

Dr. Sara Gottfried: How to Optimize Female Hormone Health for Vitality & Longevity | Huberman Lab

My guest is Sara Gottfried, M.D., a Harvard-trained, board-certified gynecologist and clinical assistant professor of integrative medicine & nutritional sciences at Thomas Jefferson University. Dr. Gottfried specializes in hormone health, vitality and longevity using precision/personalized approaches. We discuss female hormone health, puberty, perimenopause, and menopause, hormone testing, the microbiome, stress related hormone challenges, their causes, and various treatments. We also discuss fertility, birth control and tools for improving microbiome health, treating PCOS, insulin management, and the best nutrition, supplementation, and exercise programs for women. While the episode focuses mainly on female hormones, males will also benefit from our discussion because it includes actionable tools suggested for managing stress, bolstering the gut microbiome, and immunity—all of which stand to improve overall health, vitality and longevity in males and females.

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Welcome to the Huberman Lab podcast, where we discuss science and science-based tools for everyday life, I'm Andrew Huberman and I'm a professor of neurobiology and Ophthalmology at Stanford school of medicine. Today my guest is Dr Sarah Gottfried, Dr Sarah Gottfried is an obstetrician gynecologist. Who did her undergraduate training in bioengineering at the University of Washington in Seattle? She then completed her medical training at Harvard Medical School, and she currently is a clinical professor of Integrative Medicine and nutritional Sciences at Thomas Jefferson University. She has also been a clinician treating men and women in various aspects of Hormone Health and Longevity for more than 20 years. She is an expert in not just traditional medicine, as it relates to hormones and fertility, but also nutritional practices, supplementation and behavioral practices, and combining all of that expertise in order to help women navigate every aspect and dimension of their hormones. Longevity and vitality, ranging from puberty to Young adulthood, adulthood, perimenopause and menopause, and nowadays she's also treating men across the lifespan in terms of longevity vitality and Hormone Health. During Today's discussion, Dr Gottfried shares an enormous amount of information and tools that women can apply toward their Hormone Health fertility, vitality and longevity. We discussed the gut microbiome, which many people have heard about, but Dr Godfrey points out. The specific needs that women have in terms of managing their gut microbiome and the ways that that influences things like estrogen levels and Metabolism, testosterone thyroid and growth hormone and much more. We also discussed nutrition and exercise. We touch on how the omega-3 fatty acids play a particularly important role in managing female hormone Health. Dr Gottfried points out why women have particular needs when it comes to essential fatty acids and how best to obtain those essential fatty acids for Hormone Health. We also discuss exercise and she offers some surprising information about the types and ratios of resistance training to cardiovascular training that women ought to use in order to maximize their Hormone Health. We also talk a lot about the digestive system. This was a surprising aspect of the conversation I did not anticipate Dr Gottfried shared with us, for instance, that women suffer from digestive issues at more than 10 times the frequency that do men and, fortunately, that there are tools specific to women that they can use in Order to overcome those digestive issues and that in overcoming those digestive issues, they can overcome many of the related hormone issues that so many women face. Dr Gottfried also shares with you tremendous knowledge about the specific types of tests, not just blood tests, but also urine and microbiome tests that women can use in order to really

get a clear understanding of their hormone status, not just of present, but also where the trajectory of their hormones is taking them, so we have an avid discussion about puberty about young adulthood, adulthood perimenopause and how best to manage and navigate perimenopause and menopause, including a discussion about hormone replacement therapy. In addition to her academic and clinical expertise, Dr Gottfried has authored many important, important books on nutrition hormones and supplementation, as it relates to women and to people generally. The two books that I'd like to highlight and that we've provided links to in the show note captions, are *women, food and hormones* and *the hormone cure*. I read *the hormone cure* and found it to be tremendously interesting and informative, not just in terms of teaching me about female hormone health and various treatments for female hormone health, but also as a man trying to understand how the endocrine system interacts with mindset. Nutrition and supplementation more generally, so I highly recommend *the hormone cure* for anybody interested in hormones and hormone health and *women, food and hormones* in particular for women. Although again, both books are going to be strongly informative for

00:03:51 ROKA, Thesis, LMNT, Momentous

Women wishing to optimize their hormone health, vitality and longevity before we begin I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is, however, part of my desire and effort to bring zero cost to consumer information about science and science related tools to the general public. In keeping with that theme, I'd like to thank the sponsors of today's podcast cast. Our first sponsor is Roka. Roka makes eyeglasses and sunglasses that are the absolute highest quality. I spent a lifetime working on the biology of the visual system, and I can tell you that your visual system has to contend with an enormous number of challenges. In order for you to be able to see clearly so, for instance, when you go from a very brightly lit area to a dimly lit area, your visual system has to make all sorts of adjustments that allow you to still see your environment. Roka. Eyeglasses and sunglasses were built with the biology of the visual system in mind, so no matter what environment you're in you'll be able to see with perfect clarity, and they have terrific aesthetics, an enormous number of choices in terms of aesthetics. So, unlike a lot of so-called performance eyeglasses out there, that only give you the option to wear the ones that make you look like a cyborg. They have

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00:07:50 Women, Family History, Heredity & Environment

Huberman and now for my discussion with Dr Sarah Gottfried, Dr Gottfried, Sarah welcome. Thank you so happy to be here, yeah, I'm delighted and very excited to ask you about an enormous number of topics. Here we are expert in so so many things so uh. The challenge for me is going to be to constrain this walk as it were, but I'm hoping that we can touch on a great number of things today, the first of which is really about hormones and female hormones in particular - and I have a question which is: Is it ever informative for a woman, regardless of age, to know something about her mother's? Perhaps even her grandmother's experience, vis-a-vis hormones, not just pregnancy, challenges with or um ease with pregnancy and child rearing childbirth, this sort of thing. But you know what sorts of conversations should women be having with themselves and with family members to get a window into what their specific needs might be love this question, so my work is really at the interface between genetics and environment, so your question gets to both And I think it's essential that you understand what your grandmother went through. I'd even say your great grandmother, depending on longevity in your family, so I grew up with my great-grandmother. I get that and especially your mother, so I would probably start first with trauma an intergenerational trauma because I think that affects the endocrine system so hugely especially cortisol signaling, but the broader Pine system, psychoimmunuroendocrine system and then there's you know if I think about the stages. The life cycle that a woman goes through. If you think about puberty, I think I don't know how genetically determine the age of puberty is. Certainly there's a lot of environmental influences like toxins can affect it, but um pregnancy. The age at which you start to go through perimenopause menopause, many of those have a genetic component, so with pregnancy I mean you can certainly think the shape of the pelvis, your ability to have a vaginal birth. Some of that is genetically determined. I mean you do, have you know the the sperm donor affecting

some of that, but you know in my family, for instance, we have no cesarean sections, so everyone goes through this process of a relatively easy vaginal birth. I was a forceps baby, but you know for the most part um you can find out about that and then there's certain female conditions that have a very strong component, genetically most of which run in my family. So that includes endometriosis fibroids. I just had a hysterectomy. I added 50 plus fibroids

00:11:00 Puberty, Stress, Menstrual Cycles, Intrauterine Devices (IUDs)

And polycystic ovarian syndrome and of those three uh. How frequent are those - and maybe I can constrain the question a little bit by saying um. Today's discussion, I imagine, is going to be heard by men and women of all sorts of Ages, so I uh, maybe I'll direct the question a little bit toward you know at what age should these discussions start um? You know we always imagine that women in their 30s and 40s and 50s and onward should be getting certain tests and addressing things like uh, ovarian reserve and and other sorts of things. But you know, maybe we could March through and just say for a woman in her teens who's already hit puberty, what sorts of biomarkers, whether or not they're, blood-based or per or um phenotyping. You know the outward appearance of uh. Should those young women be paying attention to likewise for women in their 20s 30s? Maybe we could take it more or less by decade at starting at puberty, assuming that woman hits puberty sometime what between? What is it now? The average in the U.S is somewhere between 12 and 16 years old. Do I have that right? No, you do not, oh great, so that's to be wrong, so so it used to be 12 to 16.. I would say 50 years ago it's been moving younger and we think some of that is related to toxin exposure, as I mentioned, but I was 10 when I went through puberty so uh well, I should say menarchy and I started growing breasts much before that. So I think now I'm going to step away from the science for a moment, I'm going to do that pretty fluidly and I'll try to call it out. I think there's also a huge influence from stress and like the development of the adrenal glands. So going back to the science, the issue in teenage years is that the hypothalamic pituitary adrenal axis and I like to think of it broader, so stay with me. Hypothalamic pituitary adrenal gonadol, a recent women testes men thyroid gut axis. So that to me is the control system, so I'm kind of expressing my bioengineering side here. Well, I think it's great to include the other organs and tissue systems of the body, because, as we

both know that the narrow definition of just hypothalamic pituitary adrenal, it can't be just that right. No, it can't no yeah, it doesn't tell the whole story. So if you look at the the main sex hormones in a young woman who's in her teenage years, the hypothalamic pituitary adrenal gonadal part of that is not fully mature, so they're more likely to skip periods, especially under stress they have a lot of influences. It really doesn't get well established until you're done with adolescence, and I'm told that adolescence now is still like age 25 to 26.. I heard that, and I was like I've got two daughters and I was like that's a really long time and not just a psychologically defined or bio psychosocial, mostly psychologically defined. I heard that from a psychologist, so biomarkers you asked about in your teenage years. What I think is really interesting is to look at cortisol to look at the dance between estrogen and progesterone in those years is less helpful because I think there's a lot of variability due to the immaturity of the system. If you've got someone, who's got really regular periods, it's probably better to do some benchmarking at that age, but generally I find that benchmarking is best performed in your 20s or 30s are periods not that regular in terms of duration of the menstrual cycle. When the menstrual cycle first sets in it depends so I was like clockwork every 28 days until I had my hysterectomy in August same thing with my daughters, I've got two daughters, one's 17, the other is 23. for a lot of women, they're, not regular, and then There'S the whole piece of oral contraceptives and other forms of contraception, where you have no idea what the normal cycle is - and I hope we'll have some time to talk a little bit about oral contraceptives, because I think it is. This is now opinion again and not science. I think it is the number one endocrinopathy that is iatrogenic for women uh. We will definitely talk about it. I get a lot of questions about oral contraceptives, um in the social media space and also questions about iuds. Quite a lot totally in particular copper iuds, non-non-hormonal IUD, so we will definitely touch on that. I'M an IUD Crusader, so I just want to you know: give you that warning you're you're a fan. Do I have that right or you're anti? I am a huge fan which iuds in particular, so I like copper, because it's non-hormonal it's as effective as getting your tubes dyed. Who would have thought right? I mean it's that toxic to the sperm Mobility. Is that how it works? That's my understanding of it is that that it basically it's like a more or less an electric fence to the the sperm cap and just that's it. Electric fence is a bit of a harsh analogy, but I'll work with that. But it's it's. For 10 years, so that you really have complete autonomy and sovereignty over your sexual life, that's profound and to not get all those Downstream risks, they're associated with a birth control pill. The other thing that's important to know about it. I know this is a sidebar

women who use the copper IUD, have the highest satisfaction rate of anyone on contraceptives, the highest satisfaction rate, and yet it is the least used of all forms of contraception. Now my favorite is vasectomy but short of vasectomy. I think the IED is a really great choice. There are some risks associated with it. I'm not saying it's risk-free, but I love IUD and I love it for younger women too, because it used to be that when I went through my training, which was 30 years ago, we were told you know, don't put it in someone.

00:17:26 Tool: Sex Hormones, Microbiome, Estrobolome & Disease; Biomarker Testing

Who hasn't had a baby, and that is patriarchal messaging, but getting back to your original question, which is about biomarkers per decade in your 20s? That's when you want to do some base casing with estrogen, progesterone and testosterone. So I think it's really helpful to know about this. This Tango you're from Argentina or your father. I have Argentine lineage. Yes, my grandparents did Tango into their late 80s. I I am I'm in my late 40s and I I still haven't started so I suppose there's time it might be time for you to okay and it might be a factor in their longevity. Did they have good health span and my grandfather Smoked Cigarettes daily remained mentally sharp until he died in his late 90s, but um almost burned down their apartment several times falling asleep with a cigarette in his mouth. So I don't recommend anyone Smoke by the way uh, but it was uh, coffee, mate, uh, red meat and cigarettes and they lived into their 90s so that side of my family has the genetic Advantage, the other side less so um, but in any event, uh Tango. Um is a 2023 goal. It has been every year, um the uh, I'm gon na hold you accountable today, okay, we'll do and there no, there will be no YouTube. Video of me do at least not initially Tim Ferriss. Actually, a phenomenal podcaster, as we know, is uh he's a badass he's a badass Tango Tango dancer. I know this through various sources. Yes, yeah, I've seen yeah, so this Tango between us and progesterone is incredibly important. You want to have the right lead. Do you want to have the right follow between the two hormones? Again, I'm stepping away from my science hat, but what happens a lot of the time is that estrogen dominates in that Tango and when that happens, it sets you up for greater risk of fibroids endometriosis. Breast pain, probably in association with the microbiome and the estrobolome, can you familiarize me with the estrobloom yeah, I'm delighted to know that I don't recognize the term yeah, so the estrobolume is the set

of microbes in and their DNA their DNA, mostly in the gut microbiome. That set of microbes in their DNA, so it's in the. If you look at the totality, the subset of particular bacteria modulate estrogen levels. So a lot of this work was spearheaded by Martin Glaser, and what we know is that there are some women who have an estrobolume that makes them have a greater risk of certain estrogen mediated conditions like breast cancer, endometrial cancer and a men prostate cancer. So the estrobulum is incredibly important. There'S not a lot of attention paid to it, but I always think in terms of my patients you know, could this be someone who's got a faulty, a strobe and we need to adjust it with. You know some of the microbiome modulating uh nutrients nutraceuticals that we have so that they're less likely to have that that Tango, that's not working with estrogen progesterone, so getting back to the biomarkers. If, if you gave me an unlimited budget, which I kind of have with some of my um clients that I work with now, what I would want to know is estrogen progesterone testosterone, and I want the timing right for that. I'D want to know about DHEA and sort of the whole Anderson pathway. I'D want to know about the metabolites of estrogen, because some of them are protective and very helpful. Others are a bit like Homer Simpson. I mean they're just like causing all kinds of problems in your body: increasing the risk of Quinones like DNA damage and potentially an increased risk of breast cancer. Although that data, I think, is mixed. I'D also like to know about their stool. So I want to know about the microbiome, so the best that we have right now is to look uh. When we do stool testing, I do a lot of stool testing. We can look at things like beta glucuronidase. Are you familiar with BG, I'm familiar with it? As a term and so for those listening it very often not always when you hear an ace, ASE you're dealing with an enzyme, so we can take a stab there and - and it sounds like it's somehow involved in um glucose metabolism of some sort or is it Clickeronautation, so it's involved in when you produce estrogen in the body. This is like the simplified version, but when you produce estrogen, you are meant to use it like, send it to The receptors where it's meant to go and then lose it like. You don't want to keep recirculating the estrogen like Bad Karma and that's what happens with people who have high blade beta gluconidase. So it's this enzyme, that's produced by three bacteria, in particular in the gut, and I see a lot of men and women who have elevated beta glucuronidase and then they have some estrogen dominance related to. That is that the total reason we don't really know, but it's one of the drivers, it's one of the levers and it can be detected from a microbiome, AKA stool sample, that's right and in terms of blood testing or various tests. For these other biomarkers, getting estrogen, testosterone and

other ratios I realize there are people have different means financial means, but in general people wanting to do a blood test. It sounds like they're going to need to do it. What women will need to do it at different stages of their menstrual cycle if they had to pick one, you know either in the follicular phase and or in the luteal stage of their ovarian menstrual cycle. Excuse me ovulatory, menstrual cycle. When would you suggest they do that if they had to pick one? So if you forced me to pick one, I would say probably day 21 to 22 for someone in her 20s, so we're focused right now in that decade. So for most women they've got a menstrual cycle, Dave that averages out at 28 days, so this is about a week before they start their period for women or more irregular. It's harder to do that as women get older and we'll talk about this in a moment. Usually the cycle gets a little shorter, so as they start to decline in their progesterone production, their period gets a little closer together, like mine before August, was about every 26 days. So at that point you want to test sooner like day 19-20 and I'm not talking about blood tests. So a blood test is the cheapest thing. It's usually what's covered by insurance, but my preference would be to do dried urine. I like to use saliva for cortisol. I like to use dried urine so that I get metabolomics in addition to the levels of these hormones and if I'm forced to I'll use blood testing, and that's certainly the gold standard for all of these hormones that we're talking about but um. It's not as comprehensive and, as you know, it's a quick little snapshot while the needle's in your vein, for you know, 30 seconds yeah. The salivary cortisol makes sense to me because my understanding is that you get free cortisol, which is the active cortisol. You said with urine you're also getting the metabolites, that's right and then um for blood testing you're, getting it it's sort of a crude window into the

00:25:11 Nutritional Testing; Vegetables, Microbiome & Disease

Averages ecstatic total level so uh. Let me go back and say one other thing about biomarkers, a big part of the testing that I do in phenotyping, my patients, I practice Precision medicine. So I like to almost start with nutritional testing. I don't think I've ever had a teenager. I've got some NBA players that are 19, 20 21, so maybe those count but uh. Those are men obviously, but for nutritional testing. That would be a potentially a helpful thing to do in your 20s becomes less important. As you get older and you develop more micronutrient deficiencies, but micronutrients play a huge role in terms of

hormone production. Magnesium. You know the Magnesium is hugely involved in the way that you get rid of estrogen as an example, so micronutrient testing. What I usually do is a combination of blood and urine, and so I'm looking at all of the micronutrients that we can measure that have some clinical scientific basis behind them. If I could do that for a teenager, I think it might be helpful because I recently gave a lecture on breast cancer risk reduction. Another quick sidebar and I was sad to find that intake of vegetables polyphenols is such an important predictor. A future risk of breast cancer like when you're a 50, 60 plus and the most important time is when you're a teenager. Now I have one daughter that eats vegetables, she loves them and I have another daughter who eats food. That's beige and it's very hard to get her to eat the volume of vegetables. You know five colors a day, which is what I do, and if you have evidence that you could show a 17 year old, that they've got micronutrient gaps. I think that would be a motivator for them to eat differently at a time when it's so critical, even though it's you know 25 years in the future that it's going to potentially change this Arc that they're on. What do you do for a young woman who doesn't like vegetables is or is not somehow able or willing to to get those five colors a day of vegetable to help support the microbiome? You know our supplements a useful tool in that case um. What other sorts of tools, Behavioral or otherwise, are useful, such a good question, so here I'm going to invoke Rob Knight at UCSD, so I think his his uh, his gut project has really been helpful in terms of understanding what kind of modulators are going to be Important, so what I try to get that person to do - and I don't see many teens anymore other than NBA players. What I try to get them to do is to have a smoothie very hard to get them to have a smoothie every day. But if I could get them to have a smoothie three times a week and to throw some of these vegetables in that makes a huge difference. I mean we know that makes a difference in terms of microbiome change. She should be blending up broccoli or kale cauliflower. So cauliflower is great, even they're, putting things into the Smoothie yeah. I don't know if you can get a teenager to do that, but they often will use like. I have them. Do steamed broccoli, that's in the freezer, because it's got very little taste so that they could do that in a chocolate smoothie. They could add some greens, I, like greens, powders, are super convenient so that, with you, know, kind of a taste that they like whether that's chocolate, which is what most my clients want, or you know, vanilla with berries and that sort of thing. So that can go a long way if you don't like vegetables and short of that, I would say some supplements, but I would say that's a distant second to making a smoothie. I've got one patient that I have to mention because um he took us to

the extreme, so he is a retired physicist, professor at UCSD. He found out that his microbiome was a hot mess and developed autoimmune disease, and so he became hell-bent like only a physicist. Could on changing his microbiome and he dramatically shifted it by having a smoothie every day with 57 vegetables and fruits in it? 57 independent 57 independent. So I mean this just warms my heart, the way that he did this, but he would go to the farmer's market. He would just get a bunch of this, a bunch of that and he would go home, make the smoothie and then stick it in the freezer. So he'd have a serving every day and he became a completely different person. Based on this microbiome change. His uh autoimmune disease is in remission. He um he dropped a huge amount of weight. He went from being you know, kind of this phenotype that I know you know well of a professor High performing traveling around the world on so many boards, so much Innovation, so many great ideas, super computer guy to being someone who gets up in the morning gets In his hot tub exercises for like one to two hours a day and then does a little work like he completely shifted the way that he lives and his microbiome shift. You know who knows what What's the chicken and what the What's the egg there, but he had a huge change in his physiology. Glucose went from being quite high, he had and he tracks all of this. Of course it's like Jupiter, after all, right and retired. I suppose might have had and he's retired, but he is he's, got the longest time series of anyone. I know and he's tracked his glucose and Insulin going back 20 years, so he can show you, okay. Here'S where I started having my smoothie

00:31:13 AG1 (Athletic Greens)

and here's how my glucose and Insulin changed as a result of that I'd like to take a quick break and acknowledge one of our sponsors athletic greens athletic greens now called ag1 is a vitamin mineral probiotic drink that covers all of your foundational nutritional needs I've been taking athletic greens since 2012 so I'm delighted that they're sponsoring the podcast the reason I started taking athletic greens and the reason I still take athletic greens once are usually twice a day is that it gets to be the probiotics that I need for gut health our gut is very important it's populated by gut microbiota that communicate with the brain the immune system and basically all the biological systems of our body to strongly impact our immediate and long-term health and those probiotics and athletic greens are optimal and vital for microbiotic health in addition athletic greens

contains a number of adaptogens vitamins and minerals that make sure that all of my foundational nutritional needs are met and it tastes great if you'd like to try athletic greens you can go to athleticgreens.com Huberman and they'll give you five free travel packs that make it really easy to mix up athletic greens while you're on the road in the car on the plane Etc and they'll give

00:32:22 Microbiome, Prebiotics & Probiotics, Inflammation

You a year's supply of vitamin d3k2. Again, that's athleticgreens.com Huberman to get the five free travel packs and the year supply of vitamin D3 K2. Is there a case for I'll say young women, but young women and men using over-the-counter probiotics as a way to enhance the microbiome? This is something I hear about a lot. I've heard that excessive doses of capsule probiotics can give a brain fog like condition. I personally don't use capsule probiotics unless I feel like my system, is under a significant amount of stress, in which case I might add that in for brief periods of time or if I've just taken antibiotics for a period of time, do you ever recommend that the College student or the high school student that she or he take capsule probiotics, assuming that they're getting let's say three to five servings of vegetables per day, either in smoothie form or some other form. What are your thoughts on on supplementing probiotics? It sounds like such a simple question. It is such a complex answer and I don't think we really have the answer so I'll tell you the way that I approach it. I look for randomized trials to support my use of probiotics and, frankly, I'm underwhelmed. So I've seen some data. If I invoke my um NBA players for a moment, almost every player I've tested has increased intestinal permeability. They just have such a high training load, probably mediated by cortisol very high glucosis when they drain that they have increased intestinal permeability. So those tight junctions in their intestine become loose. They develop a lot of inflammation as a result of that and when you're, a professional MBA player and you're making 20 million a year like you, don't want a lot of inflammation. You want a little bit to like help your muscles recover, but you don't want it to be um, adding to problems when you develop an injury, so this is leaky gut leaky gut yeah. I don't love that term, but yeah we'll use it here. So there's a there's a particular probiotic that is helpful in athletes with leaky gut. So that's the kind of specificity and randomized trial that I'm looking for the rest of it. I think there's support if you find help from it as you described. If you take a course of antibiotics, I mean first of all, I would question whether you need them, but I try and

avoid them. There have been instances where they've been prescribed and I took them mostly in the past. I was in college. They seem like they kind of gave them out. You had a sinus infection to give you Pro, you know antibiotics using like yeah the worst treatment ever yeah. So, if you're coming off of antibiotics, I think that's a good time to do what we call replacement dose. Probiotics, I think, What's far more interesting is prebiotics. I think the data is much better for prebiotics and um a selective use of polyphenols. How would a person in their teens and 20s or any age for that matter, know what whether or not they have nutritional deficiencies? What is the best way to analyze if one is getting enough magnesium and for that matter, what is going to be the best way to test the microbiome? You said stool sample and I'll come right back with the same question, I asked about a blood test. What time of day when, during the month, um to establish a baseline, so this would be prior to embarking on a you know, 97 vegetables, or how many years per day 57.. Well, I love the idea that you're telling us if I'm gathering correctly, is that? Yes, there's a case for probiotics, but for the typical person, regardless of age, eating more vegetables or drinking more vegetables, as the case may be, is going to be beneficial for the gut microbiome. Perhaps without the need to go test. Whether or not one is making a certain

00:36:08 Microbiome Testing, Magnesium, Constipation & Thyroid

Number of estrogen related metabolites or not just that that's a great starting Place, eat or consume more vegetables um. But if one wants to analyze their gut microbiome, are there good tests available to the general public? This has been I'm not going to name companies, but I've been tracking this over the years, and it's never been clear to me that we know what constituents of the gut microbiome are are best. We know that dysbiosis is bad yeah and we know that diversity of the microbiome is good. We hear this yeah, but no one's ever told me that you want a particular ratio of one microbiota to another right in a way that has made any sense to me at least totally I'm not a microbiologist, but whereas, with you know, with testosterone in men, we Hear: okay, you want your free testosterone to be about two percent of your total. Perhaps with women you, women are gon na, have more testosterone than estrogen on average, but still less than men when you look at testosterone, etc, etc, but you can kind of get some. Some crude measures, but for the microbiome it just seems like long lists of microbiota,

for which I just get dizzy. I just if you just wrote out a bunch of I's and L's and s's you'd. You can go halfway a bit bit the same information, I'm not trying to poke at that field. It's a beautiful field, but they haven't told me what to what I what my microbiota ought to look like like. What's a healthy microbiome chart? Well, that's because we don't know, I mean the best we have is Rob Knight's work, but even that is limited in terms of you know. Can I tell you that a a woman in her 20s should have this particular pattern with her microbiome? No, I can't so um. Let me go to your first question because I think you just asked about six. Your first question is about nutritional testing. What I like to do with nutritional testing is run a panel. That's looking at antioxidants so like vitamin A vitamin C alpha, lipoic acid, um plant-based antioxidants, because you can measure that in the blood I like to look at some of the key vitamins, especially the B vitamin range because, as you probably know, if you've got a particular Genetic um polymorphism, so you might be less likely to be absorbing the right level of vitamin B9 folate, vitamin, B12, Etc. I'M also looking going back to the antioxidants at glutathione because I think that's such an important lever when it comes to detoxification, which we haven't talked about yet and then I'm looking at some of the Minerals. Magnesium is really the most important and we know that somewhere around 788 of Americans are deficient in magnesium. That's like the the lowest hanging fruit. I would be curious, for instance, like with magnesium, if that number of people are deficient. Does that mean that that number of people should be targeting their nutrition towards foods that contain magnesium and or supplementing with magnesium? And if so, what forms of magnesium we've talked about? Mag, three and eight for Sleep, there's a Mexican there's so many forms it can be a little bit overwhelming to people. So any any detail in sourcing would appreciate it great so, first in terms of testing, what I prefer to do is to mention one more than one lab and more than one brand um, and I can just I'm speaking mostly from experience so uh for testing. I do a lot of Genova neutrals during the pandemic. They developed an at-home test, normally with a neutral valve, you have to get your blood drawn and you have to do a urine sample. So a lot of people can't do that. The great thing about this test is your insurance usually pays for most of it, and so the copay is about 150 dollars. So during the pandemic they developed another test called metabolomics, which does much of the same testing, but it's a finger prick. So most of my patients prefer that in fact they haven't gone back to the nutribal. Second lab is spectracell. I use Spectra cell occasionally. I find it not quite as easy in terms of fitting into my practice, but I've got friends and mentors like Mark Houston. Who does a lot of kind of Precision, cardiometabolic Health? He

thinks spectrosol is the best test out there. So you asked about magnesium, you have to measure red blood cell magnesium like whole blood and with deficiency. It's interesting with supplementation for my patients, who tend toward constipation and that's frankly, about 80 percent of the women that I take care of really, yes, wow I'd be curious as to why that that is um is it I, I can guess, diet, stress, um, patriarchy rage To psychosis so Pine, the um, the pine system right psychology, Immunology neural and endocrine factors combined. Is that yes, and then I would say, there's another Factor which is being female is a health hazard. So we have twice the rate of depression. Insomnia. We've got three to four x: increased risk of multiple sclerosis. We've got five to eight times the risk of thyroid dysfunction. So if you just look at that and you look at subtle, pre-clinical thyroid dysfunction, a huge number of the women that I take care of. Well, let me back off a large number of the women that I take care of have thyroid dysfunction, that's contributing to constipation, and if we go back to that control system, the hypothalamic pituitary adrenal thyroid Canal gut axis, and they have a lot of perceived stress together with this borderline thyroid function that no mainstream medicine doctor has told her is A problem, and then she's got a problem with the Tango between estrogen and progesterone she's, going to tend toward constipation women have a lot more constipation than men. The gut is about 10 feet longer in women compared to men. We should talk about some sex and gender differences and Define those sure, and they are much more likely to have a torturous colon

00:42:25 Female Colonoscopy; Network Effect & Modern Medicine, Stress Factors

And the way you know that, is you get a colonoscopy and they tell you yeah it's really hard to like get in there and do what we need to do as a brief tangent. But I think this is the time to ask um at what age now do Physicians insist their female patients get colonoscopies for men. I think the age used to be 50. Now it's getting ratcheted back to 45 or 40.. Again, these are recommendations, not requirements, but they're. Pretty strong recommendations from depending on where you live, Etc, um for women. How early do you think they should get a colonoscopy to to explore for possible polyps and or colon cancer? Yeah? It's a really good question. I don't know the answer, so what I've always operated with is 50.. The way that I answer, that is, to go to the U.S preventive task force rating to determine, based on their synthesis of the data. What age is the most

appropriate? Has it changed, as you just described, for men from 50 to younger? I don't know so. We should fact check that all these um additional health hazards for women um - you mentioned some of the you broadly mentioned psychological impact right and, of course, these things are all related psychology, immunology and one of the, I think, wonderful things about neuroscience and Science in general And medicine is that there's now an understanding that all the organs are connected to one another: it's a network, it's a network and that the microbiome sits at had um at a key node within that Network um, and I think most people accept that now. Yes, yeah. That seems to be a theme that, at least in the last 10 years is really wonderful because um certainly for Neuroscience. It was thought that you know unless it's in the cranial vault, it's not neural, which is ridiculous, because there's lots of nervous system outside the skull. But in any case, can I interrupt for a second? Yes, please, so I think you're right that there's an understanding about the network effect, but I think that as much as I love mainstream medicine and I trained in it and I'm so grateful for my education, I still think it is a silo based way of taking Care of patients, so even if there's an understanding of the network effect more at the science level or as you described in Neuroscience, there's still, you know if you are a woman who has constipation fatigue um, maybe an autoimmune condition feel stressed out all the time feel, Like your hormones are out of whack you get sent to the gastroenterologist for the constipation you get sent to the rheumatologist for your autoimmune issues. You maybe get sent to an endocrinologist if you've got thyroid problems and there's very little collaboration between these groups. So

00:45:13 Constipation, Stress & Trauma, Autonomic Balance

Even though there's an understanding of the network effect in real life, it's not happening. Let'S um, let's go deeper down that path, because I you point out something really important and you've mentioned constipation a few times. Can we view constipation as a serious enough symptom that it warrants an immediate intervention that is, does it flag or signal problems that are severe enough, that that should be the issue? That's dealt with uh for anybody. That's experiencing it yeah and I mean sort of an odd topic for many people because they think, oh you know. Bowel movements and sort of you know there's that kind of um pre-adolescent humor around this, but I think it's it's so important when you're. What I'm hearing you say is that constipation is far more common in women and it signals a general many problems occurring. Does that mean

that women should address constipation and if so, What's the best way to address constipation yeah? I love this question because you're doing can we have a quick little meta conversation so you're doing something that I knew you would do, which is you're teaching me something and you're changing like there's a social genomics thing happening where you're changing my thought about this. So I just wanted to acknowledge that. Thank you. Thank you. Well, I think for me you know when I hear that there's a kind of you know, you're talking about a phenotype constipation is a phenotype. It's one that people generally don't wear a t-shirt explaining it to people, but that I'm guessing anything to do with sexual health, um, bowel Health, Urology people, just don't talk about right, um for all sorts of reasons, and those reasons are probably so obvious that they're not Even worth discussing, but because and also because we won't change them except by talking about them yep. So if you say um, women are far more constipated and that's signaling a larger set of problems. Yes, then, my immediate thought is well: will relieving constipation um pun uh intended retroactively um. Will that assist in a great number of issues, and or will it get them down the road of thinking about those other issues? More specifically like do I need more magnesium, or should I be putting vegetables in my smoothie, you know so I'm curious about constipation as a Target yeah for intervention. That, then, opens up a bunch of other discussions, because there are these certain nodes in the in the mental health, physical health space that when someone you know like, we talk a lot of deliberate cold exposure. Do I think it's magic? No, but I think that, if someone's getting themselves into a cold shower once a day, it opens up a nun, a number of questions about themselves and reveals a number of things to themselves like how do I buffer stress, yeah, what sorts of levels of control do? I actually have, and on and on so perhaps not the best example, but some of us hate cold exposure right, which is we have. We have like a gene that makes us stress out, like you wouldn't believe, which I would argue, makes it um very likely that even 10 seconds of cold exposure gets you. The effect that you want, as opposed to someone who adores cold exposure like a penguin needs. A lot more cold exposure for it to have the the Adaptive response. Anyway, that's my way of gumbing through that uh, quite uh, you're you're, quite correct um. So so, let's answer those questions. Constipation issue yeah. So this is how you're changing the way I think about this, so you're asking okay, instead of looking at constipation as a constellation of symptoms. What about, if you just used it on its own as sort of a um, a key indicator or signal of dysfunction with my network or maybe something broader, and I think that's right, so it makes me think of a

few things. It makes me you're. Also changing this book that I'm writing on autoimmunity and Trauma. So thank you for that. So women experience more trauma than men. This is well established. If you look at the ace studies that were done by the CDC in Kaiser in 1998, we know that men, for the most part, middle-aged men, have about um about 50 of them experience significant trauma, as defined by the ace questionnaire. Women are at 60 and that's pretty durable since 1998., so women have more, they have different forms of abuse, much more likely to have sexual abuse. They have a different HPA response than men, their perceived stress tends to be higher and I'm generalizing. For a population side. Note you know in Precision medicine, we don't do that we do medicine for the individual individual, not the population, not medicine for the average. And so, if you look at the physiology of a female, I think that constipation and that need to like control and restrain and hold things in you know, tighten the anal sphincter. I think that's part of the physiology, so I'm veering away from the science, but I do think that it is a really important signal to pay a lot of attention to now. You also asked about microbiome testing. Should we do that or do yeah? Well, I have a couple more questions about constipation. I never thought I'd ask this many questions about concentrating, but now I'm fascinated by the way. Also this morning I taught medical students at Stanford about the fact that we are basically a series of tubes. So you talked about the the anal sphincter. We are a set of sphincters from one end. To the other I mean we are a set of tubes, a nervous system being one of those tubes and well - and I think in eastern medicine, they talk about the various locks between those tubes and Chambers, and it's not without coincidence, there's some real wisdom there. Of course wait: did you just talk about energetic Anatomy, uh more or less? I didn't say the word chakras, but uh, but I might in passage it's the bondas right are the are the are the the sphincters? Yes, yes, that's right. Uh! Thank you for for that. The um, so what defines constipation I mean, in other words, let's think about the healthy, rather than thinking about the unhealthy. Let'S, how many bowel movements should a woman or a man have per day assuming this is where it gets tricky, because some people are doing time restricted feeding some people are eating more. Some people eat more fiber, more bulk, larger meal. At the end of the day, a larger meal, the beginning of the day, we will never um, be able to sort out all those variables, but on average um how many bowel movements and his timing during the day for bowel movements at all informative. What works for you um? Well, when I'm asleep um generally, I don't want a bowel movement, so I'm going to be like most people right. Well, sleep is primary for you right exactly um. I always assumed that morning time

yeah was a was a healthy time for bowel movements. Um and I think almost everybody babies included, recognize the feeling of being lighter and more energetic when they've evacuated totally colon, totally um, in fact, so much so that I'm obsessed with Jungian and Freudian psychology that the first thing we learn when we come into this world Right is that we want something we we feel some sort of autonomic arousal stress, whether or not it's food or warmth, or the need to have a bowel movement. One of the first things that parents learn is how to recognize that not by the odor. Coming from the diaper, but by the look on the baby's face or their agitation agitation signals the need for some sort of relief, right temperature relief, food relief, um evacuating the bowel relief. So my understanding is that as autonomic arousal increases in the early part of the day, ideally after a good night's sleep that bowel movements become more likely unless that arousal becomes so great that, then people feel so quote: unquote locked up right um because of the balance Of the autonomies of features so early day, I'm guessing and again in the second half of the day, and here I'm totally guessing um and certainly not having to wake in the middle of the night um yeah. Those are my best guesses, that's great, so I would agree with that. When I was at Harvard Medical School in UCSF for residency, I was taught that constipation is having a bowel movement less frequently than whenever once every three days. So I don't think I've ever laughed out loud on this podcast as a consequence of of uh textbook medical knowledge. Are you kidding me? Is that ridiculous? Well, that sounds like, and, and here pun intended, that sounds like the uh, the conclusion of some very um constipated personally and and and in other ways, constipated individuals and again this might seem like an odd conversation, but the the discussion around conservation is is present In psychological literature, yes, because of this relationship to the autonomic system - well, it's a metaphor in literature, it's crucial! So you you spoke to a number of different threads that I think are important here. So that's the definition that I learned and I was I heard that and I was like hell. No, that doesn't work for me. It doesn't work for anyone. I know - and I spent a lot of time, especially in medical school and in my internship, where you rotate on medicine, disimpacting women like older women who come in, who haven't, had a bowel movement in a month whoa, and that, let me tell you that is not Nice for anybody yeah believe me. I became a scientist, not a physician for a number of reasons, both positive and negative. That's one of them yeah, so my definition of constipation as a western, mostly white girl, is that if you're not having a bowel movement every single morning - and you have a feeling of complete evacuation, anything less than that is constipation.

So that's how I Define it. If you're in India and you're eating food, that's got a fair amount of microbes in it. It's less. You know sanitary, I'm using that word um as carefully as I can. Generally. They have a bowel movement after every meal, but they've got a different microbiome they're exposed to different microbes here in the U.S, I would say Wednesday. You also spoke to something very important, which is the balance between the parasympathetic nervous system rest and digest and poop versus the sympathetic nervous system kind of the on button. You know fight flight freeze spawn, so I think for those of us who've got

00:55:35 Constipation Relief, Stress, Breathwork & Meditation

Issues with autonomic balance it can lead to constipation, and I like that constipation could be pulled out and kind of writ larger as an important signal. What sorts of tools do you recommend? People use to um, relieve constipation um in eating more fiber sounds like reducing stress. Is going to be a huge one? Yes, what are your favorite stress reduction tools? Um I like to divide these into real-time tools, so a big proponent of like physiological sign real time. You know these sorts of things, but things that can really lower the Baseline on stress overall to facilitate constipation and other other broad indicators of Health. So I'm not a fan of lowering stress, I'm a fan of lowering perceived stress and I think the distinction is really important. I learned when I was in my 30s that I was a massive stress case and I didn't know it. It was just sort of I think I through residency through working 120 hours a week. I just was so accustomed and sort of um that was 120, not under 20 folks yeah, not unusual in in medicine. Well, they they've changed training so that you work no more than 80 hours a week now, but that was before my time. So I became accustomed to a massive amount of cortisol massive and I would say, I've spent the past 20 years really working on perceived stress to find, I think, all of us in all a cart menu of what is most effective. So what works for me now at my age is different than you know. The the TM I did as a college student Transcendental Meditation it's different than the I became a certified yoga teacher when I was in my 30s that is very effective for a lot of people. It wasn't enough for my Matrix. I do holotropic breath work um. I didn't read it, but I saw it. She just had a paper and sell on your sign and um. It kind of it made me think like teach me how to teach teach me how to sigh like. Can you say a little bit about that like? How do you do it yeah? Very briefly, that study was we. We wanted to find a minimal, effective dose intervention yeah. I just wanted

yeah. So five minutes a day. We need to figure out what people do every day yeah and we were monitoring, subjective mood, Etc, but also Biometrics remotely. So it's kind of a nice Biometrics, HRV HRV uh nighttime sleep, cortisol uh. I wish um. So this was done during the pandemic. More than 100 subjects, the advantage was that we got data 24 hours a day because they're pinging us in their data uh wearing HRV, 24 yeah nice. So that was nice resting, heart rate, um subjective mood. We would get in touch with them daily. So when people were swapped between groups like any good study, but five minutes a day of sort of standard, if you will forgive me, meditations are just sitting no instructions about how to breathe just focusing on um closing their eyes and focusing on focusing yep um. Another group did box, breathing yep inhale, hold exhale hold for equal durations. The duration of each of those inhales and holds was set by their carbon dioxide tolerance so somewhere between three and eight seconds, depending on how well they regulate carbon dioxide. Another group did cyclic signs, so this would be double inhale through the nose, so big inhale through the nose followed by it to lungs, empty exhale that second inhale after the first big long inhale through the nose is really important because it makes sure that all the Collapsed abiola, the lungs totally snap open and then the exhale you offload a lot of carbon dioxide. That's very similar to holotropic breath work. Not yes, not not. Um not unlike holotropic, breath we're a little bit pranayama-ish, but the exhale is rather passive as opposed to active and then the fourth category was cyclic hyperventilation, which is a lot like Tumo AKA, Wim Hof, ish breathing different than Wim Hof breathing. So this would be so very active, inhales and exhales. Every 25 cycles of inhale exhale that'll be one cycle. Long exhale hold lungs empty 15 to 30 seconds, then repeat for about five minutes now the info. Everyone did that for five minutes and what we found was that the cyclic sign led to the greatest improvements in mood Around the Clock, not just around the the practice or during the practice, as well as lowered, resting heart rate, improvements in sleep, Etc. And you got it, publish and sell yeah. We were so amazing, we're very fortunate. I think um, the the thankfully the reviewers and editors understood that these minimal intervention things uh, hopefully are going to be of use to people so so useful to people I mean. How often do you read a paper like that that could offer a behavior change? That is so easy to implement. I mean I love that question. Thank you. So what about? Did you tell them not to drink, because alcohol has such a huge effect on HRV yeah? So in this case we didn't tell them to alter anything else about their behavior. Just hoping it was background kind of across the system. Yes, and some were Stanford students, others were from the

general population, any Frat Boys that were drinking heavily, probably not well during the pandemic. I think alcohol intake went way way up across the board. Um, I mean, isn't if I had a magic wand, I would I would ask that people either not drink or drink. Two drinks per week, maximum at least that's my understanding of the literature um. Are you familiar with the whoop data with alcohol? No, but we have a collaboration with through that paper, yeah um and it certainly disrupts patterns of nighttime sleep, in particular from my understanding that first phase of sleep, that's related to the massive growth hormone release that you all really need and want in different measure, growth Hormones we did not. No. The second iteration of this study will certainly include free cortisol by saliva hormone panels. Well, I'm beginning to think that we should also um be asking people how often they're going to the bathroom and what time of day. Yes, I mean this thing around constipation is uh is super interesting and I think that plus um blood markers and then I'm I'm very excited to learn that um. That urine contains additional markers that could be informative, so yeah it was. It was a fun study. Uh not easy study to do with that number of of subjects. Um takes a lot of training for your research assistants yeah. It was a big group. It was nine people in our group and three clinicians and a lot of a lot of phone calls and a lot of back and forth, but you know and thank you to the subjects who served as the uh, the real life guinea pigs so yeah. I think that stress you know people's. I think people are starting to appreciate that there are ways that they can relieve their stress, that that don't only fall under the categories of vacation right and meditation, but I want to say that meditation is obviously a wonderful tool. Um, it's just it's a it's a tool, not unlike any other tool that is great for some people and less great for others. Well, certainly it's a great tool and it's got such a scientific basis behind it, but there's so many things on this A la carte

01:02:58 Systemic & Societal Stress Unique to Females

Menu sex, orgasm, um connection, feeling heard and seen and loved um yeah. Let'S talk about that. You know you mentioned earlier that all these stress factors you you said patriarchy right yeah, but I think what if I may um at risk of uh, of just strengthening that uh statement. I I mean that that to me is, is signaling a bunch of other factors around us. You said like keeping keeping things in um. What do you think explains? Let'S talk about that because I think that that's likely to have raised a certain flag in people's minds like

what exactly is she talking about? Are you talking about less opportunity? Are you talking about less opportunity to um to vocalize? Are you talking about less opportunity to vocalize and be heard? I mean I realize that there are an infinite number of variables, but given that it sounds like a really strong input to the system, uh, what I mean by that is that psychology is influencing biology and you're, saying that that these uh, that these power power dynamics Structures and Dynamics are impacting I'd. Love. Let'S hear your thoughts on that, because uh I I hate to let a flag like that go by without fleshing it out and never waste a good flag. Well and let's preface it by by just saying that, like people will have different opinions on this and that's and I think that's healthy and like with the discussion about constipation, let's talk about what people aren't willing to talk about when it comes to health love it. So we might need to talk about patriarchy on part two, but I'll give you some material that I've been working with. I started. I did not even understand the existence of patriarchy until I was a bioengineering undergraduate at MIT. I should mention which has always had a bit of a of a male um askewed male in terms of Faculty numbers. Well, my my that's true at most universities, true well, my postdoc advisor was the late Ben Barris, who was a female to male transition, transgender interest. First, transgender member in the National Academy of Sciences were my closest friends. Unfortunately, he died of of pancreatic cancer. We were very, very close they're, actually making a documentary about Ben but Ben. This is interesting. Ben went to MIT because he wanted to be around a lot of men - yeah, that's a lesser known fact, but then he was a very strong advocate for women. He went as Barbara when he was Barbara and um by the way, he's given me permission to share all this prior to his death. I recorded a lot of conversations yeah um. I only ever knew him as Ben by the way, but when he was at MIT, he was identified female and he later talked about the intense um suppression. Oppression literally, is how he described it, especially given that he was performing so well. Yes, so you just defined patriarchy, you did it yourself, a couple things when I was in bioengineering. I took a women's studies class and it was all about teaching undergraduates about the existence of patriarchy, which I would Define, maybe at its simplest as power over I'm not saying men are patriarchy, I'm saying something very different, which is power over. Let me correct one thing that you said I didn't go to MIT as an undergraduate, so I'm from I was in Alaska, and I went to the University of Washington for bioengineering in Seattle in Seattle. Okay, I dropped out of a graduate program in bioengineering to go to the Harvard MIT program for Health Sciences and technology in Boston. Thanks for that clarification, University of

Washington also wonderful place. I have many many many many many many many wonderful, close colleagues there. It's an incredible place, especially for vision, science, it's especially good for engineering bioengineering but um yeah, so my my MD is jointly between MIT and Harvard, and it's the oldest, maybe largest, although Harvard says this a lot program for biomedical engineers and uh MD phds. Physician scientist training program - great thanks for that clarification, I'm going to blame the internet for this one. I am, I think we need to send our our Wikipedia editors out there. I think LinkedIn is correct. Okay, great well Wikipedia editors, note get out there and make that make the correction. Now you heard it um so stress that is what you're really talking about is systemic stress in the body as a concept, as a consequence. Excuse me of systemic stress of environment. That's right, you know there's particular forms of it. I would say this also relates to White Privilege. It relates to racism and when you look at you, know kind of the way that systems, including my beloved MIT, the way that they're set up is that might make us makes right and generally the people that are the strongest. You know big men, strong men they're the ones who tend to be the most successful so for people who are bipoc for people who don't have white privilege for women.

01:08:19 InsideTracker

it's a different experience and so I'm using patriarchy as kind of a umbrella here but it connects to many other things I'd like to take a brief break and thank our sponsor inside tracker inside tracker is a personalized nutrition platform that analyzes data from your blood and DNA to help you better understand your body and help you reach your health goals I've long been a believer in getting regular blood work done for the simple reason that many of the factors that impact your immediate and long-term Health can only be analyzed from a quality blood test the problem with a lot of blood and DNA tests out there however is that you get data back about metabolic factors lipids and hormones and so forth but you don't know what to do with those data insidetracker solves that problem and makes it very easy for you to understand what sorts of nutritional behavioral maybe even supplementation based interventions you might want to take on in order to adjust the numbers of those metabolic factors hormones lipids and other things that impact your immediate and long-term Health to bring those numbers into the ranges that are appropriate and indeed optimal for you

01:09:23 Testing & Future Behavior

If you'd like to try inside tracker, you can visit insidetracker.com Huberman and get 20 off any of inside hackers plans. That's inside tracker.com Huberman to get twenty percent off. I want to use this as an opportunity to keep this in mind. As I return to a question that I didn't close the hatch on earlier and it's my fault, which is I'm now clear on the fact that a woman in her late teens early 20s, ought to know something about her testosterone, estrogen thyroid cortisol levels should start at Least, thinking about her microbiome should be thinking about how many bowel movements and the timing of those bowel movements per day really and I'm, assuming that what I just described is also true for women in their 20s 30s 40s 50s. On up to hundreds. Is that correct, that's correct, but I would say that there are differential opportunities by decade. So I'm glad she circled it back to teenagers and testosterone, because I think, if you know, for instance, in your teenage years, that you have high androgens and that you've got this potential phenotype way into the future that you may not even notice. I mean. Maybe you notice you've got a few extra hairs on your chin or something if you know that your testosterone is elevated or some other androgen, it might change the Arc of how you take care of yourself. So I think that could be very helpful in your teenage years in your 20s for people, who are a stress case like me so age 27, on the words at UCSF. If I had known that I was such a high cortisol person, I think I would have done things differently. I would have changed my behavior and I don't know because I didn't base case these, but your testosterone can decline, starting in your 20s kind of, depending on how much stress your Matrix is under so for women that can start as early as 28. Usually your testosterone declines by about one percent per year. What level of testosterone do you like to see in a woman once she's sort of post, let's say after age 25? What kind of range is healthy? I know what the reference range is only because I know one could look it up. I don't know it's off the top of my head immediately, but what What's a kind of a nice reference point there? So the way I tend to describe this on podcasts is the top

01:11:55 Polycystic Ovary Syndrome (PCOS) & Cardiometabolic Disease; Stress

Half of the normal range great so that I think, is a good benchmark. You know for PCOS

generally it's much higher than that. You know I've seen patients with PCOS, where their total testosterone is 100 to 200.. Do they always have peripheral manifestations of that? A little bit of hair, the the skin plaques I've heard about you know so darkened skin irregular periods. Regular periods is that um. You know. I get a lot of questions about PCOS, yeah, um and you're. The first person we've had on this podcast that's really qualified to talk about PCOS in a real way um. So here we're talking about too many androgens cysts on the ovary irregular ovarian. Excuse me. I keep saying that ovulatory slash menstrual cycle um. What are some other indicators, and do you recommend that women start taking Androgen blockers or so or I mean how do seems to be a lot of PCOS out there? I'M hearing about it a lot so glad you asked about this, so PCOS is one of those really poorly understood conditions that gets it kind of flows flies below the radar until a woman wants to get pregnant or she's got some other issue that drives her to A physician, the problem is that it is a syndrome right, so polycystic, ovary syndrome, sometimes polycystic ovarian syndrome and syndromes, don't necessarily fit together into a really clear diagnostic criteria. So in this instance, there are three different criteria that we look for. So this is on the ovaries having um clinical manifestations of hyperandrogenism, so that could be hirsutism, acne other things and then usually irregular periods and the way that that's defined, at least by the uh latest criteria, is having a period every 35 days or less so typical Cycle length, 28 is 35 days. You know you're skipping a period here and there, so those are the those are the criteria that we use to diagnose PCOS. There are about four different systems out there in the literature for diagnosing PCOS, which is where it starts to get confusing. So there's some women who have gnosis on their ovaries, but they've got hirsutism and they've got irregular periods. Could you define haircicism here? Statism is increased, hair growth, usually in places that you don't want it so for women, it can be, you know, kind of male pattern. They might notice it on their breasts on their chest um and then there's of course, a familial quality to that like. I was just looking at a paper last night, looking at Israelis and how much hair statism they have and whether this is related to CH E repeats on the Androgen receptor. Do they get um, not Israelis, but um. Do women who um, who might have PCOS experience? Um androgenic alopecia, so hair loss, that's sort of of the quote-unquote male pattern, baldness. Of course it's Androgen pattern baldness as opposed to male we're talking about testosterone, DHT related. Sometimes you know this is where I'm going to invoke clinical experience rather than what I've seen in the literature. Women definitely can have some androgenic alopecia. I tend to see it later in

life, but this is an important point because we think of PCOS. As you know, I was just talking about it in teenage years like wouldn't it be nice to know that you have this phenotype and you're at risk for all the things that people are at risk for, and we haven't talked about glucose and Insulin. Yet we should what we know is that PCOS is not just a problem in terms of irregular periods and then difficulty getting pregnant. So those are mostly problems in your 20s 30s early 40s, but it is a massive risk factor for cardiometabolic disease as you get older. So many people tend to pigeonhole. Pcos is a problem of reproductive age. We have to be thinking of it over the entire female life cycle and I would say it's even more important to consider it over the age of 50. You know average age of menopause is 51-52 because we know that that elevated testosterone, the high androgens, are probably the greatest cardio metabolic driver of disease for women with PCOS wow. Now one other thing I want to mention - and I still have my notes - that we're going to talk about microbiome testing because that's such a fun subject what I was taught to do again saying this was so much love for the people who have taught me how To do medicine, what I was taught to do is that if you have a woman with PCOS, you make the diagnosis. You measure her testosterone, you see if she has acne blah blah. You ask that woman. One question: do you want to get pregnant or not? So then you have these women with PCOS who get started on a birth control pill. If they don't want to get pregnant, if they want to get pregnant, then you help them get pregnant by addressing some of these PCOS issues like maybe you give them Clomid or you do something to make them ovulate more frequently. That is the way that most conventional medicine approaches this and it does women at gigantic disservice. So one of the things, I'm speaking into is the gender gap that exists. So I my feeling is that the research money that goes into women's health is abysmal compared to what goes into mental health really - and I think that's changing, but there's also a huge lack of awareness of sex and gender differences when it comes to the way that We construct clinical trials and other experiments. Well, that's absolutely true. I mean I sit on. I've sat on NIH review panels for more than a decade. Now I'm a regular standing member, which is only to say that I see the research as it's being proposed. Yes, and now it's required no Grant will get funded without sex as a biological variable, and here I'm by the way, folks, this is sex. Biological sex, the noun, not sex. The verb both are super interesting, obviously, but um when we say sex is a biological variable, meaning even if it's a study on mice. How did that start, though, that didn't start that long ago it must have been. I think we can think I don't want to miss attribute here. I think we can thank Francis

Collins for insisting on this amen. Francis Bernadine Healy has done so much to help us, but you know she made the Women's Health Initiative, which I hope will get to, which is a hot mess like so confusing. The data that came out of that yeah so and these trials are long, and so the data are only now starting to emerge. So, just to be clear I mean I have a question that I don't think is going to take us off track. But this is I'm going to pose this question as a hypothesis, because I think it's likely to be a little bit of a not a barbed wire question, but maybe like a prickly question when people first hear it, but it's posed as a hypothesis. You mentioned some of the psychosocial stress issues based on at the organizational level institutional level, societal level, maybe right down to the family and and just life that are biasing Health outcomes for the worse in female populations. Okay, you refer to as the patriarchy I'm just trying to put it, make sure that we're both talking about the same thing and that's non-exhaustive. I realize that's just a subset of the issues. I'm also hearing there's a lot more PCOS, which is hyper androgenization of the ovary in there we're talking about you mentioned. You know, excess testosterone which females naturally have more testosterone than they do estrogen anyway, but we're talking about elevated levels. Here's a hypothesis, one hypothesis, would be that the increased androgens and the piece of PCOS are a consequence of the psychosocial conditions that are, I don't say forcing but are biasing. The need for females to um think behave. React act in certain ways to survive, let alone Thrive. Is that a I don't say this for any kind of political correctness, hypothesis? This is a in my. This would be a fun interesting and I think, important study to run right depending on stress and the conditions. The specific type of stress do females under produce or over produce androgens, or is it a neutral effect? Does that make sense? I love this question, so let me just paraphrase the last part of it to make sure I got it. It sounds like what you're asking is: could PCOS, or at least some phenotypes of PCOS be a response to what I'm calling patriarchy and then you add a second part to it, which is do healthy? Women like what is their production of testosterone like? Is that right? Yes, and and with the acknowledgment I mean you're, the expert here - um you're, the physician, clinician, an expert in hormones and I'm not, but with the understanding that absolute levels of hormones are interesting but perhaps not as interesting as the ratios of testosterone to estrogen. So when we're talking about excess testosterone, we're really not talking about oh women, making a lot of testosterone because frankly, they already make a lot like then most people that weren't aware of that. I wasn't aware that women make more testosterone right, and so it's not saying that testosterone in women is bad

or is always a reaction to the environment. Yes, but when it becomes um super physiological or hyper elevated is, I could imagine all sorts of social conditions that would create that so in males and females, but here we're talking about PCOS and females in particular, so I'd love for you to speculate um. Should we run the study, we should totally run the study because I don't know the answer. I suspect that you're onto something it may not explain all of the women with PCOS because, as I mentioned, there's a lot of different phenotypes, but I think it could explain a significant portion - and you know you're almost you're saying if we look at the gene environment Interface, this environmental influence of having being someone who's got power over you. If, if PCOS was a response to that, the way that we treat it would be completely different. So, on the one hand, I want to be careful not to dismiss the suffering and experience of women with PCOS. I've got a lot of women with PCOS in my family, and it is there's so much pain and suffering. You know, especially if you want to have a baby and you try for years and you just can't ovulate. On the other hand, I read a paper recently, and maybe we could cite this

01:22:57 PCOS, Insulin, Glucose Monitoring and Management; Data Access

That compares the phenotype of a woman with PCOS to a man who is hypoandrogenic, and I think that's a really interesting way to look at this, because the thread we haven't talked about with PCOS is the the role of insulin and glucose. So, for some of the phenotypes of PCOS, the problem is hyper insulin, emia High insulin in the blood is driving those thika cells and ovaries to overproduce testosterone. These women are insulin insensitive, so more insulin is being cranked out, and these cells in the ovary are therefore making more Androgen. You don't like to say, insulin resistant, oh I I can uh. I don't have a problem saying: okay, I'm just a little bit outside the lane lines of my expertise, so I was trying to use it. What is the correct nomenclature so that we can make sure? Well, what I like about insulin, insensitive, the way that she just said it is that I think that offers people a way in, and I love to do that in terms of messaging insulin. Resistance starts to lose people because they don't really get what that means. At a receptor level, I think I say insulin insensitive, because when people hear insulin sensitive, it almost sounds like a bad thing, but that's actually what you want. So I think I think that's how I defaulted to insulin. What's your insulin, I don't know what I'm due for a

blood test. Yes, you are I'm due for a blood test um I had blood work done for eight months, um sure that'd be great. I uh I'm always um experimenting with different supplements and different behavioral regimens and I've kept charts. Since I was 19., oh you're, like my patient, I I've been sort of Obsessed by this and I would say everybody if you can afford it and at the time. Actually, I had to save up Insurance wouldn't cover it. Um get some basic blood work done, so you have a reference, do it as soon as possible, because even you know the we've been talking about these women over the life cycle. I wish I knew what my insulin was when I was a teenager. I wish I wish. I knew what my fasting insulin was. I really wish I knew my postprandial insulin like in my teenage years in my 20s in my 30s. Well, I knew it in my 30s starting at 35.. Are you a fan of continuous glucose monitors, the hugest most gigantic fan of cgms. I've never seen any tool that I've ever used in medicine change, Behavior the way that cgms do wow. Why do you think they are so effective at changing Behavior I've tried one, and I really liked it. I learned that in the sauna my insulin or my blood glucose goes up. Probably, by a bit of dehydration, I learned what kind of foods work for me which don't um. I thought it was fascinating. I learned how every Behavior you could possibly imagine, use your imagination, impacts, blood glucose, totally totally fascinating to me, including how a two-way wake-ups during the middle of the night versus one versus none impacted blood glucose the next morning fascinating for a data junkie. Like me, it was like I was in heaven um. Why do you think they are so effective in changing behavior? Is it because of that that people can see that real-time control like scan in and like? Oh, that's, the that's the sandwich. I think it's. I think it's many things. I think it's generally the enchantment of learning about your own chemistry and biology. I love it and I think for me what I've seen you know I feel like. Doctors are basically marketers like the sacred marketing, like our job as a physician is to convince people to do something that we think is good for them, based on the best science. But we can't just say here: I wanted to fill this prescription for a ctm. You have to Market it. You have to say. I think this completely changes, the way that you approach your pre-diabetes. I think this could dramatically affect your risk of Alzheimer's disease that you're so worried about that your mother has so our job as Physicians is to be that sacred marketer. So cgms are one of my tools that I think are so crucial. So enchantment number two yeah. It's the real-time effect, so if you go get your glucose and Insulin, measured or maybe you do like a two hour glucose challenge test where you look at glucose and Insulin at the fasting point, one hour later, two hours later or more frequently, that does not have The same kind of

behavior effect as having continuous data where you can say. Okay, I drove to see you Andrew from my place in Berkeley and it was stressful. It was torrentially raining, and I know my glucose was elevated, like I think, really understanding what the the mediators are of your glucose control is essential. Now that said, it's also kind of a later effect. I mean I'd rather know your insulin and we know from uh the white hat white Hall study that insulin, especially postprandial insulin, vascular, insulin, 2 can change years and years before you get a change in glucose, so um that's more for pre-diabetes and diabetes. So I think those are the main reasons why I think it's such an important tool. Third thing: is it democratizes data which you do too? I mean incredible how you do that with your podcast, but I think one of the most hopeful and exciting things that I'm seeing right now in the health space. Is that we're going from this patriarchal relationship where doctors hold the power and are The Gatekeepers of data to patients and clients having much more access to that enchantment about their own chemistry and their own biology? So to me that is so exciting like for me to be able to I've got. You know, probably 100 patients that are in a data stream with me where we're looking at their glucose - and I can I mean I'm on sabbatical. So I'm not doing this so much anymore, but I can call a patient be like. Why is your glucose so high like? What did you do? Oh it was my birthday. I had a piece of birthday cake like that kind of collaboration. That also is teaching the patient to be their own clinician to me, that is a loop of benevolence and integrity that I think is essential to creating Health. We've got a disease care system. We need the democratization of data to become a health-based system, Amen to that a million times over. We share that sentiment. I can tell it at a deep level. I I think the pandemic actually assisted in well harm to many things, but it assisted in people's understanding that um no magic fairy nor the government, nor any anyone was going to arrive at their door with a kit of things to make them healthy right that provide Sunlight movement, sleep and all

01:29:48 Behaviors for Vitality; Exercise & Body Phenotype; Cortisol

The various aspects of nutrition, no, nothing, nothing that everyone has to have access to first and foremost, and then Implement those things as best they can, speaking of which and kind of circling back to this idea of people in their late teens, 20s, 30s and onward. If you had a magic wand - and you could give like two or three don'ts or to make

it personal, if you could go back in time and erase certain behaviors, what would the the don'ts category be? Um, you can tell us more than two or three um, but if the goal is to maximize vitality and Longevity and those are not always uh parallel to one another right, they're, certainly not the same thing, sometimes orthogonal, but, let's just say, fertility being a proxy for Vitality and Longevity, I think people will sometimes forget this - that fertility isn't just about people who want to conceive children, it's also it's a it can serve as a proxy for vitality and Longevity. So what would you like to see patients let's focus first on female patients, but um if it extends to male patients as well? What would you like to see them not do yeah or do far less of I really like that. So I would say a few things I'll just headline them and then we can go into detail number one sleep. I do want to diverge from you a little bit on some things, but sleep is probably not one of them. Oh well, feel free, I mean you're. The one that worked 100. 120 hours a week sleeping much then I can't imagine unless, unless you lived in a different reality than I do, um uh, you know - and there are times in my career where I was pulling all-nighters and sleep deprived, there's just it. I don't recommend it, but I did it yeah. I hope you don't do that anymore, no longer if I can avoid it, but there were years many years where it was like all right here we go and I'm quite um Adept at it for one cycle yeah, but two nights. I kind of start to fall fall apart totally yeah. So I would say: sleep, alcohol, High perceived stress and I'd love to talk about, maybe um the date on telomeres and what we know so you'd like to see people get enough sleep. So don't don't just yeah! Not all of these are concordant, so um, not enough sleep too much alcohol, too much perceived, stress, eating the wrong Foods, toxic relationships and isolation and then number six um not moving enough or not moving and exercising in a way that really fits with your body. So we start with that one actually, just because it's such a and then work backwards, um uh, that's interesting. I I think nowadays people appreciate the need for quote unquote, cardio. I know that the the exercise physiologists cringe and and dissolve into a puddle of Tears when I say that, but getting the heart rate up over some period of time longer than 10 minutes in order to generate cardiovascular, health circulation so and resistance training of some kind. Maybe flexibility, what do you mean by Body phenotype or and exercise I'll speak from personal experience? So what I did through I mean I gave up my 20s to Medicine and during that time I occasionally got to the gym. You know at UCSF on Parnassus. You could go to the gym and then, as soon as your beeper went off you're back into the hospital, but I didn't exercise much. I had um. Do you remember Nordic tracks? I had a Nordic Track in my house and that was that was like it. What I

believe, because, for me, the primary outcome that I'm interested in is cardiometabolic health, so when it comes to exercise what I really feel, if we're going to be at a population level, I feel that about a third cardio two-thirds resistance training is based on my Synthesis of the literature, the best combination - and, I think, there's you know, as you described with your sign um study, I think, there's a minimal, effective dose which for a population is about 150 minutes. I think most of us need a lot more than that per week per week, but I think you know for me, because I have a phenotype that produces a lot of insulin kind of depending on how I'm on my game, I have a lot of glucose. So I have to exercise a lot more to dispose that glucose, so I think you then have to move from medicine for the population or prescriptions for the population to what works for the individual. I think that recommendation is fantastic um, I think resistance training. Well, let me put it this way: I'm neither a trainer nor a physician, but I've seen in family members that were doing, I wouldn't say a lot of cardio, but just cardio that when they add resistance, training, everything in terms including their biomarkers um have improved dramatically. Yes, in particular for female members of my family, well, one of the one of the mediators that I think is important, especially for people who do what I call chronic cardio, which is what I did is cortisol. So we know that Runners, especially marathon runners, people who do a lot of cardio and don't do much resistance training. They tend to have much High cortisol levels and you can buffer that with vitamin C, vitamin C can decrease the effect, but chronic cardio doesn't always serve people. So quick personal example when I first started measuring hormone panels. In myself I went to my physician and I said: I'm 35. I've had one kid. I want to have another kid. I've never been so exhausted. In my life. I just feel like I'm pushing a rock up the hill. I've got this belly fat that I don't like and um. I don't want to have sex with my husband. So what do you think? What can we do about this and he offered a birth control pill and an antidepressant? Oh goodness, so I left him and I went to the lab and I ran a hormone panel and my cortisol was three times what it should have been. My insulin was in the 20s. I was fasting. My glucose was 105., my thyroid was mildly abnormal. My progesterone was low, and that set me on this course of realizing that what I was doing as a physician taking care, especially of women, was not getting to some of these root causes that are so essential, and I would say I had to start first with Cortisol at that time I was running four miles three times a week four times a week. That was just racing. My cortisol further

01:36:40 Cortisol Supplements: Ashwagandha, Rhodiola, Fish Oil, Phosphatidylserine

So that was not the right exercise for me. I needed more adaptive exercise. I started doing Pilates more yoga that helped to lower my cortisol. I mean it started me on. You know changing the way I was managing perceived stress and it also changed my supplement. Richmond, can we talk about that and what the moment you said, lowering cortisol thought of the two supplements that come to mind are um ashwagandha, which I think can potentially reduce cortisol. But I've heard some recommendations about cycling. It and I've always wondered about time of day. For ashwagandha intake, because sort of quote unquote want cortisol elevated in the early part of the day. Yes, and we know this uh, we know you do not want cortisol peaking later in the day. No, you do not interfere with sleep, interferes with sleep um and then the other supplement is uh. Rhodiola rosea do I am I pronouncing that correctly yeah. So radiola is very effective. It's been shown in multiple randomized trials to lower cortisol, so that could be very effective. What sort of doses I've started taking it recently by the way, and I made a huge mistake - I like to make the mistakes first, so then my audiences don't make them um. As I was taking it. I heard it was an adaptogen, so I thought oh I'll, take it before resistance training. But of course you want the cortisol Peak during resistance training, because that's going to set in motion the Adaptive response, so I start taking it later in the day and it's really improved. I would say my late day. Second half of the day cognition. This is subjective to be fair. I just feel like I'm in a more even plane of attention in the second half of the day, so you're describing an NF1 experiment right, which is organic data. Well, it is not anecdotal, so I was taught at Harvard Medical School that the hierarchy of evidence starts at the lowest with expert opinion. You know case studies, then you've got cohort studies and you've got observational data, that's prospective, then you have randomized trial, but the highest quality. Evidence of all is the end of one experiment where you serve as your own control. So what you're describing with rhodiola? I would frame that as an end of one experiment, where you have a washout period and you compare before and after and I'd like to measure some other metrics to see. If there's an effect, including your cortisol, so radial has been shown in multiple randomized trials to reduce cortisol. The other thing that I think is super effective is phosphatidylserine PS for short fish oil also, more modestly reduces cortisol. Ashwagandha is interesting. So in my first book the hormone cure, which I read by the way you did I did I was hoping that was the one you read. I did, I read it and it's spectacular and I thought going into it. I had this,

like you know, let's just call it what it was, it's called male bias like. Is there going to be anything in here for me because uh, I'm, I don't have ovaries and you know it's gon na be and it was immensely informative um. So, thank you, yeah. I have very fun Recollections of the the walks I took listening to it and then I own the print version too. So I like to switch back and forth. So thank you for that. It's a it's a superb book for anyone to read. Yeah yeah, I so appreciate that so in chapter four, you may or may not remember that ashwagandha at least the time that I wrote that book ashwagandha's data is not great, but lack of proof is not proof against. So with ashwagandha. Most of the data comes from thousands of years of using it in ayurvedic medicine, and it's considered again not my science hat. It's considered a double adaptogen so that it's potentially helpful when you are a high cortisol phenotype like I was like, I sometimes still am or low cortisol. I haven't found that in my patients, although I'll give you one exception, so ashwagandha is mostly based on animal studies. There's not as much human data, but it is used a ton in Integrative Medicine. The um there's one supplement that I found to be incredibly helpful for people who tend to have high cortisol at night and that's called a cortisol manager, it's by integrative Therapeutics. I don't have a second um supplement manufacturer that makes something similar it's their number one selling supplement, because it's so effective. Is it a cocktail of several things? It's a combination of phosphatidylserine and ashwagandha. So tell me more about phosphatidylserine. I am familiar with it for it's been mentioned by some guests that were on the Tim Ferriss podcast long ago. For other reasons, I think related to sleep, yes, um and maybe that's another reason why you like it um, but before we move on from rhodiola, is there a dosage of rhodiola rosacea that you um? So I would refer people to my book because the randomized trials and the doses that were used are in there. So I can't remember with rhodiola, although I took it this morning to prepare to be with you yeah. We can look it up and put a show, note caption, so I can remember the dose with phosphatidyl serum, because I take that regularly so 400 to 800 milligrams is the typical dose for PS and What's interesting is that in the randomized trials that were done, 400 Milligrams was more effective than 800 milligrams. Interesting. I've found that for several supplements that the lower dose was more effective. Yes, um yeah, I won't it doesn't matter what those were, and so, when you say PS, you were referring to by the way folks not PCOS, just because scientists and clinicians are familiar with and Military very familiar with acronyms uh, phosphatidylserion PSO 400 to 800 milligrams, 400. Being more effective taken later in the day or early day, does it matter it depends on when your cortisol is

high, so for me I tend to you know: What's the pattern for cortisol? Typically, it rises to its peak 30 to 60 minutes after you get up, then it has this gradual kind of asymptotic decline until you go to bed. So if you're, someone like me who Peaks like way crazy high - I don't do that anymore, but that's what I used to do. I needed phosphatidylserine in the morning.

01:42:36 Cortisol, Anxiety & Immune System; Adrenal Function, Resilience

For people who are high at night, who have What's known as a a flat cortisol pattern or a inverted pattern, you want to take it at night and the flat pattern. Just quick sidebar is that that's associated with a number of conditions that most mainstream Physicians don't know about. So a flat pattern where it's low in the morning and it's high at night is associated with anxiety, depression, uh decreased survival from breast cancer that was studied at Stanford by David Spiegel. That's that he was my um collab close, even collaborator, even uh on the breath. Work study that we oh interesting, yeah he's our associate chair of Psychiatry now, so a wonderful human being has amazed has been a guest on this podcast and and I'm now fantasizing about a conversation that includes uh a panel of of uh, Incredible Minds like you and David from the clinical side, so in any case um yeah, the late shifted, cortisol, not good, not good, and it seems to have the worst immune, Downstream issues of any of the cortisol patterns. So that's really important to know about because it then maps to things like um, it's related to PTSD. So that's the pattern we see like in vets. Who've got PTSD as well as others. It maps to autoimmunity it maps to fibromyalgia. I was told that 1 in 12 people um have are heterozygous, so one mutant copy or a hypomorphic for some some mutation in adrenal related genes, so congenital adrenal hyperplasia, is that true and if so, that means that 1 in 12 people walking around are cranking out Far too much cortisol or not enough cortisol or the cortisol system is already skewed in a direction that makes life more challenging at the levels we're talking about um. Did I hear that correctly, because that 1 in 12 is not a small number? It's not a small number, it fits with what I see clinically I mean I want to see that data just to see um. What does that mean and could you modulate it with environmental influences, but it certainly fits with what I see you know. I was taught once again in mainstream medicine that, in terms of adrenal function, it's very binary how most clinicians think about it. You either have Addison's disease and you don't make enough cortisol or you've got cushions or Cushing weed pattern and you

make too much cortisol and anything in the middle is normal, and my experience is that hell no like there are. Those of us like me who make a lot of cortisol - I don't have cushions. Maybe I've got one of these. I wouldn't call it a mutant Gene. I would call it more of a vulnerable Gene, so maybe I have one of those. Maybe that's part of the reason why I make you know two to three times what I should be, I'm aware of certain groups of individuals from within the military sector that um have there's a more frequent occurrence of some mutation in CCH, congenital adrenal, hyper prevention, not Necessarily two copies, which will, if people look that up they're going to go. Oh wow, there's all these phenotypes and um but sort of hypomorphic type thing. So you know less than or too much cortisol and they are very good at staying up multiple days per night. Right, multiple nights in the series, so they can pull all-nighters very easily yeah. They can push harder when most people would quit and everyone thinks well, that's a great phenotype to have, but guess what it's, because they hyper produce cortisol, yeah and um. So that's interesting and I think if we were to panel medical students and graduate students - and you would look at you - know - who's pulling excessively long hours, who's stressed out a lot even outside of Academia and medicine and pushing pushing pushing really hard. I think the ability to push and not crash, we think of it as adaptive, but in some sense it's maladaptive over a series of years which is sort of what you described earlier yeah. It's such a good point, because you know you in some ways you want to select for that in certain professions like in the military like in medicine um, but I would wonder for those folks about the downstream consequences of producing so much cortisol. Oh, it's got to be detrimental for their health, it's got to be in the long run and - and you see that, but even the data shows that if you're someone like me, who makes a lot of cortisol higher rates of depression like 50 of people with major Depression have high cortisol levels, higher rates of suicide, um much more metabolic dysfunction. We know that trauma as an example maps to an increased risk of glucose metabolism issues and certainly High cortisol. Does that because it's one of the jobs of cortisol is to manage a glucose and it's it kind of sets you up for um this one number five, which is toxic relationships. You know someone who hyper produces cortisol it's hard to live with someone like that. It's also, I would say, people that have this um: let's just call it biological resilience, it's not always adaptive, because you can stay in bad circumstances, longer the ability to to crash provided it's not suicide or life life destroying or you know, long Arc of

01:48:07 Tool: Omega-3 Fatty Acids, Inflammation, Specialized Pro-Resolving Mediators

Of pause and the requirement to you know take two years off from work or school or something um. The ability to keep pressing on is a double-edged sword. Let'S put it that way. Um, I want to make sure in staying within this conversation uh, because you mentioned Foster dial serine. We talked about rhodiola rosacea, we talked a bit about ashwagandha. You've also talked about Omega-3s and fish oil, in particular. I'D love to know your favorite sources of these. I think nowadays, there's more General acceptance that getting these essential fatty acids is important. Do you have a threshold level of sort of grams? I I've encouraged uh um podcast listeners to consider, depending on what they're eating, to try and get a gram of EPA or more per day. Does that seem excessive and what are the real data on epa's, because then the cardiovascular experts always hit back and say? Oh, no, you know it's not good for cardiovascular health and then you go. Oh it's better than antidepressants and other studies and they go no. So I feel like if you really want to make your life difficult. If you want to raise your cortisol, you go on Twitter and you say something positive about Omega-3s and fish oil and um, and you learn a lot um. What are your thoughts on Omega-3s? I take a lot of them. I've always been a big fan yeah. So this is where I personalize, I think some people need more than others, and what I do is I measure your level, so this gets back to nutritional testing. So for you, I would suggest an Omega Quant or one of my favorite cardiometabolic panels is to do a Cleveland heart lab. So I think they they give me the most reliable information, not just for lipids and subclasses, and you know NMR fractionation, but it also gives me an insulin resistance score. It gives me um levels of Omega-3s great, we'll, provide links to these different sites, so that people, but one quick thing about that. The whole story is not Omega-3s and taking fish oil. So the work of Charlie Sirhan at the Brigham is showing that the way that we resolve inflammation, our understanding of it, is really, I think, in the learning to crawl stage. And so, if you look at the omega-3 6 pathway in the body, fish oils can help. You know kind of push the reactions in a particular direction, but typically they're not enough for the resolution of inflammation. Now what most people do, including my MBA players? Is they pop an ibuprofen or something like that when they've got inflammation, that's got lots of other side effects that are not so good for you, and we know in terms of the resolution of inflammation, that taking something like ibuprofen reduces the amplitude of inflammation by about 50 percent, but then it potentially blocks the complete resolution of inflammation. So there's these new supplements that you may

have heard of called specialized, pro-resolving mediators there's a lot of different supplement companies that make them and that combined with fish oil seems to be the best combination and what I do for athletes. Who've got. You know kind of the normal aches and pains of the training load. They have is all combine a little aspirin small dose just like 81 milligrams or two of those baby aspirin together with fish oil plus specialized pro-resolving mediators and there's some that are NSF they're certified. For sports, but the the dose, I would say with my patients, some of them only need a thousand milligrams. Your Gram that you mentioned for the population, some of them need six grams together with spms, so I think it has to be personalized how young um is it? Okay for people to start taking Omega-3s, for instance young women and their teens people in their 20s and their 30s young guys in their 20s and 30s, should they take fish oil if just as a assuming they're, not going to get anything tested. I'M thinking about the college student who is really into biomarkers and that sort of thing we'll go, do some of this um, but many people won't, but they want to do the right thing. So they'll try and drink a little less. Hopefully, hopefully they won't smoke or vape, please don't smoke or vape the idea that vaping is okay. It's like we had. It was so bad, so bad for everything. We're talking about. Let's end that, it's like exactly so just you know avoid hopefully they'll try and avoid those things. Hopefully, they'll avoid hard drugs um, hopefully they'll avoid getting any STIs if they do they'll resolve them quickly. Hopefully yes um so, but they might say: oh well, okay, I'm willing to you know, take some magnesium or take some phosphodel serine buffer. My cortisol eat some vegetables um. Should they consider taking fish oil as a kind of across-the-board inoculatory thing, so I put to rank order these, I would say, fish oil. Yes, I think a thousand milligrams as a general recommendation is good, but I also have a food first philosophy, so my preference would be that they're having salmon or some kind of Smash fish and they're getting that as the primary source of their Omega-3s. And then the days that they don't have fish, I recommend it probably twice a week that they take fish oil. Then I would put magnesium next since so many people are deficient, then I'd probably put vitamin D what how many IU of vitamin D per day? Well, you keep asking me this like for the the population yeah well for the. Let me put it this way for the laze, for the lazy person or - and this is an or not an and or the person who um just doesn't have the finances to go. Get measured, yeah levels measured because you know our audience is a huge range. We've got people who can have tons of disposable income that list in the spot. We have people have no disposable income, so a thousand to two thousand international units. But my you know what I do is I dose to a

serum level, that's between about 50 and 90. great, and so I have a vitamin D receptor, uh snip, and so I need to take about 5 000 a day to get to what I need a Lot of people don't need that, and you know there's some supplements that I don't know if they need so you

01:54:20 Oral Contraceptives, Benefits & Risks; Ovarian Cancer; Testosterone

Mentioned phosphatidylserine for someone who's a college student and their cortisol is completely normal. They're wasting their money on PS. They don't need it, they might need it later, but they don't need it now. I'd like to make sure that we Circle back to birth control, in particular oral contraceptive birth control, and we should touch on iuds, perhaps a little bit more. But what are your thoughts on sort of pure estrogen, birth control? This is what I learned when I was in college is that birth control is basically tonic, estrogen, so constantly taking estrogen estrogen women are taking estrogen so that they don't get the estrogen priming of progesterone you're, not getting any ovulation, and I've known women that have been Taking oral Contra or that took oral contraception as like estrogen pills, basically for 5, 10 15 years. Are there long-term consequences of this, as it relates to pregnancy, PCOS menopause? What? If so, what are some of those consequences? Um? What are your concerns? What do you like about oral contraceptives? What do you dislike about them? I like how balanced you ask that question. So women who take oral contraceptives as long as you're describing like 10 years or longer, we call those Olympic oral contraceptive users in terms of benefit. I think that, especially when they first came out, and even now it gives women reproductive choice and That's essential. As you may know, a reproductive Choice has been declining recently. So I'm a big fan in that regard and we've got a lot of data to show both the risks and also the benefits of it. So I'll speak first into the benefits because uh I'm gonna get on a soapbox a little bit about the risks. So we know that it reduces the risk of ovarian cancer. So there's something about this idea of incessant ovulation. That is not good for the female body. So if you look at, for instance, women who are nuns who don't take oral contraceptives and they have a period every single month of their reproductive lives, they have a greater risk of a brain cancer. So if you look, then at women who have uh several babies and they've got a period of time when they're pregnant that they're not ovulating, and then they breastfeed for some period of time. They have a lower risk of ovarian cancer, so oral contraceptives help with reducing ovulation and reducing risk.

We know that if you take the oral contraceptive for about five years, it reduces your risk of ovarian cancer by 50 and that's significant because we're so poor at diagnosing ovarian cancer early there's really no method, that's really effective. We use ca125 and ultrasound screen, especially in women, who are at greater genetic risk, but even that often we diagnose it. You know in a later stage, maybe just because that statement is going to highlight for a number of people. The question of what are some of the some earliest symptoms that people can recognize without a blood test so as ovarian cancer. Is it going to be pain, so the problem is the symptoms are so vague and they're, so non-specific one of the most common symptoms is bloating and we've already talked about constipation we've talked about how women have this longer track, GI tract and so bloating is a Really common experience for most women, you can have bulk symptoms. You know feeling like your. Your lower belly is kind of pressed out, so the way that we inform women in terms of watching for this is to get regular, gynecologic exams for women who are at high risk, where they have, for instance, an ultrasound. For some reason. It shows a mass that we're concerned about there's a way to triage that in terms of what kind of evaluation that they need and that's the situation where you might get a blood test called the ca129 CA 125., the um yeah. The problem is the symptoms. Are so vague it could be, it depends on how big the tumor is, how much bulk you have, what it's pressing on so, if um taking estrogen and thereby reducing the frequency of ovulation, lowers the risk of ovarian cancer. Should women that are even women who are not sexually active, so they're they're not actively trying to get pregnant or avoid getting pregnant, but if they're not sexually active, then the probability of conceiving unless they go through some IUI or some other route is, is very low. As far as I know um, so I was taught in high school anyway um would they be wise to suppress ovulation for periodically using hormone-based contraception just so that they can offset the risk of ovarian cancer? That's a very rational question and I would say that's what mainstream medicine has had at its back to recommend oral contraceptives, not just for women who are seeking contraception, but for acne for painful periods for really kind of the drop of a hat they're prescribing oral contraceptives. That's what I was taught to do, but there are so many consequences and I think the issue here is more about consent, because in OB GYN and I started out as a board-certified, ob gyn and I now mostly see men. But I was taught as an OB GYN to convince women to go on the oral contraceptive and I think a lot of that is pharmaceutical influence. So maybe we could talk about the risks and why the answer is no to your question. Um as we do that. Could I just ask: is the um the so-

called ring the new it used to be called The nuva Ring? Maybe that's a brand name, but when I was in college there was all this discussion about the ring all right by both men and women for reasons that don't belong on the podcast um use your imagination folks, so um is the the ring. Obviously it's not oral. It's not oral hormone contraception, but it's hormone based right. The rate is releasing estrogen locally as opposed to taking it orally. But would you would you slot it under what you're about to tell us in terms of the concerns, so we have less data about the ring. So the oral contraceptive is two hormones, it's ethanyl estradiol and it's a progestin. So it's not the normal uh progesterone that your body makes such ovaries make and your adrenals make. It is a synthetic form of progesterone and it is the same progestin similar same class. That was shown to be dangerous and provocative in the women's health initiative. So I'm not a fan of progestins. I do not recommend them for any woman unless the consequence of not taking them is surgery or some other um. You know unless it gives them some freedom. In some way, so I don't like Protestants, the uh nuva ring is estrogen plus progestin, but it's released transdermally through the vagina. So, given the the way that um it's delivered to the vagina, the doses are lower than What's taken orally, but in terms of some of the risks that I'm about to talk about, we don't know about much of the data. We think that it's similar, there's, probably a spectrum of risk and maneuvering, is a little more towards the middle than you know. What I'm talking about with oral contraceptives? Are you ready for that yeah, I'm ready for the risks? Okay, so like with almost any pharmaceutical. The oral contraceptive depletes certain micronutrients, so magnesium there's certain vitamin B's that are depleted uh. It also affects the microbiome that data is not as strong, but there seems to be some effect and there's also an increased risk of inflammatory bowel disease in autoimmune condition. It increases inflammatory tone, so the studies that I've seen increase one of the markers of inflammatory tone, High sensitivity CRP by about two to three x. It seems to make the hypothalamic pituitary adrenal axis more rigid so that you can't kind of roll with the punches and Wax and Wane in terms of cortisol production. The way that you can off the birth control pill it can affect thyroid function. I'M thinking of the slide that I have that has like 10 problems associated with oral contraceptive, but that's what I can remember right now, that's very helpful and it makes me wonder whether or not if, on the one hand, oral contraceptives are protective in women. It's ovarian cancer, but then they have these other issues. Yeah, there's one other I want to mention. Please anytime, you take oral estrogen. It raises sex hormone by Nick globulin and you've talked to other podcast

guests about this Kyle. I think sex hormone, binding globulin. I think of as a sponge that soaks up free, estrogen and free testosterone. So when you go on the birth control pill, you raise your sex hormone, binding globulin. It soaks up especially free testosterone and for some women it's not a big deal. They don't notice. Much of a difference, but then there's a phenotype, maybe related to CAG, repeats on the Androgen receptor, who are exquisitely sensitive to that decline in free testosterone. So this then opens the portal of talking a little bit about testosterone in women. So we've mentioned already that it's the most abundant, biologically the most abundant hormone in the female system, even though men make almost 10 times as much or even more than 10 times, it is so important for women. It is essential to so many things. Not just sex drive and muscle mass and seeing a response to resistance training, but also confidence in agency, and so those women who are so sensitive to their testosterone level. They've got this high sex hormone, binding globulin, their testosterone declines. What they describe is vaginal dryness. Maybe a decline in sex drive, but there's also this bigger issue related to confidence in agency, even risk-taking from studies that we've done with MBA students. That, I think, is a serious problem. Maybe the most important out of all of these things is that it can shrink the clitoris by up to 20 percent twenty percent, and that includes the regression of the of the nerves that innervate the the clitoris is that I mean that's a very good question. As a neuroscientist yeah, I would think uh I used to teach uh the neural side of of reproductive Health. We need to do a series on Sexual Health. Maybe you would co-host that with me. We could certainly use your expertise. I think um yeah, that's a dramatic! That's interesting number yeah, but then let's go back to the sacred marketing. If I've got a woman that I think should not be on the birth control pill, maybe she's taking it for acne or she's taking it, because her periods were a little painful. What I'm going to do is say: let's leverage these other ways of making your period less painful. Let'S take the message of your painful periods and figure out. Okay, it's your inflammatory tone and we give you some fish oil and spms, maybe a little aspirin when you've got your period like, let's find some other ways to deal with it, then, to take the oral contraceptive which you have not received informed consent about, because it Can trick your by up to 20 now that usually convinces most people to come reversible? The elevation in sex hormone, binding globulin, does not seem to go away when you come off the birth control pill. To me, that is the biggest problem with prescribing oral contraceptives. Now the data that we have is limited, there's one woman who uh Claudia, has something something who looked at sex hormone, binding globulin a year

out from stopping the birth control pill, and it was still elevated. It wasn't as high as it was when they were on the pill, but it was still elevated. So your question about reversibility - I don't know if we know the answer to that.

02:06:50 Fertility, Follicular & Anti-Mullerian Hormone (AMH) Assessments

Wow, okay, um, that's yeah! That's a significant statement and something that for consideration related to this, although this might seem not related it is how early do you recommend that women go get their follicle number assessed, in other words, to get a size, a sense of the size of the ovarian reserve And their amh levels measured um, I'm gon na I'm an amateur Outsider, as I say this, but we have an episode on a fertility where I just described the ovulatory menstrual cycle, yeah um and I'm not the best person to answer that yeah. Well, I'm too far out from it: okay, well, um! I suppose, then, from taking the perspective of somebody who thinks about fertility it in terms of at least congruent with vitality and Longevity, given that it's fairly non-invasive, it's an ultrasound or a blood draw for amh or both. Is there any reason why a woman would not want to get her follicle number assessed or her amh levels assessed? Is there any reason why? Because I was shocked to learn that most women don't do this until they're, hitting their late 30s or early 40s and yeah they're having conceived or they suddenly decide that they want to conceive - and I thought why doesn't every doctor insist that their female patients get have Their amh level addressed so that if they need to freeze eggs cost it's cost yeah. So I think if you've got the disposable income to do it, go for it. It's not included in a standard blood panel, no wow, the only women in my practice, who've had amhs done and have looked at their follicle count are women who want to freeze their eggs or, and that requires disposable income or they um are having trouble getting pregnant. So they are in the reproductive Endocrinology system and they're getting an evaluation and then they're also um the women who have symptoms of early menopause, so premature, ovarian insufficiency, which is before age 40. uh. Those are the women that I see getting attested and I think you're right that it should be offered more broadly. It speaks to the democratization of data again and I think most women don't know that so you're doing a huge service. I think to be speaking into this one other point related to that is that what I see in conventional medicine is that when a woman asks for a hormone panel and she's not trying to get pregnant, she usually gets told that hormones vary too much. It's a waste of money, you don't need it or, if you're feeling

hormonal, why don't you go on a birth control pill unless she's trying to get pregnant if she's trying to get pregnant? Suddenly those same tests are very reliable and they get you know their their testosterone, their free testosterone, their thyroid panel. They get their estrogen and progesterone. Maybe they get their cortisol, they get their amh. So there's a double standard between those who want to get pregnant and those who don't and that needs to end. I totally agree as I've learned more about um ovulatory cycle and amh and and the antral population of follicles on it. It's fascinating. It just seems to me wow a relatively straightforward test. One definitely invasive ultrasound, but I don't consider that yeah, that's not I'm not terribly invasive, but invasive uh, at least but the other one. Just pure blood.

02:10:29 Menopause & Hormone Replacement Therapy; Women's Health Initiative

Test just seems like why, wouldn't I wouldn't this be offered or covered by insurance or or you know that anyone that wanted, but now now I understand why you mentioned menopause huge topic, enormous topic. We had a guest on the podcast who's, not a clinician who said something in passing, so I wan na I'm likely to get this wrong um. But what they said was that the results of the large-scale trials on hormone replacement therapy for women for menopause said something to the effect of. If the hormone therapy was started early enough, it was very beneficial for yes, vitality and health outcomes, whereas if women went through menopause and then initiated the hormone therapy hormone replacement therapy that it could be detrimental to their health. So, first of all, do I recall that statement correctly and then, second of all, what sorts of hormones are being replaced? Is it just estrogen, and how is that done? Is it done through birth control, so oral contraceptives nuvarings? What are your thoughts on menopause? When should people start thinking about it and what is the palette of things available so that we can do an entire episode with you on on this topic in the future? But just to I you know, I get a lot of questions about this and and I'm guessing based on everything. You've told me today that there are women in their 30s that, while they may be 20 years out from menopause, probably should be doing things now. In anticipation of that yes, so we haven't talked about the 30, something, but I totally agree with you, the more you know about your phenotype, your hormonal phenotype, when you're in your 30s you're set up in terms of what to do in the future, especially things like Your thyroid, your estrogen and progesterone levels, because you can replace to a state of Youth thyroid

whatever that is for you, you can replace. I don't usually go exactly back to where the estrogen and progesterone levels were, but we can get pretty close. So in your 30s, having a base case, I think is really essential. So you spoke to the Women's Health Initiative, which was published in 2002, and we went from a huge number of women taking hormone therapy to a very small percentage like in the range of five percent, and that means we've got millions. Millions of women who are suffering needlessly with things like insomnia difficulty with their mood difficulty with sex drive, feeling like they are closing the store in terms of sex because they're not on hormone therapy. I would agree with the statement that you made that hormone therapy particular forms that are similar to what your body always made when it's given judiciously at the right time, typically within five to ten years of menopause, which is 51 to 52, that it is incredibly safe. So it's a complicated study, the women's health initiative, but it was the the wrong study in the wrong patients with the wrong medications and um with some of the wrong outcomes. So it was powered to look at cardiovascular outcomes. It was not powered to look at breast cancer. It was stopped because of breast cancer risk, but what happened in the control arm of the study was that they had an incredibly low rate of breast cancer and so, as a result, they ended up having this increased risk of breast cancer at five years and they Stopped the study now the study was done with synthetics. It was done with conjugated equine estrogen known as Premarin and medroxy progesterone acetate. Those were the so-called estrogen and progesterone. Those are synthetic hormones. We think, especially the progestin is associated with the greater risk of breast cancer. Although the the subsequent re-evaluations of the data now 18 years out, have shown that um this problem with the control group and no increased risk of breast cancer um and for the women who got estrogen only those who had a hysterectomy, the Premarin, they actually had a Decreased breast cancer risk and decreased breast cancer mortality. So there's a lot to be said about this: I'm trying to keep it really brief. But if you look at the women 50 to 60, So within 10 years of menopause they're, the ones who seem to have the greatest benefit, so they had a decreased subclinical, atherosclerosis, so less cardiovascular disease. They had an improvement in terms of bone health, um, less progression to diabetes and then over the age of 60. They started to have greater risk of certain outcomes such as cardiovascular disease, myocardial,

02:15:30 Perimenopause, Cerebral Hypometabolism, Metabolism & Estrogen

Infarction and so on, you asked about um. What do I do and to me, this problem is not just menopause. What's more interesting is to talk about perimenopause, so perimenopause is the the period of time before your final menstrual cycle and for most women depending on how it's tuned, you are to the symptoms. It can last for 10 years, so I'm still in Period menopause. It's been like 20 years, because I've been tracking it so carefully. It usually gets kicked off by having your cycle get closer together. So that could happen in your 30s or your 40s. You go from 28 days to 25 days. That sort of thing you may notice that you start sleeping more poorly, because progesterone is so important. You talked about that with Kyle. You may notice it as more anxiety. Difficulty is sleeping, and that probably is related to the estrogen receptor. So your Alpha is estrogen receptor. Alpha is anxiolytic, it increases anxiety, ER beta is associated with an anxiolytic activity and then there's a total of about six estrogen receptors. Now there's the the g-protein-coupled estrogen receptors and those are mixed: anxiolytic anxiogenic, so um, there's this whole period of perimenopause and What's Most Fascinating to me, and we've got to talk about this either today or another time is that there is this massive massive change that happens in the female brain that people are not talking about enough and so looking at the work of Lisa Moscone at Cornell from uh starting around age 40., there is this massive change in cerebral metabolism, so you can do fdg pet scans. You can look at glucose uptake and there's about on average, a 20 decline from pre-menopause. You know up to like age 35 to perimenopause, to post menopause the women who are having the most symptoms in perimenopause menopause, The Hot Flashes, the night sweats, the difficulty of sleeping those are the ones who have the most significant cerebral hypometabolism. So it's almost like a um. I don't. I don't want to scare people with this language, but it's a low level or let's call it pseudo dementia of sorts. Yes it. It seems to be a phenotype that you can then map to Alzheimer's disease, because that's Lisa moscone's work she's, looking at okay, Alzheimer's disease is not a disease of old age, it is disease of middle age. What are some of the biomarkers that we can Define? That can tell you what your risk is. I've got a mother and a grandmother with Alzheimer's disease. You can believe I am all over this data and insulin resistance. It's a huge part of sensitivity, as we talked about before um seems to be somewhere in there, which I think when that first, when that idea first surfaced a few people like really, but then of course right I mean the brain is just incredibly metabolically demanding organ. You deprive neurons of fuel sources, they or you make them less sensitive to fuel sources. They start dying, they certainly start firing less. It makes perfect sense, and I think now it's thanks

to Lisa's work, work that you've you've done and talked about. Quite a lot is um in your books and elsewhere. I think has really you know, highlighted for people that metabolism and metabolomics is going to be as important as genes and genomics when it comes that's right, dementia, perhaps especially in women, is it safe to say that I think I think so, because we believe that this System is regulated by estrogen, so the decline in estrogen starting around age 40, 43 is kind of the average seems to be the driver behind cerebral hypometabolism. The way I describe it to my patients is it's like slow brain energy, so you walk into a room. You can't remember why, like you just notice that you can't manage all the tasks, the way that you once could like things are just a little slower, and I say that to women and they're like I have that like help me so this is then circling back To Whi, where women are scared to death of taking hormone therapy, and we've got all of these women that are Marching toward potentially a greater risk of Alzheimer's disease. And they have this opportunity in their 40s and their 50s to take hormone therapy. And they may not be offered it, because the typical conventional approach based on Whi is to say, unless you're having hot flashes and night sweats that are severe. I'M not going to give you hormone therapy, and I I just want to call that out. I would say: no that is not the way to approach it further. The concept right now in conventional medicine is that hot flashes and night sweats are these nuisance symptoms that we will take care of temporarily, maybe with a little bit of estrogen, progesterone or birth control. Pill because it's given a lot or that they pass or is that this idea, you know suck it up suck it up, doesn't matter that you're, not sleeping anymore. You know turn down the temperature in your room and that's not right, because hot flashes and night sweats are a biomarker of cardiometabolic disease. They are a biomarker of increased bone loss. They are a biomarker of changes in the brain. So many of these symptoms that occur in perimenopause are not driven by the ovaries. They are driven by the brain yeah. It's the the bi-directional crosstalk between the body and the brain keeps you know, I think, is this resounding theme: uh. We had Chris Palmer on here. A psychiatrist who's talking about ketogenic, diet, mental health. I know uh you, we could have a whole other discussion and we will. I hope if you'll agree to it about nutrition and as it relates to hormones, uh, specific diets and and so forth, but the and that's a question too whether this problem of cerebral hyper metabolism. Could we solve it with estrogen

02:21:49 Intermittent Fasting, Ketogenic Diet, Metabolic Flexibility

And or increased metabolic flexibility, so I just wanted to footnote that sorry to interrupt you. No please uh, please interrupt um uh. I know Europe as long as we're there. I know you are a fan in some instances of intermittent fasting time, restricted, feeding and or ketogenic diet. Yes, um to get cells sensitive to insulin, which is not to say, if I understand correctly, which is not to say that women need to stay on the ketogenic diet for long periods of time or intermittent fast. For my only time, restricted, feeding for eight hours or six hours a day, but that by increasing you said metabolic flexibility, excuse me, but by increasing cells, sensitivity to insulin and then maybe returning to a more typical eating pattern and periodically switching back and forth. That might actually benefit be beneficial. Do I have that right, yeah? I love the pulse, so I feel like it's much more physiologic than say going on a ketogenic diet and staying there for years. All of the data that we have on the ketogenic diet. It's pretty Limited in terms of duration. You know the the longest players that we have in terms of the data are the focus with epilepsy and that's just a different phenotype. So I think in terms of microbiome effects - diversity dysbiosis some of those issues. We really don't know in terms of long-term effects, so I prefer, with a ketogenic diet that it's used as an NF1 experiment and that to do it for four weeks. Maybe you measure biomarkers before and afterwards. Maybe look at your stool before and afterwards we still haven't talked about stool tests yet, but you could measure your fasting insulin and your glucose

02:23:29 Stool Testing

You could just start there do four weeks of Keto clean keto, including vegetables, it doesn't have to be 57 a day and then measure it again afterwards, since you mentioned a mentioned stool testing. Yes, what? What is your recommendation about stool testing? So my recommendation? This is again in the the field of if you have the disposable income, so I usually start with Genova, because they've got a good copay system with insurance. That's what I typically use, so I usually do their one day, stool test, where you have to go digging through your stool and send it off to the slab. That's in North Carolina. I usually do the one day unless I'm concerned about parasites. In that case, I tend to do three days. I do that for people who travel a fair amount and go to places where there's greater risk - or they just have gut symptoms. Another test that I do a lot is um, because I always like to mention two Labs is a test by longevity, and this is much more of a data

wonk uh type of test, because it's powered by AI. It was designed by um a guy who's got inflammatory bowel disease and he is a um he's a PhD deep, phenotyping bioinformatics guy who wanted to make this really easy. So the test is, is Under the Umbrella of thorn and um. They just call it got bio. They might have another name for it and they just improved it so that it's just a wipe instead of digging through her stool, and so my athletes will do it now they were not so into digging through their stool before. Is anybody really? No one is, I don't want the answer. I know the answer. I prefer to that, but that's a super interesting test, because it's you get much more dense data. The issue is um, with apologies to my friends at Thorne. The issue is that there are recommendations. End up being sworn

02:25:32 Coronary Artery Calcium (CAC) Test, ACE Score & Disease

Supplements so that can be very easy for people who want to you know, connect the dots. That's not always the way that I like to do it uh. First of all, three things: um you've shared with us, an immense amount of knowledge, and in that first statement I also want to apologize, because I threw at you the entire life span of uh female lifespan, reproductive Health, contraception, diet, uh, microbiome, so many things but um. I first I just want to say you've taught me a tremendous amount um, including, I think something that most people, including myself, have not thought about enough, which is the psychosocial impact on things that we're all familiar with constipation bowel movements, what we eat, what we avoid. I have to say really a huge thank you for that, because it's not something that's been discussed on this podcast before sort of know that brain communicates with body psychology and biology are linked. But I think this is the first time that anyone's ever directly linked circumstances and biology and psychology in such a concrete way. So that's that's the first thing and I speak for many people in that. Second of all, we barely scratched the surface of your knowledge and um, which is both uh frustrating for me because uh it. I always want to learn more, and I know many other people do as well, but also very, very exciting, because uh with uh, hopefully without much persuasion, we can have you back on to talk about something at all. Like meant uh, I know you're working with men. Now Men's Health um some particulars around, I think, there's more for us to explore in terms of PCOS, menopause, contraception and all of the above, but then something that you and I were talking about off camera um before we started, which I think is a really important Factor that ties back to this issue of of

trauma and stress and the bi-directional relationship between biology and psychology, hopefully someday. We won't even separate those two which is the use of specific medicines, including plant medicines, yes, and how that can influence overall health, which no doubt will include Hormone Health. So I say all of that for two reasons. First of all, to queue up the we won't even call it a part two, but a sequel to the to this with um. I'M gratified to hear that you you'll join us for that and then also to just really extend a huge. Thank you. The amount of knowledge that you shared is is immense and uh is going to be very, very useful and actionable for for men in terms of their thinking and their actions, and for women in particular. Today's discussion, in particular for women in terms of how to think about their health and biology, how to think about their psychology and the environment that all of that's embedded in so I just want to say an enormous. Thank you. Thank you Andrew. I so appreciate that, and I so appreciate what you offer to the world in terms of a weigh-in a way to understand physiology and how, to craft a architect a better life um. Can I just add one last thing, because I didn't talk about it since we didn't get to the 40s and the 50s and those listed biomarkers. So I feel like if people, if women went away with one thing today, it would be to do a coronary artery, calcium score by age 45 and sooner if you've got premature heart disease. How is that taken? So it's a CT scan of the chest. You can self-order it like, I think, at Stanford Hospital you can self-order it last time a patient checked. It was 250, so again disposable income, but it tells you it. It almost gives you this fork in the road in terms of how much you need to pay attention to cardiometabolic health as a woman and it's uh 45 for men too. So if you haven't had one, if you had one, no, you need one insulin, cortisol CAC great. So I'll run all that by you. It's really essential and it's um yeah. It's it's so fascinating because you know there's some women who have a zero. So my score is zero and that's great so often you can just keep doing what you're doing, but if you're 45 and you're starting to be elevated or you've got you know, maybe you've got PCOS or you've got some other biomarkers tending you in this direction. Toward the number one killer, really it's nine out of the top 10 killers in the US that allows you to really start to make changes, and I I think it's essential to know that data. It's not it's, probably not going to be offered by your doctor. Certainly Peter attia is going to offer it, but most conventional doctors are not going to do it and then the last thing I want to say before you mention. So if I were to go to my doctor - and I just say I want a cardiac calcium score - that's what people coronary artery, calcium, scores, CAC! Okay, so everyone hear that and know that, if you're 40 or older - and maybe if you're, 45, 45 or older get get it so the last thing is - and this is for

men and women - is there a score so adverse childhood experiences? Knowing your a score is so essential in terms of a baseline, for how much trauma your system, your Pine system, endured when you were a kid, and we know that childhood trauma, whether it's abuse or neglect, or you know, having an alcoholic parent that maps to disease In middle age - and it can give you so much Insight I'll give you an example: I've got a patient who had an elevated, coronary, artery, calcium score, who does everything right with her food? I think it was her trauma that elevated her CAC when she was 45.. So I think an a score knowing your a score, starting as a teenager like knowing it and knowing how to work with that is really essential. There are certain people, they are exceedingly rare, but you are one such person that when they speak, knowledge just comes from comes out of them and it's incredibly useful and helpful knowledge. So thank you. I'M gon na get both of those things. Good um and I highly recommend everyone else pursue ways that they can get those or if they can't get them that they. You know Your Mark, those as things to get at the point where they they can obtain

02:31:56 Zero-Cost Support, YouTube Feedback, Spotify & Apple Reviews, Sponsors, Social Media, Neural Network Newsletter, Momentous

Sufficient uh, disposable income sounds like that. The health uh, the detriments to health that those can offset would be well worth the cost totally. Thank you. Thank you for joining me for Today's discussion. All about female hormone Health, vitality and Longevity with Dr Sarah Gottfried. If you'd like to learn more about Dr Gottfried's work, please check out her social media channels. We've provided links to those in the show note captions. In addition, please check out one or all of Dr Gottfried's excellent books that she's written about nutrition, supplementation and various treatments for Hormone Health, longevity and vitality, we've linked to two of those, notably women, food and hormones, and her book. The hormone cure in our show note captions if you're learning from and or enjoying this podcast, please subscribe to our YouTube channel. That's a terrific zero cost way to support us. In addition, please subscribe to the podcast on Spotify and apple and in addition on both Spotify and apple, you can give us up to a five star review. If you have questions or comments or topics or guests that you'd like me to cover on the Huberman Lab podcast, please put those in the comments section on YouTube. I do read all the comments. In addition, please check out the sponsors mentioned at the beginning of and throughout Today's episode, that's the best way to

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