

Huberman Lab #15 - The Science of How to Optimize Testosterone & Estrogen

Published - April 12, 2021

Transcribed by - thepodtranscripts.com

Introduction

Welcome to the Huberman Lab podcast where we discuss science and science-based tools for everyday life. I'm Andrew Huberman and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. This podcast is separate from my teaching and research roles at Stanford. It is, however, part of my desire and effort to bring zero cost to consumer information about science and science-related tools to the general public.

Before we begin today, I just want to acknowledge that if you're watching this on YouTube - yes, I have a bandage on the left side of my face. I was trying to cook something for Costello and I - and I got burned - burned myself. It was a cooking accident. I'm fine. No need to dwell on it. We can move on. But I just wanted to let you know everybody's going to be okay. He got a great meal. I got a burn and a great meal.

Today's episode is brought to us by Four Sigmatic. Four Sigmatic is a wellness company that makes mushroom coffee. For those of you that haven't heard of mushroom coffee before, I just want to make clear these are not psychedelic mushrooms. And no, the coffee does not taste like mushrooms at all. It tastes amazing and it tastes like coffee. I started using Four Sigmatic coffee a few years ago. And then, we actually stocked it in my lab. We still stock it in my lab because it tastes really good. And it also happens to have two types of mushrooms in it that I particularly like because of their supplement and medicinal qualities. And those two are lion's mane mushroom, which has been shown in several research studies to have a mild anxiolytic - meaning anti-anxiety effect and mood elevating effect. Those are from research studies done independently. As well, it has chaga mushroom. Chaga mushroom has been shown to increase growth factors that impact the nervous system like nerve growth factor. So, that's the reason I drink it, and that's the reason we stock it in the lab, and that's the reason why I drink it at home. If you'd like to try Four Sigmatic, you can go to foursigmatic.com/huberman - that's F-O-U-R-S-I-G-M-A-T-I-C.com/huberman. And you'll get up to 40% off your order plus free shipping on their mushroom coffees. That's foursigmatic.com/huberman for up to 40% off and free shipping.

Today's episode is also brought to us by Blinkist. Blinkist is an app that has thousands of non-fiction books condensed down to just 15 minutes of key takeaways that you can read or listen to. For me, I really like listening to books on Blinkist - even books that I've already read. Typically, the way I consume information is - unless it's fiction, I'll listen to a non-fiction book or I'll read the actual physical hard copy of a non-fiction book. And then at the end, I like to take some notes about things that really stuck with me or key takeaways that I'd like to teach or share with other people. With Blinkist, it allows me to go back to those books and get all the essential items - some of which I might have missed in the course of listening to or reading the full-length version. And if I haven't read a book before, it also gives me a sense of whether or not I'd like to read the book. Blinkist has some terrific science-category books. For example, my colleague and friend David Eagleman's book, "Live Wired" - which came out recently - is all about neuroplasticity. It's a fantastic book. I read the full-length book. And I've listened to it on Blinkist and it's a terrific synopsis of "Live Wired". That's in there. David Sinclair's book, "Lifespan". Many of you probably know that David Sinclair, professor of genetics at Harvard Medical School - is a real pioneer in the aging and longevity field.

His book, "Lifespan" is terrific. I've read the full-length book. I've listened to it. And I've listened to it on Blinkist. And so, it really captures a lot of the essential elements that you would want to get from that book. Blinkist is also just a great way to get through many books on the bookshelf that you've been meaning to get to, but you haven't had time. With Blinkist, you can get unlimited access to read or to listen to a massive library books, not just science books. And they're all condensed in this way of - just 15 minutes will allow you to get all the key information. So right now, for a limited time, Blinkist has a special offer just for Huberman Lab podcast audiences. You go to blinkist.com/huberman and you can try Blinkist free for 7 days and save 25% off your new subscription. That's Blinkist - B-L-I-N-K-I-S-T.com/huberman to start your free 7-day trial and you'll get 20% off, but only when you sign up at blinkist.com/huberman.

Today's episode is also brought to us by Theragun. Theragun is a handheld percussive therapy device that releases deep-muscle tension. I was introduced to Theragun on a dive expedition for my laboratory a few years ago. On that expedition, we were working very hard. We were diving all day. We were carrying pelican cases with equipment. We were carrying tanks - very sore - very tired by the end of the day - as was everybody else. Someone brought along a Theragun and pretty soon that thing was getting passed around and became the most coveted device on board because it really works to relieve the soreness and deep-muscle tension that accumulates with physical work, exercise - even just sitting too long throughout the day. So when I got back, I got a Theragun. I still use the Theragun daily. It's terrific because it's very quiet, so you can use it while watching a movie or even while having a conversation without it feeling intrusive. It really gets down into the meat of the muscle if you want or you can use it more superficially if you'd like. If you want to try Theragun, you can go to theragun.com/huberman. They have several models available. The first one starts at \$190, which, if you think about it, is comparable to the price of a professional massage - except that unlike a professional massage, you can use the Theragun for as long as you want throughout the day and for as many days as you'd like. That's theragun.com/huberman and I should mention that there's also a 30-day money-back guarantee. So, if you don't like the product, you send it back. You get your money back.

This month on the Huberman Lab podcast, we're talking all about hormones. These incredible chemicals that can impact our mood, our behavior, our feelings of optimism or pessimism. The amazing thing about hormones is that hormones impact all those things. But all those things - how we feel, and what we do, and what we think also can impact our hormones. So, it's a really fascinating area of biology that impacts every single one of us every day - both in wakefulness, and in sleep, and throughout the lifespan.

Today, we're going to be talking about hormone optimization. And we're mainly going to be focusing on estrogen, and testosterone, and their derivatives. Last episode of the Huberman Lab podcast, we talked about sexual development - that is how the chromosomes, the gonads, and hormones impact what we call sexual development - leading all the way up to puberty. Today, we're mainly going to talk about processes that happen from puberty onward - although, we might talk a little bit about development as well. So today, we're going to talk a lot about basic biology, but we're going to

weave in a lot of practical tools along the way for how to optimize these incredibly powerful things that we call hormones.

Salutogenesis

Before we dive into our discussion about hormone optimization, I want to raise what I think is a very important point that at least I hadn't heard of until recently - which is the concept of salutogenesis. Many of us are familiar with the concept of pathogenesis - the idea that there are all these scary diseases like dementia, and heart disease, and stroke and all these things that await us if we don't take good care of ourselves and that might await us even if we do. That's the pathogenic model. Salutogenesis is something I learned about from one of my Stanford medicine colleagues, which is a different orientation toward health and well-being where you're taking on particular behaviors - you're taking on a particular stance towards nutrition, and exercise, supplementation, etc. in order to promote well-being above where you would be if you were not doing those behaviors. If you think about these two things - salutogenesis and the pathogenic model - are really two sides of the same coin.

But I'll just give an example of how this might affect you in a real way. If you like exercise because it feels good, great. But many people exercise or eat well for that matter in order to avoid heart disease or to avoid dementia - to avoid - you know - negative changes in body composition. And while that's powerful - and it certainly is the case that exercise will help you move away from all those things - the salutogenesis model differs in that it involves a mindset and an orientation towards doing those things in order to feel good - in order to enhance your level of energy - in order to improve endocrine function and metabolic function. So, it's really part of the pathogenic model. And yet, salutogenesis is really more of a mindset toward why you would do these particular behaviors. And really, the most powerful mindset is going to be one where you are thinking about the pathogenic model - doing things so that you don't end up sick, etc. - and to move away from sickness - as well as the salutogenic model where you're doing things in order to move towards health and well-being. We think of health and wellness nowadays, or the wellness community, or wellness practices - and in many ways, that is the essence of the salutogenic model. But I found it very interesting to know that within the field of allopathic medicine, these two models exist, but we don't hear about the salutogenic model quite as often.

So, it's just something to keep in mind - especially because of some of the mindset effects that were discussed in previous episodes. I'm not going to go into these in detail again right now, but if you might recall from the episode on food and mood, we talked about some of these incredible studies that were done by a Alia Crum's group at Stanford and others - showing that if you tell people that the behavior that they're about to do - in this case, it was people cleaning up hotel rooms because that was their job - if you tell them that it's good for them, then you see much greater positive health effects than if they aren't aware of that information - that it's good for them. So, we should really be thinking about not just moving away from disease and negative things, but also why certain things are good for us because it's well established now from really good scientific

studies that keeping in mind the positive effects of things can really have an outsized effect on well-being - right down to the level - level of our physiology.

Estrogen & Testosterone

So, let's talk about hormone optimization. Today we're going to talk about hormone optimization in reference to estrogen, and testosterone, and their derivatives. Now estrogen, and testosterone, and their derivatives are what we call sex steroids. Now the sex steroids immediately call to mind sex - for obvious reasons - and steroids, meaning anabolic steroids. But I just want to emphasize that estrogen and testosterone are present in everybody. It's their ratios that determine their effects. So, today we're going to talk about how you can optimize their ratios depending on your particular life goals because the ratio of estrogen and testosterone in every individual has profound influence on feelings of well-being, feelings of optimism, feelings of anxiety or lack of anxiety, on reproduction, on sexual behavior independent of reproduction. They are profoundly powerful molecules and we all make these molecules to some degree or another, but there are also important behavioral tools, supplementation tools - as well as prescription drugs that can impact ratios of testosterone and estrogen in really powerful ways. So, we're going to cover all of that. I want to emphasize that when you hear sex steroids or steroid hormones, most people think about anabolic steroids. And of course, anabolic steroids are derivatives of testosterone or testosterone itself and they are heavily used and abused in the sports community - as well as outside the sports community. But there, of course, are many steroids that are not anabolic steroids that are also abused in sports. Today we're not talking about drugs in sports, but I think that it carries such a heavy weight. When people hear the word "steroids," they think about anabolic steroids. So, while today's discussion will certainly be relevant to physical performance. In fact, we're going to talk about how specific types of exercise, particular patterns of cold exposure, as well as particular patterns - believe it or not - of breathing can impact sex steroid hormones - both estrogen and testosterone. The discussion isn't really geared towards performance enhancement in sport - although, we will do an entire episode - perhaps even an entire month related to performance enhancement in physical enterprises.

So, one of the first things to understand if you want to optimize your hormones is where they come from. There are a lot of different glands in the body that produce hormones. There's the pineal gland. Some hormones are made in the hypothalamus. Hormones are made by the gonads - the ovaries or the testes. You've got the thyroid gland. There are a bunch of different glands that make these different hormones, but when we're talking about the sex steroid hormones, estrogen and testosterone, the major sources are ovaries for estrogen and the testes for testosterone - although, the adrenals can also make testosterone. Now, there are also some enzymes. Enzymes are things that can change chemical composition. And the enzymes that we're going to talk about today are the aromatases, mainly. The aromatases convert testosterone into estrogen. So in a male, for instance, that has very high testosterone, some of that is going to be converted into estrogen by aromatase. And aromatase is made by body fat. It's also made in the testes themselves. A lot of people don't realize this, but the testes actually have the capacity to manufacture estrogen and

aromatase - albeit, at low levels. But this turns out to be important for optimizing hormone levels in males at later points. And we'll discuss that.

It's important to note that there's a huge range in terms of the levels of hormones, testosterone and estrogen, between individuals. And it actually occurs within individuals across the lifespan. I'm not going to throw out specific numbers of X picograms per deciliter, etc. - today - because that's going to vary a lot. It's going to depend on whether or not you're measuring in picograms or nanograms and that sort of thing. If you want to examine your hormones, you should do that in conjunction with a medical doctor. Ideally an endocrinologist can help you sort out that information.

But the important thing to note is that prepubescent females make very little estrogen. And when we talk about estrogen, we mainly talk about estradiol - which is the most active form of estrogen in both males and females. So prepubescent females, very low levels of estrogen. During puberty, levels of estrogen - a.k.a. estradiol - basically skyrocket. And then across the lifespan, estrogen is going to vary depending on the stage of the menstrual cycle. But as one heads into menopause - which typically takes place, nowadays, somewhere between age 45 and 60. Levels of estrogen are going to drop. And then postmenopause, levels of estrogen are very low.

As well, testosterone will fluctuate across the lifespan. Testosterone is going to be relatively low prepuberty - prepuberty in males. During puberty, it's going to skyrocket. And then, the current numbers are that it drops off at about a rate of 1% per year - although, we're going to talk about some data that show that there's actually tremendous variation in testosterone levels. There's actually a lot of examples of men in their 90s - their 90's - who still have testosterone levels that mimic puberty levels - which is remarkable and speaks to the huge variation in testosterone levels across individuals.

So, let's talk about other sources of these hormones. And then, it will make clear what avenues you might want to take in order to optimize these hormones. The other glands and tissues in the body that make these hormones - testosterone and estrogen - as I mentioned briefly - are the adrenals. So, the adrenals ride up top the kidneys. And the release of these steroid hormones from the adrenals - in particular, testosterone and some of its related derivatives - are mainly activated by competition.

Competition / Foraging-Type Behaviors

So, let's talk about competition because it turns out that competition is a powerful influence on the sex steroid hormones, and the sex steroid hormones powerfully influence competition. So, most people don't realize this, but most males of a given mammalian species never get to reproduce. In fact, they never even get to have sex at all. And we don't often think about that, but testosterone plays a powerful role in determining which members of a given species will get to reproduce - which ones of that species will actually get access to females. And so, here I'm not talking about humans, specifically, but it's well known in species like elephant seals, in species like antlered animals, and rams, for instance - that the higher levels of testosterone correlate with access to females. Now, one interpretation of this is that the females are detecting which males have high testosterone and selecting them. They're more receptive to them. We're going to talk about receptivity for mating in a moment. But it's actually more so that the males that have higher

testosterone forage further and will fight harder for the females. And this is really interesting because there's very good evidence now that testosterone can reduce anxiety, promote novelty-seeking, and promote competitive interactions. And so, before you leap too far with this in your mind and think about all these human behaviors, just stay with me because there's a little bit of biology here that makes it all make sense and it turns out to be pretty simple.

We have a brain region called the amygdala. In Latin, that just means "almond". But the amygdala is most famous for its role in fear. We hear a lot about fear and the amygdala. But the amygdala is really involved in threat detection. It sets our thresholds for anxiety and what we consider scary or too much. Testosterone, secreted from the gonads and elsewhere in the body, binds to the amygdala and changes the threshold for stress.

So, I've said before on previous versions of this podcast and on other podcasts that testosterone has this incredible effect of making effort feel good. But what I was really referring to is the fact that testosterone lowers stress and anxiety - in particular, in males of a given species. Now, this is important because we often think of testosterone as creating - whatever - masculinization or it's - you know - virilization - or all these - these terms are thrown around. But what it's really doing when it comes to mate choice and competition? What it's doing is it's reducing the threshold for anxiety. And in doing so, it selects individuals of a given species to push further - being willing to - you know - suffer more - although, it also reduces pain - so, maybe they also suffer less - in pursuit of reproduction in females.

Now, it's well known in humans that both males and females who have elevated levels of testosterone will engage in more novelty-seeking. And I do want to point out that even individuals without testes have testosterone. And peaks in testosterone have similar effects regardless of whether or not someone has ovaries or testes. Testosterone increases generally lead to more foraging, more novelty-seeking, increases in libido, and increases in desire to mate.

So, it is the case that increases in testosterone promote competitive and foraging-type behaviors in - in humans and in nonhuman mammals. But it's also true that competition itself can increase androgens such as testosterone. I want to repeat that. Competitive environments themselves can increase testosterone. Now, some people have come to the conclusion that if you win, your testosterone goes up. And if you lose, your testosterone goes down. And to some extent, that's true. But that's not a direct effect on the gonads. That's actually mediated by the neuromodulator dopamine. We talked about dopamine in the episode on motivation and drive. And dopamine and testosterone have a remarkable interplay in the body. Dopamine is actually released in the brain in ways that has the pituitary - this gland that sits over the roof of your mouth - release certain hormones that then go on to promote the release of more testosterone. And indeed, winning promotes more dopamine and later, more testosterone. However, in the short term, just competing increases testosterone - independent of whether or not you win or lose. So, the short version of this is that competition increases testosterone.

And this may be an ancient mechanism whereby the androgens such as testosterone are feeding back to encourage more competitive-type behaviors. Because every species - whether or not you're talking about reproduction or other resource allocation - is involved in competition. Not every individual of a species gets access to the same number of mates or the same quality of mates. And this is true in both directions for males, and females, and everything in between.

Mate-Seeking Behavior

So, I just want to emphasize once more - in case I went through it too quickly - that increases in testosterone in females are also going to lead to increase in reproductive behavior or seeking out reproductive behavior. They increase libido. In fact, there's a particular phase of the menstrual cycle where testosterone peaks just before ovulation that, on average, leads female humans to seek out sex more than they would otherwise during their cycle. And this is all by self-report, but this is also while measuring things like testosterone, estrogen ratios, and so forth. So, it's really interesting that a single molecule - regardless of chromosomal or gonadal background - is increasing seeking of mates across individuals, increasing desire to compete or willingness to compete, and lowering the threshold for stress and anxiety.

It's important to point out that while increases in testosterone promote seeking of mates and reproduction in both males and females, in females, it's actually increases in estrogen that promote receptivity to mating. So, testosterone is driving the seeking of sex and estrogen is promoting the actual act of sex from females - so-called receptivity - consensual receptivity. In males, it's interesting to point out that testosterone is promoting seeking of sex, but it's also estrogen in males that's important for libido. If estrogen levels are brought too low, then men will completely lose their libido. This is often not discussed or overlooked in the discussion about testosterone therapy and performance-enhancing drugs. People think that hyperandrogenized individuals - meaning people that have very high levels of androgen - will have very high levels of libido. And they will provided estrogen is available in sufficient ratios to match that testosterone. So, it's not simply the case that high levels of testosterone produce a lot of sex and mating behavior and low levels of estrogen are good across the board. You actually need both in both males and females. It's just that in females, the testosterone levels are always going to be lower than the estrogen levels. And in males, the estrogen levels are always going to be lower than testosterone levels.

So, testosterone promotes sex-seeking behavior and the real question then is: Does sex itself promote testosterone? And the answer is somewhat complicated, but the short version is: Yes. And as you recall, sex has multiple stages. So, there's the physical act of sex. There's the seeking of sex. And then, there's orgasm and ejaculation. Now, it's important to distinguish between these because whether or not sex itself increases testosterone depends on whether or not the male ejaculates. And this is very important to understand because on a previous episode, I mentioned how dopamine increases with sexual activity. Remember, dopamine and testosterone tend to increase linearly with one another. But then after ejaculation, there's a release of prolactin and prolactin actually sets the refractory period in males during which he can't have sex again. And the duration of the refractory period will vary tremendously depending on how much and how long that prolactin

release occurs. I also described in a previous episode how some people take vitamin B6 - I'm not suggesting anyone do this - but take vitamin B6 in order to reduce prolactin levels and thereby reduce the duration of the refractory period.

Observation of Sex / Sex / Abstinence Increases Testosterone

But getting at this question about testosterone and sexual behavior, it's important to distinguish between these different phases of reproduction or reproductive behaviors. So, there are studies showing that sexual behavior itself can increase testosterone. There was a study published in 2011 from Escasa et al. - E-S-C-A-S-A. This is the stuff of textbooks. This is on PubMed. These are quality studies showing that men who observe sex - so, I guess this would be observing pornography - will have slight increases in testosterone during the observation. These people actually were willing to have blood draws taken while watching pornography. They had increases in testosterone that were very modest - of about 10% - whereas when people participated in sex - they actually did this study where people had blood draws and they had real sex with their partners - and they had 70% increases in testosterone. So, there are increases in testosterone that are quite significant during the physical act of sex and far less so during observing sex.

Now, the question that I often get - in fact, is one of the questions I get most often in the comments on YouTube - I don't know why that is - is whether or not ejaculation adjusts testosterone levels. And it turns out, there are two studies that I could find that were quality studies on PubMed that addressed this - that sex and ejaculation itself does not reduce testosterone levels - although, it will increase prolactin levels for the reasons I described a moment ago. However, abstinence or sex without ejaculation for a week or more will increase testosterone levels up to 400%. So, the answer is actually complicated. It's not straightforward. What it means is that sex itself increases testosterone. However, abstinence also increases testosterone even further. So, it's a nuanced answer. And I hope this is satisfactory - no pun intended - to those of you that have been asking me, "What is the relationship between sex and ejaculation and testosterone and dopamine?" It is nuanced. And you have to understand that nuance if you want to understand how certain behaviors impact hormones and how hormones impact those behaviors.

As I mentioned before, in females, testosterone also primes the motivation to seek out sex. And sex itself also increases testosterone. But it also increases prolactin. So, in both men and women, sex increases prolactin post-sex. It's just the way that the system works. It's that testosterone and dopamine increase in the seeking out and the behavior of sex. And then after sex, prolactin levels go up. There's kind of a quiescence. The whole nervous system is promoted towards calm. And this may actually have something to do with pair bonding and the encouragement of individuals to spend more time together to exchange different smells, and hormones, and maybe even pheromones. We're going to talk about pheromones in a moment.

DHEA

A few years ago, there was a lot of excitement about the hormone DHEA - which is mainly made by the adrenals. DHEA has been promoted as kind of a catch-all for increasing testosterone and

estrogen in males and females. And indeed, DHEA will increase both testosterone and estrogen. This is something to be mindful of if you're thinking about taking DHEA or you're taking DHEA already. DHEA will increase both testosterone and estrogen. And the extent to which it increases one or the other will depend on whether or not you're starting off with more estrogen than testosterone, or whether or not you're starting off with more testosterone than estrogen, and whether or not you have a lot of aromatase. So for individuals that have a lot of aromatase being made by the testes or body fat, if you take DHEA, there's a good chance that a fair portion of that is going to be shuttled towards estrogen production and not towards testosterone production. Whereas in individuals that have low levels of testosterone to begin with - high levels of estrogen - there's a good chance that the DHEA is going to promote mainly estrogen production. At least that's what I could find from the research studies that I examined. So, the way to think about DHEA - it's a - kind of - global promoter of the sex steroid hormones and its specific effects are going to depend a little bit on where you started and whether or not you have ovaries or testes.

Behaviors That Decrease Testosterone

So just as there are behaviors that can increase testosterone, there are behaviors that can decrease testosterone. And one of the most well-characterized ones in humans is becoming a parent. So, expecting fathers have an almost 50% decrease in testosterone levels - both free and bound testosterone. As well, their cortisol levels - a stress hormone - dropped by almost threefold - which is incredible. And their estradiol levels double. So, their estrogen levels double. So, expecting fathers - many people have known put on additional body weight. Everyone always thought that it's because they're eating in parallel with their pregnant wife. But it turns out that these effects of reduced testosterone, increased estradiol, and reduced cortisol can all be explained by an increase in prolactin. So not just in humans, but in other species as well - when the male and female of that species are expecting young, they lay down more body fat. The assumption is that this is to prepare for long nights of no sleep - which occurs in many species, not just in humans. So, it's really interesting that this hormone prolactin can start suppressing whole categories of hormones - sex steroid hormones - and can start increasing whole categories of other ones. So, we hear about the "dad bod". There are a lot of explanations for the "dad bod" that extend well beyond this podcast episode. But it is a well-known phenomenon that testosterone is going to drop. Prolactin is going to increase. Estradiol is going to increase in males and females that are expecting children.

Now, how long that lasts is very interesting. It actually has to do with how much contact and how much contact with the smells of the baby - of the offspring - the father happens to have. So, how available or unavailable he is will actually impact his level of hormones. Now, I am definitely not promoting the idea that fathers or mothers take time away from their offspring in order to keep their testosterone levels higher - to restore them. It's not what I'm saying at all. It's just interesting to point out that these evolutionary mechanisms push us toward or bias us toward particular categories of behaviors by influencing our hormones - which then feed back and promote more of that particular behavior. Because as I mentioned before, peaks in testosterone in males and females cause individuals to seek sex, not promote parenting. Whereas reductions in testosterone,

increases in prolactin, and decreases in cortisol move individuals of both sexes toward parenting behavior and less toward reproductive behavior.

Illness / Increased Levels of IL-6

The other behavior that markedly reduces testosterone in both males and females and markedly reduces the desire for seeking sex and sex itself is illness. And many of you might say, "Well, duh. When people don't feel sick, they don't feel like seeking out mates. They don't feel like having sex." But have you ever wondered why that actually is? Well it turns out that it can be explained by the release of what are called inflammatory cytokines. So, cytokines are related to the immune system. They travel in the lymph and in the blood and they attack invader cells like bacteria and viruses. And under conditions of illness, we make a lot of different cytokines. Some of them are anti-inflammatory, but some of them are pro-inflammatory. And the best known example of a pro-inflammatory cytokine is IL-6. And it's known that IL-6, when injected into individuals, will decrease the desire for sex and eventually will reduce levels of testosterone and estrogen independent of feeling lousy. So, the reason why people don't want sex when they're sick is because levels of IL-6 are increased. Now, this is important because as we start to think about the different ways to modulate the sex steroid hormones - so-called optimize the hormones - keeping levels of IL-6 low is going to be important for them to exert their effects. Now, IL-6 doesn't just travel to the gonads and shut down the gonads. It actually has ways to interact with some of the receptors that the steroid hormones - estrogen and testosterone - bind to. And impact those receptors so that the sex steroid hormones can't have their effect. In short, and put simply, inflammatory cytokines like IL-6 are bad for sex steroid hormones. And so, we're going to talk about how to modulate IL-6 in the direction that you would want and how to increase another cytokine called IL-10 - which is anti-inflammatory - in ways that can help promote or at least support the sex steroid hormones. So as we move forward, we're going to now start to consider what sorts of behavioral practices - as well as other things - can modulate the sex steroid hormones in the directions that you want them to go.

Pheromone Effects

But before we do that, and in order to step the stage for that, you should be asking yourself: How is it or why is it - at a mechanistic level - that behaviors can modulate hormones at all? If you think about it, it's kind of strange that just the mere act of being a parent or parenting can change testosterone levels so dramatically or estradiol levels so dramatically. What is it? Is it the sweat of the baby? Is it their saliva? Is it the sight of the baby? Is it holding the baby? Or is it all those things? It turns out that many of those effects are because of smell - or in some cases, even possibly, pheromones.

Now, I talked about hormones. Hormone - again, are chemical - travels in the body - impacts tissues and cells elsewhere in the body. A pheromone is a chemical that's released by one member of a species that goes and impacts members elsewhere, but of the same species - or even of other species. Now, pheromone effects are absolutely well established in lots of animal species, but they are very controversial in humans. Today, I'm going to talk about some of the well established ones in

animals. I've mentioned one or two of these before on previous podcasts, but I haven't mentioned several of them. And I'm going to talk about the evidence for pheromones in humans that are well established.

So, the main ones in animals that are discussed are called the Lee-Boot effect, the Whitten effect, the Bruce effect, and the Vandenberg effect - named after the people that discovered them. The Lee-Boot effect is when you house females of a given species together with no males, they start displaying longer - what are called estrous cycles. In many species, they don't have menstrual cycles - which are 28 days. They have estrous cycles - which tend to be 4 days or some variant thereof. It's an interesting phenomenon because what it means is that the presence of the male itself is changing the ovulation cycle. Now, many people out there - I imagine mostly the people that are ovulating out there - will say, "Of course. I notice I ovulate differently - or my cycle changes - when I'm in the presence of my partner or I'm not." But the pheromone effect that mirrors this Lee-Boot effect in humans has still not really been identified. Nobody knows what the exact chemical is, but nonetheless, this is a strong effect in some animals.

The other one is the Bruce effect. And this is a very dramatic effect whereby a pregnant animal will abort or reabsorb her fetus if the dad of those animals - the father that sired the litter - or because these are animals, they're litters - is removed and a novel male is placed in her vicinity for about 48 hours. And what's interesting is the way that this happens is a pheromone that comes from male urine activates the gonadotropin-releasing hormone system and causes a reintroduction of the estrous cycle and a spontaneous abortion of the fetus. Now, a lot of people have taken the Bruce effect - kind of - to its extreme and asked whether or not in humans, miscarriages are caused by detecting the pheromones or odors of novel males - meaning the non-dad male. And that's still an open question. Nobody knows if that's true or not. So, I want to emphasize that.

The other one is the Vandenberg effect. And this is one I alluded to in a previous episode of the podcast - which is that puberty in females can be accelerated by placing a novel sexually competent male in with a young female who has not undergone puberty. There's also a version of this which I haven't described - which is delay of puberty - where you take juvenile female animals that have not undergone puberty and you put them with more mature females of the same species. And that introduction of more females will cause a delay - a significant delay - in the onset of puberty. So, these are all pheromone effects. And we know they're pheromone effects because they're not conscious. They also don't require actual contact with the other members of a given species. These are all effects that can be mediated by the urine from a given species or by the sweat of a given species.

Stern & McClintock Study - Synchronization of Menstrual Cycles

And speaking of sweat, the one pheromone effect that I'm very aware of from the published literature is a paper that was published in 1998 by Stern and McClintock - which was getting at this question of synchronization of menstrual cycles. Now, the whole idea of synchronization of menstrual cycles is pretty controversial. For a long time, people said, "Oh, this is absolutely a

well-characterized phenomenon. People living in dormitories, their menstrual cycles would synchronize. People living in environments together with - their menstrual cycles would synchronize." And then, some studies came out that - kind of - undercut those data and said, "No, this actually doesn't happen." And it was kind of controversial. But there is a very clear effect that was described by Stern and McClintock. What they did actually was they took females, they charted their cycles, and then they had other females wear pads in their armpits, and they collected sweat from those females, and then they took the sweat from those pads in those females armpits, and they introduced them to women who had never had contact with the people who had sweated. They only had contact with their sweat. In fact, they swabbed it underneath their nose. But if that sounds gross, they dilute it in alcohol so much so that they can't actually detect the odor of the sweat. It's actually very important because it's not the - the smell - it's the pheromone chemical itself. And it turns out, the pheromone chemical itself can modulate the menstrual cycle. Although, it doesn't necessarily synchronize it with the sweater. What it does is it changes the duration and the pattern of ovulation relative to so-called follicular phase. Long and short of this is that the sweat and pheromones of females can modulate the menstrual cycle patterns of other adult females. It's just a question of whether or not they synchronize.

If you're kind of rolling your eyes now and saying, "Well, of course they do. And this is really detailed." This is how the science is done. And the reason why people are so skeptical about the presence of pheromone effects in humans is that there's no well-identified pheromone organ. You know, we have an area of our nose that's responsible for smelling. That's well established. It's been observed in MRIs many, many times and cadavers as many, many times - in pretty much all individuals. But the vomeronasal organ - which is the pheromone detecting organ - hasn't really been found in humans. There's something called Jacobson's organ - which is thought to be the - the organ in the nose. It's actually on the top of the roof of the mouth and in the - kind of - back of the nose. This is for you wine tasters. I never can pronounce this. What are they called? Sommelier? Sommelier? Whatever - the people that are excellent at drinking and detecting the essences of wine - that you have to go through all these tests in order to get certified as one of them. Somebody tell me. They are using probably a similar mechanism of mixing taste and smell. And Jacobson's organ, if it exists - the vomeronasal equivalent in humans - is thought to be a combination of smell and taste.

Study - Boyfriend's T-shirt

Now, it gets even weirder and cooler when you think about a given study that was done in humans where if you take hundreds of t-shirts from boyfriends. Keep them separate. You take those t-shirts. You wash them many times separately. And then, you offer them to the girlfriends - the long-time partners of those guys - and what you'll find is that the girlfriend can pick out her boyfriend's t-shirt among hundreds of other t-shirts. Not because it smells different, but because something about it seems different. It might smell different to her in some way that's kind of imperceptible - even to her. And the level of accuracy in detecting that t-shirt - her partner's t-shirt - is way above statistical significant thresholds. So much so that you almost have to say there's something about these effects that are real pheromone effects. Although, people still argue that there are no pheromone effects in humans - that it's all through olfaction. I think these are

interesting and important to understand because it means that a lot of things coming through our nose - whether it's pheromones or smells - are impacting hormones and our ability to attach memories and - kind of - recognition of mates and other people - including our children, not just our mates.

Perfume

And of course, perfume manufacturers have really picked up on the idea of pheromones and have entire laboratories set up to build chemical compounds into perfumes that are designed to attract other mates. This is a well established and well-documented phenomenon.

Flehmen Response

And the last point I'll make about pheromones is that this combination of taste and smell is such a real thing in the animal world that there's something called the flehmen response. During the mating season for different animals - you can actually even see this in horses - but for animals that are seasonal maters, they'll do something called the flehmen response - where they actually open their lips and their mouth and they expose their gums so that they can capture pheromones that are floating in the wind in the environment. They actually are looking for mates using their mouth and - kind of - sniffing around.

If you own a dog and you watch the way that the dog will sniff around - selecting where they want to urinate - males and females - there's often - they're bringing molecules into their nose. I know it sounds kind of gross - sniffing urine - but there are a lot of pheromones in urine of animals. A lot of pheromones are traveling in the wind.

Again, whether or not this is happening in humans, I don't know. But then, you think about the perfume thing and here people are putting these scents on themselves that contain putative pheromones - human pheromones - and walking around hoping that their scents are going to evoke mate-seeking behavior from other individuals of the same human species. So, we are among the animals in this behavior - independent of whether or not you believe pheromone effects exist.

Apnea

So, let's get back to behaviors that can help optimize hormone levels. One of the main behaviors that's been shown to be associated with poor levels of estrogen - relative to age-matched controls - for people with ovaries - or lower levels of testosterone - compared to age-matched controls - for people with testes - is apnea. Apnea has everything to do with underbreathing and the buildup of too much carbon dioxide in the body. There are other effects of apnea as well. But if there's a consistent literature in this whole story about aging and reductions in hormones and general health and reductions in hormones, it's apnea. I went deep into the literature on advanced menopause or when menopausal symptoms are exacerbated. And I went into the literature on andropause or early-onset andropause - so, levels of testosterone that are far lower than they should be for a given age. And in every case, you could find multiple papers that showed that apnea - or poor-efficiency of breathing - and buildup of too much carbon dioxide in the body was a problem.

Mostly sleep apnea - although, apnea in general was shown to be an issue negatively impacting hormones. Now, the directionality of this effect isn't entirely clear. It could be that reductions in estrogen cause apnea and, actually, there's some reason to believe that might be the case. I found at least one paper showing that there are estrogen receptors on some of the neurons that actually innervate the lungs and allow for the perception of how full or empty the lungs are. In other words, reductions in estrogen may adjust breathing by changing our sensitivity to our own lungs. Now, that was true for males and females - remember, estrogen in both males and females. But as well, I found papers in which testosterone reductions were associated with apnea and testosterone receptors are also found on a lot of cells in the so-called viscera - including the lungs. So again, the directionality of the effect isn't clear. But what's really interesting is that there are very clear ways in which patterns of breathing - especially patterns of breathing in sleep - can modulate hormones in ways that are immediately actionable and can serve to optimize both estrogen and testosterone regardless of whether or not you have ovaries or testes.

So, what is apnea? Apnea is underbreathing or mainly cessation of breathing during sleep. So, people are holding their breath and then they'll - they'll suddenly wake up. Actually, I've talked about the physiological sigh on previous episodes of this podcast - of this pattern of double inhales, followed by exhales that one can do consciously to reduce stress and anxiety and offload carbon dioxide. That pattern of breathing is actually what kicks in spontaneously anytime we have an apnea episode in sleep. Although in many people who have apnea, they don't engage the physiological sigh.

People who are dramatically overweight also suffer a lot from apnea during sleep. There's actually a lot of buildup of carbon dioxide in the body and that can lead to excessive sleepiness during the day - inability to access the deeper phases of sleep. And it's well established that going into deep sleep and getting the proper patterns of slow-wave sleep and REM sleep are important for hormone optimization. I talked about how to modulate sleep and optimize sleep in the first month of the Huberman Lab podcast, so please check out those episodes if you have sleep issues or you want to work on your sleep. Also, check out Matt Walker's terrific book, "Why We Sleep". And that will help you find various protocols to help you optimize your sleep.

Mouth vs Nose Breathing

But the issue of breathing itself can be adjusted in the daytime - waking hours - in ways that can powerfully impact both sleep - reduce incidence of sleep apnea and apparently from some emerging literature, can also help to optimize various hormones - even just by breathing in particular ways while awake. So, here's how this works. There's now a lot of literature showing that breathing through the nose - not through the mouth - is powerful for improving lots of things. First of all, it improves cosmetic features of the jaw and face. This was first well established by my colleagues at Stanford in a book called "Jaws: The Story of a Hidden Epidemic". This is by Sandra Kahn and Paul Ehrlich, who are both faculty at Stanford - has a forward by Robert Sapolsky - the great Robert Sapolsky - and it also has a heavy endorsement upfront by Jared Diamond, the author of "Guns, Germs, and Steel" - the Pulitzer winner. So, a lot of heavy hitters on this book, "Jaws". It's

not a book that a lot of people know about unfortunately, but it really describes the benefits of nasal breathing and the terrible things that happen when people - in particular, children - but adults also - are heavy mouth-breathers. So, mouth-breathers have changes in the cosmetics of their face and jaw that are really bad in terms of attractiveness. And this was done in twin studies. You can look in the book and see some of this. It's really dramatic - how being a mouth-breather tends to make the chin drop back behind the upper mandible. There's a lengthening in the face - a drooping of the eyes. It can be quite dramatic or modest depending on how much mouth-breathing. Now, sometimes we have to breathe with our mouths.

But there's also a lot of data and studies described in this book, "Jaws" - that describe how nose-breathing in wakefulness and in sleep promotes all sorts of positive things related to not just cosmetics, but also the improvement of gas exchange of carbon dioxide and oxygen in the body. And as well, it can modify levels of different neurotransmitters and neuromodulators in ways that positively can impact hormones. So, believe it or not, being a nasal breather and avoiding being a mouth-breather can actually positively impact hormones - and, in particular, the hormones testosterone and estrogen. Although, the way that it does that is by making you a better sleeper - which allows you to produce more testosterone and the appropriate amounts of testosterone and estrogen. But it does that, in part, through indirect mechanisms - because deep sleep supports the gonads - the ovaries, and the testicles, and their turnover of cells, and the production of cells. Remember, in the ovary, particular cells and the egg follicles themselves make estrogen. And in the - in the - in the testicle - that the sertoli cells and the leydig cells are important for the formation of sperm and for testosterone, respectively.

So, what does this all mean? This means we have to be breathing properly. It almost sounds - kind of - you know - like kind of new-agey - like, "Oh, you have to breathe properly. Get your hormones right." But no, you have to breathe properly to get your breathing and sleep right so that your sleep can actually be deep enough and you're not entering apnea states. And then, that will support gonad function. And I would be putting this out as one of the main behavioral tools up front if it weren't for the fact that the effects of apnea on these hormones are dramatic and terrible. And the positive effects of getting breathing right on these hormones - testosterone and estrogen - are dramatic and wonderful.

So, let's talk about a few of those studies briefly so I can underscore the value of proper breathing in order to optimize hormones. So, I was able to find at least four quality studies showing that when apnea is reduced in sleep or eliminated, there are significant increases in testosterone in males and in proper estrogen-to-testosterone ratios in females. And the way that it works is very interesting. Apparently, it works by reductions in cortisol. Now, cortisol is a stress hormone that is released early in the day as we wake up and serves healthy roles in protecting us against infection, reducing inflammation, etc. But you don't want cortisol to be too high and you certainly don't want it elevated too long throughout the day and night.

And so, we all know - because now we've been told a lot in the last decade or so - that getting proper sleep is important for all these aspects of health. Getting proper sleep can really offset all the reductions in testosterone and estrogen and reductions in fertility that occur if we don't get enough sleep. But seldom is it discussed how sleep actually adjusts things like testosterone and estrogen and it does it by modifying cortisol. So, the molecule cholesterol can be converted into testosterone or estrogen. But there's a competition whereby the cholesterol will turn into cortisol and not testosterone or it'll turn into cortisol and not estrogen if stress levels are too high. So, the simple version of this is getting your breathing right during the waking hours - meaning primarily - unless you're working out really hard or there's some other reason why - you're maybe eating or speaking - that you need to be breathing through your mouth - you should be a nose-breather. There's really good evidence for that now. And in sleep, you also want to be a nose-breather because that's going to increase the amount of oxygen that you're bringing into your system and the amount of carbon dioxide that you're offloading. There are other positive effects of it as well, but you're basically reducing apnea. Breath-holding in sleep leads to buildup of carbon dioxide and leads to increases in cortisol - which then decrease testosterone and decrease estrogen in negative ways across all sexes, okay?

Tool - CPAP Machine / Taping Mouth Shut

So, the simple version of this is: Get your breathing right. So, how do you do that? How do you get your breathing right? Well, for some people that have severe sleep apnea, they're going to need the CPAP machine. This is a machine that you actually put on your face and it helps you breathe properly in sleep. Many people, however, are starting to do this thing of taping their mouth shut. Now, this sounds a little bit extreme and you certainly don't want to do this in any way that's dangerous. James Nestor talked about this in his book, "Breath: The New Science of a Lost Art" - that simply taping shut the mouth with some tape that will allow you to open your mouth if you really need to. During sleep can allow people to shift over from being mouth-breathers and snorers to nose-breathers.

Tool - Dilating Nasal Passages

In the daytime, the best way to get good at nasal breathing is to dilate the nasal passages because a lot of people have a hard time breathing through their nose. And one way to do this is to just breathe through your nose more. And one way to do that is that when you exercise - in particular, cardiovascular exercise - most of the time, provided you're not in maximum effort, you should be nasal breathing. Now, for a lot of people, nasal breathing during exercise is hard at first, but as you do it - because the sinuses have a capacity to dilate over time - you'll get better at it. The sinuses - if you haven't ever held a skull - I've - I've held - because of my job as a neuroscientist, I've held a lot of skulls - taken a lot of brains out of a lot of skulls. I teach neuroanatomy and I've done that for - goodness - God knows how many species have done that for - including human. But what the sinuses are is they're actually - what you've got are these little portals in the bone that run - you know - up here and down here - behind the - behind the nose and into the jaw. If you've ever had a cold and your sinuses are stuffed up - you feel like you have congestion here and here - and around your ears, and in your cheeks, and in your face. And that's because the sinuses are actually portals

where the bones are fused together - kind of interdigitated like this. But they're lined, of course, with mucus membranes. And as you start to nasal breathe more, the nasal passages will start to dilate more. Don't worry, you're not going to get giant nostrils. But what's going to end up happening is you're going to have an easier time breathing through your nose just from waking.

So, my advice would be breathe through your nose while exercising unless you're in maximum effort. Pretty soon, what you'll find is you actually can create more output than you would if you were breathing through your mouth. And of course, there are exceptions to this. If you're swimming, follow that breath protocol. For fighters and martial artists, there's a reason to do the - kind of - exhale breathing through the mouth - the "shhh" kind of thing - you know - there are reasons to do that sort of thing for particular sports. But for most people who are kind of recreational athletes or exercisers, learn to be a nasal breather. It has positive cosmetic effects. It reduces apnea. It offloads more carbon dioxide. It increases lung capacity. It dilates the sinuses and it prevents apnea in sleep. So, unless you have severe apnea and you need the CPAP, becoming a nasal breather can have all sorts of positive effects by reducing cortisol, reducing apnea, and indirectly raising testosterone and estrogen in the proper ratios. So, this might seem kind of foundational and indirect. But when you go into the scientific literature, it comes through as one of the most powerful things that you can do that is zero cost. It takes a little effort, but it's zero cost. And it has all these positive effects across the board - you know - both cosmetic, and in sleep, and hormonal, etc. So, that's the first piece of behavioral advice.

Tool - Viewing Light

The second piece of behavioral advice relates to the viewing of light. And many of you have heard me talk about this before and I'm not going to belabor the point that viewing bright light within the first hour of waking - whether or not it's from artificial light or ideally from sunlight - has these powerful effects on sleep and wakefulness. But we have to return to this if you want to understand how light can impact hormones because hormones - light and dopamine have a very close-knit relationship. So much so that your light-viewing behavior can actually have a direct effect on hormone levels and fertility. It can have a direct effect on hormone levels and libido. It can have a direct effect on hormone levels and your ability to heal quickly. And I'm not talking about shining light on particular injuries. That may or may not have positive effects. You know, we can argue about that on a subsequent episode. It may. But what I'm talking about is viewing light with your eyes.

So, let's talk about that now because the scientific literature on this are robust and they extend back several decades. And yet, I think most people don't really understand how powerful this relationship is between light, dopamine, hormones, and all the great things that the sex steroid hormones do when they're available in your body in the proper ratios.

In order to understand the powerful effects that light can have on the sex steroid hormones, we need to understand seasonal-breeding animals. Now, humans are not seasonal breeders. But if you

understand the biology of how light impacts various neurotransmitters and hormones, you'll set yourself up for a deep understanding of what you should do with your light-viewing behavior. So, several species of animals - many species of animals, in fact - like rabbits, and fox, and various mustelids - like ferrets and ermines - change their pelage color across the seasons. This might be - kind of - a "Duh." - but fox, in winter, are often white or light gray. And those same animals will be brown or darker colored in the summertime and spring months. Now, those same animals breed in the spring and they shut down breeding. They actually shut down ovulation. They often shut down testosterone production in the winter months. So, right now I'm just correlating color of fur with tendency to breed. Tendency to breed, as we know, is going to be related to the levels of sex steroid hormones estrogen and testosterone.

Now, why would these two things be linked? Well, it turns out that dopamine is the link between them. So, dopamine has a precursor. That precursor is tyrosine - which comes - which is amino acid - comes from food. And when dopamine levels are high - as I mentioned before - there's a tendency for more gonadotropin-releasing hormone, luteinizing hormone, follicle-stimulating hormone - all the hormones that come from the hypothalamic-pituitary axis and stimulate estrogen and testosterone release from the ovary and testes. Dopamine basically increases all of that. The precursor to dopamine is tyrosine, but the precursor to a lot of the melanin-producing elements of cells that give pigmentation - including for the hair - is tyrosine and tyrosinase - an enzyme. So yes, the same amino acid-based pathway and many of the same enzymes that are devoted to dopamine and dopamine increasing the sex steroid hormones are devoted to giving pigmentation to the hair and skin.

And this is why in the summer months - when days are longer - animals are breeding more. And this is also why in the winter months - when days are shorter - animals are breeding less. This is also why in humans - many people, not all - feel an elevation in mood in the spring and summer months because of the amount of sunlight they're getting is increased relative to the winter months. Now, some of you may be saying, "I love the fall. I love the winter." Sensitivity to light in these dopamine systems has a strong genetic component. So, you go to some areas of the world. I have relatives who are Scandinavian. And in some areas of Scandinavia, people know that there's a - kind of - seasonal affective disorder. There's kind of a seasonal depression. And people get sadder and more quiescent in the winter. There's actually less going out and therefore, there's less sexual behavior. There's less partying and things of that sort. But other people will say, "No. During the winter months, I feel great and I love the holidays around winter." - etc. So, there's a lot of variation. But in general, the pathway is the following. Increased viewing of sunlight - and it has to be to the eyes. It's not to the skin. Increased viewing of sunlight increases dopamine levels in the brain. Increased dopamine levels in animals and humans increases the amount of these melanocytes and the activity of these melanin-producing cells - which give pigmentation to the skin and hair - and indirectly, increase the amount of testosterone and estrogen - and thereby, reproductive behavior, feelings of well-being, social interactions, reductions in anxiety, etc. - all of which should make sense based on what we've talked about already in terms of the biology and the impact of these steroid hormones on various aspects of the mind and body.

So, how does this translate to a protocol? This translates to the protocol of: If you want to optimize testosterone and estrogen, you need to get your light-viewing behavior correct. It's not just about optimizing your sleep - which is also important. It's about getting sufficient amount of light in your eyes so you have sufficient levels of dopamine. So, the simple protocols for that - I've reviewed before - but it means getting anywhere from 2 to 10 minutes of bright light exposure in your eyes early in the day. It is not sufficient to do this with sunglasses unless you have to do that for safety reasons. It's fine to wear prescription lenses and contacts. If you can't get sunlight for whatever reason, you want to use bright artificial light. But that is absolutely critical for timing the cortisol release properly - limiting cortisol release to the early part of the day - getting increases in dopamine that are going to promote the production of testosterone and estrogen to healthy levels. The other aspect of light-viewing behavior that's extremely important is to avoid bright light exposure to your eyes in the middle of the night. If you're viewing bright light in the middle of the night, you are suppressing dopamine release. If you're suppressing dopamine release, you are suppressing testosterone levels. So much so that I would wager that a major effect of sleep deprivation on reducing testosterone and estrogen is not necessarily because of the lack of sleep per se. It's because usually when people are not getting enough sleep, they're getting too much light in their eyes in the middle of the night as well.

A study on this has not been completed yet. But there are two studies published in Cell and Neuron - both Cell Press journals - excellent journals - showing that viewing bright light with the eyes in the middle of the circadian night has a detrimental effect on dopamine and therefore, has a detrimental effect on things like testosterone and estrogen. So, you can't even begin to talk about supplements and other ways to optimize testosterone - diet and its effects on testosterone, and estrogen, and fertility, and reproductive behavior, etc - until you get your breathing right - until you get things like your light-viewing behavior right. So, bright light early in the day and throughout the day is great. If you view as much bright light - ideally sunlight - as you can - as much as you safely can. You obviously don't want to burn your retinas or damage your retinas. So, never look at any light that's so bright it's painful to look at. But getting a lot of light in your eyes is not just about adjusting your sleep-wake rhythms. It's also about optimizing your sex steroid hormones. And avoiding bright light in the middle of the night is not just about not disrupting your sleep. It's also about optimizing the sex steroid hormones. And now that you understand a bit of how the sex steroid hormones work and how powerful they are for reducing anxiety and all these other effects, this should be straightforward to do - or hopefully, it's inspired you to get your light-viewing behavior and your breathing behavior correct.

In fact, in thinking about tools, for many people that are suffering from low levels of estrogen - if they want higher levels - or low levels of testosterone - if they want higher levels - just getting the breathing and light-viewing behavior - which will indirectly support sleep behavior - can be a huge and positive effect on levels of sex steroid hormones. I can already anticipate that in hearing this, you might wonder whether or not viewing light is going to, for instance, increase your testosterone a lot when in fact you want your estrogen increased - or it's going to increase your estrogen a lot when you want your testosterone increased. Everything I'm describing here is for people regardless

of chromosomal or gonadal background. So, I'm trying to basically offer all this information in one - in one swoop. But basically, if you're somebody who naturally has ovaries and has higher levels of estrogen than testosterone, then viewing bright light early in the day - because of dopamine's effects - is going to promote more estrogen and subtle increases in testosterone. Whereas if you're somebody who starts off with more testosterone and lower estrogen - so, somebody presumably who has testes or maybe you're supplementing with testosterone through other sources for whatever reason - bright light viewing is going to increase testosterone and estrogen in parallel, but you're still going to maintain the ratio of testosterone estrogen. In short, you don't have to worry that you're going to increase the wrong hormone. This is all about optimizing the ratios of hormones that you already have.

Okay, so we've talked about breathing. We've talked about light. Let's talk about a third element that there seems to be some excitement about lately for other reasons, but that can actually have some pretty profound influences on hormone levels. And that's heat and cold. So as always, rather than just offer a tool, I'm going to tell you the underlying science as it relates to naturally occurring phenomenon - because in understanding that and understanding the mechanism, you're going to be in a far better position to understand the tools, and mechanisms, and how you might want to adjust them for your own life. So, now you understand the relationship between light, daylength, dopamine, and hormone levels. And everyone should realize that temperature and daylength are linked. And I'm sure as I say that, you're probably thinking, "Oh, of course." In summer - when there's more sunlight - days are longer, nights are shorter - in general, it tends to be warmer out. And in winter - when nights are longer, days are shorter - it tends to be colder out. And in the winter months, testosterone and estrogen tend to be lower in many animals and in humans. And in the summer months - because of the role of dopamine in promoting a sex steroid hormones - when days are longer and it's warmer, humans tend to make more estrogen and testosterone relative to the other months of the year. Now, these effects can be somewhat weak and modulated - as opposed to in seasonally breeding animals where they're really dramatic, okay? But the point is that temperature, and daylength, and sunlight - those are all intimately related because of the systems that we evolved in, right? So, before we had artificial light, and artificial heating, and artificial cooling - our biology evolved under systems where temperature, daylength, and the hormones were correlated with one another.

Heat & Cold

So nowadays, there's a lot of interest in using cold as a way to stimulate testosterone. This is mainly because in the - you know - in the sports community - in particular, in the bodybuilding community - they are always seeking ways to maximize testosterone/dihydrotestosterone - keep estrogen to its minimum required to still have libido, and still have - you know - skin elasticity - but also walk around with Saran Wrap skin. And all this - kind of - extreme stuff that happens there has led to a recent movement where - believe it or not - I heard this and I couldn't believe it - I went and checked - although, I didn't buy them - that on Amazon, you can actually find - people have - they're literally underwear that have ice packs - or I think they are ice pack underwear. So, that people are making themselves cold at the level of the gonads in order to try and increase testosterone and libido.

Sounds pretty crazy. But believe it or not, that and things like ice baths and cold showers can have positive effects on the sex steroid hormones - both testosterone, mainly in males - and estrogen, mainly in females.

Tool - Cold Exposure

And you might say, "Wait, I thought cold makes the reproductive axis kind of shut down a bit or reduces testosterone and estrogen." But it turns out, it's not actually the cold that's having these effects in people. Things like the ice bath, cold showers, cold-water swims, these ice underwear - whatever they are - can't believe that these actually exist, but they do exist - what happens is there's a rebound in vasodilation after cooling. So, cooling causes vasoconstriction. And then after the cooling, there's a rebound vasodilation and there's more infusion of blood into the gonads. There's also an effect that's neural. So, let me explain how this works because there are only a few studies on this - none of which looking at the frozen underwear - but that have looked at cold exposure and levels of - of androgens and estrogens. And it's kind of interesting. So, you have to remember that the gonad - the ovaries and the testes - are heavily vascularized. Remember, even at the level of the brain, GnRH - gonadotropin-releasing hormone - comes from neurons - that believe it or not - start off in your nose early in development - migrate into the hypothalamus. I'm not making that up. They start off in your nose and migrate into the hypothalamus. Those neurons extend processes - we call them axons - into the pituitary and release GnRH into the pituitary. There's a lot of vascularization within the pituitary. So, now those hormones - or GnRH - can - can stimulate follicle-stimulating hormone - luteinizing hormone - which then are released and travel into the bloodstream. Then those hormones reach the ovary or testes and they have to get into the ovary and testes. And the way they do that is through the vascular system. And people forget, but the vascular system and how constricted or dilated vessels are is controlled by neurons, alright?

This is - we discussed this during the discussion about stress in the stress episode. But it's well known to neuroscientists that the best way to shut down neurons is to cool them. So, we - there are a lot of examples of this in the scientific literature, but most people aren't aware of it because you're not digging around in the methods section of these papers. But when we want to shut down neurons, we can do things like inject drugs that will do that - like lidocaine - you know, the stuff that makes you numb at the dentist - or you can use different inhibitors. But one of the best ways to do it experimentally is to just cool neurons.

When you make neurons cold - because there's a temperature dependence of when neurons can be active and when they can't - the neurons shut down. So, the most plausible explanation for why cold exposure - either through - you know, 1 to 10 minute ice bath - or cold shower - or the ice underpants thing - would increase testosterone or increase estrogen - is that you're cooling the neurons that control vasoconstriction and vasodilation - and shutting down the entry of blood - or at least reducing it - and hormones into the gonad. And then, when the gonad and the surrounding area heats up again, you're getting a rebound hypervasodilation that delivers excessive levels of - not excessive - but increased levels of GnRH, and other hormones, and carriers, and carrier proteins, and so forth - that would then stimulate the gonad to more testosterone - or would

stimulate the gonad to release more estrogen. That's the most plausible explanation I can come up with.

There aren't a lot of studies looking at direct effects of temperature on the gonad. And it's going to be a difficult study to carry out, in any case, because unless it were done in vitro - in a dish - it's very hard to eliminate all the other things - like vasoconstriction and vasodilation. Put simply, we don't know whether or not cold and heat directly affect the production - the production of testosterone and estrogen. We only know that cold and heat can modulate those probably through indirect mechanisms - like controlling the amount of blood flow by way of shutting down or activating the neurons.

Now, there's a lot of lore around heating up the gonads too much. There's actually a whole set of pseudoscience web pages out there saying, "Well, if you want a girl, you should conceive the child at this room temperature. And if you want a boy, you should conceive the child at this room temperature." I - I don't think there's really any firm scientific evidence for that - for either one. But there's some interesting literature about temperature dependence of production of hormones. And I think that it probably relates to these mechanisms of vasodilation and neural control over vasodilation.

Room Temperature Myth

And of course, excessively high heat is not good for the testes, for sperm production, or for sperm health. Sperm have all sorts of proteins in the cap - things like pentraxins and other things - that cause them to swim faster when they're expressed properly and in the right locations. And heat actually alters the location and the function of a lot of those proteins. They're very heat-sensitive. And so, that's why excessive heat is truly not good for fertility - which may be independent of heat's roles in promoting estrogen or testosterone.

How to Exercise

Okay, so now we've talked about breathing, light, and temperature. We talked about parenthood. We talked about competition and we talked about some pheromone effects. Now, let's talk about particular forms of exercise and how they modulate the steroid hormones. And then, we're going to talk about various supplements - both in reference to testosterone and in reference to estrogen. So now, let's talk about how exercise in its various forms - weight training, endurance work, weight training to failure, or less intense weight training - can impact testosterone levels. But I want to remind you that we're talking about testosterone both in males and females. And based on what you know from earlier in the episode, testosterone can have numerous positive effects in both males and females provided they're in optimal range.

So, if you look on the web, people say, "Oh, you know - testosterone is increased by weight training. You want to do big, heavy compound movements - squats, and deadlifts, and chin-ups, and things of that sort." But what about the scientific studies? Like what's the actual basis for this? Because if you just take a step back and look at this from the perspective of a scientist, you'd say, "Okay, what

is a squat?" A squat is loading up a bunch of weights on a bar and then - you know - sitting down, essentially - and standing up over and over again. "What's a deadlift?" It's lifting heavy weights from the ground. Why would that increase testosterone, right? This is what's often not discussed in the weight training or even the exercise science community. What - what would actually stimulate the release of testosterone from the adrenals and/or testes? And which one is it? Adrenals, or testes, or both? And that's often not discussed. But as a neuroscientist, these are the kinds of things we think about because we think always that genes don't create behavior. Immune systems don't know when to be activated, lungs don't know when to inhale or exhale, hearts don't know when to beat - except for the information that it gets from neurons. The nervous system controls all of that. And so, really the answer has to be in the neural system that's related to these particular types of weight-bearing exercises.

So, when you go into this literature, it's kind of hard to find real mechanism. You see a lot of effects. You'll hear things like, "androgen receptor content..." - meaning testosterone and its derivatives - "...receptor content following heavy resistance exercise". And you'll find some examples that for instance - you know - they do muscle biopsies. They can actually see receptor increases - looking at either high volume or low volume - really intense exercise. And you - you can find a lot of that, but not a lot of mechanism about how the nervous system would do this. And the reason you'd want to know how it can do it is that you could potentially build better protocols or figure out exactly what about these movements is triggering increases in androgen receptors and testosterone.

So, what's interesting is when you start digging into the more mechanistic studies, what you find is that heavy weight training. So, this is weight training where the - the sets are done with anywhere from - you know - kind of - one to eight rep range. So, this translates differently depending on the ratio of muscle fiber type and so forth. But where basically people are working at anywhere from like 70% to 95% of their maximum or sometimes even going right down to their one repetition maximum - really kind of - you know - max effort. What you find is that using the nervous system in a way in which they're moving heavy loads. So, that I would translate to recruitment of high threshold motor units - for you muscle physiologists. And there's a rule in muscle physiology about the neuron recruitment for moving muscles - where you basically use the minimum number of motor units - of neurons - to activate muscle as you possibly can. As loads increase, you have to recruit more and more neurons. You always hear about, "recruiting muscle fibers" - but really, it's recruiting more neurons to recruit more muscle fibers. And what you find is that heavy weight training, but not weight training to failure - where completion of a repetition is impossible - leads to the greatest increases in testosterone.

Now, I'm sure there are a bunch of exercise jockeys out there that are going to - you know - come at me with a bunch of things where, "Oh, yeah. But high volume..." - and this and - "training to failure..." - and that. Sure. If you're willing to - kind of - put things side by side - adjust for exogenous testosterone treatment and all the rest - which was done in these studies - what you find, in general, is that weight training with heavy loads - so, anywhere from one rep maximum to somewhere in the - you know - six to eight repetition range - in males or females - increases testosterone significantly. And it does it for about a day - sometimes up to 48 hours.

And the studies that I found - which seem to hold the most rigor or weight based on where they're published - as opposed to being published in the journal of "Never Heard Of It" - they're published in good quality exercise physiology journals. And for instance, the paper by Ratamess - R-A-T-A-M-E-S-S et al. - which was published in 2005 - which talks about modulations in androgen receptor content after heavy resistance exercise - looks at going to failure and not to failure. The work of Izquierdo et al. - published in 2006 - "Differential effects of strength training leading to failure versus not to failure on hormonal responses, strength, and muscle power gains". You know, there are a lot of studies here and I will certainly put the links to these in the caption. Many of these actually include Duncan French - who runs the UFC training center - who I've had the privilege of meeting and discussing some of this with before - as well as other authors, of course. But they all point to the fact that there's something about the engagement of the neurons that recruit high threshold motor units in muscle when moving heavy loads - but not to failure - that has to provide some sort of feedback signal - either to the gonad to produce more testosterone - or is increasing the activity of receptors in the body.

Now, why do I say that? Well, this is the puzzle, right? How is it that a particular movement - just like how is it that interacting with your child - is increasing or decreasing testosterone? This is the - kind of - fundamental question at the mechanistic level. And we answered the question for child-rearing. It has probably something to do with smell and pheromones - although, I'm sure there are other cues as well. But there's clearly an influence of hard work at the neural level - and then, at the muscular level - for increasing testosterone. And there's also clearly an effect of working too hard and presumably increasing cortisol too much - although, I'm speculating there - in terms of reducing testosterone. And so, the reason we're getting nitty-gritty about this is because ultimately we'd really like to understand what are the optimal protocols. You know - out there in the literature you hear, "Move heavy objects to increase testosterone. Some of that will be converted to the more powerful androgen, DHT, by 5α -reductase" - etc. But we really don't understand yet how these particular behaviors increase testosterone and whether or not it's doing that by modulating the receptors or it's modulating testosterone released directly - presumably, testosterone released directly and the sensitivity of the receptors. That's what most of the muscle physiology studies that I was able to find point to. But this basically boils down to a particular set of protocols where if you want to increase testosterone - for whatever reason - that weight training with heavy loads but not to failure seems to be the best supported - at least, scientifically supported - solution to that. Now, it may not raise your testosterone levels as high as you want, but it's definitely taking things in the correct direction.

Tool - Weight Training Before Cardio

Now, many of you might be endurance athletes or also enjoy exercise besides heavy weight-bearing exercise. And there are several studies exploring whether or not endurance activity can increase or decrease androgen levels - and whether or not you combine endurance activity and weight training - whether or not that has any effect - if you do the endurance activity first or second. And the takeaway from all of this was that endurance activity - if performed first - leads to decreases in testosterone during the weight training session - as compared to the same weight training session

done first followed by endurance activity. In other words, if you want to optimize testosterone levels, it seems to be the case that weight training first and doing cardio-type endurance activity afterward is the right order of business. Now, when these are done on separate days, it doesn't seem to have an effect. They showed no statistical interaction. But it seems that if you're going to do these in the same workout episode that it's move heavy loads first, then do cardiovascular exercise.

So, there's a little bit of data looking specifically at how endurance exercise impacts testosterone and its derivatives. And it's very clear that high-intensity interval training, sprinting, etc. - which somewhat mimics the neural activity that occurs while moving heavy weight loads - is going to increase testosterone. And there's ample evidence for that in the literature. And that endurance exercise that extends beyond 75 minutes is going to start to lead to reductions in testosterone - presumably by increases in cortisol. But of course, the intensity of the exercise is going to be important too. You know, no one ever - I don't think anyone really believes that hiking for the 3 hours is going to reduce your testosterone. It - whereas I think if one were to go out and run hard for 3 hours, that you can imagine there would be reductions in testosterone by way of increases in cortisol. And so, while this area certainly needs more research, it's pretty clear that limiting the endurance exercise to 75 minutes or less - not making it too intense - is one way to keep cortisol from going through the roof. But I've talked on previous episodes and there are a lot of others who have talked out there about how to clamp cortisol - how to keep cortisol more reduced.

This is also one of the reasons why you can imagine that various individuals - either for competition or just for their own purposes - are - rely on testosterone therapy - exogenous testosterone - not just for weight training, but for endurance exercise. So, this is one of the reasons why, every once in a while, professional cyclists will get popped for performance and drugs - meaning they'll get caught. And it's not just that they're increasing red blood cells through EPO and things of that sort. Oftentimes, they're also taking testosterone - not because they want to be large or have massively hypertrophied muscles, but because they're injecting testosterone, they don't have to worry about cortisol-induced reductions in testosterone. They can just clamp or keep their testosterone levels high. Not something I'm recommending, but I'm just justifying the rationale for why an endurance athlete would want to do that at all.

Menopause

So, now let's switch over to talking about estrogen. So, there are many people who are trying to optimize their estrogen levels. And one of the places where this shows up a lot - and I get a lot of questions about - is menopause. So, menopause - as I mentioned earlier - is this fairly massive reduction in the amount of estrogen that is circulating in one's blood - mainly because the ovary is now depleted of some estrogen production of its own, the eggs are not being produced, they've been depleted, etc. So, menopause is characterized by a variety of symptoms. And it's multifaceted - probably deserves an entire episode on its own - but things like hot flashes, things like mood swings, things like headaches - in particular, migraine headaches. There can be a lot of brain fog. It can be very, very disruptive for people.

Now, you sometimes hear about andropause - which is thought to be the - kind of - analog to menopause, but menopause has certain characteristics that make it a very robust phenomenon for most women. Whereas for men, andropause is going to sometimes happen - sometimes won't. In fact, without going into the details of the - the graphs and the - and the data - it's very clear, as I mentioned earlier, that some men maintain levels of - of circulating androgens that are quite high - even as - similar as they were in puberty, in their teen years, and 20s - well into their 60s, 70s, and 80s if they're optimizing a lot of other things - and probably genetics plays a role as well. Whereas some males won't. But within the female population - or population of individuals that have ovaries - there's a very stereotyped and characteristic reduction in estrogen levels as the number of eggs becomes depleted and that's what we think of as menopause.

Tool - Supplemental Estrogen

So, what are the various things that one can do for menopause? Well, one of the most common ones is that physicians will prescribe supplemental estrogen. So, this is hormone therapy where somebody takes either oral estrogen - or they'll take - they'll use a patch or a pellet - some way to secrete estradiol into the system. And that has varying success depending on the individual. Some people respond very well to it. Other people really have challenges with it. And there are a lot of side effects associated with it for some people - not others. In addition, there's a concern, always, about supplementing estrogen when there's a breast cancer background in the family or there's concern about breast cancer for any reason because a lot of those cancers are estrogen-dependent. And that's why drugs like tamoxifen, and anastrozole, and drugs that block either aromatase or block - excuse me - estrogen receptors directly were initially developed. You see them a lot on the internet, again, for all the sports folks who are trying to increase testosterone and reduce estrogen. But remember, those drugs were initially developed as ways to prevent estrogen binding to the estrogen receptor - as cancer treatments.

So, I want to be very clear. And I've said this many times. We always put in the - in the caption of each episode, of course - that I'm not a physician. I'm not an MD. I don't prescribe anything. I'm a professor. I profess things. I'm here to translate the scientific literature and point to what might be some useful avenues for exploration. But this is just for information purposes. You should definitely talk to your doctor about anything that I'm talking about now or in any episode for that matter. So, if you look at the literature on menopause outside of just standard estrogen therapy, there are some very interesting compounds out there that have been used and that are supported by quality peer-reviewed studies. And again, I'll refer you, once again, to this amazing website - examine.com - where you can put in essentially any condition or any supplement and it will point you to the human effect matrix - not animal studies - but human studies that have explored these things. Now, there are a huge variety of them here, but - so, I won't go into all of them. But some of the pro-estrogenic compounds that have been shown to be powerful in the context of menopause - as well as other conditions where estrogen is lower than one would like - include a description and some of the literature.

Tool - Black Cohosh

I'll get into this in a moment - of something like - black cohosh. I think that's the correct pronunciation. It's literally the word "black" and then C-O-H-O-S-H. And it's very interesting. There are 13 peer-reviewed studies that have reached prominence in the - kind of - commercial landscape where this substance - black cohosh - has been promoted as a way to increase estrogen. It turns out that the effects are consistent but are fairly minor - fairly minor increases in estrogen. So, it does seem to be a real effect. It is significant over the placebo effect, but there's also a significant placebo effect in some of these studies as well. So, what's interesting when you look at these studies is that many of them were carried out over a period of - you know - 6+ months. They're double-blind studies, etc. And almost all of them led to modest increases in estrogen and modest decreases in menopause-related symptoms. Now, a few additional details about these studies. They were generally carried out on women aged 45 to 64. In some cases, they looked specifically at women that were clinically obese or overweight - although, not always. The subject size pools are pretty big - you know - anywhere from - you know - 50 to 87. These are decent size. 132 subjects, etc. So, these look to be like quality studies and they basically point to the fact that black cohosh can have a modest effect in improving menopause symptoms.

Tool - Panax Ginseng / Maca / Valeriana Officinalis

The other one is panax ginseng - so P-A-N-A-X ginseng - has been shown to decrease some symptoms associated with menopause - mostly related to libido - although, the other effects were unreliable. Other things like maca - which is known to increase dopamine, actually - had minor effects. Things like - the names here are a little hard to pronounce, so forgive me - things like valeriana officinalis - has shown that there can be some improvement in the hot flash symptoms and some of the insomnia associated with that. So, that might be worth exploring. Again, discuss with your doctor. But these were both - you know - 100+ subject - age 45 to 64 individuals - double-blind placebo-controlled studies - that showed significant but modest effects.

Tool - Pueraria Mirifica / Kwao Krua

There was one substance in the gallery of the - of the compounds that was looked at that turns out to be particularly interesting. And this one is also particularly difficult to pronounce. And it's pueraria mirifica. So, I'm going to spell this out for you. It's P-U-E-R-A-R-I-A - pueraria mirifica - M-I-R-I-F-I-C-A. And there are four studies on this compound that show, in every case, it to be very potent. In fact, comparable to estrogen therapy - estrogen-replacement therapy - in reducing the symptoms of menopause. So, this was pretty striking because when you go through these studies and you look again - that they seem to be pretty well controlled - as far as I could tell. And they explored a pretty wide subject pool. And it seems that every single one of these studies - when looking side-by-side at pueraria mirifica - which is also called - and now, this is really hard to pronounce - "kwao krua" - I guess that's the name that they use in - in various countries - that it was comparable to estrogen-replacement therapy. So, I mention this because a lot of people contacted me and said, "What about the insomnia in menopause? What about the headaches in menopause?" Now, I'm not suggesting you run out and immediately start taking any of these compounds. Please talk to your doctor. You know, any hormone-related compound is a serious consideration because

of the relationship to breast cancers. But just in general, these compounds are - estrogen and testosterone - are exceedingly powerful in terms of controlling our mental and physical states. And so, you want to approach them with caution. But I thought that that one, in particular, was interesting in for which there are quite a few PubMed-documented peer-reviewed studies in quality journals.

Tool - Vitamin D / Zinc / Magnesium

Okay, so now let's talk about the role of specific compounds - some of which - many of which can be taken in supplementation form or extracted from diet and nutrition in order to optimize sex steroid hormones. And again, I just want to emphasize that I'm not suggesting anyone take anything or stop taking anything. This is purely for informational purposes, but some of the data on these is quite striking and impressive. It's very clear that certain collections of nutrients are useful for promoting testosterone and estrogen production in their proper ratios. And those things are what I would call the sort of usual suspects. Vitamin D, which is important for so many biological functions - including endocrine functions. Zinc, magnesium, etc.

And if you want to look into this more deeply and you want to understand exactly what the negative effects are of not having sufficient zinc, magnesium - and what those levels might actually be. There's a paper that's available. You can go on PubMed. I can't pronounce this last name. I'm sorry. It's - it looks to me like Wrzosek. But it's W-R-Z-O-S-E-K. I hope I didn't butcher that too badly - Wrzosek et al. - 2020 in Endocrinology and Metabolism Review. So, this is a recent paper in a good peer-reviewed journal that talks mainly about how the hypothalamic-pituitary-adrenal axis and the sex steroid hormones are negatively impacted by deficiencies in magnesium, deficiencies in vitamin D, and deficiencies in zinc. However, that doesn't point to the levels that one should take in order to optimize. So, it doesn't say, "Take X amount of zinc, or X amount of magnesium, or X amount of vitamin D."

For that information - because it's so context-dependent and individual-dependent - I highly recommend you go to [examine.com](https://www.examine.com). You can put in "zinc", or "magnesium", or "vitamin D" and they will give you ranges of dosages that are supported by specific studies. Again, that information is completely free to you and it's very useful in figuring that out. I personally have supplemented with zinc, magnesium, and vitamin D for years. And - but many other people do that as well. And the question is always: How much? And that's why I'm a proponent of getting blood work done because that's how you know whether or not your androgen levels - as well as things like vitamin D levels, etc. - are sufficiently high. So, the takeaway from these studies is looking at what deficiencies cause in terms of deficits in testosterone and estrogen really point in the direction of make sure you're getting adequate zinc, magnesium, and D3 unless you want these steroid hormone levels to be reduced for whatever reason.

Opioids

One of the things that's been shown time and time again to have very negative effects on sex steroid hormones - testosterone mainly in men - estrogen mainly in women - is opioids. There's this

whole issue, of course, of the opioid epidemic. It's deserving of an entire episode. We are going to talk about that with experts in addiction, and people that treat pain, and so forth. But the opioids dramatically reduce levels of testosterone and estrogen. And they do that mainly by disrupting the receptors on gonadotropin-releasing hormone neurons - these neurons within the hypothalamus that communicate to the pituitary. And in fact, people that take large amounts of opioids or even take low levels of opioids for long periods of time will develop all sorts of endocrine syndromes. That's been shown over and over again. Gynecomastia or male breast development in males - disruptions to the ovary in females. It's really a quite terrible situation. So, excessive opioids are very problematic for sex steroid hormones. I don't think anyone will have any trouble finding any literature on that. You can just go into PubMed, you can put "opioids", "testosterone or opioids", "estrogen". But the major effect is actually way up in the hypothalamus to shut down the production of GnRH - the very hormone that stimulates testosterone and estrogen release.

Tool - Deer Antler Velvet / Ground Cow Testes

Now, there's an entire industry devoted to supplements and various things that people can take to increase testosterone - some of which have scientific data to support them - some of which do not - and some of which have anecdotal support - and some of which do not. This ranges so broadly. I mean - things like the material of deer antlers - which is high in supposedly IGF-1 - which is in the growth hormone pathway - all the way to actual consumption of bull testes. There are - you can go on Amazon right now. I certainly don't suggest that you do this. And you can actually buy ground-up testes from - from cows. And you can consume those. Now, a lot of that's going to be broken down in the gut. I'm certainly not suggesting you do that. But just to point out, this is a huge and vast literature. And it actually dates back hundreds of years - even though testosterone wasn't discovered that long ago as a specific hormone molecule and characterized and then resynthesized. It has a huge industry because of the powerful effects that it has. Likewise with estrogen, the development of the birth control pill was only made possible by understanding the structure of estrogen and estradiol. And we're going to talk all about birth control, and how it works, and its influence on various other pathways in a future episode. But there are these supplement compounds that are supported by the scientific literature in terms of their ability to adjust androgens - things like testosterone and dihydrotestosterone.

Tool - Creatine

One of the ones that has really good evidence for it is creatine. It's very clear that something about creatine - although, the mechanism isn't exactly clear - either increases 5 α -reductase or makes the testosterone molecule more susceptible to certain enzymatic reactions that leads to increases in DHT. DHT - dihydrotestosterone - as I mentioned in the previous episode, has this dramatic role in creating a - kind of - masculinization of the brain prenatally. It also defines the primary sex characteristic of the growth of the penis, etc. And beyond infancy and early childhood and later in life, it has powerful effects in creating balding, in beard growth, etc. And it has a much higher affinity for the androgen receptor than does testosterone. So, creatine can increase DHT - which means that if you take creatine and you're very DHT-susceptible, then you might experience some hair loss. This has been heavily debated. Does creatine cause baldness? It's going to depend. It's

going to depend on how much 5 α -reductase you have and how prone to hair loss you are. Some people can take creatine without any problem in terms of hair loss. Some people cannot. They start losing their hair to levels that, at least for them, aren't comfortable.

There are a few other things that can increase testosterone and it has to do with the way that testosterone exists in its free and its bound form. So, testosterone - the molecule - is - kind of - total testosterone - that's usually what's measured. This is the - kind of - levels of - that are typically thrown around from 300 to 900 being the - kind of - natural range. And then, supraphysiologic getting up into 1200 to 1600 range. But testosterone isn't just roaming around free in the blood. At least, most of it isn't. Most of it is bound to either sex hormone binding globulin (SHBG) or to albumin. They - they're needed as transporters to get testosterone into cells so that testosterone can have its effects on gene expression as well as other pathways within the cells.

So, people talk about - that the level of free testosterone is really what's important and that you want to optimize free testosterone. That's a little bit of a tricky statement. That's kind of like - it's - it's true. And yet, it's not really reflective of a thorough understanding of how these binding globulins work. Remember, these binding globulins aren't there to soak up all your testosterone just to make it hard for you to free up testosterone and - you know - make gains in the gym or whatever it is - or having increases in libido. They're there to actually transport testosterone to specific tissues - to shuttle them to specific tissues and to set the rate of bound and unbound testosterone so that it's not all unbound at once. And - you know - it's always interesting to look in the literature and see how everyone wants to free up their testosterone so that it can work. But sex hormone binding globulin can bind up too much testosterone to the point where it's having negative effects on libido or on - on muscle growth, and fat loss, and things of that sort. This is true in males and females. Or it can be doing exactly what it's supposed to do, which is shuttling testosterone to the proper tissues and organs where it has all these effects - including the brain.

Tool - Tongkat Ali / Longjack

So, there are supplements - in particular, tongkat ali - which is - has this other name. It's something - I've called tongkat ali. Sometimes it's called - and forgive me that it's hard to pronounce - but eurycoma longifolia jack. They always seem to have these names that - kind of - that - kind of - allude to androgenic features, like I don't know why - longifolia jack. I don't know. I think it's kind of obvious why that sounds sort of androgenic. It - this has been shown in several studies and you can find these on examine.com or you can go to PubMed if you'd like. I've looked at these. But it does seem to have some pro-fertility, pro-free testosterone, and subtle aphrodisiac effects. And it does also seem to be a slight anti-estrogen. So, the reports of this - people take this anywhere from 400 to 800 milligrams a day. Again, I'm not suggesting you do that, but that's - kind of - what's out there. And there is some decent scientific literature to support the fact that it liberates some of the bound testosterone and allows more free testosterone to be available. Some of the reported quote-unquote "side effects" are things like excessive alertness, and insomnia if it's taken too late in the day, and so forth. But I encourage you to explore that further if - if that's - if increasing free testosterone is something that you're interested in doing.

Tool - Nettles

Examine.com includes a lot of other things that can increase testosterone. One of the things that's been purported to free up testosterone in the blood are things like nettles - stinging nettles. Although, I should point out that the literature points to stinging nettle also have some fairly potent effects on the prostate and on the - on the liver. And so, it might be a tricky molecule - maybe not an attractive one for people to take.

Tool - Boron

So, we talked about creatine, we talked about tongkat ali. It's clear that boron - which is really interesting. Believe it or not, I think boron comes from - I think these were like meteors that landed on Earth. And now, they extract boron. It's - you know - one of these crazy stories that when you look at it, you go, "How could that possibly be?" But there's actually - that's how it works. That boron - there's some scientific support for it freeing up more testosterone.

And again, freeing up testosterone may be exactly what you want. I just don't think that we should demonize these carrier proteins like albumin and SHBG. In fact, albumin is very important for testosterone to be able to make it into the brain to have some of the pro-androgenic effects on the cognitive effects of testosterone. Because in both males and females, testosterone can shift these behaviors - like mate-seeking, reductions in anxiety, and so forth - that we talked about before. Only by making it into the brain - and there is this thing called the blood-brain barrier - which is fascinating and deserving of an entire episode also. And getting molecules across the blood-brain barrier - even if they're sex steroid hormones - which are lipophilic and can pass through cell membranes - requires carriers. And those carriers often are bound to or include albumin. And so, it's not the goal - it - you know - to free up all your testosterone. But getting free testosterone into a range that works for your particular goals and needs is an attractive one and that's why we're discussing these particular tools. The amounts of boron that people take - and - and you can find this again on PubMed or Examine - but people take a couple grams of it a day.

Cancer

I'm not aware of any specific side effects. But you always, always, always want to examine for the particular side effects. And - you know - people with different backgrounds and conditions - as we talked about for menopause and estrogen - have to be careful. Because when you're starting to modulate hormones, you're starting to modulate not just the tissues that thrive on binding of those hormones - but remember, the reason why there's so much breast cancer - and there's a reason why there's so much testicular cancer - is that any tissue that undergoes rapid reproduction of particular cells. So, there's a lot of reproduction of cells, and shedding of uterine lining, and the reproduction of cells and eggs in the ovary. And in the testes, there's the production of leydig and sertoli cells and there's this - kind of - ongoing production of sperm. That's why those tissues are particularly vulnerable to the development of cancers. And many of those cancers are androgen-sensitive. That's why one of the major treatments for prostate overgrowth or prostate cancer is to give antiandrogenic drugs. It's not just to shut down all things related to being androgenized. It's really about trying to prevent testosterone from encouraging growth of tumors.

So, I want to - you know - really emphasize the caution there because it's easy when thinking about "optimizing estrogen and testosterone" and just think, "Oh, more is better." More is definitely not better. And it's not just because they can aromatize or convert into other things. It's because cancers - or any tissue that has a lot of turnover of cells - is going to thrive on androgen. Anything that promotes growth, it's going to thrive on estrogen. Remember, brain tissue doesn't turn over that much. There isn't really much production of new neurons. Brain cancers happen, but they're kind of rare. And when they do happen, they tend to be glial cells - which have a lot of proliferation. Glial cells can proliferate. Adult neurons don't create more of themselves. They don't create more neurons in general - except in a few places in the brain and body. So, any tissue that recycles itself is prone to cancers. And those tissues thrive on androgens and estrogens to create more tumors. So, you have to be careful anytime you're modulating hormones - especially androgens and estrogens.

Tool - Ecdysteroids / Turkesterone

And in my scouring of the literature and looking at - kind of - what's out there and what people are talking about - and I also mean in the scientific literature - one of the things that is new to me anyway - probably not new to a lot of the gym rats out there but - or the people that spend a lot of time on YouTube videos talking about androgens - are these - forgive me for butchering the name again - are these ecdysteroids. So, ecdysteroids are molecules that come from things like spinach - believe it or not - that have a lot of similarity to the cholesterol molecule. The one that's being discussed a lot out there right now is something called turkesterone. I wish I knew why it was called "turkesterone". Someone tell me why it's called "turkesterone". Does it have anything to do with turkeys? I don't know why it's called "turkesterone". Perhaps someone will - will know. In any case, these ecdysteroids are similar enough to cholesterol. Remember, cholesterol is the precursor to testosterone, cortisol, and estrogen. And it appears that some of these ecdysteroids do have bioavailability or their metabolites are bioavailable. And this was something that - for many years, people talked about whether or not insect hormones or hormones from other species could actually be used by humans - or whether or not it would have any effect at all.

And it's pretty clear, based on a study that I was able to find - there's a paper that came out in 2019. It's a comparative study in the Archives of Toxicology. This is Isenmann et al. - I-S-E-N-M-A-N-N et al. - that talks about the ecdysteroids and was given - in conjunction with strength training - strength training or no strength training. This is a 10-week intervention. And their conclusion is that these ecdysteroids had a fairly significant - above placebo controls - increases in muscle mass, strength, hypertrophy effects - all the sorts of things that one would expect with increases in androgen. Their conclusion of this study is not my conclusion - although, I may or may not agree with them. This isn't about my opinions. It's just I want to be clear. These are their words, not mine. But they - their - they say that - in their words - quote, "Our results strongly suggest the inclusion of ecdysteroid in the list of prohibited substances." So, they're saying these things are so powerful that they should be on the list of banned substances, - which might be upsetting to some - or some of you might be thinking, "Well, who cares?"

The whole issue of augmenting hormones in sport is a very interesting issue. In fact, if you just want a little anecdote about that - I can't reveal names here, of course - but what I learned recently - was very surprising to me - which is that many athletes in pro sports are taking testosterone and they are able to do that legally - not just because it's available by prescription - but they are allowed to do that under the rules of their sport - in the fine print that no one, including me, had ever seen - if they've had an injury. So, if athletes are injured, then it opens up the door for certain forms of testosterone augmentation and other types of augmentations that are not available to them if they're not injured - which always makes me wonder now when I see them getting injured - whether or not that's an attempt to get some of the support - because there's absolutely no question that estrogens and testosterone modulate gene expression, modulate strength, modulate the way the brain works, modulates our relationship to effort and anxiety, etc. And while we're talking about supplementation, the effects of supplementation - I would say - in some individuals can be quite dramatic. But they're always, always, always - except in extreme cases - going to be far subtler - excuse me - far more subtle - to use the - the proper English - far more subtle than would be, for instance, just injecting testosterone, or injecting estrogen, etc. So, I think we should just be honest and upfront about that.

Tool - Human Chorionic Gonadotropin (hCG)

So thus far, in terms of talking about optimizing hormones and in the discussion of supplementation, I haven't really talked about things that actually affect the brain directly - that increase the pituitary output and things of that sort. We've mainly been talking about things that free up testosterone or the increased estrogen at the level of the periphery. But if you remember way back to the beginning of this episode, hormones are made in different locations in the body and there - there are hormones that promote the release and the production of - of hormones from other tissues in the body. And one of the main hormones for that is luteinizing hormone. Luteinizing hormone, again, comes from the pituitary - circulates - and either goes to the ovary to promote various aspects of egg maturation - as well as production of estrogen - and to the testes to promote testosterone and sperm production. And the prescription version of increasing luteinizing hormone is something called hCG - or human chorionic gonadotropin - which has been synthesized and is now available as a prescription drug. It's taken in various contexts for increasing fertility - both by males and by females. It can increase - for all the reasons that now make sense - it can increase sperm production, it can produce ovulation frequency, it can produce the number of eggs even that - that are deployed in a given ovulation - although, that's not always a good thing. It basically is pro-fertility, pro-testosterone, pro-estrogen - depending on your background.

And what's interesting is hCG was initially synthesized - collected and synthesized from pregnant women's urine. And believe it or not, before it was synthetically made and sold as a prescription drug, there was actually a black market for pregnant women's urine - where people would buy the urine. I don't know. I'm guessing that they probably just consumed it - which is weird. But in any case, human chorionic gonadotropin is now available as a prescription drug and it's one of the things that many people use to increase testosterone or estrogen for increasing fertility.

In some cases, I think it's used to increase sports performance or when people have shut down their - their gonads for whatever reason - because of excessive hormone therapies or they have some sort of - sometimes they're actually lesions to the - to the pituitary. Sometimes people have a tumor in the pituitary. It's actually not common. But among brain tumors and neural tumors, it's one of the more common ones. And then, you get deficiencies in LH and FSH. And so, people will take hCG to stimulate the gonads. So, there are a variety of reasons why these drugs were created.

Tool - Fadogia Agrestis

But there are certain supplements - not many - that apparently can increase luteinizing hormone and thereby, can increase testosterone and estrogen. And one of the more well-documented ones is fadogia agrestis. That's F-A-D-O-G-I-A - separate word A-G-R-E-S-T-I-S - which, at least according to the literature that I was able to find, can increase levels of luteinizing hormone and thereby, levels of testosterone or levels of estrogen. And again, if an individual were to take fadogia agrestis, what they would probably find is that testosterone and estrogen would increase in any one of any chromosomal or gonadal background. But remember, it's the ratio of both. So, both - if someone has low estrogen, high testosterone - let's say they have testes, just by way of example - then both of those should - would be expected to increase. And if someone has high estrogen and low testosterone - and let's just say has ovaries - then both of those would increase by taking fadogia agrestis. The side effect profile of fadogia agrestis hasn't really been documented, so it's a little unclear.

I just want to emphasize that anytime someone's going to start taking supplements that - or modifying sex steroid hormones - getting blood work done is extremely important for safety reasons - and also just to know whether or not things are working. And because all of these things are subject to negative feedback - talked about this previously - previous episode - but if testosterone goes high or too high, it can feed back and shut down luteinizing hormone, which will then shut down for testosterone production. Likewise, if estrogens are going too high or they're going too high at various phases of the cycle, that can start to throw off various other hormones - including FSH, progesterone, LH. The menstrual cycle itself is a just - absolutely exquisite balance of feedback of luteinizing hormone kept low and constant - at least for the first 14 days of the cycle. Then mid-cycle, there's a peak. And that's typically when ovulation occurs. That's why pregnancy is most likely during the middle of the 28-day cycle. FSH - kind of - goes up and then down across the first 14 days. So, taking anything or really modifying one's estrogens or testosterone on - on that background of the menstrual cycle is really going to disrupt the way those things interact. And it's just such an exquisite feedback loop. So, I'm not saying don't do that, but you definitely want to be aware of what you're doing. And blood draws are one way to do that. Monitoring cycles for ovulating females is another way to do that. And in males, having a good window into what's going on with testosterone, DHT, aromatase, estradiol, LH, etc. - is just vital and it's really part and parcel with the practice of thinking about optimizing these incredible things that we call sex steroid hormones - estrogen, and testosterone, and their derivatives.

Bulbine Natalensis

The list of supplements and molecules that can adjust estrogen and testosterone is vast - and I only touched on a few of these. I - I really tried to emphasize the ones for which there are human studies - or that have mostly human studies - or maybe even just one human study. There are other things out there for which there are scientific data - things like bulbine natalensis - which definitely has support for increasing testosterone, but all the studies were in rats. I think there is some evidence in humans, but the evidence is - mainly comes in the form of what we call sponsored research, so companies paying for research - which is different than independent research by people who are not biased in terms of the outcome. And the reason I didn't throw out things like bulbine natalensis is they seem to have liver toxicity similar to high levels of anabolic exogenous steroids. There are some problems associated with them that make them - you know - important to think about if you're curious about this area and - and the endocrinology, but also somewhat precarious. And - you know - that's one category. So, stuff that doesn't have a lot of evidence in humans - might actually be dangerous.

The other category of things that has been shown to improve - or levels of - or increase, I should say. I don't want to say "improve" because it's up to you whether or not you would increase estrogen and testosterone. That's highly individual. How could I know? Are the things that are - kind of - housekeeping for production of estrogen and testosterone - things like magnesium - things like D3 - things like zinc. You know, those are the things that are going to create an overall milieu of opportunity to produce normal endogenous levels rather than increasing endogenous levels further. And so, I really want to highlight that there's a difference between taking something to create a - kind of - backdrop of general support and taking something that's going to create a big inflection in the levels of a given hormone.

Recap

So once again, we covered a tremendous amount of information. We covered some basic science of hormones and pheromones - estrogen, and testosterone, and their derivatives. We talked about supplementation and behaviors - competition and parenting - and how all these things interact. And I hope that you'll come away from this with a deeper mechanistic understanding of how the brain and body are interacting to control the output and the ways in which these incredible things that we call sex steroid hormones work and influence us. I hope you'll also come away with some ideas of things that you can do - in particular, behavioral practices that can improve sleep and your relationship to light, etc. - because those things really set the foundation not just for healthy steroid/hormone output, but for all sorts of health effects - and for both the psychology and the biology of your nervous system.

Conclusion

So, I'm sure there'll be many questions. There are many things that I couldn't get to today. I do try and limit these episodes to about 90 minutes - which is the optimal ultradian cycle for learning. It's a lot of information, but we've timestamped everything for you. So, feel free to look over it in parts or circle back where you might want deeper understanding. And please put your questions in the

comments section below. Please put suggestions for future episodes and things that relate to hormones in the comments section below. We do look at those and we do use them to inform the content for subsequent episodes.

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