is what often happens in medicine, I think, particularly with this gene era in which we live (the post-genomic era), is that we get into discrimination and kind of a meta-eugenic argument and what I call genetic determinism. It becomes very, very disempowering for people because we start thinking somehow that because of these genes we've just analyzed that they're determined to get a certain disease. It's kind of a recasting of a eugenic argument that we tried to get rid of in the early 20th century but still sticks with us, and it discriminates against that person and puts them in a class, and now they become that class of what we treat. We forget about the individual and now we treat that class because we've labeled them. And what you're really speaking to so beautifully is ways of modulating the expression of these characteristics by changing the environment, changing both the micro- and the macro-environment. That's a different kind of medicine, by the way, I believe, philosophically, than the way

that we grew up from our view that disease is caused by a vector that you treat with a molecule and you then have a self-limiting condition where the body gets well. These conditions that we're speaking about that plague us in the 21st century are very complex situations that relate to pattern disturbance across multiple parts of our physiology, and no one magic bullet is going to treat it. It requires this much more sensitive orchestration that you're speaking to so beautifully in the Gottfried Protocol. As I listen to you, I can just envision how you speak to your patients, and how it must be very empowering for them to go from the model that they're flawed to the model that they're in control; they have a locus of control. I bet you have a lot of "a-has" with your patients.

How Will Medicine Make Genetic Testing Actionable?

SG: Well, I believe that is true. I think so many of the women who land on my doorstep—you know, they first come to me because they want to get their hormones in balance, and of course that's just the tip of the iceberg. But, you're right that many of them have been dismissed, or they feel like they're doing something wrong. You know, they feel like a stress case because they can't get to yoga often enough, or they don't want to sit on a meditation cushion every morning, and I think it is so important to do what you're describing—to really validate their experience and to talk about, "Here's the biology. Let's address the biology and then figure out if there are any emotional/psychological components that need to be addressed once we have improved your biology." I completely agree with that, and also I think you're calling out something very important. I don't think we've got good language around it, but this idea of new paradigm medicine, or personalized medicine, and the fact that I've heard some predictions—and maybe you can chime in here—what I understand from when I was at MIT and they were working on the Human Genome Project was that it cost about three billion dollars to sequence the first genome. And now, it costs about 10 grand—10 thousand dollars—to sequence your entire genome. But in 2015, it is predicted that it will cost about 100 dollars to sequence your entire DNA. So that's an incredible opportunity, but I really believe that old school medicine has no idea how to make this actionable, so it's an incredible opportunity for functional medicine, for the practitioners who are listening to us, to really understand, "Okay, how do we help people going forward? How do we message this? How do we help them with their short serotonin transporter gene, or the Amish gene (one of those thrifty genes that you're talking about, where your tendency is to put on weight, and—if you're like me and you're trying to fit in your skinny jeans—you're fighting it all the time? How do we help people make this information actionable, especially as the costs significantly decline in the next few years for sequencing your genome?" Do you have any thoughts about that, Jeff? Can I ask a question back to you?

JB: Absolutely. This is a dialogue that's really fun. Well, I think you're right on point. I just went to a meeting, here, a month ago in Mountain View, California, that was the global personalized medicine symposium, and for three days there were speakers every 15 minutes that were, like, the head of the FDA, the head of Medicare, the head of Aetna, the head of Blue Cross, the head of NIH. I mean, this was a very esteemed panel of presenters and it was all focused on this question that you're raising, and that is, "What are we going to do now that the cost of having a full sequence of your genome will be accessible to virtually every patient?" In fact, it is suggested that it will start with infants, and every infant will ultimately get their full genome screened, and then it will transfer from that into other members of our society, but eventually—within a period of probably 10 years—everybody will have on a smart card the full sequence of their genes, which is the ultimate lab test, by the way, because if you think about it, every lab test you ever want to do or will be done (developed in the future) has information that's really encoded in your genome and your epigenome. These are major paradigm shifting, seismic changes in the way that we

can enlist technology into understanding certain strengths and weaknesses of our uniqueness. The question is always—and that was the principal question out of the meeting—"Okay, what do we do with it? Is this all going to be doom and gloom that now you know how you're going to die, or is it really how you figure out how to live, and how to live effectively to the limits of your biological potential, whatever that might be--a century-plus of good living, compressed morbidity, and you know, have natural death that James Fries talked about in 1980 in the New England Journal of Medicine?" This is a new medicine that's going to emerge to support this technology. I mean, it's not the old medicine. The old medicine is wait until it is broken and fix it, and we see how efficient that is with the rising cost of health care, so this new medicine will be prospective rather than retrospective. It will be functional-focused rather than pathology-focused, and it will change curricula, education, training, and reimbursement for health care and how it's delivered. So we are at the front edge. One can argue how long it will take to occur and certainly I have been recently criticized that I am always the guy talking about how the change is right over the horizon and then the question is, how far away is the horizon? But this is an inevitable change, this is not a fad or a fancy, this is something of substance as important as was the discovery for infectious disease—that bugs can cause illness—and that's where we are right now in society.

The Difficult Part is Not Making a Plan, it is Implementing It: Daily Lifestyle Challenges

SG: I completely agree, completely agree. And I think it's so important for folks who are listening to understand that this is coming and to prepare for it—you know, to really invest in your knowledge, you know, whatever your niche is, however you want to start taking this on and helping people with understanding how you uplevel the expression of your DNA. You know, my particular niche is the neurohormonal dashboard. I've tried to make it astonishingly simple in The Hormone Cure, but I find that the challenge—even with all the science that we have, even with all the randomized trials that we have for how to work with your neurohormonal dashboard--what I find is the difficulty for folks is not how to make a plan, but rather how to implement it—like, some of those daily lifestyle challenges that keep people from being able to do the things that they know to do. When I start off a talk sometimes I'll ask people to raise their hands if they know what to eat in order to lose weight, and all the hands go up. And then I ask them, "Okay, how many of you are doing it?" and the majority of the hands come down. So we know so much about how food, and exercise, and the right dose of mental retraining, and the right supplements, how they influence your DNA, and yet I still think there's a big gap in terms of helping people implement and maintain. Do you have any thoughts about that piece, Jeff? I mean, I found that yoga was one of the best ways to do it, but I would say more often than not in my practice when I suggest yoga to people, they look at me bug-eyed, like that is the last thing they want to do. They don't want to go sit in a yoga class. Do you have any thoughts about this particular piece, about the implementation and the maintenance?

JB: Well, I think you are one of those leaders who is helping us to understand how to translate intention into action. That's why books are important. That's why books from leaders who know what they're talking about are important. That's why being mentors, and guides, and role models and walking the talk as well as talking the walk is very important, and I think that's why your book is a substantial contribution, because I think "The Hormone Cure" gets down into some of the issues that you're speaking to in a very sensible way that comes from your experience, both as a person—as mother and as a person walking the world as a woman—and as a professional who understands the intricacies of how physiology plays out. I think you're part of the matrix of change. I'd like to think that we are, in some small way, as well. How many individuals does it take to change a lightbulb? I'm not sure, exactly,

because we're trying to change the light that lights up global society, but I think this is a movement that is enlisting all sorts of people from different backgrounds who are seeing the light and are becoming advocates for a transformative state of thinking, which has to happen because this old model of thinking…the proof of the results are already in. It wasn't a controlled study, but enough data are there that we can pretty much understand what the strengths and weaknesses were of that study, so now what are we going to do? Are we just going to continue to do the same and hope for different results, which is the definition of insanity? I think that you're absolutely—in your book—talking about the answer to your question of me.

Cortisol, Thyroid, Estrogen: Charlie's Angels

SG: It's true. I guess I'm always trying to ask that question and answer it because I want to reach as many people as possible with, "We need to make these changes—the upstream and the downstream changes—that aren't painful and don't feel like a gigantic project." I'm always trying to find the small hinge that swings the big door. That happens to be yoga for me, and we know that yoga helps you with the mental retraining. It helps you with tendency towards cortisol resistance. It helps with limbic hijack, and then downstream we know that it reduces cortisol, it reduces IL-6 (one of those cytokines you talked about). It also raises melatonin. So I'm a big fan of making that list as long as possible. I really want to offer people an a' la carte menu for working in this way, for both the upstream control systems, as well as that downstream place that I call altered Charlie's Angels. I think about your hormonal Charlie's Angels for women, which is your cortisol, your thyroid, and your estrogen; and in men I call it the Three Amigos, which is your cortisol, your testosterone, and your thyroid. I found that those three seem to be very important, especially for women. I also realize, for women who are reading my book, I wanted to offer the content in two ways. I wanted one option to be very streamlined, where you take a questionnaire, figure out the root cause of your symptoms—for why you feel like you're rushing from one task to the next, or feel tired but wired, or have endometriosis or fibroids or painful breasts, and then to be able to go to the chapter that corresponds to that particular problem. I did quantitative surveys in my patients to figure out what the top 7 hormone imbalances are, and those are the chapters of my book. So I have this very streamlined way that you can do the book, where you figure out your root cause and then you go to the Gottfried Protocol, this functional medicine approach to solving the problem, starting off with filling nutritional gaps and lifestyle tweaks and moving on to step two, which is proven botanicals, and then step three, bioidentical hormones (but for the shortest duration and at the lowest doses). I did that because I had some friends who read my book, and they said to me, "Sara, I love the book, but clearly that whole Harvard/MIT geek is coming out. Like, there's so much science here. You make it really interesting, but if you say 'adrenals' one more time, I'm going to smack you." So I wrote the book in these two different ways, and I wrote it, honestly, also for practitioners, so that they could have the data consolidated around how to address these top 7 hormone imbalances that women face. Have it consolidated in one place, and especially in chapter 4, where I address cortisol. I wanted to have that science consolidated and ready to have conversations with conventional physicians. That was a really important piece for me.

JB: I think that's probably why I loved the book so much, is that it really spoke to hemispheres of my brain. Obviously, I like to think that it's a male brain, but the female influence came through very strongly. I think that you did a really nice job of treading that balance between enough of the science to demonstrate the rigor of authenticity, but put in the context of a useable program that really addresses the uncertainty of life and the process by which we navigate through life. It's really a useable program. I'm very, very impressed. I guess one of the last questions I really should ask you—we could go on and on, and

I'd love to in this conversation, but I know you've got a life to lead and things to do here—let me ask you, in making this practice that you evolved over 20 years and defining your professional and personal identity, you've undoubtedly run up against individuals who maybe have questioned how you've approached this. Maybe they've said, "Well, gee, you should stay in ordinarily confined areas and do what I want you to do"—this whole control of the guild-type model. How, as a physician, have you been able to make this change in your professional life? How do you make a living at it? How do you go through the daily world of peer oversight? All those kinds of things that we live in that become part of the reality, as you were saying, of putting our legs in our pants every morning. How has this worked for you?

The Devils We Know: Premarin and Provera

SG: I would say it has worked fabulously well. Whenever I answer a question like that, my default, which I think is similar to yours, Jeff, is to go to the data. I go to the data. To me, I think the first part of your question is about the doubters or the people who maybe feel threatened about the way that I take on conventional medicine and address these gaps that I came up against myself when I was in my 30s, and I know millions of women come up against them, too. The first part of that is that I really feel it's important to be rigorous about the data. What I've emphasized in my book is the randomized trials. A well-designed randomized trial, as you know, Jeff, and our listeners know, is the best quality of evidence that we have; it's got the least amount of bias, as long as it's done well. I really feel like we've got a shameful past, especially in women's health where we were using synthetic hormones—not just recommending them—and you know the devils I'm talking about, here. The devils we know: Premarin and Provera. We were prescribing them for 57 years before we had a randomized trial showing that they are dangerous and provocative in 1999 with the HERS study, and then confirmed again with the Women's Health Initiative in 2002. Now, of course there were many flaws in that study—I don't really even want to get into that—but I just think it's shameful that we had 57 years of prescribing these hormones to women in a vast, uncontrolled medical experiment. I was taught not just to suggest them but to really proselytize them in my training.

So I feel that it's very important that we keep women safe, and that we have randomized studies to support the recommendations that we make. So the data that I have, the recommendations that I have, the solutions in my book, are all supported by randomized trials. Getting back to that question of the haters…my daughter said to me the other day…someone called my publisher and complained—she said that I didn't go to Harvard Medical School—and that's because I had my maiden name when I was at Harvard Medical School, and she also said, "Dr. Gottfried is recommending estrogen without a prescription and I disagree with that." And she didn't understand that I'm talking about the way that you eat, move, think, and supplement as a way of changing the tango between estrogen and progesterone. Getting back to that bridge that I want to build with conventional medicine, I really feel like this us/them paradigm is not good; it doesn't serve anyone. And so I want to meet the conventional physicians in the middle. I am fortunate to have gone through the same medical training. I know what it's like. I'm not blaming them for these gaps that we have in what women want. But, I also feel like we need to work together to find the right solutions. The first part of your questions is really, "How do you deal with the haters?" and I would say start with the data because that's a lot harder to argue and there's less of an emotional tone to it. The second part of it is, "How is this working for me?" and I think dialing back to when I was in my 30s, when I was working in McMedicine and struggling so much with PMS, and low sex drive, and wanted a glass of cabernet pretty much every night as a way of dealing with it—which, oh, by the way, raises your cortisol, it's not a good solution—what I found was that when I really stepped into my own authentic ideas

about how to take care of people, everything downstream was better. So that made a huge shift for me, and now, you know, I wanted to go from the one-to-one conversation that I was having with clients in my office to the one-to-many conversation, and I really love that. I think there's something very sacred about leverage, about teaching online, about doing what you're doing, Jeff, with how you train practitioners. I'm super excited about that. That's another reason why I'm so excited about the book, but the short answer is: it feels a lot more authentic to be working with people in this way.

JB: I think that's a powerful, powerful sound bite that really relates to the advocacy that probably all of us feel when we step a little bit out of what was considered the standard of thinking at the moment. It's not that every different idea is always right. You can get into the Galilean dilemma—because Galileo said that the sun was in the center of the universe and he was excoriated—anybody that thinks differently is a Galileo. I don't think that's always true, but I think there is something very special about being authentic to your purpose and using the best of the information you have from your colleagues, your training, your peers, but not being bound by it. The brain is still there to create solutions that we probably didn't even know were going to come about until time moves on, so I want to just compliment you not only for the writing of the book, which I think is brilliant, but really for your advocacy, for the way you language things, for the sensitivity you have within your practice and your world. I think it's a model for what many of us in the functional medicine movement are aspiring to be known by and be imprinted with. Thank you so much. We've spent a lot of your time going through this discussion, but every moment for me has been very, very rewarding and I thank you for all your hard work and your advocacy for your patients.

SG: Thank you so much, Jeff. It's been such a pleasure to be with you. Every time I talk to you it raises my oxytocin, and we know how good that is.

JB: That's a good way to end. I think we both are on an oxytocin high. Thanks so much, Sara. We'll be in touch, and good luck as the book moves forward.

SG: Thanks, Jeff. Thanks, everybody.

Bibliography

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