

Dr. Kyle Gillett: How to Optimize Your Hormones for Health & Vitality | Huberman Lab Podcast #67

My guest is Dr. Kyle Gillett, MD, a dual board-certified physician in family medicine and obesity medicine and an expert in optimizing hormone levels to improve overall health and well-being in both men and women. We discuss how to improve hormones using behavioral, nutritional, and exercise-based tools and safely and rationally approach supplementation and hormone therapies. We discuss testosterone and estrogen and how those hormones relate to fertility, mood, aging, relationships, disease pathologies, thyroid hormone, growth hormone, prolactin, dopamine and peptides that impact physical and mental health and vitality across the lifespan. The episode is rich with scientific mechanisms and tools for people to consider.

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- Welcome to the Huberman Lab Podcast, where we discuss science and science-based tools for everyday life. [lively music] I'm Andrew Huberman. And I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. Today my guest is Dr. Kyle Gillett. Dr. Gillett is dual board-certified in family medicine and obesity medicine and practices out of a clinic in Kansas and via telemedicine. He provides full-spectrum medicine, including hormone health, preventative medicine, obstetrics, which is the branch of medicine and surgery concerned with childbirth and the care of women giving birth and pediatrics. I first learned about Dr. Gillett from a podcast of all things and was immediately struck by the breadth and depth of his knowledge on all things hormones and hormone optimization. As you'll see very soon today, Dr. Gillett can teach you how to optimize your hormones using behavioral tools, nutrition, exercise-based tools, supplementation, and hormone therapies if those are appropriate for you. There are many professionals out there including many medical doctors of course, talking about hormone health. What really sets Dr. Gillett apart from the pack is his ability to understand how the different factors that I described before, nutrition, supplementation, exercise, and hormone therapies, how those interact with one another and the safest and most rational ways to approach hormone optimization. During today's episode, you will learn how to optimize your hormones, not just testosterone and estrogen, but also prolactin and other hormone pathways that impact your mood, mental health and physical health. Dr. Gillett is also an avid educator about hormones in other aspects of health. He does this on zero cost to consumer platforms, such as Instagram and other social media. On Instagram, he is kylegillettmd, that's K-Y-L-E-G-I-L-L-E-T-T, no E at the end, MD. So kylegillettmd on Instagram. And he is Gillett Health on all other platforms, including LinkedIn, Twitter, YouTube, TikTok, and Facebook. If you go to his Instagram or his other social media, you will learn a lot about hormone health, about the latest science impacting obesity and metabolic health. He is a wealth of knowledge. And again, he's providing all that information at zero cost to you, the consumer. What you are soon to hear is a conversation between me and Dr. Gillett about all things hormones and hormone health and hormone optimization. We dive deep into mechanisms, but we are clear to establish what each word or set of concepts mean. So if you have no

background in biology or even if you do, I'm sure that you'll come away with a wealth of valuable knowledge. We also talk about specific protocols related again to lifestyle factors, nutrition, supplementation, and where appropriate, hormone replacement therapy. I know there's a lot of interest about these topics. Dr. Gillett is very thorough about addressing both male and female issues and addressing hormone health for people at all stages of life. I'm sure that you'll come away from this episode with the same impression that I did, which is that Dr. Gillett is an extraordinarily clear communicator and that he has tremendous compassion for his patients,

00:03:10 The Brain-Body Contract

and that he has a deep love of understanding biology and medicine in ways that can benefit you. I'm pleased to announce that I'm hosting two live events in May, 2022. The first live event will take place in Seattle, Washington on May 17th. The second live event will take place in Portland, Oregon on May 18th. Both are part of a lecture series entitled, "The Brain Body Contract" during which I will talk about science and science-based tools. Many of which overlap with the topics covered on the Huberman Lab Podcast, but most of which will not and will be completely new topics and tools never discussed publicly before. Both live events will also include a question and answer period during which you the audience can ask me questions directly about any aspect of science or science-based tools and I will attempt to answer them. Tickets for the two events, again, Seattle on May 17th and Portland on May 18th, are both available at hubermanlab.com/tour. Before we begin with today's episode, I want to emphasize that this podcast is separate from my teaching and research roles at Stanford.

00:04:10 Thesis, InsideTracker, ROKA

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. Our first sponsor is Thesis. Thesis makes nootropics. In fact they make custom nootropics. Now what is a nootropic? Technically nootropics means smart drug. Frankly, I'm not a big fan of the word nootropics, because what is smart? I mean, there's creativity, there's focus, there's task switching, different aspects of our brain and body engage different aspects of

cognition, many of which we can call smart. There's emotional intelligence, there's analytic intelligence, there's logic, there's creativity. Thesis understands this and has designed custom nootropics designed to bring your body and brain into the specific state that you want. So for instance, they have specific nootropics for creativity, other nootropics for focus, other nootropics for motivation, and so on, and so forth. In addition to that, each nootropics is custom designed for you. They use only the highest quality ingredients, things like alpha-GPC and phosphatidylserine, which I've talked about on this podcast before. They also use ingredients like ginkgo biloba, which many people use, like and benefit from. However, there are also people like me who can't take ginkgo biloba, because it gives me terrible headaches. I learned that a long time ago. And so I simply can't take any nootropic or any supplement for that matter that includes ginkgo biloba. I'm sure I'm not alone in the fact that some ingredients work for me and others do not. Thesis has solved this problem of individual variation by creating a brief quiz. So if you go online to takethesis.com/huberman and take a three-minute quiz, and then Thesis will send you to four different formulas that match your specific preferences. Again, that's takethesis.com/huberman. And if you use the code HUBERMAN, you'll get 10% off your first box of custom nootropics. Today's episode is also brought to us by InsideTracker. InsideTracker 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 longterm health can only be analyzed from a quality blood test. There are a lot of blood and DNA tests out there, but a major issue with many of them is that you get numbers back about levels of hormones, metabolic factors, lipids, et cetera, but you don't know what to do with that information. InsideTracker has solved that problem by creating a personalized dashboard. So you take your blood and/or your DNA test, you get the results back, and where certain values might be too high or too low for your preference, you can click on that and it will direct you immediately to lifestyle factors, nutrition, supplementation, et cetera, that can help you bring those numbers back into the ranges that are ideal for you. So it not only gives you information about where your health stands, it gives you directives as to how to improve your health. If you'd like to try InsideTracker, go to insidetracker.com/huberman to get 20% off any of InsideTracker's plans, that's insidetracker.com/huberman to get 20% off. Today's episode is also brought to us by ROKA. ROKA makes eyeglasses and sunglasses that are the absolute highest quality.

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00:08:24 Preventative Medicine & Hormone Health

And now for my discussion about hormone health and optimization with Dr. Kyle Gillett. Dr. Gillett, welcome. - Thank you for having me. - Well, I'm super excited to talk to you, because I found out about you on a podcast and it immediately became clear that you are an encyclopedia of knowledge about hormone health for men and for women across the lifespan. So I have many, many questions, but before we dive into those questions, I'd love to just get a little bit of your background in terms of your medical training and what your particular orientation is toward treating your patients. And how do you think about this whole landscape that we call hormone health? What is a hormone? How do you envision people managing their hormones? If you could just kind of fill in a few of those blanks for us, I think a lot of people would appreciate it. - Absolutely, so I'm dual board-certified in family medicine and obesity medicine. I've kind of tailored my training in order to provide what I call a balanced approach to total health, which includes body, mind, and soul. I recently saw a podcast with Joe Rogan and Mr. Beast. And Joe asks Mr. Beast, "How do you become such an amazing YouTuber and have all these great clickbait videos, and how did you become good at it?" And it turns out he just became obsessed when he was a teenager. And that's essentially how I've tailored my education as well. I've become obsessed with optimal human performance, their body, their mind,

and even their spirit. So I attended med school at the University of Kansas, which is one of the few med schools that still emphasizes full-spectrum care. They emphasize exercise is medicine. They emphasize food is medicine, of which I was active in both of those interest groups. In residency, I was active in a lot of mindfulness curriculum. And then also things like Walk with a Doc where you emphasize preventative medicine. That's something that we've kind of got away from. And that niche led me to hormone health. It didn't really start as hormone health, but it's a very important component of health in general that many people don't emphasize. - Great, well, this idea of preventative medicine, I think, is starting to really take hold in the general population, especially given the events of the last few years, people realize that they are showing up to health challenges at a bunch of different levels. And with some people feeling very robust, other people feeling back on their heels. When someone comes to you as a patient, what are some of the first things that you want to know about them? I mean, obviously you want to know their blood pressure. You want to know something about their mental health and family history. But in terms of hormone health, what are the sorts of probe questions that you ask and what are you looking for? And I ask this because I'd like people to be able to ask some of these very same questions for themselves. - Yeah, so when you do a physical exam and a history, you have a lot of different parts. You have your history of present illness if they have a complaint, maybe the patient doesn't have a complaint. In that case, things like their social history and their family history are extremely important, because that gives you an insight into their genetics and an insight into their hormone health. So patients will tell me, oh, I'm doin' okay, but it helps to ask them, well, how are you now? Let's say the patient is 50. How are you now versus when you were 20, and what has changed? So I've gotten the question the lot, how do you get your doctor to order a better lab workup or to even include your basic hormones? And there's no magic answer to that, but what really helps is you tell them, my energy is not as good as it used to be. My focus is not as good as it used to be. My athletic performance is not as good as it used to be. So you don't have to have a pathology in order for a lab to be indicated. You just have that pertinent symptom. - I think that's going to be really helpful, because for many people, the idea of getting a blood test to look at their hormones just seems like such an enormous hurdle to get over, and many doctors won't prescribe them. And would you say that it's, using the approach you just described, that it's equally effective for men and women or do you find that, for one reason or another, that men and women have different challenges and advantages in trying to

access their deeper hormone data? - Yeah. It's slightly different. With women, there's a lot more objective data. So if they're having menstrual irregularities or if they're not having a period, if they're having too heavy of periods, then those are things that they talk about very frequently with their doctor. Men are more hesitant. So men really want to know what their testosterone is, but at the same time, they really don't want to tell their doctor how their libido is or how their energy is, because it's almost like they feel less masculine or they feel less like a guy when they say that even if they're just talking to their doctor about it. - Yeah, I think that that raises a really important point, which is that the whole discussion around hormone health is a bit of a barbed wire topic, because in many ways when we hear the word hormone, we think testosterone and estrogen, we think notions of masculinity and femininity. And of course testosterone and estrogen are present in all sexes, right? All chromosomal backgrounds. And just varying degrees in ratios. But it also raises all these issues about sexual health that it's kind of interesting, 'cause I'm surrounded by medical doctors in my lab at Stanford. And the more physicians that I surround myself with, the more open is the discussion around sexual health and reproductive health. But in the general population, I think some of these topics are a little bit taboo or against kind of barbed wire. And so I think that people are seeking a lot of this information on YouTube and through communities that may

00:14:17 The Six Pillars of Hormone Health Optimization

or may not be very educated about the actual biology. So along those lines, we could probably assume that hormones are changing across the lifespan, right? Certainly from childhood and puberty and onward. If you would, I'd love to just kind of take a snapshot of what you think everybody should be thinking about or doing to optimize their hormone health, male or female, in, let's say in their 20s. And then maybe we could migrate that to their 30s and 40s. But before that, could you just tell us what everyone should be doing for their hormone health from puberty onward? - Yeah, the law of diminishing returns applies. So doing a little amount of what I call lifestyle interventions over a long period of time is going to be far more helpful or efficacious than doing a lot and then doing nothing or doing a lot and then doing nothing. So I talk about the big six pillars. The two strongest ones are likely diet and exercise. For hormone health, specifically resistance training is particularly helpful. For diet, caloric restriction can be particularly helpful, especially with the epidemic of metabolic syndrome that is continuing to on go in this

country and in developed countries in general. So those are the two most powerful. So number one and number two are diet and exercise. For the last four, I have a little bit of alliteration. So there's stress and stress optimization. That has to do with cortisol, that has to do with your mental health, that has to do with societal health, and collective health of your family as well. When you're a member of a family or even a very close friend trying to achieve optimal health together is very important. It's the same thing with nicotine cessation. It's the same thing with hormone optimization. If you do it as a household unit, it's far more helpful. So after stress, you have sleep optimization. Sleep is extremely important, especially for mitochondrial health as well. And then you have sunlight, which encompasses anything that's outdoors. So you move more, you have cold exposure, you have heat exposure, that's sunlight. And then last one is spirit. So that's kind of the body, mind, and soul. If you have all the other five in, they're dialed in completely, but you don't have your spiritual health, whatever you believe, then that's going to profoundly impact your body and your mind as well. - Yeah, and we're definitely going to touch into this notion of spiritual health, because I think for some people that might draw connotations of certain things that may or may not be accurate, but I know a number of academic laboratories that are focused on this and a number of, not just functional medicine clinics, but research clinics and hospitals throughout the country that are achieving some really interesting data, not just in people that are quite sick, but in healthy people who are trying

00:17:14 Diet for Hormone Health, Blood Testing

to further optimize health. So we will definitely touch back to that. If you would be so kind as to maybe give us a little bit more detail about some of these other areas. So when people hear diet, I immediately think, okay, now we get into the combat around vegan, plant-based, carnivore, et cetera. But I think that my general view of this is that most people should probably be eating as few highly processed foods, highly palatable foods as possible, which doesn't mean eating foods that don't taste good, of course. But what other sorts of things do you recommend in the realm of diet? And then I also want to know about caloric restriction, because my understanding is that a caloric surplus can actually support certain hormones like testosterone. So how does one combine caloric restriction and still optimize hormones? But what would you say is a really terrific way to think about an approached diet? - Yeah. Diet should be an individualized approach. So if

you have a car, each car is made different and requires a different sort of fuel, whether it's a race car, whether it's a diesel truck, they have different fuels for different performance outcomes. So if you're trying to tow something or you're trying to go fast. So it's the same way with athletes. It's pretty well studied. The more intra-workout carbs ultra long distance athletes take, in general, they do better. I think they've studied this in cyclists quite often. It also depends on your genetics. So you can have a genetic polymorphism and you metabolize carbs and sugar better, even when they're unopposed by fiber. - How does one determine whether or not they have such a polymorphism? I mean, I'm an omnivore, so I do eat some high quality meats, not in huge quantities, but I also eat vegetables and starches, I feel fine. I've never done an elimination diet. I think I did a very low carb diet once and all it gave me was a lot of psoriasis and poor sleep, so I backed off. I probably didn't do it correctly, but I know a lot of people that do quite well on a very low carb or zero carb diet. - Yeah, particularly those who are at risk of cancer, because you have less glucose that can be easily uptaken into cells. And then also people with autoimmune diseases. - They tend to do well on auto- - On lower carb diets, yeah. But yeah, as far as the how do you know, basically you can use your biofeedback, how you're feeling, to guess what you tolerate well, or you can just get genetic testing, which can be fairly expensive, but most of all, it requires a physician or someone who knows how to interpret the test accurately. - And if someone had the means or would you say that getting regular blood testing is a good idea? And if so, what is regular blood testing? Is it every three months? Is it every six months? Of course the backdrop of life is changing too, stress levels, et cetera. - Yeah, every three to six months for preventative purposes, at times you need blood tests at faster frequencies than that. And then you should also get a blood test when you're fasting and when you're not fasting. So if you're looking for damage to the beach, you don't just look at low tide, you look at high tide and you see what's happening

00:20:21 Exercise for Hormone Health

at high tide as well. - I think that's a great way to put it. And in terms of general recommendations around exercise, I mean, I'm of the mind, based on the data that I've seen, that almost everybody should, or everybody should be getting 150 to 180 minutes minimum of Zone 2 cardio per week that kind of could continue while having a conversation, but if one were to exert any more effort, it would have a hard time getting

the words out. At least that, right? For cardiovascular health and general brain health and musculoskeletal health plus resistance exercise. Is that more or less the contour of what you recommend? - Yeah, that's more or less the contour. The more you're doing your Zone 2 cardiovascular exercise,

00:21:06 Caloric Restriction, Obesity & Testosterone

the slightly less important a long duration of caloric restriction is. - Interesting, and that brings us to caloric restriction. So it's very clear that caloric restriction can allow one to lose weight, right? This is the classic CICO, C-I-C-O, calories in calories out. We are not disputing calories in calories out. But somehow that always has to be stated 50 times in any forum because of whatever follows, people I think will anchor to, and assume that we don't mean that, but I know you and I both agree on calories in calories out as a fundamental law of thermodynamics. But it's clear to me that based on what I've read that when one is in a slight caloric surplus that hormones like testosterone can be optimized, but is that true for somebody who's showing up with excessive body fat? How does this all work? Because body fat is manufacturing enzymes that convert testosterone to estrogen. So in other words, how does someone know if they should use caloric restriction or avoid caloric restriction? - Yeah, here's how to parse that out. So before I delve into the details a bit more, I should say, as a board-certified obesity medicine physician, obviously the laws of thermodynamics apply. And then in addition to that, there is nothing special about intermittent fasting or caloric restriction or exercise when it pertains to losing body weight in general. When you do lose weight, about 33% of that is lean body mass. And about 10% of fat cells, adipose cells are actually lean body mass as well, because it has proteins and water and things like that in it too so the reason for exercise and the reason for caloric restriction in general, including intermittent fasting, is health reasons. That's how you increase your health span. It's not necessarily going to make the weight on a scale change, but that doesn't matter as much. It's been fairly well studied in both mice and humans. It's much easier to study in mice. So that's a precursor to our six types of people, the ones that care about mice studies and the ones that care about human studies. But if you correctly restrict mice by 40%, than they can have improved testosterone parameters, but only if they're obese to start. And it appears to be that same way in humans as well. So the easy way to think about it is if you're obese or you have metabolic syndrome, caloric restriction will improve your

testosterone. There has been a study and they talk about all these studies in a systematic review from the Mayo Clinic Proceedings in March of last year. And they note that there is a study in young, healthy men and they calorically restrict them and their testosterone does decrease. So if you're young and healthy and you don't have metabolic syndrome, then caloric restriction will likely decrease your testosterone.

00:23:55 Intermittent Fasting, Growth Hormone (GH), IGF-1

- That clarifies a lot for me. And I believe it will clarify a lot for other people as well. And I'm delighted that you pointed out this distinction about intermittent fasting not being the only way to achieve caloric restriction. There are a number of young, healthy, or older, healthy people I know who like using intermittent fasting, even if they're not trying to lose weight, for a couple of reasons. Some believe that it might extend lifespan. I think that's still a bit of an open question. It's a bit of a hard experiment to do, because the control group is, no one wants in the control group as I say. - It does in mice. - Right. Exactly. - Captive audience. - Exactly, and the other feature of it that's a little bit tricky is that many people like intermittent fasting because of the mental effects, the clarity of mind that they feel during fasting, the increased pleasure in eating when they finally do eat and here I'm referring to intermittent fasting of the sort where eating windows are anywhere from 8 to 12 hours a day. Not extended fasts of 24 hours or more. So the question therefore is, for the healthy lean enough person, right? Non-obese person, is intermittent fasting a bad idea in terms of hormone health? Is oscillating between this period of kind of feast and famine within a 24 hours a problem if one is getting sufficient calories to maintain weight? - Yeah, so if they're in a caloric maintenance, then it's not going to be, it's not going to be deleterious. It's not going to be bad for their hormone health. There's a couple different hormones that we can talk about. We can talk out testosterone. We can talk about DHEA, which usually go hand in hand. And then we can also talk about growth hormone, which is not a steroid hormone, but it's a peptide hormone. So it's a chain of proteins, amino acids that are put together instead of a sterile, think of sterile hormones as coming from cholesterol. So intermittent fasting, you do get a little spike in growth hormone after you eat, but you also get a huge spike in growth hormone, a more significant, less negligible spike overnight. And that is improved if you are intermittent fasting. So it's probably going to help your growth hormone and subsequently IGF-1 levels, which will help more in the older age groups than younger age groups. - And I like

to eat dinner. So for me, that means sometime around six or seven o'clock, sometimes eight o'clock. I confess last night, 'cause I was working late, I ate pretty big, it was basically my only meal of the day, at 10 o'clock. That's a rare thing for me. Can I still achieve a high degree of growth hormone output if, let's say I avoid food in the two to three hours before going to sleep? Or does one have to be very deep into a fast in order to achieve the increase in growth hormone? - There's still pretty good growth hormone output even if you eat two or three hours before you sleep. It's just the law of diminishing returns, the longer you go, you get slightly more and slightly more. - Right, and I know a number of people think of growth hormone in the context of the exogenous growth hormone and the fact that that can, in some cases, be associated with cancers. I've been asked many times before, can the increase in growth hormone from things like saunas or intermittent fasting cause levels of growth hormone that are so high that they cause cancers. My impulse is to say, no, it seems like it's not like to happen, but I should probably verify that statement with you. - Yeah, so quite unlikely. I think about growth hormone, and especially IGF-1. And there's actually an IGF-1 and IGF-2. But I think about it in terms of endocrine IGF-1, mostly IGF-1 that's synthesized in the liver and released in the liver versus IGF-1 that's released classically. An example of this would be your IGF-1 levels increase after resistance training or exercise. And that's more of like paracrine or autocrine, and they have more local action. So that IGF-1, it's pretty well studied that if you just give people IGF-1, it's not going to, at physiologic levels, it's not going to improve their body composition. However, that IGF-1 that's autocrine and paracrine just working in those local tissues and muscles is likely part of the reason why you get an improved body composition response after exercise. - I see, and just to clarify for me and for others, what can we say are the major functions of IGF-1 and IGF-2 that are distinct from just growth hormone? Are they just kind of the active hormone growth hormone? The kind of the pickaxe end of the assembly line? - Yeah. So they have a much longer duration of action. I believe the half-life of IGF-1 is several days almost a week, whereas growth hormone has an extremely fast half-life of only hours. So growth hormone acts significantly on the liver to produce IGF-1. So it's around

00:29:08 Sleep Quality & Hormones

in the serum in the blood long enough to where it's producing an effect pretty much all the time. - Very interesting. - Yep. - Well, and then your other pillars, stress, we've talked

a lot about stress on this podcast before and tools for managing stress. Sleep obviously is a big one. I think, if nothing else, I will either put people to sleep with my podcast. Certainly not one, but my solo episodes or hopefully convince people that sleep is the foundation of mental and physical health and performance. Are there any aspects of hormone optimization that can improve sleep? I know sleep can improve hormone optimization, but are there any aspects of hormonal optimization that can improve sleep? And for people that are suffering from this common syndrome of going to sleep and then waking up at 03:00 or 04:00 in the morning, we know that can be associated with depression, but are there any hormonal indications that might lead to that kind of situation? - Yeah, there's three big ones. The first one is not super common, but it's a very direct correlation. If you have a growth hormone deficiency, a true deficiency, whether you're an adult or a child, then your sleep is likely going to be affected. And let's say you're a child with growth hormone deficiency, once that is replaced with therapy, your sleep is going to get significantly better. The second one that's a very common scenario is if you're having what's called vasomotor symptoms of menopause or vasomotor symptoms of andropause which are also applicable. And that's where your progestogenic activity, so your main progestogens are progesterone and then and pregnenolone and then 5-alpha, 3-alpha-progesterone, which is- - Where are those manufactured in the body? - So they're manufactured in a few places. In men, they're manufactured some in the testes in the Leydig cells. In women, they're manufactured in the ovaries until menopause. And then they're also manufactured in the adrenal gland. So if you're pre-adrenopausal where your adrenal glands are still working fairly well, usually still have a decent amount of progesterone around, and this can be measured too. So after menopause, women make progesterone from their ovaries, or sorry, from their adrenal glands. If that progesterone crosses the blood-brain barrier, especially if it's 5-alpha and 3-alpha reduced, so it's modified a little bit, then it is both a GABA agonist, which helps sleep just like GABA does, gamma-amino butyric acid, the main inhibitory neurotransmitter of which lots of things work on, alcohol works on GABA as well. Gabapentin also works on GABA. Migraine medicines, many of them work on GABA. Benzodiazepines, and also non-benzos. So an example of a benzo would be Xanax. An example of a non benzo would be Ambien. So those all work on GABA. So GABA is also helped by the progestogenic activity as well. That's why a lot of women in menopause feel like their sleep is much worse is because they have lower activity of those progestogens. - And for men in so-called andropause, low testosterone, is that also one

of the causes of poor sleep. - Low testosterone can lead to poor sleep, but my third scenario is actually, if a man begins TRT, then they develop poor sleep because of sleep apnea. It drastically raises the risk that somebody is going to have sleep apnea. And then a lot of people, especially when they first started in the first month or two, it puts them into this hypersympathetic state, because they have overactive androgen receptors, especially after a long time of being hypogonadal. Then they have a physiologic dose of TRT and that causes the sleep issue itself. - Interesting, I have a lot of questions about TRT, testosterone replacement therapy. I should just mention that when you say it increases sympathetic activity, you don't mean that taking testosterone increases sympathy for others. It may in fact do the opposite. Although it's very clear from my discussions with my colleagues in the endocrinology side and also with the great Dr. Robert Sapolsky that increasing testosterone merely exacerbates existing features of people. So the jerks become bigger jerks, kind people become even more kind in general, but I want to get into TRT in depth, but it's very interesting to me to hear that testosterone replacement therapy increases the risk of sleep apnea. And I want to make sure that I ask that is that also the case in people that are using TRT who are not hypogonadal? Because in the classic situation, if somebody isn't making enough testosterone, they're below 300 nanograms per deciliter on the chart, they go in and take TRT. But many people nowadays, let's be honest, are taking doses of testosterone even though they are in the sort of standard range, because the range is so large because of other symptomology, is that right? - Yeah, I do love the analogy that Dr. Sapolsky had about monks taking testosterone and making them more and more generous. So that does appear to be what testosterone usually does, is it exacerbates, if you will, what you're previously like. So it's not going to change you as a person. But if you're eugonadal before you start testosterone- - Meaning? - Meaning you have normal testosterone, and then you start TRT or self-administered TRT, steroids, however you want to look at it, then your risk of sleep apnea still goes up in a dose-dependent fashion. So the higher the dose, the more risky. With the sympathetic and the parasympathetic nervous system, the sympathetic is the fight or flight nervous system, the parasympathetic is the rest and digest.

00:35:03 Testosterone in Women

So if you have too much fight or flight, and stress can cause that too, then you're not

going to rest as well at night. - I want to touch on testosterone in women because there is testosterone in women. I'd like to know where that testosterone comes from, which tissues, I'd like to know whether or not testosterone replacement therapy make sense in women. I'm hearing more and more about women using testosterone. And I'd like to know whether or not knowing a woman's testos, for her to know her testosterone is of equal, less than or more value than knowing, for instance, progesterone and estrogen levels? Because I think there are a lot of misconceptions about the roles of testosterone in women. - For health optimization, testosterone is just as important to know. For pathology prevention, for example, breast cancer, osteoporosis, estrogen, and progesterone are more important to know. So when you're thinking about women, women think that they have such a tiny amount of testosterone, because you test it, most people test a free testosterone, so a testosterone that's unbound, which is by far the smallest proportion of testosterone. Any androgen is bound by lots of different steroid-binding proteins. But the ones that are most pertinent are called SHBG, or sex hormone-binding globulin. And that binds the androgenic steroid, for example, DHT or dihydrotestosterone. It's associated with prostate enlargement, it's associated with male pattern baldness. It binds that the most strongly, and then it binds testosterone next most strongly, and then it binds things like androstenedione or DHEA, dehydroepiandrosterone. And then it binds the estrogens, the weakest, like estradiol. So if you look at the total amount of testosterone, women actually have, almost all women, not all women, but almost all of them have significantly more testosterone than estradiol, but it's because it's in different measurements. So estradiol, a lot of time is picograms per mil as opposed to nanograms per deciliter. So women have more testosterone than estrogen and significantly more DHEA than either. - Interesting. Do women make dihydrotestosterone? - Yeah. - And where does this testosterone come from? Because they don't have testes. - Yeah, so most testosterone in women that are premenopausal can come from theca cells, T-H-E-C-A. So theca cells are cells in the ovaries that can produce testosterone. And a lot of people have actually heard about hyperthecosis, not the term itself. But a lot of Olympians that are, their chromosomes are XY, they're females, and they're not taking any- - Wait, they're XY, but they're females? - Or sorry, they're XX. - Oh, okay. - Yeah. Thank you. So they're XX, they're not XY, and they have never transitioned or been on any sort of hormone replacement or testosterone, but they naturally produce a huge amount of testosterone, as much as many men. And some of these women, I believe they were from Botswana, were banned from competing in the

Olympics in certain distances. I believe they were banned from the 400 meter and 800 meter, because their natural testosterone was deemed to be too high. - So they mistakenly thought that they were using steroids? - They actually knew they were not using steroids. They knew it was their theca cells were just genetically gifted, I suppose. And they still made them change distances. - [Andrew] Wow. - So one or two of these athletes changed to, I believe it was the 3K or the 5K, and they still did quite well, but it was not their best event. - Interesting, yeah, that's turning out to be a very interesting and controversial area of this notion of hormone therapies and natural variation in hormones on different chromosomal backgrounds. Fascinating, we should probably do

00:38:55 Dihydrotestosterone (DHT), Hair Loss

a whole episode about that, 'cause it's very much of the times. So men and women both make DHT. I'd like to ask about DHT in men. So often we hear about testosterone in men and free testosterone being the unbound form of course. But dihydrotestosterone, where does it come from in men? What is the cascade of events that takes testosterone to dihydrotestosterone and what are some of the quote/unquote positive and negative effects of, here I'm only referring to endogenous dihydrotestosterone. And in fact, I'll make it very clear whether or not I'm talking about taking something or one's own natural production. Here we're just, I think up until now we've just been talking about natural production. So tell us about DHT in men, such a powerful hormone during development obviously. But what is it doing? - DHT is a very androgenic hormone. So whether you're talking about DHEA, which is a weak androgen, or testosterone, which is a relatively strong androgen, or DHT, which is a very strong androgen, they bind to the androgen receptor in both men and in women. So the effect of all three of those is mediated by the androgen receptor. There's a couple different beta-estradiol receptors and alpha-estradiol receptors, but there's only one androgen receptor. Intriguingly, it is on the X chromosome, so men get their androgen receptor gene from their mother. Women get one androgen receptor gene from their father, one from their mother. Often the one that is more sensitive to androgens and people with PCOS, that's the one that's active. The other one is methylated and inactive. - Can I just pause you one second? Sorry to interrupt, but I have to ask this question before I forget. And I know a number of people are probably wondering, I've heard that whether or not one develops male pattern baldness, whether or not a male develops male pattern baldness, just to be very precise,

you could get some information about that by looking at your mother's father, and that would, in keeping with what you just described, that the X chromosome, which of course is handed off through the mother, is carrying the genes that encode for the number and distribution of these androgen receptors that DHT will bind to, 'cause of course, I think as you'll probably tell us, that DHT is responsible for male pattern bald and beard growth, is that right? Should I look at my grandfather on my mother's side to determine what I'm likely to look like in terms of my DHT-ness, is that a word? - Yeah, it's the best guess that you could make purely from phenotypes. Now you can measure your genotype and get a better idea of that. Assuming that it's true male pattern baldness, it's related to the gene transcription of the androgen receptor. So I like to think of it as how much of this androgen receptor gene is activated by any androgen? So if you have an extremely sensitive gene, which usually means you have very few CAG repeats, which is basically just a certain, CAG encodes for a certain amino acid, and if you have very few of the repeats, then your androgen receptor gene works better. Think of it as a corollary to Huntington's disease where if you have very few of, called trinucleotide repeats, then it's not as severe as a disease, but after you get more and more CAG repeats, which by the way are, in the population you're getting more and more CAG repeats, so it's a natural selection of process that has been ongoing for a variety of number of reasons. But anyway if you have more repeats, then that gene activates in the cytoplasm and moves to the nucleus and causes gene transcription more often and hair loss more often. - So does that mean that we're seeing more hair loss now due to elevated levels of DHT than we were 50 years ago? - Probably not. The hair loss 50 years ago, well, not 50 years ago, but 500 years ago, was probably more significant, because on average, 500 years ago, people were more sensitive to androgens. So there's a syndrome called androgen insensitivity syndrome, AIS and that syndrome was related to when men, who have the copy from their mother who is a carrier, their AR gene, or androgen receptor gene, is completely insensitive. So think of it, it's not related to the CAG repeats, but think of that receptor as just not working at all. So there's a continuum, so everybody's receptor works a little bit better or a little bit worse. And the better your receptor works,

00:43:46 DHT in Men and Women, Turmeric/Curcumin, Creatine

the more likely you are to have male pattern baldness. - To zoom out from this, but still keeping an eye on DHT, what do you like to see all women in all men do to optimize

DHT? And here I'm talking about regardless of age. So we're still in this from puberty onward phase. We haven't yet micro-dissected out decade by decade, which we will do, but what do you like to see people do to keep DHT in check? But before you tell us that, could you tell us what positive things DHT does when it's in the proper range? - Yeah, so DHT helps a lot for, it's the same reason why testosterone helps, it activates the androgen receptor gene. It helps effort feel good. So it can be motivating. So that's how it's active in the CNS. It also is active in cardiovascular tissue. So if you look at someone that has heart failure or if someone has cardiac hypertrophy, the level of DHT can matter because it's also binding to the androgen receptor in the myocardium or in the heart itself. So you think of the classic bodybuilder heart. It's an easy example to make. They have very thickened muscle. Their muscle is very strong, because they're pumping blood often with high blood pressure and that DHT and the testosterone and any DHT derivatives like Masteron or oxandrolone, preambles and also bind to the heart, and they cause even more hypertrophy or enlargement of that muscle tissue. So then let's say the person stops and they're recovering, and they're trying to have cardiac remodeling, which is where you take a very thick heart, and cardiac remodeling's important in a lot of different cardiac pathologies, but if you give them finasteride or dutasteride, which inhibit the enzyme that converts testosterone to DHT, so making less activity at the androgen receptor gene, they have cardiac remodeling, and their heart health improves.

- I see, so for the non-body builder, the typical woman or man, younger or older, what sorts of things support DHT, and thereby heart health? Presumably DHT she is involved in some of the other things that testosterone is famous for in both men and women. Things like libido, as you mentioned, making effort feel good. So motivation, drive and vitality is, I guess, could be the general phrase. What sorts of things support DHT? What sorts of things create problems for DHT? - There's lots of dietary changes and supplementation that you're probably doing right now that's affecting your DHT. - You mean me personally? - Well, everybody. All of the listeners. Because let's say you have a diet high in plant polyphenols, many of those inhibit the enzyme that converts testosterone to DHT. - Could you give us an example of one of those, either in supplementation form, or in food form? - Curcumins, certain curcuminoids, depending on the structure, will inhibit the enzyme called 5-alpha-reductase that converts testosterone to DHT. - Turmeric? - Yeah. Turmeric. Black pepper extract. So it's used often to increase bioavailability. It's also called BioPerine. It's also a 5-alpha-reductase inhibitor. And on top of that, people have different genetics too. So some people, they're 5-alpha-

reductase enzymes, there's three of them. They're on chromosome two, three, and four, I believe, but some of them are active in the prostate, some of them are active in the brain. And so it depends on which tissue, they're tissue-specific enzymes that depend on how much DHT you convert. - Do you recommend that people avoid curcumin and turmeric for that reason? And is there any specific recommendations for men versus women. - If a man or a woman, by the way, in women, a lot of times, if you just ask your doctor for a DHT check, it's the same units as in men, so it's essentially undetectable. So you have to, especially if they're on oral contraceptives, which is a front topic, their DHT is very likely undetectable, especially if it's free DHT. You can measure both a DHT and a free DHT. But if someone's DHT is already low, or if they have somewhat insensitive androgen receptor via genetics or via lifestyle, then I recommend they avoid bioavailable curcuminoids like bioavailable turmeric, black pepper extract, and they might be a good candidate for creatine. Creatine, like creatine monohydrate, can significantly increase the conversion of testosterone to DHT. - Interesting, there's also a lot of really interesting data coming out now about the role of creatine as a brain fuel, and maybe even as a cognitive enhancer over time. The data is still ongoing, but some of the studies in humans are pretty impressive, at least to me. I'm glad you mentioned this thing about curcumin and black pepper. I wish we had had this conversation six years ago, because I had the experience of jumping on the bandwagon of the excitement around turmeric, and I took a turmeric supplement. It was a couple capsules of what I thought to be, and I think was high quality turmeric, and I've never felt as poor as I did in the subsequent few days, flat line of, let's just say everything that one would want to have in life, energy, vitality, just it was a cliff. And a friend somehow knew that curcumin could inhibit 5-alpha reductase. It converts to testosterone to DHT, as you pointed out. I stopped taking it, it was the only new addition to my diet and supplementation, and things bounced back within about three, four days. But it was remarkable. I mean, I felt like garbage. And it was actually kind of frightening to experience the sharpness of that cliff. But I know that some people like turmeric for its antiinflammatory properties, et cetera. Sounds like people either need to experiment, and if they do, obviously to approach that with caution. Anytime you add or remove something, you need to talk to your doctor. You're a doctor, and I'm guessing that if one were to experiment, would you say that most of these effects of things like curcumin are reversible as they were in me? Or is there any potential of permanent damage if people have been taking them for a long time?

00:50:10 5-Alpha Reductase, Finasteride, Saw Palmetto

- The effects are nearly always reversible when you're talking about 5-alpha reductase inhibition, so what turmeric does, but stronger. The most common story that we hear is regarding a supplement known as saw palmetto, which a lot of older men take for their prostate health or finasteride, which you can take for your prostate, or your heart, or your hair, or dutasteride. So if you're having side effects on these, then it's probably because of a couple different reasons. One can be your ratio of androgens to estrogens is off, and that needs addressed. Another one can be it's inhibiting the conversion of your progesterone to that other type of progesterone, the 5-alpha, 3-alpha, that we talked about earlier that's helping with your sleep and your brain, and your calmness. And that's definitely an effect. Another one is depending on the type of supplement or med, they inhibit different isoenzymes of that 5-alpha reductase. So if they're just inhibiting one and two, then that's going to be a different effect than if they're inhibiting two and three. So finasteride does two and three, saw palmetto does one and two, and then dutasteride does all three. The third one is active in the brain and dutasteride inhibits that third one a little bit weaker in vivo, but strongly in vitro. So it's really hard to parse out. You can use biofeedback and experimentation. I do think with supplements it's safe to experiment. The time that it takes to set in is usually about three months. So the risk of, and this is anecdotally, there's been lots of research published about if post-finasteride syndrome is real or fake. And it is real, but it's one of those things that's a combination of organic and inorganic disease. Almost kind of like fibromyalgia where it's definitely real, And there's lots of things that you can do to help with it, but it's very unlikely to occur if you stop taking your supplement or medication after you have side effects. - Interesting, well, I certainly feel better when I'm taking five grams of creatine monohydrate per day. I know most people take it for muscle growth and tissue repair and things of that sort, mainly I think brings water into the muscle tissue, et cetera, but I take it for the brain effects, and also because I like to think that it gives me

00:52:30 Hair loss, DHT, Creatine Monohydrate

a little bit of a DHT bump that I can actually see in my blood charts when I've done them. I know many people want to avoid the hair loss that can sometimes be associated with DHT levels going too high. And so I've been asked many times, does creatine

monohydrate cause hair loss? It would make sense that if creatine increases DHT and DHT binding to the androgen receptor on the scalp can induce hair loss, that that would be the case. Is that that true or are people just overly concerned about something that's trivial or non-existent? - Each male and fem, so yes, it can potentially add it. I don't like to say it causes it, but it can be a little bit more fuel to the fire. So just like everybody has a different sensitivity of their androgen receptor, they have a different amount of gene transcription that is going to cause death of the follicle. That's an arbitrary threshold. So you don't really know until you start losing hair. - And if somebody takes a little bit of creatine to increase their DHT, maybe for the cognitive enhancing effects, or for whatever reason, and they notice a bit more hair falling out in the sink, and they stop taking it, you said death of the follicle, which sounds very dramatic. Are those little stem cell niches that reside in the follicle, which hairs grow from, are those then abolished, like there's no going back, or can one rescue at the hair? - It takes months, if they're still there, the hair will come back. So the loss of the hair itself is a normal part of the hair cycle. So you have your antigen phase, your catagen phase, your telogen phase, and then your hair loss, and then a new follow. - Of the stem cell niche in the hair follicle. - Yeah. Yeah. Think of it like sharks have teeth. So shark loses a tooth, and they have a new one that comes through. Or losing your baby tooth, and you have a new one, but your hair just always keeps coming through. So it's natural for it to die and lose. That's that's why when you start 5-alpha reductase inhibitors, often you have a big shed. So what happens during that big shed is all of these cells that are unhealthy, they immediately jettison that hair and then they start making a much healthier new follicle. So a lot of the hairs that are at the end of their telogen phase, then they have what's called telogen effluvium, which also happens after pregnancy, also happens in thyroid pathologies. So you shed it, a new one in place, and you think that you're having a horrible hair loss caused by your finasteride or whatever you're doing. And minoxidil does this too, but you're really just having a new, healthier follicle. If you go a really long time, if you go a year,

00:55:07 Hair Regrowth, Male Pattern Baldness

then those hairs might come back, and they might not. - So for simplicity's sake, if somebody is concerned about, or is experiencing hair loss, male or female, what are their options of ways to offset that hair loss that are not going to negatively impact other

tissues sensitive to DHT? And what I'm basically saying here is, I could imagine taking a DHT inhibitor, a pill of some sort, or an injection of some sort, and offsetting hair loss, maybe even stimulate more hair growth. It's clear that I'm not doing that, but I know people that do, but then experience some of the other negative effects of blunting DHT, reduced affect, reduced libido, reduced drive, disruptions in prostate function, or even sexual function generally. So what can people do if they want to maintain or grow back hair, but they don't want all those other effects? What should they avoid and what should they perhaps consider talking to their doctor about? - Yeah, there's a whole host of options. I try to separate alopecia or hair loss into two different categories, male pattern baldness, or androgenic alopecia, also known as androgenetic alopecia, versus other types of alopecia, usually telogen effluvium. And if it's androgenetic alopecia or male pattern baldness, even if they're female, perhaps say PCOS, something like that, then you want some sort of strategy to decrease the activity of that androgen receptor. - So women can get male pattern baldness? - [Kyle] Absolutely. - Okay, I'm going to have to wrap my head around that one, but okay. - So there's a lot of different things that you can do that are topical. The most promising is called dutasteride mesotherapy. Essentially what it is is it's very localized injections in areas that are prone to male pattern baldness, whether they're female or male. And it acts locally only. And you repeat these injections from time to time, it decreases the conversion of testosterone to DHT just in the scalp. - So that can avoid prostate effects. And what are some of the negative effects of blocking DHT in females, in the periphery? Meaning not on the scalp or in the brain? Where is DHT doing its stuff? - Yeah, so it's both DHT, and then also that 5-alpha, 3-alpha progesterone, which is called THP or dihydroprogesterone or tetrahydro, trihydroprogesterone. So they're active in the central nervous system, but it's also just active, again, binding to the androgen receptor in a female as well, causing them to have that effort feel good, motivation. A lot of women that are sensitive to DHT, 'cause women can be sensitive to DHT as well, feel very different when they start an oral contraceptive, not because it alters their DHT to a huge amount. It does to some degree. Because the negative feedback inhibition in the pituitary and less produced in the ovaries, but it increases SHBG really high.

00:58:12 Polycystic Ovary Syndrome (PCOS), Inositol, DIM

So because their SHBGs are significantly higher, their free DHT is way lower. - I see,

how does a woman know if she has PCOS, polycystic ovarian syndrome? What are the issues with polycystic ovarian syndrome? What can be done about PCOS? I confess, I was naive to PCOS. That wasn't supposed to rhyme, but since it does, I do confess I was completely naive to it. And I started getting a lot of questions about it in various forums. And I think that's actually the reason why I initially approached you. I know you have treated a lot of PCOS. What age women should be about PCOS, what's PCOS? Teach us about PCOS, please. - Yeah, so PCOS is polycystic ovarian syndrome. And this is one of those conditions which is underdiagnosed. So its prevalence is much higher than we think it is. There's been a lot of studies. And some studies say a prevalence of 10%, some say 20%. It's not completely clinically penetrant. So most people don't know they have PCOS until they have infertility or subfertility. - And is PCOS happening at this frequency in 20-year old women, in 30-year old women, in 40 and onward? - Most women find out they have PCOS in their 30s, especially, it's on a spectrum or a continuum, like a lot of things, where you can have a weaker version, or a very severe version. - What are the symptoms? - There's criteria called the Rotterdam criteria. And in the Rotterdam criteria, there's a couple different ways that you can diagnose it. You're looking for androgen excess, insulin resistance, and you could also look for polycystic ovaries. You don't actually have to have polycystic ovaries or to get an ultrasound of your ovaries to be diagnosed. If you have androgen excess, for example, androgenic acne, or hormonal acne. If you have hair growth, like a hair growth on the chin, it's called hirsutism. Or if you have, like deepening of the voice, any symptom of too much. And male pattern baldness, if you're female, that's a symptom of PCOS as well. Then you can also have insulin resistance. So this is obesity. It's pre-diabetes, a high fasting insulin, a HOMA-IR over two, a fasting insulin of over six. So if you have significant insulin resistance and also androgen dominance, that's a sign of it. Androgen dominance often leads to what's called oligomenorrhea. So if you're having more than 35-day intervals in between a period or if you have less than nine per year, then that can be a sign that you have oligo, which means too little, menorrhea which means menses. So that's a very common sign of PCOS. If you have infertility, so if you're under the age of 35 and you've been trying for more than a year, or if you're over the age of 35, and you've been trying for more than six months, then that can also be, it's a very common presenting complaint when somebody presents with PCOS. - And assuming that a woman is doing all these other things is paying attention to the six pillars that you talked about earlier, diet, exercise, caloric restriction, in some cases, right? Not everyone

needs to be caloric restricted. Stress, sleep, and sunlight, spirit. Assuming that they're doing all those things, what other things in the realm of diet or supplementation can help them avoid PCOS if they have subclinical PCOS or they have not developed it, but don't want to develop it? 'Cause it doesn't sound like a good thing. - Yeah, so depending on where they are, if they're very strong on the insulin resistance spectrum, then optimizing their body composition, decreasing their body fat, and treating that metabolic syndrome can help. So a lot of people ask, well, does everybody that's on, like does everybody need to be on metformin that has PCOS? Not necessarily, but metformin is one of the tools that can help with insulin sensitization. Other tools that can help are inositol, so myo-inositol is an insulin sensitizer. Its cousin D-chiro-inositol is a weak antiandrogen. A lot of types of inositol have both of those in it. So depending on if you're a female or a male and you're on inositol, the type of inositol does matter. - Yeah, this is a very important point. Just today I said I'm trying this new supplement inositol for its role in perhaps enhancing sleep even further. My sleep's generally pretty good. Lately it's been a little bit off for a number of reasons. So I took it for the first time last night, and I said, I thought it helped, and just subjectively, and you said, "What kind of inositol is it, because inositol is a very potent androgen inhibitor. It turns out I was taking myo-inositol, which is not an androgen inhibitor. The other type that you mentioned, which is an androgen inhibitor is? - D-chiro-inositol. It's usually in a ratio of 1 to 25 or 1 to 40, in a much lower amount compared to myo-inositol. - In a supplement or in the body? - In a supplement to help induce ovulation. - But for women who have PCOS who might want to try and reduce androgen, then they would perhaps want to take a form of inositol that reduce the androgen receptor activity. Correct? - Yeah. They want both. So if you're a woman and you've ever talked to your doctor about getting on the oral contraceptive or spironolactone, which is also an anti-androgen, but it happens to be a potassium-sparing diuretic blood pressure medicine as well. D-chiro-inositol might be a better option. DIM or diindolylmethane is another kind

01:04:00 Oral Contraception, Perceived Attractiveness, Fertility

of weak antiestrogen, antiandrogen that a lot of women should consider as well. - You mentioned oral contraception. I've done a few posts on these. Let's just call them, they really are perceptual effects whereby it's been demonstrated in humans several times now, and what appeared to me to be very solid studies where women that take oral

contraceptives, there is both a shift in their perception of men, 'cause these studies only looked at heterosexual, the sort of arrangements here, where women who are on oral contraception, because it blunts some of the peaks and valleys of hormone output, no longer experience the same peak and valleys in their assessment of other men's attractiveness. So it sort of flattens their perception, so to speak. They still find certain men attractive and certain men unattractive, but the degree of difference is kind of mellowed out. And likewise, men, these data say that men perceiving women's attractiveness, they still see women on oral contraceptives as attractive, but a woman taking oral contraception eliminates this kind of peak in her attractiveness that men would otherwise perceive. In other words, oral contraceptives are changing the way that we perceive each other, at least in terms of these male/female experiments. What is going on with that? Is that because oral contraceptives, blunt the increase in testosterone that occurs just before ovulation, or is it because of a complex cascade? What is going on? I find this fascinating. - Yeah, so there's differences in how your, and I wouldn't use the word change necessarily, but alter the severity or alter the peak, as you said. So just like TRT is not going to change you as a person, an oral contraceptive will not change you as a person. It will just change your day to day peaks and troughs in libido and attractiveness. So one of the main effects of oral contraceptives, almost all of them have a synthetic estrogen and a synthetic progestogen in them. One common type of synthetic estrogen is ethanol estradiol. There is another new synthetic estrogen that's out there as well, but that anecdotally, that seems to have even more side effects. So this ethanol estradiol is 100 times more potent than endogenous or bioidentical estradiol in the liver. So it binds to the estrogen receptor in the liver, and it's going to increase sex hormone-binding globulin, which secondarily, as you mentioned, decreases your free testosterone, and especially your free DHT. So that little testosterone hump that you get when you're a female that's ovulating, that's really flatlined and it's a pretty insignificant difference. It's not negligible, but it's a little bit of a hump and you have significantly less of that when you're on a oral contraceptive. - And does that blunt the associated increase in libido that normally would occur from that increase in androgen? - Yes. - Yeah. Interesting. And what about other forms of contraception, right? 'Cause there are, there's copper IUD, there's various implants. There's rings, there's a huge number of different forms of these. So what we're talking about is, as I understand, it is only the effect of oral contraception that impacts hormone output. Is that correct? - Yeah, there's a lot of other effects as well. For example, your choice of synthetic progestin will alter

how high your platelets and SHBG go. It appears to be the higher your platelets and the higher your SHBG, the your higher risk of a blood clot. So a lot of women know that if they're on a oral contraceptive and they're already predisposed to a blood clot or a venous thromboembolism, in their vein they have a blood clot in either their leg, or their lung, then it can increase that chance. So you can choose a synthetic progestin that is not going to have as high of a response, but there's various pros and cons. Some synthetic progestins are weak anti-androgens as well. For example, there's one known as Slynd, which is made from spironolactone. So some women are on spironolactone and that as well, which is made from spironolactone, which probably isn't particularly necessary unless they need it for a diuretic or a hypertensive effect. - I see, I'm just going to intentionally interrupt, and I apologize, but specifically because I wanted to ask about, there is this notion that oral contraception taken over long periods of time can disrupt fertility in ways that are independent of just the age-related decrease in fertility. Is that true? - It depends on what you mean by a long time. 6 to 12 months, it's possible. Past that, it seems very unlikely. However, the persistently elevated SHBG can be present for quite some time. - Wait, so if a woman takes oral contraception for 6 to 12 months and then stops, will she essentially be aware she would've been anyway in terms of her fertility at that age? Or are you saying that it can cause permanent damage? - Her fertility would be equitable as if she had never taken it if she's certainly 12 months, but probably six months off. - And what if she... I know of women that have taken an oral contraception for many years are, in addition to the age-related decline in fertility that occurs that's inevitable, of course the slope is going to be different depending on the individual, but are they quickening the transition to infertility? - Probably not, you could make a case that because they've been on a oral contraceptive, they may have been slightly more predisposed to insulin resistance and/or lower lean body mass. But that's probably going to be a negligible difference compared to their resistance training and also their caloric restriction or caloric maintenance so- - And of course there are also effects of having children. - Yeah. - Yeah. Right, I mean on all these parameters, right? 'Cause it's a major lifestyle shift, right?

01:10:31 Testosterone & Marijuana or Alcohol

That obviously people contend with and have since the beginning of human time anyway. I want to ask some questions about male hormone therapy and male hormones

generally. But before I do that, I have a couple of burning questions that I get very often that I'm just going to insert now. Marijuana, I've heard that it can decrease testosterone in men and women. I've heard that it can increase testosterone. Alcohol, I think there's general consensus that high alcohol intake, high barbiturate intake does in fact reduce testosterone. What about modest increase of alcohol? I'm not a drinker, so I'm not asking these questions for me. I don't smoke pot, and whatever. I just never really liked marijuana or alcohol. They're not my thing. But many people want to know the answers to these. And the data that I've seen are very confused and conflicting, so what about marijuana, does it reduce testosterone to a significant degree or not? - Cannabinoids itself, whether it's THC or CBD, are not going to reduce testosterone by themselves. If it's smoked marijuana, then it's very likely to increase your aromatase, which increases your estrogen. And that's going to, it's aromatizing from testosterone. So that is going to decrease testosterone. When you have an increased estrogen, like estradiol, that's going to work on your pituitary to make less hormones that cause release of testosterone. So you're going to have less LH and less FSH. So it's almost kind of like opiates are well known to, opiate agonists, they're going to decrease LH and FSH and subsequently testosterone. Smoked marijuana will as well. As far as alcohol, high alcohol will decrease testosterone as will any very potent GABA agonist, whether it's a barbiturate, or benzodiazepine, or a non-benzo or alcohol, they're definitely going to. Moderate alcohol, I guess it depends on what your definition of that is. The American Heart - I guess I'm thinking like, some people I know that don't seem to be alcoholics, at least by my assessment, will have a glass or two of wine four nights a week, which to me seems like a tremendous amount, only because I don't like alcohol. I don't have a problem with other people liking alcohol, but I think for many people that would be considered low or moderate intake. - Yeah, I would consider that low intake. The American Heart Association for men recommends between one and two drinks a day on average. - They recommend it? - So around, yeah. So around one per week. - Wait, so I'm making my heart less healthy by not drinking alcohol. - Yeah, they recommend a very low amount of alcohol intake for men. For women, they recommend zero to one. So that's kind of hard to interpret, zero to one. But the protective effect of alcohol, especially if it's a red wine with polyphenols in it, outweighs the deleterious effect. - Interesting, 'cause I've seen some studies that point to the idea that even low intake of alcohol over a prolonged period of time might actually decrease brain volume or at least volume of particular brain areas. But of course we don't know the consequence of decreasing the

volume of a given brain area either. I mean, one can imagine it's decreasing the size of one's amygdala and making them less stressed. Although there's no evidence to support that. I've been told that I need to drink many, many times, but I always reply that I don't need to drink anything in order to speak my mind. So again, individual differences. Very interesting, so it sounds like smoked marijuana may in fact reduce testosterone or at least increase the conversion of testosterone to estrogen, correct? - Yeah. - Okay. - And with alcohol and GABA agonists, it's important to remember that it shouldn't be daily. So one drink of alcohol a day is actually very mildly immunosuppressive. So it's better to have two drinks of alcohol one day of the week and then two more drinks

01:14:27 Sleep Supplement Frequency

of alcohol another day of the week and then no alcohol the rest of the time. The same could be said even for supplements that have GABA in them. A lot of sleep supplements have gamma-aminobutyric acid, which is GABA, so- - Yeah, I occasionally take, oh, sorry to interrupt. I occasionally take 100 to 200 milligrams of GABA in order to enhance sleep. But I do it maybe every third or four nights. No more than three or four nights a week. - Yeah. - Yeah. - That's perfect. - Okay. - So there's a lot of sleep supplements that should not be taken daily and GABA's one of them. Another one of them is Trazodone. And melatonin is kind of arguable and it depends on the situation. But in general, if you're taking a sleep supplement, it should not be taken every night. - The sleep supplements that I understand are okay to take every night or nearly every night are things like magnesium 3 and 8, apigenin, if that's not true, correct me. I certainly take them every night unless I forget them back home when I'm traveling. - Magnesium's one of the exceptions. L-theanine is also another exception. - Great, well then at least I haven't put anything into the world that's wrong in that category yet.

01:15:34 Testosterone Supplementation & Prostate Cancer

And hopefully I won't. But if I do, I'll correct myself. So let's talk about testosterone in males. You see these headlines all the times now that testosterone levels are dropping, sperm counts are dropping. Phenotypes of men are changing over time. And I can't quite follow the literature on that, because obviously those are hard controlled experiments to do, because techniques change over time, and sensitivity of techniques change over

time. But regardless, I'm aware that a lot of people are considering increasing their testosterone by taking testosterone. A few years ago that was considered steroid use, and it was really extreme kind of stance. Nowadays it seems like there's more discussion about it. First off I'd like to know does testosterone supplementation, and here I'm talking about prescription from a doctor, does it make one more prone to prostate cancer? That seems to always be the first question that comes out. - Yeah, and there is a huge amount of misinformation about this too. So testosterone is not going to cause a prostate cancer. However, normal aging causes prostate cancer and testosterone will grow your prostate cancer. So if you're a 80-year-old male and you have an autopsy and there's at least say 50% percent chance that you have a prostate cancer, if you're 90 or 100 years old, there's at least a 90% chance. So for humans with a prostate, it's only a matter of time until you get a prostate cancer. So that begs the question, do you want to take something that's going to grow it for sure once you have it? So it's an individual assessment and it's important to follow things like PSAs as well. - So a PSA of four or less, I mean, ideally you wouldn't be at four, 'cause that's kind of the upper threshold, is the simplest read out of whether or not there's excessive prostate growth. There's benign prostate hyperplasia where the prostate is growing, but it's non-cancerous, correct? And then of course there are the symptomologies, like people have challenges with urination, they have sexual difficulties, et cetera. I'm always struck by the correlation that people draw between testosterone and prostate health and the fact that, or I should say the claim that testosterone makes prostate health worse. Because if you think about it, young males have high testosterone often, if not always, or certainly often. And you don't see a lot of prostate overgrowth and cancer in young males. So something's going on here. How should we conceptualize this? - So if you have a PSA of 3.9 and you're a 25-year-old male versus a 75-year-old male and you have a PSA of 5.9, the 3.9 PSA is significantly more concerning. So think of your prostate as taking cumulative damage from, not only testosterone, but also estrogen and also growth hormone. So that's why obese individuals have higher incidences of prostate cancer as well, is because they don't have those cell checkpoints where your immune system takes a second and says, all right, stop replicating as fast prostate cells. Let's see if there's any atypical ones and then it finds those and it prevents them from reproducing. That's why immunotherapy in cancer is so promising is because they can target these certain things. So the older male is going to have that cumulative damage happen already and arguably prostate cancer is a normal, with aging, fast aging is abnormal. Very slow aging is normal. There's a fine

line to walk between those two. But there's a lot of things that can be done to decrease the turnover, decrease the inflammation, and decrease the congestion of the prostate over time. There's also a lot more than just PSAs that can be done. There's prostate MRIs and things like that that can look at the structure and the function of the prostate. - So what should every male do to maintain the health of their prostate? And I realize that younger males probably aren't thinking about it at all. Although it seems like nowadays I get these kind of what I call cryptic questions. I think women are more comfortable talking about their hormone and sexual health because of they cycle, because of menstrual cycles. They're used to fluctuations that sort of give them the experience of what it's like to have different levels of progesterone, estrogen, testosterone, et cetera. But I get these kind of cryptic questions often in my direct messages where what I think people are asking is, is there something wrong with my prostate? What should I do for my prostate? These are often indirect questions

01:20:24 Prostate Health, Dietary Fiber, Saw Palmetto, C-Reactive Protein

for other aspects of their life where they're suffering. And I don't say that ingest. I think more direct discussion would be great. So what should all males do to maintain prostate health throughout the lifespan? - Maintaining prostate health can be looked at similarly how you can maintain a good natural optimal testosterone. So you look for things that can hurt it. You don't necessarily look for one thing that can improve it or boost it. So for young males, those are prostatitis, so it goes hand in hand with epididymitis. So different infections of the prostate. The younger the male is, the more likely it is related to something that could be sexually transmitted. But another very common cause is what we call gram negative and anerobic bacteria. The prostate is right by the end of the colon. So if you have chronic constipation or if you have colitis or if you, even just an E-coli overgrowth in the colon is very likely to cause an infection of the prostate as well. - What should males do to prevent that? - Have a diet that has good, healthy prebiotic fiber, probiotics as well. Make sure that they're having regular bowel movements, that they don't have chronic constipation. Have good sources of dietary fiber, which is also as soluble fiber, and enough insoluble fiber. Most people get enough insoluble or non-dietary fiber. So that can help prevent the chance of diverticulitis, which is another type of infection. It can also decrease the chance of colitis and decrease the chance of prostate infections as well. - Are there any foods and/or supplements that men should

take or avoid? What about, you hear or about saw palmetto, yeah, supplements for, or supplements that support or cause issues for the prostate? - Yeah, if there's a strong genetic predisposition to enlarged prostates, or even just really early prostate cancers that grow fast, then they could consider taking saw palmetto or even curcumin as an anti-androgen, as long as they're able to tolerate it. It's an individualized basis and depends on their history. As far as making sure that their prostate is not congested, there's an interesting correlation between having girls and having prostate cancer. - Having girl offspring? - Yeah. - So if your offspring are females, then you're slightly more likely to have prostate cancer. There's hypotheses that link estrogen to prostate cancer rather than testosterone. So if you have hypoestrogenism, your prostate has more atypical cells. In general, the higher your C-reactive protein, which is the general marker of inflammation in your body, we call it CRP, and the test order is hsCRP, or high-sensitivity CRP. If your CRP raises up very high, if you have an autoimmune disease, like if you have a Crohn's flare or if you have lupus or an infection or a sexually transmitted infection, or even a colitis, or even the flu, your CRP is going to raise significantly. - That you would detect in a blood test of course. - Correct. Yeah. - Yeah. - So you want to get a baseline CRP when you haven't had any of those things recently. And if your CRP is higher, you also have more female offspring. If your CRP is higher, then your reactive oxygen species, which are causing mutations and atypical cell turnover

01:24:05 Prostate Health & Pelvic Floor, Viagra, Tadalafil

in the prostate are also likely higher. So you want to keep a very low CRP. - Interesting, and what about blood flow, and pelvic floor in general? We should probably do a whole episode on pelvic floor. There's so much interesting data coming out of the fields of clinical and research urology. I realize it's kind of the Netherlands of biology and medicine. People probably aren't thinking so much about this, but pelvic floor is obviously a confluence of a ton of of vasculature, of nerves, and of course the prostate resides there. And of course the genitals reside there as well. So I would imagine that one of the six pillars, exercise, being able to maintain adequate blood flow to those regions is key. What about just postural things? People sitting too much, not hydrating well enough, you mentioned avoiding constipation. What are some other things, including medications that can serve to support the prostate over time and maybe even

support pelvic floor in general, both in males and females over time? - Absolutely, and this is something that's rightfully getting more and more attention. The way I explain the pelvic floor is your abdominal cavity, which includes your peritoneum or where most of your organs are, your retroperitoneum, your pelvic space. Think of it as a box. And your abs are the front of the box. Your back muscles are the back. Your diaphragm is the top of the box. And your pelvic floor, that's where your port is to the outside world. Especially important, it has muscles as well. And you can do exercises. Pelvic floor physical therapists are becoming more and more utilized, especially after childbirth, but in other situations as well, including by men getting care from urologists. So you want to both strengthen that pelvic pelvic floor and make sure that the tubes that are docked to the outside world are working well enough, but they're not too loose. They're not working too well. So there's a lot of medications that can be positives or negatives for your pelvic floor. We kind of talked about your gut and colon health in general. As far as your prostate health and as far as your bladder and urinary system health, you think about a couple different classes. So you have your phosphodiesterase. You have your tadalafil. Basically this is going to help decrease congestion in the prostate. A lot of people take it for ED, but it can actually help you decrease your- - Could you define that? - A lot of men take to tadalafil, generic is Cialis, has a much longer half-life than Viagra or Levitra. Its half-life is almost a day. So you can take a very low dose of it. Instead of taking 20 milligrams, you take two or two and a half milligrams. - So you're saying that a lot of men take it for erectile dysfunction? - Yes. - But that at it at lower doses, it may have served purposes for prostate health, independent of erection? - Correct, the most common scenario is if a male is waking up twice at night to pee, on average, it'll cut that down to once. So if they're waking up at four times at night, then it can cut that down to twice at night, just because you have easier blood flow. We used to use other medications like Flomax, which is tamsulosin. That's an alpha antagonist, so it basically binds to a receptor in smooth muscle, and it helps relax that. There's several other alpha antagonists. And then you also have your medications that are hormonal like finasteride that a lot of people take for prostate health to decrease the enlargement of the prostate. The periurethral area, or periurethral lobe, there's several lobes of the prostate, that tends to be especially enlarged in cases of BPH and- - BPH? - Prostate hyperplasia or an enlarged prostate. And if you are able to shrink that area, then at that point, it's just a plumbing problem. And the urine is able to get by easier. - Yeah, my understanding is that now there's a growing, I don't want to say a movement, [chuckles] but the idea of

taking very low dose, like 2.5 milligram or 5 milligram tadalafil, even daily is becoming pretty common for many men who do not have erectile dysfunction, simply to either maintain or enhance prostate health. Is that correct? - Yeah, that's correct. - And do you see any negative effects of doing that? - There can be negative effects. It can lower blood pressure. So theoretically it can increase your chance of vasovagal syncope. A lot of people take it as an alternative to pump, because it kind of works similarly to citrulline, or different pump products in pre-workout, and it can certainly help with that. But if you're about to go do a deadlift where you might pass out anyway, it can certainly increase the chance of that happens, because you don't have that compensatory exercise, hypertension response. - Could someone just take it away from exercise? - They could, if you took tadalafil, then that's going to be, has a long half-life. Whereas Viagra and Levitra is just a few hours, tadalafil almost today. Some interesting studies on Viagra have been done as well. It can potentially alter your rays and cones in your eye. So the usual recommendation for pilots that need to have red-green discrimination from very long distances with very small indicator lights is to not take Viagra. So I usually say if you're a pilot and that's your profession, perhaps hold off from that for a while. There's also studies with Viagra that significantly, which is also known as sildenafil as the generic now, it can increase eyebrow hair growth. So potentially what it does is it helps vasodilate and relax the veins, especially in older men. And when those veins are relaxed, you have better blood flow. That's one of the proposals or theories behind why older men get the androgenetic alopecia more. You're having less blood flow in the scalp. So theoretically it can also help prevent that, but it's not going to- - So in theory, increasing blood, oh, because it increases blood flow systemically throughout the body? - Yeah. - Not just in specific tissues. Well, I find it incredibly interesting that, yeah, there are these online forums building up now around low dose tadalafil, daily use of low dose tadalafil, again, not for sexual or erectile dysfunction, but for sake of longterm prostate health. Is there any reason why women might want to take low dose tadalafil? - tadalafil is also a weak androgen receptor sensitizer, kind of like L-carnitine, where the density of the available androgen receptors to bind increases slightly.

01:30:54 Testosterone Replacement Therapy (TRT)

So there could potentially be a benefit from that, but most of the time it's used in men. - Very interesting, we haven't really talked about testosterone and optimizing testosterone

in males. Assuming someone is paying attention to the six pillars, there's kind of a gap as, I see it, between doing all those things and TRT, hormone replacement therapy. And again, the R, the replacement in TRT is a little bit of in quotes nowadays, because a lot of people who have testosterone in that 300 to 900 nanogram per deciliter range opt to take low dose testosterone anyway. My understanding is that there have been some new kind of movements in this area toward, for instance, not doing big, large doses injected infrequently, but rather low doses quite frequently, obviously prescribed by a doctor, monitored by a doctor, et cetera. Is that generally what you like to see in your patients if they're going to take this route? - If they're a hypogonadal patient whose benefits outweigh risks of TRT, then you want to have a nice even steady state. It's not going to be exactly the same as producing pulsatile testosterone release endogenously from your own body. When you have a steady state, you don't have a peak or a trough. And when you have a peak, that's when the antigen receptor gene is overactive, that's when you get more erythropoietin or EPO release, and that leads to a lot of the side effects of thick blood, so higher hemoglobins, and hematocrits. And then when you have a crash, you don't feel good. So it's definitely not optimal. There's a lot of ways to get around this. So when you're doing testosterone replacement, if you're someone that needs it, you can have different types of esters, or you could do topical testosterone. So the Ester is basically something that's attached to increase the biological half-life. The most common ones are cypionate, enanthate, there's also a very short-acting propionate, which has almost no clinical relevance. And there's also very long-acting ones, decanoate, and undecanoate, and different mixtures of all those. So if you're someone who has a very, very low SHBG, you're going to have trouble of regulating your serum testosterone in the long run. If you do it topically, then the testosterone is absorbed, hopefully bound to SHBG, and then a lot of times you reapply twice daily or once daily, but you have lots of variations. So for most people, especially for people who can't absorb it well, that's not going to be a great option. So injections would be preferred. Most people end up injecting, because they have either side effects from too high, too low, or just too much of a varied dose when they do topical. There's also a capsule with a special lymphatic absorption. So it's not being absorbed through the liver, it's not hepatically metabolized, but it's absorbed through the lymph. And it's essentially testosterone undecanoate, and then put into a capsule. And that's taken twice daily. It has fairly steady half-lives, but you have to take it at specific times of the day. So that being said, and it's new enough to where there isn't a huge amount of data on it, but it is

FDA approved. So it is brand name now. it's called JATENZO. But the injectables in general, the lower your SHBG, the longer of an ester you want, because when you inject it, whether it's intramuscular or subcutaneous, just talk to your doctor about the risks and the benefits of those. Subcutaneous has slightly longer active half-life, because the esterases take longer to reach that supinate or an esterated clavate. So most men, a lot of people ask me about like what a usual dose is. For most people, it would be a total of about 100 to 120 per week for an actual replacement dose. - Milligrams? - Milligrams. 120 to 100 milligrams per week administered two to three times per week. - And you're not, so you're saying dividing that into two or three, right? 'Cause I'm sure a bunch of people out there are thinking, oh yeah, 103 times a week, which is actually quite a high dose. Yeah, there really does seem to be a shift toward spreading these dosages out into,

01:35:17 Estrogen & Aromatase Inhibitors, Calcium D-Glucarate, DIM

dividing them into two or three smaller doses. And then along those lines, 5, 10 years ago, it was common to hear about inhibiting estrogen through aromatase inhibitors. Nowadays you hear, and I think it's true, at least by my read of the literature, that inhibiting estrogen can disrupt brain function, can cause connective tissue issues, and even can cause reductions in libido. So a lot of people think they estrogen, if you crash estrogen, that basically libido goes up, but actually the opposite is often true. You don't want estrogen too high or too low, is that correct? And for that reason, do you shy away from people taking aromatase inhibitors? - Yeah, very few people truly need aromatase inhibitor. There's almost always lifestyle interventions. It can just depend on which gene, how active your aromatase gene is. Some people's aromatase gene is very active. A lot of times these individuals have pubertal gynecomastia, which is breast tissue growth in males, even despite no other risk factor. - Even if they're lean? - Some people get it if they're lean. - I remember growing up - It's possible. - There were a few kids that got mild cases of gynecomastia that were transient. Like it's sort of like they developed gynecomastia and then it went away. - Often it's unilateral on one side too. So growth hormone a lot of times is the fuel to that fire. - Oh, interesting. - Yeah. - Yeah, there were a couple of kids. I mean, they took some teasing 'cause back then, there wasn't online discussions about hormones and things like that, but then it would seem transient. And they were, the people I'm thinking of were actually lean individuals. So they weren't

overweight, which of course can cause gynecomastia, because adipose fat tissue can convert testosterone into estrogen. So it sounds like, except in special cases, that avoiding aromatase inhibitors is probably going to be a good idea. - Yeah, there's several other ways that you can control your estrogen and keep it at a healthy level, which you do have to check. There's a lot of patients who assure me that their estrogen's going to be sky high and it's actually very low and vice versa. But calcium D-glucarate is a supplement that can help with estrogen control. - What's a typical dosage of calcium D-glucarate? - 500 To 1,000 milligrams. - But is there the risk that if someone's estrogen is in normal range and they take the supplement, that their estrogen will go too low? Is it that potent? - It's not that potent. It's not near as potent as an aromatase inhibitor. So it helps with excretion and also the sensitivity of the estrogen receptor itself. And it kind of like helps outcompete it. Some people will also take DIM or different cruciferous vegetable, they get 'em from cruciferous vegetables like kale but, or broccoli and that is both an antiestrogen and an antiandrogen. So if you're on TRT and you're on that, then you're probably just on too much TRT. - Yeah, I remember a few years ago I had a friend, and it truly is, it's not like I have a friend thing, 'cause I'm very cautious just about which supplements I take. I think people might get the impression that I'm very cavalier about this, but I'm not. I always alter one thing at a time. I talk to physicians. What I suggest other people do I actually do and have done for a long period of time. And I recall wanting to take DIM, 'cause I thought, well, back then you hear, okay, reduce estrogen. My estrogen levels weren't out of range, so they were fine, but I thought, well, what would the experience be of bringing those down? But someone I know is quite informed in this area said, yeah, exactly what you said, which is that DIM can reduce estrogen, but also testosterone. So I just never opted to try and take it. I do want, we're sort of airing in this direction, but we went straight from the six pillars to TRT or to what some people now call sports TRT, which is basically code language for saying taking exogenous testosterone even though one doesn't need it to get into a semi-super physiological range or a high end, like 900 to 1,000 nanogram per deciliter range. And people always point out, I should mention that, oh, well in certain countries, the high end range is 1,200 nanograms per deciliter. In the US, it's 900. And so if you're 1,200, are you really super physiological?

01:39:28 Lifestyle Factors to Increase Testosterone/Estrogen Levels, Dietary Fats

All that aside, I neglected to ask about that gap in between where individuals could think about supplementation, meaning non-prescription approaches to increasing testosterone, and here we should probably also talk about things like, is it true that ice baths increase testosterone or not? Lifestyle factors that go beyond the six pillars for increasing testosterone. If you could comment on those, that would be terrific.

Supplements that are useful. And it'd be wonderful if you could mention where some of these same practices and supplements might be useful for women as well as men to increase testosterone for all the reasons we talked about earlier. - Yeah, so this is where a true individualized approach comes in. When you're talking about what dose of TRT you should be on, one thing to keep in mind is the law of diminishing returns. Quality of life is a subjective thing and it's different for each person. So some people are more willing to give up a little bit of athleticism or body composition. Some people are more willing to give up, or not willing to give up libido or sexual health. And as we mentioned earlier, everybody's androgen receptor is less or more sensitive. So you can make a case that if somebody's androgen receptor is half as sensitive as somebody else, the person with the less sensitive receptor does need a level of 1,000 or 1,200. There's no great way to know that. And you can alter the sensitivity of your androgen receptor with things like L-carnitine and tadalafil as mentioned. - And we'll definitely come back to L-carnitine, because I'm really intrigued by the data on L-carnitine, both for women and men in terms of egg quality, sperm quality, fertility, and a bunch of other interesting effects. So we'll come back to L-carnitine. - But a lot of how you feel, the biofeedback or subjective, I feel like this, comes from the ratio of your androgens to your estrogens. And a lot of that is lifestyle. So if someone's also on hCG, that could upregulate aromatase as well. - hCG, you might want to just, human chorionic gonadotropin? - [Kyle] Yeah. Used to be found in pregnant, is still found in pregnant women's urine. - Still found in pregnant women, yeah. - But used to be, believe it or not, there was a black market for pregnant women's urine before this stuff was developed synthetically. So in other words, what we're saying is men typically would buy pregnant women's urine through black markets in order to get the hCG in order to get the testosterone-enhancing effects of hCG. So in other words, men were using pregnant women's urine for hCG. I do not want to how they got it into their body. Let's just skip to what you were going to say next instead. - Yeah. So that's hCG. There's a lot of other things that upregulate estrogen. Alcohol significantly increases aromatase. So if you're very sensitive to estrogen, then you probably shouldn't even consume two glasses three times a week. High fat meals also upregulate

aromatase. So if you're on a ketogenic diet, but you have hyperestrogenism, then you should take care with that as well. - All kinds of fats or just saturated fats? - I'm not sure if it's just saturated fats, but fat definitely increases, both fat and your body and consumption of a high amount of calories increases aromatase. - So the it's the ratio of testosterone and estrogen. I don't want to break your flow, but since we're talking about fat, I have to ask, since estrogen and testosterone are both synthesized from the cholesterol molecule, I've heard that ingesting some amount of saturated fat can be useful because of the way that cholesterol can serve as a precursor to these molecules. Now I once said on a podcast that I like butter so much that I occasionally eat pats of butter. Somehow that got misinterpreted to mean that I eat entire many pats of butter. I'm saying like one or two pats of butter here and there, and I have no guilt or shame about it. My blood lipids are in great shape also, so I feel good. But is it possible that people who are ingesting too little of saturated fats could directly or indirectly reduce or somehow disrupt the proper ratio of testosterone to estrogen in men and women? - It's theoretically possible, but it probably doesn't happen in developed countries just like it's theoretically possible to have not enough omega-6 fatty acids, but that probably does not happen in developed countries. - So I don't need the butter pats, but I'm going to do it anyway. I'm just curious. - Yeah. - Okay. - Grass-fed butter has good omega-3 content as well. So grass-fed foods in general. It's not the end all be all and everybody doesn't need grass-fed foods, but they are one of the only sources of healthy trans fat. So a naturally occurring trans fat comes from ruminants. So ruminants, think of like cows and the rumination in the different stomachs can change your omega-3 and omega-6 to trans-linolenic and trans-linoleic fatty acids. - Which are healthy for us. - Yeah. So it's actually omega-3s and omega-6s that just happened to have a trans instead of cis-isomer. - And these healthy trans fats would be found in ruminant cheese and milk and butter from ruminants and the meat- - And the meat. - And the meats? - Yes. - And for people who are following a purely plant-based diet or mostly plant-based diet, are they at risk of not getting enough of certain types of fats or other nutrients to maintain that healthy ratio of testosterone to estrogen or not? - If they're a vegetarian, they're probably not at risk. If they're a vegan, they very well could be at risk. Most vegans are aware of this very acutely and they'll supplement with algae or they'll supplement with other sources of healthy fats. - I see, so the takeaway that I'm drawing from this is that less so than getting saturated fat, it's key to get these healthy trans fats from ruminants. - [Kyle] Yes. - Or the food products of those ruminants as well as to get proper amounts of

omega-3s. - Yeah, and to be clear, you don't need any trans fats.

01:45:34 Aromatase Supplements: Ecdysterone, Turkesterone

It just happens that those omega-3s and omega-6s are in a trans-isomer. - I see, okay, so that's nutrition. What other supplements can support healthy testosterone to estrogen ratios? - Anything that alters aromatase can support healthy testosterone to estrogen. And your testosterone to estrogen ratio, think about it as how much estrogen activity do you have at the beta estradiol receptor and your alpha estradiol receptor. - How would I know that? - So [chuckles] it's hard to tell, but depending on what you're eating, if you have a lot of plant-based diets or polyphenols, many of these are beta estradiol receptors. People know about Turkesterone and also Beta-Ecdysterone, which are two ecdysteroids that are beta estradiol receptor agonist. So they activate the beta estradiol receptor. So if you have a very low amount of estrogen naturally, you're probably a better candidate for it. - For taking Turkesterone or ecdysterone? - Yeah, ecdysterone. - I've never tried them, but I know my understanding is that they work tremendously well for some people. - Yeah. - And not at all for others. And so one just simply has to try. But in promoting the activity of this estrogen receptor, is there a risk that Turkesterone or ecdysterone could cause some of the quote/unquote problems associated with increasing estrogen activity, like reduced libido, water retention? - Water retention, yes. Reduced libido, probably not. Closing growth plates in the bone, no,

01:47:04 Tongkat Ali (Long Jack), Estrogen/Testosterone levels

because that's the alpha-estradiol receptor. - I've talked before on a couple of podcasts about tongkat ali, which is Indonesian herb, I guess, is also made and found in Malaysia. But it seems to be the Indonesian variety of tongkat ali that's most effective for potentially for reducing sex hormone and binding globulin and thereby freeing up testosterone. Whether or not the effects are through that pathway, through another pathway, a lot of people report improvements in things like libido and maybe androgen-like phenotypes, right? Feeling more vital, et cetera. And of course, some of that could be placebo, correct? But what are your thoughts on tongkat ali? And please challenge my statements about tongkat ali if they're incorrect. I'm not looking for validation here. I just really want to know what your thoughts are on it. Do you ever recommend it to

patients, when? Men, women, one or the other? - Yeah, so tongkat ali or longjack has multiple mechanisms of action and there have been several placebo controlled studies on it. Some of them show decrease in SHBG, at least one of them did not show any change in SHBG. However, it does act on aromatase very weakly. Probably not so strongly that you would have to be concerned of hypoestrogenism. - So it reduces aromatase and thereby can reduce estrogen. - Correct. - Okay. - It's also a weak, it's not SERM, so it's not a selective estrogen receptor modifier, but it's probably a weak, it's probably an ERM as well or a non-selective estrogen receptor modifier. And that should help with decreasing negative feedback inhibition of estradiol in various locations and also increasing testosterone. - Interesting, yeah, the dosage that I've been using for years now is, it's 400 milligrams taken once a day, typically early in the day, 'cause it can kind of have a mild stimulant effect, very mild. And I know that some of the products out there recommend dosages that are much higher. Anytime I've taken more than 400, I don't feel very good. I don't know how to describe it other than it's just a little overly stimulatory in terms of makes me kind of, it's like drinking too much coffee. - [Kyle] Yeah. - So that's interesting. And so would women ever want to take tongkat ali for any reason? - Yeah, absolutely. So there's a lot of women that have hyperestrogenism and unlike adrenal fatigue or andropause, there's actually ICD 10 codes for hypoestrogenism. - ICD 10 codes? - Yeah. - That's doctor speak, right? - Yeah. - Okay. - So there's codes to where your doctor can actually diagnose you with something. So if you go to your doctor and you say, I have adrenal fatigue, they can't diagnose you with that. Or if you say I have andropause, they also can't diagnose you with that. But if you say you have hypoestrogenism, the most common complaint that comes with it is endometriosis, which is overgrowth of the lining of the uterus. And those people could potentially, I think, that's one area where we might see tongkat supplementation more and more, because not only does it decrease aromatase. Like we mentioned, testosterone in females is higher than estrogen in females. So a lot of females get estrogen from aromatization as well. Peripheral estrogen is sometimes what we call it, because it's not directly produced in the ovaries. But they could be good candidates for tongkat if that's the case. - Very interesting and my understanding is that people should be looking for sources of Indonesian tongkat ali in particular. - Correct. - Right. - Another interesting application is essentially a, I'll call it a PCT, but essentially- - What that means is? - PCT means, I'll defined it as post-cycle therapy. - Physicians love acronyms, scientists love acronyms, military love acronym, but we, yeah. PCT, post cycle therapy,

so this would be people coming off hormone therapy or steroids. - This would actually be for women that are coming off of their birth control pill, because perhaps it can help lower that SHBG back to normal, which is sometimes persistently elevated, and then it can help prevent the subsequent hypoestrogenism that happens. - Does tongkat ali need to be cycled? When I first started taking it, I would cycle it. I would do a few, three, four months, and I would take some time off. Now I've just been taking it continuously for years. - [Kyle] Yeah. - And I should say I do blood work to check my liver enzymes and everything else and I don't see any reason for me to cease taking it. - Yeah. Probably not. There's been human studies on both tongkat and Fadogia. And full disclosure, I did help design Derek's new testosterone optimization supplement, which has both Fadogia agrestis and also tongkat ali in it. - Yeah. Let's talk about Fadogia separately in a moment. But let's say someone is only taking tongkat ali for whatever reason, do they need to cycle off? - Likely not, but I would just to be safe, because it does both affect your aromatase and it's an estrogen receptor modifier. - And what would be a reasonable cycle off? So how long to take and how long to stop before taking it again? - Yeah, there's a couple different protocols that you can do, but 11 months on, 1 month off for tongkat is pretty reasonable. Now I guess this is, we'll talk about this later too, but if it's combined with Fadogia, the protocol that I would do is three weeks on,

01:52:25 Fadogia Agrestis, Luteinizing Hormone (LH), Frequency

one week off. - So that's tongkat ali. But I'm curious what your thoughts are on Fadogia agrestis, this Nigerian shrub or this extract from Nigerian shrubs that at least in my experience, in my read of the literature, has the potential to increase testosterone and probably other hormones as well by way of increasing luteinizing hormone. Something that we haven't really talked about much up until now. What are your thoughts about Fadogia agrestis? What are your ideas about the proposed mechanism or mechanisms and where might this be useful for people on or off hormone replacement therapy? - Yeah, Fadogia agrestis has just reached a point where we have enough evidence till we know it probably helps both with luteinizing hormone release, which stimulates Leydig cells in the testes to produce more testosterone. And probably with LH receptor sensitivity as well, which is a good combination of the two. It does come from the Nigerian shrub, but there is not quite enough evidence for me to be able to say it's safe for someone to take this all the time, which again, full disclosure, that's why I

recommended that we recommended for people to cycle this supplement. So three weeks on, one week off, that's likely safe. The only toxicity studies in general are in rats and in humans, it looks quite safe. - My understanding is that the toxicity studies in rats showed toxicity to the testicular cells, so that's certainly concerning, but that the dosages that were used or translating the dosages used to humans would lead to a situation where the dosages that humans would have to take would be very, very large. So the amount of, I no longer take Fadogia, but I took it at 600 milligrams per day for a long time. And I ceased taking it because I was experimenting with other things and I didn't want to confound those things. Not because I had any negative side effects. In fact, I was monitoring blood work, and other biological parameters that would've told me if there was testicular toxicity, and there wasn't. Let's put it that way. - Yeah. I think it's extremely safe. And I'm just not convinced that there's enough overwhelming evidence for longterm consistent administration. - So do you recommend this to people who are not taking TRT and do you recommend to men and women? - Yeah, so if you have a really high LH, then there's probably a gonadal issue, whether it's heat damage to the testes, a varicocele, a history of testicular cancer where your LH is going to be higher. So if your LH is already very high, increasing it even more is probably not going to help. However, if your LH is low, then obviously try to find out is it low? Is it deficient or is it just a little bit low? If it's low and you don't have an issue with prolactin, you don't have an issue with opioid receptor antagonism, and naltrexone can actually potentially help antagonize that to increase LH as well, especially in people recovering from opiates or likely even alcohol. So you're looking for a subclinical secondary hypogonadism, which is essentially, just think of that as low LH. So in people with that lower LH and their estrogen is fine and their prolactin is fine, then Fadogia is a particularly good option. - Interesting, so three weeks on, one week off for 600 milligrams Fadogia, 400 milligrams tongkat ali, Indonesian tongkat ali could potentially you be good. And of course, everyone should always check with their physician, clear this, do blood work, et cetera. I always say we don't just say that to protect us. We say that to protect you, meaning the consumer. And it's very, very important. You don't want to get, you don't want to fly blind with any of the stuff. You want to do blood work, right? - That's the catch-22 with supplements is most of them are safer than medications, but the only difference between them and a medication is one's prescribed and one's not. - And oftentimes with supplements, it's unclear whether or not what's listed on the bottle is actually what's in the bottle but. - Yeah. - But I think there are a number of reputable brands now.

01:56:44 Boron, Sex Hormone Binding Globulin (SHBG)

The other supplement I want to talk about in terms of testosterone augmentation is boron. What is boron thought to do? Does it actually do that? And do you ever recommend boron? - Yeah, so boron is actually an element. And you can find it on the periodic table. It's more plentiful in rich soils. So frequent farming can deplete the soils of boron. It's very plentiful in the Mediterranean area like Greece and Turkey, so a lot of people will just eat dates or raisins that are grown there. - I thought you were going to tell me people eat dirt, but there are people who eat dirt. - There are people who eat dirt. - And there's a phenomenon called pica, right? Where people in a, and that's not a good thing, they- - Often assign a iron deficiency. - Okay, but they're eating grapes and dates that were grown in soil that has high amounts of boron. Is that right? - Yeah. Yep, so boron can help regulate SHBG, but its effect is mostly acute. So it's unlikely to have a bad effect, so a lot of people take boron because it's probably not going to hurt and it will lower SHBG even if it is for a short period of time. So I guess you could make a case that maybe cycling boron can help too. - What sorts of dosages are useful for boron supplementation? - Three to six milligrams once to twice a day. - Oh, interesting, so that's higher than the amounts that I've been taking. I've long been doing this cocktail of tongkat ali, again, I stopped taking Fadogia, but for a long time with Fadogia, and boron, I think it was two to four milligrams per day,

01:58:13 Human Chorionic Gonadotropin (hCG), Fertility

but maybe I could afford to go higher. Although my blood work is where I want it, thankfully. So circling back to Fadogia. Fadogia was attractive to me as a supplement, because I saw increases in LH, testosterone, and free testosterone. My estrogen stayed in check, but I also did not see a down-regulation of LH when I would cycle off. Whereas with hCG, human chorionic gonadotropin, which does now arrive in forms not from pregnant women's urine only, but the synthetic forms that people inject, that, as I understand, it can actually suppress endogenous hormone output if one takes it for a long period of time. So why would a man or woman want to take hCG? And what are the potential risks and benefits of taking hCG? - Yeah, so hCG or human chorionic gonadotropin is actually very similar to TSH. - Thyroid stimulating hormone? - Correct,

so when a woman is pregnant, she produces more hCG, especially in the first trimester. When you take a pregnancy test, whether it's qualitative or quantitative, you see the hCG rise, and it actually doubles every 48 hours. So if you're five weeks pregnant, you can get a hCG level. And then two days later, five weeks and two days, you can see your hCG, and maybe it went from 500 to 1,000. So it precipitously increases. It does a few things. One thing is it prevents hypothyroidism or hypothyroxinemia of pregnancy, which is one of the most common causes of miscarriage. It's also why if you are, if you have hypothyroidism and you get pregnant in the first trimester, you want to increase your dose from 25 to 40% to keep your free T4 high as much as possible. And the reason why you have to do that as opposed to somebody who does not have hypothyroidism, is if you have hypothyroidism, then likely your thyroid will not respond to either TSH or hCG. So the increased hCG does not compensate for that. So if you take hCG, then it can potentially improve your thyroid function. So that along with selenium are likely the two best things that you can do for thyroid health. - hCG and selenium? - Yeah. - Well, I definitely make sure I get enough selenium by eating three to five Brazil nuts per day. - Yeah. - Which I very much enjoy the taste of also. Who should take hCG and can hCG suppress one's normal luteinizing hormone output? - Yeah, it suppresses LH in a dose-dependent manner. So the higher the dose of hCG you take, the more it suppresses LH. A common dose for fertility, fertility is usually why hCG is prescribed. - In men or women? - In both, is 10,000 IUs all at one time, which is quite a bit. - That's a tremendous dose. - Yeah, in fact, some formulations, some brand names of hCG come in autoinjector pins to where you cannot even dose lower than 5,000 units at a time. - Wow. - Yeah. - But I know a number of people who take hCG to maintain testicular function while on testosterone therapy or augmentation of some sort. Does it work to do that? - Yeah, some people are on hCG monotherapy. It can be slightly better on your lipids than being on TRT. - Oh, so people are using hCG alone as a kind of neither sort of an indirect hormone augmentation. - Yeah. Some clinics advertise it as a non-suppressive alternative to TRT, but it is suppressive of LH. - But it could also increase estrogen pretty potently? - Yeah. - And is it true that increasing LH and/or hCG can improve sensitivity of the genitals? And is that true for men and women? Yeah, I've heard this anecdotally. People say hCG makes sexual activity more pleasurable for people because of some, is it a direct effect on some of the nerve cells in the genitals? - Yeah, so LH is also an agonist in the prostate and in genital tissue in general. So it's a very common treatment for post-finasteride syndrome or post-5-alpha reductase when

you've blocked the conversion of DHT for a long time, it helps re-upregulate DHT. - So someone who's been taking finasteride to prevent hair loss, comes off it, maybe 'cause they felt lousy, but then feels even lousier for reasons that you talked about earlier. And then they might use hCG as a transition treatment to transition back to normal hormone health. Is that right? - Yeah. - It's extremely helpful in many cases. Now when you come off the hCG, then you need to have a strategy of how to return to your normal as fast as possible as well. But it will upregulate those 5-alpha reductase enzymes. You have, in your genital skin, both scrotal skin and penile skin, and perineum in general, you have, I believe what's called stratum lucidum. It's skin layer that is very, very thin, but it has the highest concentration of 5-alpha reductase. So you have a lot of activity. And after you've been on something that inhibits the enzyme, the 5-AR enzyme in those tissues, then you do something else to upregulate those enzymes, whether it's waiting and taking time, whether it's trying tadalafil, whether it's trying creatine even, or whether it's trying HCG, a lot of times those are the go-tos for post-finasteride syndrome. - Any risks for women taking HCG on their ability to get pregnant or risks generally? - Yeah, obviously it'll make any pregnancy test positive. So that's a risk that some women don't know. - So one could, in theory, fake a pregnancy test by injecting hCG. - Absolutely. - Interesting. - Yeah. - I have no motivation to do that.

02:04:18 Prolactin & Dopamine, Pituitary Damage

I was just curious. [Kyle chuckles] - Yeah. - What about prolactin? The simple version of this that I was taught, because I was taught mainly from the neuroendocrine perspective was dopamine is a kind of close cousin of testosterone, and also estrogen for that matter, drives appetitive behaviors, including pursuit of sexual partners, sex itself, motivated behaviors generally, then postcopulatory, post-orgasmic states are accompanied by a prolactin increase. That's the refractory period for mating in males, and maybe even in females as well, involved in milk letdown, et cetera. What are sort of the general contours of syndromes or things that people could be on the lookout for of having too much prolactin or too little prolactin? And I'm aware of a number of people who take dopamine agonists, L-tyrosine, cabergoline, things like that, to really boost their dopamine levels. And that isn't always a good thing as it turns out. Oftentimes people become kind of hyper-dopaminergic and so they have the drive to do all these appetitive things, fill in the blanks, but they don't always have the ability, because it

seems, just as testosterone and estrogen need to be in the proper ratios, dopamine and prolactin need to be in the appropriate ratios. So how should we think about and perhaps act on our prolactin systems? - Absolutely, the way I describe it is the dopamine wave pool. So if you're increasing your dopamine too much, you're going to overflow and then you're going to have that wave crash too much. So you want to have nice even waves that are not going too far above the pool of dopamine and prolactin will follow. So prolactin and estrogen are quite close cousins. Estrogen upregulates a gene called the PRL gene or prolactin gene that directly increases prolactin synthesis. So prolactin is going to also inhibit the release of testosterone from the pituitary. So if you're using a dopamine agonist, then you're to help decrease the prolactin-producing cells, including if you have a prolactin-producing microadenoma in the pituitary. - How common are those? Because, I mean, I hear a lot about these hypogonadism or, and of course that can be due to an issue at the testicles or hypergonadism could also be of course in like ovarian syndromes and then there's of course the brain side of it where the signals aren't coming from the brain. Not enough gonadotropin, not enough luteinizing hormone. And there are ways of teasing this apart with an endocrinologist that are quite elegant in fact, right? Using stimulating hormones, too much to dive into here. But how often does one actually have one of these pituitary tumors? I have heard that people that play a lot of high contact sport, so boxing, football, people that headed the soccer ball quite a lot, sadly people whose jobs force them to take head blows for, could be military. And so they were firing 50 caliber guns and the kind of woodpeckering of the brain inside of the skull. And construction workers or just a concussion can cause the pituitary to go malfunctional. Is that really common or is this something that is a rare like 1%? - Yeah, it's extremely common. It's another one of those conditions where a lot of people never know they have it. They just feel a little bit more fatigued. They have that high prolactin feeling all the time. Pituitary microadenomas can be non-producing as well. So your prolactin can be totally normal. Your growth hormone and IGF-1 can be totally normal. That's the second most common producing microadenoma, is growth hormone causing either acromegaly, which is growth of cartilage or gigantism. - This is the big brow. - Yeah. - Yeah. - So those are fairly common causes of adenomas, but a lot of people that have a very small adenoma, much less than one centimeter, it's hard to see on imaging even if you have a contrast that specifically looks at the pituitary and many people aren't symptomatic. So it's one of those things along with PCOS and pre-diabetes that are much more frequent when it comes to prevalence, which is the amount,

02:08:34 Augmenting Dopamine Levels: Casein, Gluten, Vitamin E, Vitamin B6 (P5P)

the percentage of people that have it in the general population. - I'm glad you mentioned the dopamine wave pool. I know nowadays there's a lot of interest in augmenting dopamine. I know a number of people that do this through prescription drugs, Adderall, Ritalin, modafinil, and those drugs of course hit many transmitter systems, but dopamine is certainly involved. People taking antidepressants like Wellbutrin tap into that system. And of course people are trying to inhibit prolactin and promote serotonin or reduce serotonin. To me, it all seems like a very delicate dance, right? I mean, to just imagine the arousal arc for mating behavior, for sexual reproduction, is such an elaborate dance between sympathetic drive and parasympathetic drive, even with across the span of minutes, right? I mean, I've talked about this before on the podcast that the arousal is kind of more parasympathetic, orgasm in itself is a sympathetic response, a completely different set of neurons. And so where do you see people getting into trouble just trying to hit the gas pedal on dopamine and where do you think there is a place for people who perhaps are experiencing low drive and motivation, not just sexual, but in general, to increase the amount of dopamine circulating in their brain and body? How do you think about that, given this wave pool analogy? - Yeah, so it's important to parse it out and start with the least powerful interventions. So if someone's concerned about dopamine or maybe they have a slightly higher prolactin, then they eliminate things that could be increasing that prolactin. - Such as? - Casein or gluten, which are mu opioid receptor agonists or any mu opioid receptor agonist in the gut. - Casein, so milk protein? - Correct. - Can increase prolactin? - Correct. - Interesting. - In addition to that, they should, if they need a pituitary MRI, then they should get a pituitary MRI. If they don't have an adenoma or if they don't have a high enough prolactin level to where they need an MRI, if they're having visual symptoms, or if they're having olfactory symptoms with the nose, then it's more likely that they do. But if they don't, a lot of times a prolactin under about 40 is not too big of a deal. They can take dopamine agonist that agonize that D2 receptor like P5P, which is essentially vitamin B6. It's pyridoxine-5-pyrophosphate. And pyridoxine is vitamin B6. So that can help, 50 milligrams once to twice a day. Vitamin E can also help, especially if it's mixed to tocopherols. A lot of people have high levels of vitamin E, but low levels of the gamma form of vitamin E. So that can also help. - Fascinating, I'm so glad you mentioned vitamin B6 and P5P. I have

heard that one can shorten the refractory period after orgasm, essentially to be able to have sex again, to be quite direct about it, by way of vitamin B6 blunting of the prolactin response, which turns out to be quite potent. But I've also heard that vitamin B6 can be neurotoxic, especially in the periphery, that it can cause peripheral neuropathies if it's taken at high doses. But that P5P is the safer form. Is that true? - It's pre-activated, so it does not build up. Think of it as an allegory to how folate can build up. It's not methyl folate, but it builds up and it can increase levels of homocystine. Or if you have too much vitamin B12, another water soluble B vitamin, you can have too much methylmalonic acid or MMA. So depending on what your enzymatic conversion is to the active form of the enzyme, often it's just safer to take the active form of the enzyme. - Yeah. Very interesting. - Yeah. - Okay, well, at risk of going down every hormonal pathway and talking about supplementation, lifestyle factors,

02:12:30 L-Carnitine & Fertility, TMAO & Allicin (Garlic)

I think touching on, as we have, testosterone and estrogen, and now prolactin, I'd love to chat a little bit about L-carnitine. We talked about this earlier, but I want to raise this discussion about L-carnitine, not in the context of L-carnitine itself, but in the context of fertility. Because my read of the literature is that L-carnitine can be very beneficial for enhancing sperm quality and egg quality and even rates of conception. What forms does L-carnitine come in that people can reasonably consider? Again, talk to your doctor, folks. What is it doing? And do we know how it's doing it? And do you often use this in your patients? - Yeah, so the way I think about L-carnitine, and I'll try to tie this in with creatine, and other things as well, is if your cell is an energy factory or car, then L-carnitine is the shuttle that helps get the fuel into the motor to use the motor. The motor is mostly due to lifestyle factors. So like your diet and your exercise. And the type of fuel itself is NAD+. We don't need to get into NAD precursors or NMN or NR, anything. And then the accessory fuel tank is your creatine phosphate. So creatine is your accessory fuel tank. Your NAD status, which is largely determined by your REM sleep and quality sleep and exercise along with supplementation as the fuel, the carnitine shuttle is carnitine palmitoyl coenzyme A. And that takes medium-chain fatty acids, it takes different molecules of fat. You have two main energy sources other than ketones. You have your glucose or carbs. You have your fat or fatty acids. And that takes it across the layer of the mitochondria so that it can be utilized. So upregulates that, that's why things

that have flagella in general, the flagella are going to work better, like sperm. - The flagella being anything, sort of the wavy little tenders on cell types of which they're everywhere, right? In the gut too, right, yeah. - Yeah. - Yeah. - So those are going to work significantly better. And in general, your mitochondria are going to work better. So the worst your mitochondria are off the bat, the better they're going to be helped by these shuttle that shuttles them across. It also slightly increases the density of the androgen receptor as well. - Is that a local effect? So if an L-carnitine is injected into a particular muscle, will it increase the density of androgen receptors in that muscle? - Likely so. - So how are people taking L-carnitine? There are capsule forms and there are injectable forms. Most people are going to be taking the capsule forms, because that's all they're going to have access to. And then we should also ask, can you get L-carnitine from food? - Yeah, so L-carnitine is just a combination of, it's actually a very small peptide. So glutathione is just a three amino acids. L-carnitine is the smallest peptide, two. So peptide is just a protein that has amino acids between two and about 200. And L-carnitine is just two amino acids. - Amazing, so it's like a micro-peptide? - Yeah, so your body synthesizes enough. It likes to absorb the amino acids by themselves. And then if it puts them together, there it makes L-carnitine. It's not very bioavailable if you take it. A lot of people take L-carnitine, L-tartrate, or an acetyl-L-carnitine, and that's about 10% bioavailable. So if you want 1 gram or 1,000 milligrams of L-carnitine, you can take 10 grams of oral L-carnitine. - Is the one gram the typical dose, you recommend one gram per day? - For fertility and androgen receptor upregulation. - So that means taking 10 grams of the capsule form? - Yeah. So it's about 15 to 20 capsules, which is a lot. - [Andrew] That is a lot. - It can also potentially increase TMAO. - Yeah, I want to ask about that, because TMAO on your blood chart is, when that's elevated, that's going to cause some concern. You taught me a trick, however, that one can take 600 milligrams of garlic capsule for the allicin. Is that what it's called? - Allicin is in it, yeah. - It's like the name Allison but with two L's? - Yeah. - Okay. And that had a remarkable effect in reducing TMAO. So that's quite potent and also was it just coincidence that it really brought my LDL down as well? - I'm not sure if the LDL is a coincidence, but depending on your gut microbiome or your microbiota, some microbiome beneficial bacteria will convert carnitine and also choline. So any choline precursor like Alpha-GPC or phosphatidylserine, it'll will convert them more or less to TMAO. So TMAO is something that you can get measured in a blood test and see if it's high or low. Some people might not even need allicin. - Interesting. - Some people do benefit from it. - Interesting,

although I think it was you that also told me that allicin in garlic can have positive effects on cardiovascular tone and blood flow generally. Is that right? - Yeah. - Okay. So is 600 milligrams garlic an excessive amount or can I just eat garlic? - You can just eat- - I mean, I like eating garlic. - Yeah. - Yeah. So, okay, so one could also just eat garlic. If one were going to take L-carnitine in injectable form, how much of that is bioavailable? - 100% if you inject it. It is in an aqueous solution, so it's bacteria static water essentially. So it's not in a carrier oil. So it's going to burn a lot if you inject it subcutaneously. So it's going to be absorbed faster and more evenly and also just hurt a lot less if you inject it into a muscle. - But one could then just take one gram per day injected or divide it up into a couple doses? - Yeah, or 500, the minimally efficacious dose for injectable's probably around 200 when it comes to sperm motility,

02:18:19 Blood Test Frequency

the androgen receptor upregulation. So it really depends on why you're taking it. - In terms of fertility, and in terms of blood tests generally, I always say that if possible, either by way of insurance or by way of some other way, affording it, it would be great for people to have blood tests to know what their hormone levels and other levels of other things like metabolic markers and lipids were in their 20s, also in their 30s, also in their 40s. I think there's this idea that you only take a blood test when you have a problem, but then of course one can't actually do the comparison that you mentioned earlier or state the comparison to one's physician that things are changing over time. And it seems to me that basically everyone should get at least a once-a-year blood test. Is there the hope that insurance will someday just cover it for everybody? This will be standard care? I would think that everybody should know what sorts of things are floating around in their bloodstream and what they need more of and less of in life. - I doubt it will ever be covered by insurance. In many cases, you could make an argument that it's indicated. As insurance begins to cover more of the population for pathologies, the things like FSAs or HSAs or care credit will likely cover this advanced testing, which it continues to come down and down in price.

02:19:41 Long-Term Relationships & Effects on Hormones

So it'll be affordable, but it won't be free. - Got it. Yeah. I'd like to shift gears slightly and

talk about social interactions and relational effects on hormones. Something that I just find fascinating. We touched on this a little bit earlier in terms of oral contraception, but now that we have the backdrop of what these various hormones do, some involvement in neurotransmitter systems like dopamine and prolactin and associated pathways. Prolactin of course being a hormone. Not a neurotransmitter. But there's a phenomenon in human beings where people get very excited about a new partner and that excitement no doubt is related to the dopamine system among other systems. And that excitement can be maintained or can wane over time. And here I'm talking about attraction, but I'm also talking about just general excitement in the sense of novelty, because that's what dopamine's associated with. Given that you work with human beings and they have lives and relationships and lifestyles, and they have hormones, and all these things interact, what are some of the ways that we could think about adjusting our relationships in order to optimize hormones as opposed to just thinking about how to optimize hormones for sake of our relationship? Because it's bidirectional of course. And this assumes, I should say, that one is already paying attention to the six pillars talked about earlier, that people are doing most things right. How should we think about relationships in hormones: friendships, romantic relationships, new partners, longterm partners, yeah, how do you think about this kind of stuff? - Yeah, so if you have a new partner, then it is largely regulated by the dopaminergic system, which changes over time. So people may have heard the saying that you have to go through a full calendar year with someone that you're in a relationship so that you- - Very good advice, by the way. - So that you really know what to do and what not to do. But because you experience both of your families in the holidays and all the different situations. But I would argue until you have moved in together, had a baby, and then raised that baby, preferably breastfeeding, because that's when you get the prolactin spikes, you haven't really gone through every stage in life yet. Now you can't really do that with every person that you're considering. - Well, some people do, but it can be quite costly in terms of time and finances and emotionally costly. - Yeah. - And then here, I'm definitely not referring to any personal experience of having done all that many times over, but what would you suggest people do or think about as they enter a relationship or for people that are in longterm relationships where they feel like something has shifted, and indeed those shifts may reflect the output of different hormone systems and neurotransmitter systems. It almost certainly has to be the case, right? - Yeah, so just like women who spend a lot of time together, whether they're coworkers or whatever, a lot of times their menstrual cycles will align. There is a

lot of pheromonal and hormonal crosstalk, including prolactin between men and women. So spending 100% of the time together, this is why people think it's so hard to work together and live together. They're around each other 24/7. You don't have the reprieve where you let that dopamine settle down, and then you're excited when you see them again. A lot of guys know that if they've gone on a hunting trip or if they've gone on a trip for a long time, they come back and they see their partner, and it's like a new, not quite like a new relationship, but almost like a new relationship. And they have that excitement again. And purposely building that into every relationship can help significantly, especially if you choose to have a child or get pregnant or be breastfeeding, because you just plan ahead for both of your prolactins to be high and both of your dopamines to be low. And both of your testosterone to be low. So there's a lot of planning that you can do. Essentially every relationship goes through a crisis. And that crisis is personal between the two of you. And you can plan ahead and figure out a way, maybe it's not supplementation. Maybe it's not even the amount of time you spend away from each other. But plan ahead to have good times if you know you're about to go into a crisis. - Got it, and so it sounds like time apart and time together, which is actually built into a number of cultures where men and women will purposefully avoid each other for some period of time, avoid physical touch and maybe in proximity, and then will reconvene, and yet those are very stable relationships over time often. Is the inverse also true? For instance, for people that are in long distance relationships, where they're only seeing each other three or four days a week or two days a week, does this explain the fact that some of those relationships can go on for a very long period of time without ever actually entering the, let's call it the hyper-prolactin phase of actually moving in together and et cetera, et cetera. Like in other words, is that a way in which people are spiking and troughing dopamine that keeps them attached? This kind of elusive, this sort of, what is it called? I think it's called like a cat string. Like if you play with a cat and you move the string away, they'll keep reaching, but you throw the string on the ground, they're like, they're totally uninterested in it. Is that what's going on? 'Cause that's a dopaminergic phenomenon, the cat string example. We know this experimentally. - In those cases, the relationship hasn't really progressed, in many of those cases, past the dopamine spike, the fun initial stage, honeymoon stage, whatever you want to call it. So it's almost kind of like a roommate. If you're looking for a roommate, if it was for college or after college or whatever, you can fill out forms and look for common interests, but until you're actually together

02:25:33 Nesting Instincts: Prolactin, Childbirth & Relationships

a significant proportion of the time, you're not really going to know if you're going to be compatible or not. - And is there evidence that the appearance of an infant changes, obviously there're going to be hormonal shifts. We know actually that for in both women and in men, there's a prolactin increase when couples are expecting a child. It's almost like a brooding phenomenon. You see this in birds where it's actually called brooding and it's caused by prolactin increase, but it turns out this also occurs in humans. And some people would argue this causes the dad bod phenomenon, 'cause it actually, prolactin is involved in laying down a body fat, preparing for sleepless nights. And presumably that spike in prolactin is there also to suppress sexual activity, because there are periods of time immediately near childbirth where sexual activity is not advantageous. - Yeah, you see a prolactin spike right after breastfeeding. So if you think about it, often when you have an infant, you'll breastfeed, put the infant to bed, and then immediately go to bed with your partner, which is not particularly conducive. It's almost like trying to have intercourse back to back. And it's very difficult. - Because of in the prolactin sense? - Yeah. - Yeah. - Low dopamine, high prolactin. Oxytocin is also increased significantly to help with milk let-down as well. So yeah, as far as brooding, there's definitely a human equivalent of brooding. Some humans call it nesting instinct, which is both helpful, but it's not necessarily a bad change in a relationship. It's just a change. And as long as you know that it's coming, you're going to do better with it. Just like any medication. If you are aware of the side effect and that it might happen, then when it happens, it's not only less severe, it also happens less often. - Very interesting. - If you tell the patient. - Well as a neuroscientist, I come from the framework that of course hormones impact perception and behavior, but perception and behavior also impact hormones. I find this fascinating. I also really like the example you gave of people taking time apart, but also these affiliative bonds that are non-romantic bonds can serve as kind of a reservoir to replenish dopamine that is then released upon experience going back to one's partner or some sort of regular feature of home. Very interesting, and of course this should exist on both sides. I'm guessing that from both the male side and female side, there's an interest in kind of separation and reunion as the theme. And I guess the frequency will vary for different couples and different situations. - Yeah, and I don't want to make it seem like prolactin is all bad, so prolactin does help with the

nesting instinct. It helps with breastfeeding as well. A lot of women are diagnosed with luteal phase defects, which is basically the phase after ovulation, but before a period or giving birth. A pregnancy's kind of a prolonged luteal phase. And a lot of them will go on progesterone for this. Progesterone can also decrease prolactin and prolactin is also helpful for the maturity of lungs in infants. So it helps the sphingomyelin to lecithin ratio. So if your prolactin's too low through pregnancy, it spikes up very high during pregnancy, then it can lead to increased risk of respiratory distress of the newborn. - Really interesting. Yeah. So we certainly don't want to paint a picture

02:29:05 Cold & Hot Exposure, Hormones & Fertility

where prolactin is the bad hormone to avoid. Without proactive, none of us would be here of course. It's so vital. I realized that earlier I raised the question about whether or not cold exposure could modify hormone output, in particular whether or not ice baths or ice applied to specific tissues of the body, as people are doing, one way or the other, can change testosterone levels, estrogen levels. In other words, does taking ice baths and cold showers increase testosterone and/or estrogen? - Yeah, so taking a ice bath or a cold shower or cold exposure in general, it's not going to correct a vitamin D deficiency or a metabolic syndrome. So there's a lot of things that it will not correct that are causes of hypogonadism or low testosterone, but it will help acutely, specifically the application of cold to testes that are too warm. So if you have a varicocele or if you have a little bit of a primary hypogonadism, which is where testosterone is not released by the testes, but your LH and FSH signals are sufficiently high, then you'll likely respond to cold exposure better. And there's actually undergarments that are designed specifically to help with fertility. And there's probably going to be more and more of that in the future. You just need to be careful not to get frost bite, because it's a particularly bad spot to get frost bite. - Noted. Could you define varicocele? You've mentioned it a few times. That's a varicose vein? - Yeah, so it's essentially a varicose vein. It brings warm blood and the venous flow or the flow back to the heart is not as good. Just like in the legs, it can happen in the scrotum. Usually about 20 to 25% of people have one grade of varicocele. There's grades one through four, one through five. And most people just have a very mild one, usually on the left side because the blood has to go through further to get back to the heart. And it raises the temperature of the testes. Temperature is the enemy of testes. So they like to be 5 to 10 degrees cooler than the rest of the body. - So are

saunas particularly bad for sperm production? - They can be, yeah. - When you say can be, I mean, how long could one safely be in the sauna, or would you want to go back and forth between the cold and sauna? Are there any data? - If someone is having infertility, then I tell them to avoid all saunas empirically. If someone has, if they're not infertile, but they have a low sperm count, I also tell them to avoid. However, it's mostly warmed water that can raise the temperature of the testes faster than the sauna. - So hot tubs and things of that sort? - Yeah, so hot tub and a jacuzzi. Those are enemies number one and number two of sperm. - What about ice baths and cold showers for women? Any evidence that it can shift hormone output in women? - Yeah, it can. It increases the activity of the beta adrenergic receptors, even in the central nervous system and the astrocytes as well. So it can do a few things. It can slightly decrease the drive for food, which astrocytes and beta adrenergic receptors have, some medications that are weight loss medicines also do similar things. But it can be beneficial in women too. - But no evidence that it changes estrogen output

02:32:34 Peptide Hormones: Insulin, Tesamorelin, Ghrelin

in women, correct? - Not that I know of. - No. Me either. Peptides, lot of discussion these days about peptides. Peptides of course just being strings of amino acids, as you mentioned the very small ones like two amino acids like L-carnitine all the way up to polypeptides, which just mean many amino acids. There's so many peptides that we should probably just do an entire episode about peptides, but I think one of the reasons I'm hearing so much about peptides these days is that they are not called steroids. The name steroids I think has come to be associated with anabolic steroids in the context of acne, testosterone rage, et cetera. But of course testosterone, excuse me, estrogen is a steroid hormone, right? There are other steroid hormones, as we both know. But peptides are gaining increasing popularity. I am willing to go on record saying that you can be sure that many of the incredible transformations that you see in Hollywood are the consequence of peptide use. And I'd put my name behind that because I'm well aware of people that use these to prepare for roles, but athletes use them. And then everyday people are using them too. For instance sermorelin, tesamorelin, ipamorelin, to stimulate the release of growth hormone rather than taking growth hormone. BPC-157, which is essentially a synthetic gastric juice that normally repairs the gut, being used to treat injuries. And there are other ones as well. What can we say generally about

peptides? Are they safe? Are they not safe? What about sourcing? And are there any peptides that you think could be of particular use for people? And we should probably also touch on peptides that people shouldn't go anywhere near with a 10-foot pole. - Yeah, definitely, so peptides are very heterogeneous. There's very dangerous ones and very safe ones. My favorite peptide is the original peptide, which is insulin. So insulin is a peptide and less than 100 years ago, there was a scientist studying insulin. And at some point, they saw that an animal had its diabetes cured by insulin inject, cured, by insulin injection. Less than a year later, they were injecting insulin into every type one diabetic, because it was saving their lives. - And yet insulin can kill you if you take it at the incorrect dose? - Yeah, so just like insulin should be prescribed by a doctor, there is over-the-counter insulin, ReliOn or NPH, but ideally your insulin is prescribed by your doctor for your diabetes, as it's lifesaving. Peptides should be prescribed by doctors as well. And there's several that are FDA approved. So you mentioned a lot of different ones. Let's start with tesamorelin. So tesamorelin was recently FDA approved for something called lipodystrophy. It happens where body fat is displaced into abnormal areas, often as part of aids or severe burns, things like that. And it helps redistribute this body fat and give people their quality of life back. Tesamorelin is a GHRH, which I kind of loop into the category of GHRPs, so growth hormone-releasing peptides. So it's only a couple amino acids different from endogenously-produced growth hormone-releasing hormone. So growth hormone itself is also a peptide. It's a peptide hormone. Not a steroid hormone. So you have different somatotrophs which are very similar to growth hormone. Another fun fact is that HPL, which is human placental lactogen, we love acronyms, right? Human placental lactogen is nearly identical to growth hormone. The growth hormone in pregnancy is not what causes the sugar spike in gestational diabetes. It's the human placental lactogen. So if you look at twin pregnancies, if they have two placentas or more placental tissue making more human placental lactogen, the risk of gestational diabetes is exponentially higher. So this HPL is only a couple molecules different from growth hormone. It is interesting that these different GHRHs and GHRPs actually have pretty different mechanisms of action. Ghrelin is also a hormone that's released when you're hungry. This is probably one of the reasons why you have more growth hormone release overnight. And there's a lot of peptides that are very similar to ghrelin, so these peptides are not bioidentical peptides, but they just have a couple different amino acids changed. So they're almost identical and they're probably going to be used in the future for growth hormone deficiencies,

02:37:24 Growth Hormone-Releasing Peptides (GHRPs)

including in kids, they've been studied. - So if somebody wants to increase their growth hormone output, in addition to not eating within two hours of sleep, getting good, deep sleep, doing all the other things in the six pillars that you mentioned earlier, especially resistance exercise at some point earlier in the day, what are the risks and benefits of taking a growth hormone-releasing hormone peptide like sermorelin prescribed by a doctor, of course. What should one be concerned about? How long could one take these? I've even heard that they can modify gene expression so that they really are changing your hypothalamus in very long lasting ways. - Yeah, there's definitely a lot of risk, tumor growth and cancer. So you look at a type one diabetic, they have very high incidences of various types of cancer. They have very high growth hormone, but low IGF-1 paradoxically. So they would likely give you a similar cancer risk to a type one diabetic that has very high growth hormone. However, the benefits of it, you think of lipolysis, decreased body fat, increased lean body mass. A lot of those, you can use other things to get those benefits. So then you don't need growth hormone for those benefits. It just leaves cosmetic benefit to which you can usually use topicals to get. Your hair and your skin and your nails, there's a lot of other things that you can do other than growth hormone. So a lot of people just don't need these GHRPs if they don't have lipodystrophy or if they don't have growth hormone deficiency. There is other uses of them, specifically in injuries. So I know that they've been studied, I'm not sure if it's in the military. We mentioned the woodpecker or the contrecoup injury. So that obviously. - The head jolting back and forth and the brain basically slamming up against the front of the skull. - So- - Football, heading the ball in soccer, definitely people who use the 50 caliber in military, although that's a fairly small population. And I think anyone that's hit their head hard

02:39:38 BPC-157 & Injury, Dosing Frequency

more than once. - Yeah, we can talk about BPC-157 for a bit, GHK-copper peptide for a bit. TB-500 or a thymosin beta-4 analog. And then we can also talk about bremelanotide, which is melanotan III. They have melanotan I and II, and then they also have melanotan III and IV. - Yeah, let's talk about BPC-157 and melanotan, 'cause I think those are the

ones that most people are eyeing, so to speak. - Yeah, so BPC-157 is body protective compound 157. It's identical or bio-identical to gastric protective compound 157 that's produced in the stomach. So as you age, you get atrophic gastritis very often. That's why you have less intrinsic factor, which is kind of another peptide that binds to vitamin B12. That's why you can get age-related B12 deficiencies. So that's one reason why you have more colitis, more or diverticulitis as you age. You don't have that gastric protective compound. It increases VEGF vascular endothelial growth factor, which basically makes your blood vessels grow more. So that's what causes your body to form a blood vessel. So another medication known as Avastin. It's on the WHO's list of essential medications for cancer. So many different types of cancer, including colon cancer, you treat it with Avastin, which is a VEGF inhibitor. So if you have cancer or a high cancer risk, you probably don't want to be taking a medication that's the exact opposite mechanism of action as your essential anti-cancer med. - In other words, if you have cancer, you're at risk of cancer, avoid BPC-157? - Correct, a lot of people prescribe it for six weeks and BPC-157, so bremelanotide, that is FDA approved for a hypoactive sexual disorder. Tesamorelin, that's also approved for lipodystrophy. Interestingly another one of the melanotans is also approved for lipodystrophy. And also deficiency in the melanocortin receptor. So the receptor that receives the alpha-melanocyte-stimulating hormone, it's a very rare condition. It's also approved for that, because if you don't take it, then you get obesity. But BPC-157 is not FDA approved, but it is essentially standard of care at this point. I would say it's, if you're not counting insulin or growth hormone as peptides, it's one of the most commonly used peptides and anecdotally, and in some clinical literature, it's fairly well tolerated for short periods of time. I'm not in the camp that everybody needs to do it two to three times a week or even daily for six weeks no matter what. The major benefit is when you're going to take it early on, because it's going to allow your body to increase blood flow to the injured area, and the less blood flow it has, for example, cartilage, ligaments have horrible blood flow, especially as people age, it's going to make a significant difference. So I would wager that that Russian gymnast that achilles healed in one month and completely from a full rupture was likely taking BPC-157 or something very similar. - Yeah, I'm willing to wager on that as well, a remarkable recovery. And so because it is prescription, there are non-prescription forms, my understanding of the non-prescription forms and the danger of going after non-prescription forms is that oftentimes they will contain what they claim they contain, BPC-157 in this case, but they are not adequately cleaning out the LPS, the

lipopolysaccharide which can cause inflammation. In fact, in the laboratory, we use LPS to deliberately induce fever and inflammation to study systemic inflammation. So this is a warning to people. If you're interested in peptides, you absolutely need to work with a physician, in my opinion. - Yeah. - Get it from a really good compounding pharmacy that cleans out the LPS. Because if you're buying it through a source that a lot of people, I don't want to name sources, but there are these common sources on the internet that everyone knows about. They're buying these sources, they'll ship it to anyone essentially. But then the LPS is really causing inflammation and many people experience a kind of mild fever or tingling from that when they inject it and they're like, oh, I can feel it working. That's probably LPS action, which is not good for the brain. I don't know about on other peripheral tissues. I haven't heard of people dropping dead from this stuff yet, but I certainly wouldn't want to be ingesting any LPs unnecessarily. So would you agree that you should work with a doctor? After all you are a doctor. - Yeah. Definitely talk to your doctor about this and talk to them about dosing regimen as well. So if they have you doing it for six weeks, ask 'em why am I doing it for six weeks? Why not two weeks or why not as soon as I feel better? Can I just stop it? Yeah, there's a lot of good questions like that that you should ask your doctor. And if somebody's trying to prescribe you a bunch of different things, then see, is this what they prescribe everybody or is this individualized for me? There are peptides like GHK-copper peptide which is produced endogenously in the liver more at younger ages. That's why the liver can regenerate fully, is this, the GHK-copper peptide helps. And if you're copper deficient, which not a whole lot of people are, but a lot of people that have had bariatric surgery are copper deficient, GHK-copper peptide can help significantly with your nervous system. And it's also synergistic. So any growth agonist like thymosin beta-4 made in kids in the thymus, which shrinks. That's another reason why kids heal really well. That and GHK is somewhat synergistic with BPC, but if you don't need all three, you don't want them. And if you don't need it for more than a week, you don't want it for more than a week. - I really appreciate you saying that. I often say that sometimes the best dose of something to take is zero.

02:45:23 Uses for Melanotan

It's often the case that the best dosage is zero. You mentioned melanotan. There are several kinds of melanotan. I find it a little bit of a funny conversation, because I first

learned about melanotan from reading about peptides and discovering that people were injecting melanotan to get tan, because it's in the melanin synthesis pathway. They also discovered, this isn't an individual. This is reading about this in various manuscripts and peer-reviewed papers that it could cause things like priapism, like sustained erection, that might be the last one that anyone would ever have because of damage to the vasculature. Also women taking melanotan as a way to get tan and lose body fat. So this sounds all very recreational. Are there any clinical usage of melanotan? So separate from the kind of extreme biohacking cosmetic world, which is really not the main focus of this podcast ever, more in terms of health, pursuing health optimization. - Yeah, there's actually three FDA approved indications, believe it or not. Not many people know about this, but there's three well accepted indications. One of them is the hypoactive sexual disorder, and more in women, that's for bremelanotide. - So- - Those are women that have essentially no libido whatsoever? - Yeah. - But other hormones are in check? Yeah, classically it's before menopause. So those hormonal issues are not contributing. And when you give them this peptide, it's also known as PT-141, it helps significantly. A lot of times you use it in nasal spray. It goes straight into the central nervous system and acts centrally. You can also inject it, and you can also take it via troche. - Men and women take it? - Correct. It's approved for women. But it can also help men. And it's relatively safe. The only relative contraindication that I tell people and a lot of people say, oh, there's no side effects that I know of. But if you have a family history of melanoma or potentially have a melanoma and don't know about it, that's why I'm a big advocate of dermoscopy as well on regular skin checks, then theoretically it's going to increase that alpha-melanocyte-stimulating hormone, and it can grow that. So that's definitely not a good a thing. So be very careful about longterm administration of it. It's also approved for lipodystrophy, which is the same exact thing as tesamorelin, which I believe is also known as Evista or Egrifta. And then it's also approved for the rare genetic condition where your receptors or your melanocytes don't proliferate as well, so you usually have hypopigmentation. It's not true albinism, but it's associated with morbid obesity and very be poor outcomes from that in childhood, so it's used in kids actually. - Interesting, well, peptides are a fascinating landscape, but thank you for that deep dive into several of them. We will probably return to you to talk about peptides again in the near future,

02:48:21 Spiritual Health Impact on Mental & Physical Health

because I know there's a lot more there. And a lot of interest. I want to talk about the sixth pillar, all right? So just to remind people, you said diet, exercise, where appropriate, caloric restriction, managing stress, sleep and sunlight are critical for everyone at all ages to manage and optimize hormone health. Then you have the sixth category, which is a really intriguing one, which is spirit. Which is kind of unusual thing to hear coming from a medical doctor, except that I have many colleagues and indeed our former director of the National Institutes of Health, Francis Collins has talked about this notion of spirit. We've talked about belief effects on this podcast before with Alia Crum, how one's understanding of the things that they do and their world in general really creates an important effect on everything at the level of physiology, not just psychology. So as a physician, how do you conceptualize this spiritual aspect? And how do you talk to patients about this, given that people walking into your clinic presumably have a bunch of different religious and not a religious backgrounds. I'm sure some are atheists. Some are probably strong believers. How do you deal with that? And how should people think about this? - Yeah, I believe it is surprisingly well received. You wouldn't think at first glance that a patient really wants to talk about their spiritual health with their doctor, but the way I think about it and the way that it really is is it's like a Venn diagram and you have a body and a mind and a soul. And you can't have one healthy without the other healthy, even if your mental health is phenomenal, and even if your physical health is phenomenal, the mental aspect of spirituality, if that piece is not there, then that's going to affect your body physiologically as well. And Alia Crum's done some excellent work. There's also been a lot of other studies regarding prayer. And I'm a Christian, I believe in God. And that gives me a lot of that resilience and motivation. It gives me the cornerstone or the groundwork, how I can interact with life. And regardless if someone's an atheist or regardless of what someone believes as far as religion or the origin of the species, they can know that their spirituality is going to have a profound effect on their mental and physical health as well. People like to compartmentalize it. So they like to talk to their doctor only about the physical health 'cause it's comfortable to do that. They only talk to their pastor or a mom or reiki healer for their spiritual health. And they just talk to their therapist or psychiatrist about their mental health. But you need to bring all three of those things together. It's well known that interdisciplinary clinics lead to improved patient outcomes and that's just disciplines within medicine. So that's just doctors that are specializing in this or this. So this takes a step back in the upper part of that tree before you've reached those dichotomies or the split-offs. You have your body

and your mind and your soul, so your spiritual health and your mental health and your physical health. So if you're in line in all three of those things, that builds the cornerstone for the rest of your health and the rest of your life. - So if someone comes into your clinic and they say, they're feeling one way in their body, they're feeling one way in their emotional life, you run their charts, you get their blood work, and they're an atheist or they're agnostic, what are some of the sixth pillar practices that they can consider that are in keeping with their atheism or agnosticism? Because I have to assume that people who are in participate or feel that they belong to a particular religious sex will have particular prescriptives from those religious sex that will direct them towards particular types of prayer. But how would somebody who doesn't have a prescriptive coming to them from some other source, what could they do or would they do? - Yeah, so I certainly don't force prayer on anybody or anything like that. But it's my belief that being, especially being an agnostic, it's almost the hardest thing, because if you're an atheist, then you have some groundwork and you have some spirituality, even if it has to do with the human spirits' interaction with the environment, things that can't be physically explained well, phenomenon like the work that Alia Crum does. But if you're agnostic, you're still trying to find that. So I hope that everybody does find what they truly believe in as far as their own spirituality. But yeah, that's a personal journey. From a physician's standpoint, and even if I'm friends with them as well from a friend's standpoint, I don't like to push anybody in any specific direction. So I don't think that everybody should believe what I believe. And I don't feel like there should be any pressure for them to believe something different. So I think that there can be excellent physician-patient rapport, regardless of what we believe and what our backgrounds are. - Yeah. That's wonderful to hear. I can say without revealing any names that I have close colleagues that, in every bin of this spectrum, like hardcore atheists, hardcore religious in different domains, different religions, I don't know, I don't know if I know many agnostic, as to whether or not I know any agnostics, I should say. It's not something that people commonly discuss, but in the context of science and medicine, but it's starting to happen more and more. And certainly this issue of spirituality is one of the areas in which neuroscience is asking a lot of questions. Like what spiritual experiences really are in terms of how they're grounded in the brain or not grounded in the brain. I think it's a really interesting area for discovery. And I appreciate that you bring it up, and you bring it up in the non-pressured way that you do.

02:54:18 Caffeine & Hormones

I think that it will stimulate a lot of thinking, which is ultimately the goal of this podcast. Well, I have one final question that a listener insisted I ask, and it's a very straightforward one. It's not at all a curve ball and not at all related to what we were just talking about. But it was the most common question when I told people that I was going to be talking to you, which is, is caffeine problematic for hormones? It's amazing, I received hundreds of the same question about caffeine. And since it's probably the most commonly used drug on the planet, I know it's taking us back into the very practical, but in closing, we're not quite there yet, but in closing is caffeine having an effect, one way or the other, on testosterone, estrogen, or other hormones that is positive, negative or neutral? - Only if it affects your sleep. So it works on adenosine and it can actually slightly improve allergies as well, but negligible effects otherwise. - Great. - Yep. - Well, sorry to end on such a practical brass tacks type of question, but I did promise to the listeners that I would ask that question. Listen, I want to sincerely thank you. We covered basically an endocrinology textbook, a neuroendocrinology textbook's worth of information, a ton of practical tips in there. Where can people find out more about you? We will certainly provide links. And I guess the other question is, are you taking patients? I'm sure you'll hear that in the various venues where people can contact you. But where are you active in terms of public facing work? - I'm active on Instagram, kylegillettmd. I'm also active on the social medias of my brand new clinic, which is Gillett Health. That's @GillettHealth on Instagram or GillettHealth.com. - Great. We'll provide links to those. And I should say that the content you've been putting out on Instagram is terrific because you actually pointed to specific studies and you put things into actionable context, which is very meaningful for me. Kyle, Dr. Gillett, I should say, thanks so much for your time.

02:56:19 Neural Network Newsletter, Zero-Cost Support, YouTube Feedback, Spotify Review, Apple Reviews, Sponsors, Patreon, Thorne, Instagram, Twitter, Brain-Body Contract

I really appreciate it and I know the listeners will too. - Thank you. My pleasure. - Thank you for joining me for my discussion about hormone health and optimization with Dr. Kyle Gillett. As you just heard, he is a treasure trove of actionable clear information. And again, you can find him teaching more about hormones and other aspects of health on

Instagram @kylegillett, that's Gillett with two T's and two L's, but no E, kylegillettmd on Instagram and Gillett Health on all other platforms. And if you would like more information about his practice, you can find that at gilletthealth.com. If you're learning from and/or enjoying this podcast, please subscribe to us on YouTube. That's a terrific zero cost way to support the podcast. In addition, please subscribe to the podcast on Spotify and Apple. And on Apple, you have the opportunity to leave us up to a five star review. If you have questions or comments about this, or any episode of the Huberman Lab Podcast, or if you'd like to suggest topics that you'd like us to cover or guests that you would like me to talk to, please put that in the comment section on YouTube. In addition, please check out the sponsors mentioned at the beginning of today's episode. That is the best way to support the podcast. We also have a Patreon. It's patreon.com/andrewhuberman. And there you can support the podcast at any level that you like. During today's episode and on many previous episodes of the Huberman Lab Podcast, we discuss supplements. While supplements certainly aren't necessary for everybody, many people derive tremendous benefit from them for things like optimizing sleep and focus, and indeed hormone health. Anytime you're considering taking a supplement, you want to make sure that the supplements are of the very highest quality. For that reason, we've partnered with Thorne, T-H-O-R-N-E because Thorne supplements are known to have the highest levels of stringency in terms of the quality of their ingredients and precision about the amounts of the ingredients that they put in each bottle. Meaning what is listed on the packaging is actually what's contained in those supplements, which is not true for many supplement companies out there. If you'd like to see the Thorne supplements that I take, you can go to Thorne, that thorne.com/u/huberman, and you can get 20% off any of those supplements. Also if you navigate deeper into the Thorne site, so go to thorne.com/u/huberman, but then pass into thorne.com, you can also get 20% off any of the other supplements in the Thorne catalog. If you're not already following us on Instagram and Twitter, please do so. It's Huberman Lab on both Instagram and Twitter. And there I cover science and science-based tools, some of which overlap with the contents of the Huberman Lab Podcast, but much of which is distinct from the contents of the Huberman Lab Podcast. And again, we are hosting two live events. One in Seattle on May 17th. Another in Portland on May 18th. That series is called "The Brain Body Contract" where I'll talk about science and science-based tools, some of which I have never about in a public forum before. And there will be an open question and answer format for you to ask me your questions, and

I will do my best to answer them in real time. Thank you once again for joining me for today's discussion with Dr. Kyle Gillett. And as always, thank you for your interest in science. [energetic music]