

How to Optimize Fertility in Males & Females | Huberman Lab Podcast

In this episode, I discuss the mechanisms by which human eggs and sperm are generated, the ovulatory/menstrual cycle, the conception process and overall fertility in males and females. I also explain how, regardless of whether you seek to conceive children, optimizing egg and sperm health is directly related to vitality and longevity. I cover the nutrition-based, behavioral, supplement-based and prescription approaches to optimizing egg and sperm health, the ovulatory/menstrual cycle and fertility. In addition, I explain lifestyle choices that greatly assist or harm fertility—several of which are very surprising. I provide science-based protocols for those trying to conceive children. The tools and principles I discuss can also improve overall vitality and longevity in all people, regardless of age.

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ANDREW HUBERMAN: Welcome to the Huberman Lab podcast, where we discuss science and science-based tools for everyday life. [MUSIC PLAYING] I'm Andrew Huberman, and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. Today we are discussing fertility. We will discuss male fertility and female fertility. And I should mention that today's discussion is not just for people who are seeking to conceive children or who want to know how their children were conceived, but it's really for everybody. And I say that because it is the story of all of us. All of us are here because a specialized set of cells, called germ cells-- that is the sperm and the egg. And I'll make it very clear why they're called germ cells a little bit later. It has nothing to do with infection. But it's because a sperm cell and an egg cell arrived at one

another, either in vivo-- inside of our mother-- or in vitro-- so-called in vitro fertilization-- and then we're implanted into our mother and became us. And so understanding the process of how the egg cell and the sperm cell came to be is really the key to understanding how that fertilization process came to be. Now, I know everyone's thinking, I know how fertilization occurs. It occurs through sexual intercourse and so on. And we'll talk a little bit about that. But I promise you that if you understand the menstrual cycle-- and the menstrual cycle in today's conversation can best be thought of as a biological cycle that occurs in females that allows the potential for fertilization by the sperm, because that's really what it is, and it's a beautifully orchestrated process that I'll describe to you. And I should say, all people, males and females, should really understand how the menstrual cycle works, how it impacts fertilization, but also how it impacts the brain and body, behavior, psychology, et cetera. And we'll also talk about spermatogenesis, how sperm cells come to be and how they arrive-- that is, how they swim to the egg-- and the incredible interplay between the biology of the sperm and the biology of the egg leads to this incredible thing that we call embryogenesis and the birth of the child and, of course, the development of that child into an infant, a toddler, an adolescent, a teen, and an adult. Today's discussion, again, is not just for those of you that are seeking to have children. And I say that because when you look at the data, you look at the literature on longevity and vitality, two themes in biology that oftentimes people lump together but aren't always the same-- for instance, there are a lot of things that we can do to increase our vitality that actually can harm our longevity. But there are a subset of biological rules and mechanisms that, when aligned, allow us to maximize both our vitality and our longevity. And I think it's fair to say that all of those mechanisms and tools are housed in the discussion around maximizing fertility. And that's true whether or not you're male or female. In other words, if you want children or if you don't, if you already have children or if you don't, understanding how fertility and fertilization occurs in the brain and body will allow you to maximize your vitality and longevity. And of course, today's discussion will provide an understanding of the biology and many actionable tools that will also help you conceive children, if that's your wish. So of course, as is characteristic of this podcast, we will discuss science-based tools, including behavioral tools, both the dos and the don'ts, and we will discuss nutrition-based tools and supplementation-based tools and some other practices, including things like acupuncture, which have quite good data to support them in terms of improving fertility. And we will discuss why those certain practices can work. And we will discuss

prescription drugs that your doctor can prescribe to you if, for instance, you have a deficit at the level of hormone production or neurotransmitter production at the level of the brain or the pituitary gland-- I'll explain what all of those things are soon-- or the gonads, the ovary and the testes in females and males respectively. Again, by the end of today's episode, you will have a lot of knowledge and actionable tools related to maximizing fertility, and you will

00:04:24 Maui Nui Venison, Eight Sleep, Momentous

have a lot of knowledge and actionable tools related to maximizing vitality and longevity. Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is, however, part of my desire and effort to bring zero cost to consumer information about science and science-related tools to the general public. In keeping with that theme, I'd like to thank the sponsors of today's podcast. Our first sponsor is Maui Nui Meats. Maui Nui Meats, I can confidently say, are the most nutrient-dense and delicious red meat available. Maui Nui he spent nearly a decade building a USDA-certified wild harvesting system to help balance invasive deer populations on the island of Maui. The solution they built turns the proliferation of an invasive species into a wide range of nutrient-dense products, from fresh butcher cuts and organ meats to bone broth, jerky, and even pet treats. Their bone broth has an unmatched 25 grams of protein per 100 calories. I've talked before on this podcast and I've had several expert guests come on this podcast to talk about the fact that most people should aim to get 1 gram of quality protein per pound of body weight per day in order to maximize their health, tissue repair, which includes brain tissue repair, and, if you're an active exerciser, to support recovery from exercise. Maui Nui Meats have an incredible quality protein to calorie ratio. And I mentioned the bone broth. I should also mention that their ground meats and their venison steaks are absolutely delicious, and their jerky is absolutely terrific. In fact, it's the only jerky that I've eaten consistently that I happen to like consistently over time. If you'd like to try Maui Nui Venison, go to mauinuivenison.com/huberman to get 20% off your first order. Again, that's mauinuivenison.com/huberman to get 20% off your first order. Today's episode is also brought to us by Eight Sleep. Eight Sleep makes smart mattress covers with cooling, heating, and sleep tracking capacity. I've talked many times before on this podcast about the fact that sleep is the fundamental layer of mental health, physical health, and

performance. Now, one of the key things for getting a great night's sleep every single night is to optimize the temperature of your sleeping environment. Put simply, in order to fall asleep and stay deeply asleep, your body temperature needs to drop by about 1 to 3 degrees. And waking up, on the other hand, involves a heating of your body by about 1 to 3 degrees. With Eight Sleep, you can tune the temperature of your mattress cover or mattress to be cooler or hotter, depending on whether or not you tend to run too hot or too cold, and you can even vary it across the night so that you can access the best deep sleep early in the night, the so-called REM sleep, rapid eye movement sleep, that's more pronounced in the later half of the night and in doing so really get your sleep optimized, not just in terms of duration but in terms of quality and the overall architecture of your sleep. This has a profound influence on your alertness, focus, mood, and many other important factors throughout the day. If you'd like to try Eight Sleep, you can go to eightsleep.com/huberman to save up to \$150 off their Pod 3 cover. Today's episode is also brought to us by Momentous Supplements. I want to acknowledge that not everybody needs supplements, and yet many, many people derive tremendous benefit from proper supplementation. I would count myself in that group. There are excellent supplements for improving the depth and quality of sleep, for improving focus, and for improving energy and for hormone optimization and many other factors related to our mental health, physical health, and performance. We've partnered with Momentous Supplements for three important reasons. First of all, Momentous supplements are of the very highest quality. Second of all, they ship internationally, and we know that many of you reside outside of the United States. And third, they focus on single ingredient formulations. This is very important. There is a place for blends. But in most cases, if you're going to develop a supplement protocol, you want it to be single-ingredient formulations so that you can adjust the dosages of different things according to what works and doesn't work for you, which is essentially impossible to do if you are using multi-ingredient formulations. If you'd like to see the supplements that I take and that we've discussed here on the Huberman Lab podcast, you can go to [livemomentous-- spelled O-U-S-- so livemomentous.com/huberman](https://livemomentous.com/huberman) and get 20% off any supplements.

00:08:20 Eggs & Sperm, Genes, Fertilization

Again, that's livemomentous.com/huberman to get 20% off. Let's talk about fertility. And in doing so, let's take a step back from this word "fertility" and ask, what is fertility and

fertilization really all about? Well, the obvious answer is that it's about producing offspring. But more importantly, it's about producing offspring that contain the genetic components of both parents and indeed contain half of the genes from one parent and half of the genes from another parent. Now, there are two general types of cells in the body. The most common types of cells in the body are called somatic cells. So these would be all the cells in your body except the egg in females and the sperm in males. The egg in females and the sperm in males are part of what's called the germline. And again, it has nothing to do with infection. It's just that the cells of the germline have genes that cannot be modified by the behavior of the individual that houses those genes. What do I mean by that? Well, if I were to tell you that by exercising you can improve mitochondrial function, you can change hormones by reducing stress, you can reduce cortisol by hitting puberty, for instance, you will have the secretion of hormones that then change gene expression in other cells, leading to the development of body hair, facial hair, deepening the voice, breast growth, et cetera, you'd say, OK, great. Yeah, that all makes perfect sense. But that's all occurring in the so-called somatic cells. The germ cells or the germline cells-- that is, the egg and the sperm-- are a very unique and protected set of cells that are generated in a particular way and whose genetic components are not modifiable by experience. And when you take a step back and you think about it, you say, oh, that's right. There's no reason to think that exercising will make the children that you have not yet had stronger. And you say, of course not. Well, why is that? Well, that's because there is a barrier between the genes of the germline cells and behaviors. They cannot be modified by behaviors and the various things that you do in your lifetime. Now, I suppose there's an exception in the negative direction. And what I'm referring to here is if you were to, say, be exposed to a chemical that could mutate the DNA of your egg or sperm or if you were to fertilize an embryo in a certain way or at a certain stage of life that it got an extra chromosome, for instance-- we'll talk about this a little bit later-- well, then, of course, you could end up with offspring that have modified DNA that don't faithfully represent half of the genes from mom and half of the genes from dad. But that's not the same as specific behaviors modifying the genes of those cells-- the sperm and the egg cells-- in a way that improves the offspring. So the key first thing to understand today is that there's a distinction between somatic cells, which is the vast majority of cells in your body, and the so-called germline cells, which are the egg and the sperm. The egg and the sperm are these highly protected populations of cells that, in females, actually come to be during embryogenesis. So for

all females out there, you generate what today I'm going to refer to as a vault of cells. You have a vault of eggs that are your germline. Those eggs all contain all the chromosomes of your DNA. So it's going to be-- as most of you know, there are 23 chromosomes, and chromosomes exist in pairs. So the way to think about this is each pair is one strand, and you have 22 so-called autosomes, and then you have one sex chromosome. The sex chromosome will be either X or Y. So in a female, they have two X chromosomes. So in each one of the eggs that a woman has and that she's had since she was an embryo and that's contained in this vault, those eggs are, of course, going to be very immature at birth. She hasn't undergone puberty yet. And certainly, as an embryo, she hasn't undergone puberty. And those cells are going to contain 23 pairs of chromosomes. This is very important-- 23 pairs of chromosomes. The chromosomes are essentially the wrapped-up DNA that contains all the genetic information to create any cell type in the body and actually to create an entirely new individual. Now, there are 23 pairs of chromosomes, 22 of which are called autosomes. If that doesn't make sense to you, just remember, autosome, OK, there's 22 of them. And then there's one so-called sex chromosome. The sex chromosomes are either X or Y. But this is a female, so she's going to have 23 pairs of chromosomes, and she's going to have two X chromosomes for the sex chromosomes. If this is already confusing to you, don't worry, I'll make it very clear how this all relates to fertility and how it relates to chromosomal segregation and a bunch of things that I think maybe you've heard of and that perhaps were opaque to you. But I promise to make them clear. But just understand that, within each of those eggs, they have 23 pairs of chromosomes. And for those of you that like nomenclature, I'll tell you that those cells are considered diploid. They're called the diploid, and that means that they have 23 pairs of chromosomes, as distinguished from cells that are haploid where there's only one set of those 23 chromosomes. So instead of 23 pairs, there's only 23 chromosomes. We'll come back to haploid cells a little bit later. So when a female is born, she has all these eggs in the reserve, in this vault, that she'll have for her entire life. She's not going to make any more. But they are very, very immature. So when a woman is in embryogenesis, she develops these very immature eggs. Today we're also going to talk about follicles, and we will be careful to distinguish follicles from eggs. They're often talked about interchangeably, online and elsewhere and even by fertility docs and OB/GYNs. But right now we're just talking about the egg cells, the eggs themselves, which are cells. Now, the goal of fertilization is to bring that egg cell into close enough proximity that it can be fertilized by a single sperm cell. And that sperm cell

will bring 23 chromosomes, as well, that include-- just as in the female egg, it'll have 22 autosomes and one sex chromosome. And in the male, that sex chromosome can either be an X chromosome, which then would give rise to female offspring, or a Y chromosome, which would give rise to male offspring. And today we're not talking about sexual differentiation. That's a topic of a previous and yet another future episode. But just to give you a sense of how X chromosomes and Y chromosomes can actually accomplish that sexual differentiation, both of body and brain. I'll just mention in two sentences that, for instance, if there's a Y chromosome as opposed to an X chromosome, that Y chromosome contains genes that suppress, for instance, the development of female genitalia and thereby give rise to male genitalia. So rather than the formation of a clitoris, it's the formation of a penis. And rather than the formation of ovaries, the formation of a testes. So that's more directed towards sexual differentiation. We're not going to get into that right now. We'll get into that in a future episode. But even if you're only tracking about 10% of what I'm saying right now, I promise you're doing great. If you're tracking more than 10%, well, then you're doing terrifically well, because the essence of fertility and fertilization is to bring together that haploid cell that is the sperm that only has 23 chromosomes-- but not pairs of chromosomes because that's the DNA from dad-- together with the egg, which, as I told you already, has 23 pairs of chromosomes. So part of the fertilization process has to be to get rid of one half of those 23 pairs in the female. You got to get rid of it, and you have to get the egg and the sperm in proximity so that the egg can potentially be fertilized by the sperm bringing the DNA, the 23 single strands of chromosomes from dad, into a cell that has 23 single strands from mom. So I realize I'm probably being a little bit repetitive here, but I want everyone to understand this because it really frames up fertility and reproduction in the proper way. We've got a cell from mom, the egg, which has 23 pairs of chromosomes. We need to get rid of one set of those pairs so that there's only 23 chromosomes. We need to get rid of half of those chromosomes. And then we need to bring that cell together physically with the sperm cell that contains the 23 chromosomal strands from dad. And we need to bring those together so that you get 23 chromosomal pairs from dad and 23 chromosomal pairs from mom. And in doing so, you create a cell, which then becomes multiple cells. That's going to be the developing embryo that has half the genes from mom and half the genes from dad. So I hope that's clear. That is the biological logic, which I realize is a bit of a tongue twister. But forgive me. It is the most accurate way to describe this process. We're trying to bring together the 23 single strands of

chromosomes from dad and the 23 single strands of chromosomes from mom into the same cell. Now, that requires a literal physical contact and pairing of the two cells. But as I mentioned before, all these eggs in mom are sitting in a vault, and they're very, very immature. So the ovulatory cycle and the menstrual cycle are really about first eliminating half of the chromosomal pairs in that 23 sets of chromosomes and not getting rid of, for instance, half-- just going 1 to 11 or 12 to 23. That's not the goal. The goal is to have chromosomes 1, 2, 3, 4, 5, 6, all the way up to 23, but only to have half of the chromosomes there and to bring that cell together with the sperm cell, physically, then allow them to fuse and allow the chromosomes from dad and the chromosomes from mom to fuse within a single cell and duplicate into cells that contain half of the chromosomes from dad and half of the chromosomes from mom.

00:18:28 Puberty: Gonadotropin Releasing Hormone (GnRH), Melatonin & Leptin

That's what the ovulatory and menstrual cycle are really all about. So when thinking about it that way, I'd like to just initiate the discussion by focusing first on the female component, or the egg component, of fertility and fertilization. As I mentioned before, a female has all the eggs, albeit very immature eggs, that she's going to have at the time that she's born. Now, puberty will happen at some point and will allow the ovulatory and the menstrual cycle to commence. Now, one question that you perhaps are asking is, what controls the onset of puberty? And there are a number of different results, each of which could be an entire episode of a podcast on its own. But I'll just highlight a few things that we know about the onset of menses or menstruation, or it's sometimes also called a menarche. One thing that you'll notice about today's discussion is that if you were to take any number of your notes online and put them into a search function that you would see a lot of different language used for the same thing. So for instance, some people will talk about the egg and the follicle as the same thing, even though they are not. I'll explain the difference soon. Some people will talk about menses or menstruation or menarche as the exact same thing. And in fact, they are not the exact same thing, but oftentimes these words are used interchangeably. I'll do my best today to not overload you with nomenclature but rather to use the most commonly used terms for the different aspects of fertility and fertilization. But when it comes to the onset of puberty, first of all, most of you have probably heard that the onset of puberty is happening much earlier in females now than it was some years ago. And in fact, that is the case. And I'll talk about

some statistics related to this which are pretty striking but don't necessarily point to anything detrimental. It doesn't necessarily mean that something bad is happening. What do we know for sure? Well, we know that there are a number of signals that come both through the brain and through the body-- and more likely both-- in order to control the onset of puberty in females. A couple of examples-- the first is a mechanistic one. We know, for instance, that the entire process of the ovulatory menstrual cycle is initiated from the brain. We're going to get into this in a lot more detail in a few minutes. But there's a certain number of hormones and neurotransmitters that are communicated from the brain, a structure called the hypothalamus, which roughly sits above the roof of your mouth, and that communicates with a gland, an endocrine or hormone-releasing gland called the pituitary gland. The pituitary gland looks like a stalk that essentially extends out of the brain. It's also located not far from the roof of your mouth. And that has two sort of small marble or grape-sized protrusions, the anterior pituitary and the posterior pituitary. And they release different hormones into the bloodstream. Puberty is in part controlled by the fact that, up until puberty, there are neurons in the hypothalamus that release a neurotransmitter called GABA, which is inhibitory, and that prevents the neurons in the hypothalamus from releasing a very important hormone called gonadotropin-releasing hormone, or GnRH. So the first thing I'd really like everyone to know and commit to memory today is very easy-- GnRH stands for gonadotropin-releasing hormone. This comes from the brain and will communicate to the pituitary to release certain hormones. Prior to puberty, in both males and females, there are neurons in the brain that are actively suppressing the neurons that release GnRH. It's like no puberty, no puberty, no puberty. You can't have puberty. You can't have puberty. And in fact, those cells are releasing this neurotransmitter called GABA because it's inhibitory. It prevents the firing of those neurons. So puberty is actively suppressed up until a certain point. It's also actively suppressed, at least in some species and we think at least partially in humans, by the tonic release-- that means the ongoing release, around the clock-- of a hormone called melatonin. Later in life-- in fact, after puberty-- melatonin will be secreted only in the dark phase of each night and around the time that one goes to sleep. But in children and in particular in children prior to puberty, melatonin is released more or less constantly. Now, melatonin isn't the only source of suppression of puberty. It's also these neural mechanisms involving GABA. But it is certainly a great candidate for one of the reasons why puberty doesn't generally tend to happen at, say, age four age five. That would be very unusual. Another

component of suppression of puberty is that typically in children they have relatively low body fat stores. Why is this important? Well, we know that one of the things that can trigger the onset of puberty-- in particular in females-- is that when enough body fat accumulates, that body fat releases a hormone called leptin, and that hormone leptin travels in the bloodstream, across the blood-brain barrier, and goes to the hypothalamus and can trigger the onset of puberty

00:23:38 Onset Trends of Puberty, Odors Effects

by activating the neurons that release gonadotropin-releasing hormone. So many people believe that one of the reasons that puberty is happening earlier and earlier in females is because of the accumulation of more body fat at younger ages than was observed 30 or 40 and certainly 100 years ago. Now, I can already imagine a number of people are thinking, oh, this must relate to the obesity crisis. And indeed, there is a crisis of obesity. Obesity is something that is causing all sorts of problems with people's health at various levels, brain and body, and that is far more frequent today than it was even 20 years ago. So it is indeed a crisis because it has enormous detrimental effects for so many aspects of brain and body health and longevity. But this whole process of thinking about body fat signaling leptin to the hypothalamus and the onset of puberty doesn't necessarily have to do with the obesity crisis. It might relate, but it could also relate to, for instance, improved nutrition, which is allowing body fat stores to accumulate maybe not to the level of obesity but to accumulate earlier and at younger ages in females, which is then causing earlier puberty in females. To just highlight how that might be possible, I want to review some data that talk about the onset of menses, menstruation-- that is, puberty-- in females according to country and according to age over the last 100 or more years. So what are the general trends in terms of the onset of puberty in females? Well, that's an easy one to answer. Over the last 100 years or so, the onset of puberty has been occurring much earlier with each passing decade. It's really an incredible set of statistics. I will provide a link to these data since I know a number of you are listening and not just watching on YouTube. This is from a study in which the onset of puberty has been analyzed from as early as the 1850s-- in certain countries, there are data on that-- out to the 1970s and in other countries starting at about 1900, extending out to about 1990. These are ongoing collections of data. But just to give you a sense of how the data are falling out in a couple of different countries, just to give you a flavor--

but for those of you listening and for those of you watching, the essence of all of these findings is that puberty is happening much, much earlier with each passing decade. So for instance, in the United States, around 1900 or 1903, the average age of menarche, the onset of puberty, in females was about 14 years old, whereas in 1990, the average age is 11. So that's a pretty significant, we can say, acceleration of the onset of puberty. Now, of course, these are averages. So there will be exceptions. There's a distribution of data. Today, still, there will be young females who will undergo puberty at age 11 or 10 or maybe even 9 and others who will undergo puberty at age 13, 14, maybe even 16 or 17. However, if we look at, for instance, the data from Norway, which dates back quite far-- they have excellent record-keeping-- to 1850, what we see is that the average age of the onset of female puberty in 1850 in Norway was 17 years old, whereas in 1970, it's 13 years old. So this is a dramatic acceleration of the onset of puberty. And you see a similar trend in other countries, as well. So if we were to look, for instance, in the UK, they have a smaller data set, meaning it only extends back to about 1940. But the average age of the onset of puberty in the UK in 1940 was 13 and 1/2 years old. Again, this is just for females. And in 1970, it was closer to 13, with a trend towards declining even further. Unfortunately, they didn't continue to collect data out to 2022. And as a final point, if we were to look at, for instance, in Germany and Finland, the average onset of puberty in 1870 was 16 and 1/2 years old. By 1940, it was down to 13 and 1/2 years old. So all of these data have borne out over and over again, regardless of location in the world, which is important, because when you start to think about the obesity crisis, you can say, well, that's mainly in developed countries, believe it or not-- or perhaps not surprisingly. And maybe it has to do with the obesity crisis. And yet I don't think we can conclude that at all. Something is happening, however. It could be increased body fat stores due to overeating and obesity. However, it could also be-- unrelated to obesity, it could be, for instance, improved nutrition and the availability of quality nutrition, which can signal the maturation of the brain and body mechanisms that trigger the onset of puberty, ovulatory cycle, and menstruation. So we want to be very careful about leaping to conclusions about what these trends mean, but the trends themselves are very, very apparent. And as a final point, I should also mention that there are a number of different behavioral and psychosocial, as they're called, interactions that can influence puberty as well. This has been most strikingly observed in animals. And so I don't want anyone to be alarmed or to leap to any great conclusions about the onset of timing of puberty in humans, but I'd be remiss if I didn't tell you about a certain result which shows that if a

young female is exposed to the odor-- not necessarily the pheromones. There's a distinction between odors that we perceive and pheromones, which are subconscious. We don't actively perceive, but that can impact our biology, and pheromones effects in humans are very controversial. But we know, for instance, that if you take a female animal-- and there's some evidence from humans that if you take a young prepubertal female and you expose her to the scent of a reproductively-competent male for a series of days, but maybe even as short as a few hours, and she is also not regularly being exposed to the scent of her father, that she can undergo puberty earlier. That's right. There is something about the odor and/or pheromones, or perhaps something else, that occurs when a young prepubertal female has a father that she's in regular contact with. He wouldn't necessarily have to live at home but that is around a lot that his smell is registered by her biological systems. That-- I don't want to say protects because it kind of skews the valence of the conversation, but that offsets or buffers the otherwise observed effect, which is that the scent of a reproductively-competent male, if it's present often enough or perhaps intensely enough, that it can trigger the onset of puberty in that female. In other words, the scent of a male that is not the father and we think also that is not biologically related to her can trigger earlier onset of puberty. And that effect can at least be partially buffered by her being in the presence of the scent from her biological father. Now, some of you are probably already leaping to conclusions about what this means. Should you not allow your daughter to be exposed to any males who are of reproductive age, et cetera? That's certainly not what I'm saying. There's a huge number of considerations that go into that calculation for everybody and circumstances, et cetera. But the point is that the odors of individuals, both related-- in particular, closely related-- and non-related individuals, can shape the neural systems and the hormone systems that can trigger the onset of puberty or suppress the onset of puberty. So whether or not we're talking about onset of puberty at this age or that age and whether or not biologically-related male

00:31:24 Female Puberty, Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH)

or non-biologically-related male scents around, et cetera, the thing I want everyone to know is that at some point during development, typically nowadays between the ages of 11 and 15 or so-- again, there's variability there. The suppression of gonadotropin-

releasing hormone released from the hypothalamus is removed, and then gonadotropin-releasing hormone can activate cells within the pituitary. And if you really want to know, it's the anterior pituitary in particular. And then the anterior pituitary gland, which sits at and kind of bridges the brain and the body because it allows the release of hormones into the bloodstream, that anterior pituitary is going to release two key hormones that everyone should know the name of and what they do. And when I say everyone, I mean males and females need to know about these hormones because they have an active role in both males and females. And of course, you should want to know and should know about the biology of everyone on the planet, in my opinion, because it tells you a lot more about humans than if you just focus on your own biology. But those two hormones are called luteinizing hormone, which is abbreviated LH, and follicle-stimulating hormone, which is abbreviated FSH. So the simple picture that you need to have in your mind is gonadotropin-releasing hormone from the brain, from the hypothalamus in particular, is causing the release of luteinizing hormone and follicle-stimulating hormone, GnRH stimulates LH, luteinizing hormone, and follicle-stimulating hormone, FSH. LH and FSH travel in the blood and can access all the cells and tissues of the body. This is one of the incredible things about hormones is that many hormones-- and LH and FSH are included in this group-- can travel into cells, and they can actually change the genetic expression of those cells. They can change which genes are turned on and which genes are turned off. And they can also attach to the surface of those cells and make those cells take on different properties. So they can mature those cells. So for instance, a good example of this outside of the context we've been talking about is the hormone testosterone can travel to the hair follicle and can stimulate changes in the genes of the cells of the hair follicle that can make hair grow. A different hormone, estrogen, can travel to the cells of the breast tissue and activate genes that control enlargement of the cells of the breast tissue. Prolactin, a different hormone, can travel to the mammary ducts and control the production and the secretion of milk. And in males, that can actually happen, in certain cases, although it's rare. But prolactin can also travel to areas of the brain that control libido, for instance. And just so you'll never forget it, males' elevated levels of prolactin are actually what set the refractory period after ejaculation and prevent erection for some period of time. So you'll never forget prolactin. The point being that different hormones have different effects on different cells, depending on what cells those are. Estrogen or estradiol is going to have different effects on the breast tissue than it would on skin, although as effects on both. Similarly,

when LH and FSH, luteinizing hormone and follicle-stimulating hormone, travel in the blood to the gonad and the gonad is an ovary, it will have a certain set of consequences. And when luteinizing hormone and follicle-stimulating hormone travel in the blood to a gonad and that gonad happens to be a testis, then it will have a different set of biological implications. So let's focus now on what happens when LH and FSH arrive at the ovary. And let's assume now that we're talking about a female who has already undergone puberty, or perhaps we could even frame this in the context of a female who is about to undergo puberty. FSH and LH are now able to be released because she's undergoing puberty. But the same set of processes, essentially, would occur for any point from puberty onward until menopause,

00:35:25 AG1 (Athletic Greens)

which is the depletion of that vault, that ovarian reserve of all those immature eggs. I'd like to take a brief break and acknowledge our sponsor, Athletic Greens. Athletic Greens is an all-in-one vitamin mineral probiotic drink that also contains digestive enzymes and adaptogens. I started taking Athletic Greens way back in 2012, so that's 10 years now of taking Athletic Greens every single day. So I'm delighted that they're sponsoring this podcast. The reason I started taking Athletic Greens and the reason I still take Athletic Greens is that it covers all of my foundational nutritional needs. So whether or not I'm eating well or enough or not, I'm sure that I'm covering all of my needs for vitamins, minerals, probiotics, adaptogens to combat stress, and the digestive enzymes really help my digestion. I just feel much better when I'm drinking Athletic Greens. If you'd like to try Athletic Greens, you can go to athleticgreens.com/huberman, and for the month of January, they have a special offer where they'll give you 10 free travel packs plus a year supply of vitamin D3/K2. Vitamin D3 and K2 are vital for immune function, metabolic function, hormone health, but also calcium regulation and heart health. Again, that's athleticgreens.com/huberman

00:36:34 Ovulatory & Menstrual Cycle

to claim their special offer in the month of January of 10 free travel packs plus a year supply of vitamin D3/K2. OK, so we're now going to talk about ovulation and menstruation, and let's just remember what this is all about. This is all about creating the

potential for an egg to be fertilized, and that egg needs to have half of the chromosomal pairs, so no pairs, but it's got to have 23 chromosomes just from mom. And we need to position that egg so that the egg can be met by the sperm and that sperm can penetrate that egg and donate its 23 individual strands of chromosomes to that egg so that you can bring together the DNA of dad and the DNA of mom. So the obligatory menstrual cycle occurs when luteinizing hormone and follicle-stimulating hormone have been released. And the ovulatory/menstrual cycle-- and here I have to kind of pick what I want to call it. I guess to be really accurate, we would just call it the female reproductive cycle, but that includes underneath it both the menstrual cycle, as it's sometimes called, and the ovulatory cycle. So you decide. I'm going to interchangeably discuss the ovulatory cycle and the menstrual cycle. The problem is, when you say menstruation, people often think about just the period, the shedding of the uterine lining when fertilization has not occurred. So if I start saying ovulatory cycle, just keep in mind I'm referring to the entire thing. Now, this is probably also a good opportunity to say that if you heard that the ovulatory/menstrual cycle is 28 days long, that's true in some cases, but that's not always true. It's, on average, 28 days long. There are some females for which the ovulatory cycle will be shorter-- it can be as short as 21 days-- and other females for which it will be 35 days long. Shorter than 21 days and longer than 35 days is rare, although it does occur. One of the key things when thinking about fertility is if you talk to OB/GYNs who are focused on fertility, which I have in anticipation of this episode, they'll tell you that whether or not your cycle is 21 days long or 35 days long is not as much of an issue necessarily unless it's happening to become much shorter or much longer in a kind of erratic way. So if you're somebody who's consistently had 28 day long cycles and all of a sudden you're having 30 day long cycles, that's not necessarily an indication of anything bad. But if it's 21 days one month and it's 30 days the next month and it's 17 days the next month or even if it's always falling within that 21 to 35 day long cycle but it's very variable from each month or every other month or so, you probably want to talk to your OB/GYN because that could indicate a number of different things. Which things could it indicate? Well, that will become clear as I spell out the biology in a bit more detail. But this idea that the menstrual cycle/ovulatory cycle is always 28 days, that's just false. That's just not true. I should also mention that there is a common misconception that because the average menstrual cycle is 28 days-- indeed, the average is 28 days-- and the lunar cycle is 28 days-- and of course, there is a real biology to support the fact that the lunar cycle can't, in fact, impact certain aspects of human behavior. It does, and

we'll talk about lunar cycles in a future episode. But there is zero data to support the idea that the menstrual cycle and the lunar cycle are linked in any kind of causal way. Sorry to break it to you. The lunar cycle and the tidal cycles at the ocean are definitely linked in ways that are super interesting related to the tilt of the Earth and the pull of gravity of different planets, and it's an incredible story into itself. But the lunar cycle and the menstrual cycle, despite having some weak correlation in terms of their duration or their so-called periodicity-- no pun intended-- well, there's no causal relationship whatsoever between the lunar cycle and the menstrual cycle. If any of you are aware of any real data that conflicts with what I just said,

00:40:36 Follicular Phase: Egg Maturation & Ovulation, FSH & Estrogen

please put that in the comment section on YouTube. But this is pretty well established as far as I know. OK, so we need to bring together the so-called haploid contents, the 23 individual strands of chromosomes from the egg, to a place and a position where it could potentially be fertilized by the male. So what happens? Luteinizing hormone and follicle-stimulating hormone travel to the ovary. These hormones are able to access the ovary. There's a lot of blood supply to the ovary. And FSH and LH arrive at the ovary. The ovary has this vault, this ovarian reserve of immature cells. They reside within what are called follicles. The follicles are little spherical packages that can potentially provide a nice environment for those eggs to mature. And when FSH, in particular, arrives at the ovary, a small number of those follicles will split off from the reserve, they will exit the vault, and they will undergo maturation. And the key player here is follicle-stimulating hormone. And the first 14 days of the menstrual/ovulatory cycle is referred to as the follicular phase because of this relationship between FSH triggering the maturation of a subset of follicles. Now, typically in the context of a 28 day or so ovulatory/menstrual cycle, day one is designated as the first day of the period, of the shedding of the uterine lining from the previous ovulatory menstrual cycle in which fertilization did not occur. So day one is when the period initiates. It is days 1 through 14, approximately-- because here we're just considering the average of a 28-day cycle, but it could be longer. It could be shorter. But the first half of that cycle is the so-called follicular phase, FSH, has triggered the departure of a subset of these follicles that contain immature eggs. And it is triggering the maturation of those eggs. Luteinizing hormone is also present, but also at relatively low levels. And it's during the first half of this ovulatory menstrual cycle that the

main goal is to get those follicles to mature. So inside of those follicles, the egg is developing. It's growing. It's maturing. And in doing so, it's also making its own hormones. This, I think, is one of the most elegant aspects of the ovulatory menstrual cycle that, in a few minutes, you'll learn about something which still to this day, even though I've known about this stuff for decades now because of my training, still just blows my mind that you have one hormone, follicle-stimulating hormone, triggering the maturation of some eggs inside of some follicles and then those follicles themselves making another hormone that furthers the process and then soon, as you'll learn, create a hormone to trigger the second half of the process. Just a beautiful symphony of expression of different genes and different hormones to make everything work as optimally as possible. So as these different follicles mature, somehow-- and we still don't know exactly how-- one of those follicles containing an egg gets selected. It's either because it matures the fastest or there's something about it that is still not completely understood that allows it to be selected. And all the other follicles that are maturing degenerate and die. And they're gone. They don't go back into the ovarian reserve. They are now depleted from that bank account that is the ovarian reserve. They die off. But that single egg that, keep in mind, contains 23 pairs of chromosomes-- we haven't gotten rid of one half of those 23 sets of chromosomes yet. But that one will continue to mature. And then, at some point, that egg will start to undergo a process in which those chromosomes are pulled apart by little components within the egg called spindles. They literally have a physical pulling of the chromosomes apart. So now those 23 pairs are no longer attached to one another at the middle like they were before, like two beads of strings-- or I should say, 23 short strands of beads that were at once connected to one another now are pulled apart so that you have 23 chromosomes on each side, but they're pulled apart from one another. So that diploid cell is now starting to become a cell in which half of the chromosomes, half of those 23 pairs, are physically pulled away from the others. And then the egg actually starts to form its own what we call an involution of membrane around those 23 pairs, one set of them, and encapsulates them. So you sort of got an egg with two parts where the two sets of chromosomes, two sets of 23 chromosomes, are now separate from one another inside of the egg. And then one of those actually gets ejected from the egg, and the name of that thing that gets ejected-- it's sort of like a little Hubble pod is how I imagine it, you know, from Star Wars or from any kind of Space Odyssey movie where some thing is ready to happen. A little Hubble pod shoots out of the ship. Well, that 23 pairs is now ejected from the egg. It's called the

polar body. And that's going to degenerate. It's going to go away. And in doing so, take the egg cell, which was once diploid-- it had 23 pairs of chromosomes-- and making it haploid. And now what you've got, in ideal circumstances, is a beautifully pristine egg that was selected for and has 23 single strands of chromosomes, 22 autosomes and one sex chromosome. And that sex chromosome is going to be an X chromosome almost with certainty, because female-- mother-- is creating that egg. So then the egg that contains just the appropriate 23 single-stranded chromosomes is going to fuse with the wall of the ovary, and that egg will be released and will travel into the Fallopian tube. Now, we'll get back to that egg in a few moments. But that process, which represents the first half of the ovulatory menstrual cycle, again, was triggered by FSH and to some extent luteinizing hormone. But it is the ongoing maturation of that egg which also causes the production of estrogen, which allows that whole process to occur. And you could say, why? Well, the answer to the why is a very important biological principle that we are going to return to in a number of different contexts today, both as reference to female and male fertility. And the principle is a so-called negative feedback. So when estrogen is present at relatively low levels in females in the ovary, as it is during the development of these eggs, some of that estrogen, of course, is going to exit the ovary. It's going to go into the bloodstream. And it's going to travel back to the pituitary. Now, the pituitary can release things like follicle-stimulating hormone and luteinizing hormone. But the way I'd like you to think about the pituitary for sake of feedback loops is that it's sort of like a thermometer that you would put into a pool, like a backyard pool, that is attached to the heater. And for instance, if you were to put a thermometer into a pool that you would like to keep at 70 degrees and the temperature of that pool is 60 degrees, well, then that thermometer ought to trigger some sort of mechanism where the pool would heat up until the temperature of the pool hit 70 degrees, and then it should trigger that thermometer to turn off the heating system. That's kind of a negative feedback system that would keep the temperature more or less correct. That's a lot of the way that the system's related to estrogen and also testosterone and these different things like luteinizing hormone and follicle-stimulating hormone work as well. Typically, when the level of a hormone is too high, then it shuts down the production of the hormones that would trigger further production of that hormone. I know that's a mouthful. It's a lot to think about. And some of you are probably thinking, whoa, I'm getting dizzy now with biology. But I promise you, you can understand this. In females, when estrogen is relatively low-- but not zero but is relatively low during that first follicular half of the

ovulatory cycle-- it actually triggers negative feedback on LH and FSH so that not too much is produced. But then just prior to ovulation, the levels of estrogen and the levels of some other hormones from those eggs-- you have the eggs producing estrogen themselves-- gets high enough that it actually triggers a positive feedback loop on the pituitary. So the pituitary is essentially observing the amount of estrogen in the bloodstream produced by the ovary, and the amount of estrogen towards the end of the second half of the menstrual cycle has increased and triggers a positive feedback loop. It triggers the pituitary to release more FSH and LH, and that helps trigger ovulation, that deployment or the release of that one mature proper selected egg that's haploid with the 23 individual pairs of chromosomes into the Fallopian tube. So let's just back up really quickly and just kind of summarize what's happened. Gonadotropin-releasing hormone from the hypothalamus triggers the release of follicle-stimulating hormone and luteinizing hormone. That travels to the ovary-- triggers the release of a subset of immature follicles with immature eggs. Those immature follicles and immature eggs start to mature, start to grow because of the presence of follicle-stimulating hormone. The growth of those eggs themselves increases estrogen. As the estrogen starts to accumulate in the environment, some of that travels back to the pituitary. And when levels of estrogen arriving at the pituitary are relatively low, the pituitary says, oh, we don't need to release any more follicle-stimulating and luteinizing hormone. However, at some point just prior to ovulation, enough estrogen has been produced by that one single selected mature egg and some of the other follicles around it that were maturing but then since died off that the estrogen triggers a positive feedback loop. The pituitary says, OK, and releases more follicle-stimulating hormone and luteinizing hormone. And bam, the egg, which has the proper genetic components, sets off out of the ovary and into the Fallopian tube. So-called ovulation has begun. That itself, what I just described, constitutes the first half of the ovulatory/menstrual cycle, which we call the follicular phase. And it's marked by the presence of FSH and some other things,

00:51:09 Luteal Phase: Progesterone & Estrogen, Menstruation

but we can really think about it as marked by FSH from the pituitary and by estrogen, or estradiol, made within the ovary. Then comes the second half of the ovulatory/menstrual cycle, which I personally think is one of the coolest mechanisms in all of biology, which is that-- remember the follicle that housed that one egg that was the selected egg that

became the mature egg? And that follicle, which no longer contains the egg because the egg took off and ovulated, is called the corpus luteum. And the corpus luteum starts making three hormones, which include estradiol, I think called inhibin, but the most important hormone, the one that you really need to know about, is that it starts producing very high levels of progesterone. Progesterone levels start to increase about the time of ovulation, although just prior to ovulation. And over the next second half of the ovulatory cycle-- so about 14 days if it's a 28-day cycle, a little bit longer or a little bit shorter, depending on the length of cycle. Levels of progesterone in the second half of the ovulatory cycle are going to increase by 1,400 fold compared to what they were in the first half of the ovulatory cycle. So again, if we were to characterize the menstrual/ovulatory cycle in broad strokes, what we would say is that FSH and estrogen mark the initial part the first half, the so-called follicular phase, and that the estrogen and FSH set in motion ovulation, and they prime the system for the production of a corpus luteum, which produces progesterone. And the second half of all of this is called the luteal phase. The second half of the ovulatory/menstrual cycle is the luteal phase because of corpus luteum, this otherwise discarded tissue that produces progesterone. What does progesterone do? Well, progesterone impacts the uterine lining, so-called endometrium or the lining, the mucous lining of the uterus where that egg that's ovulated is potentially going to implant if it's fertilized. And so in a kind of perfect way-- or I should say, in a seemingly perfect way-- the egg is off on its way. It might get fertilized. The remnants of the compartment that let go of that egg produce a hormone that then prepares the endometrial lining of the uterus for the potential implantation of that egg. It's basically making the bed for the fertilized egg to potentially embed in, to implant in, and then achieve all the nourishment that it needs to grow, eventually, into a healthy embryo and child. Just an amazing set of biological mechanisms, if you ask me, because what you're observing here is an incredible economy of function whereby the same cellular components that are producing the egg, well, some of them are being discarded, but they're not being discarded without purpose. They're being discarded in a way that triggers the onset of hormonal expression that then prepares the fertilized egg to be in an enriched environment in which it can thrive. Now, I realize that was a lot of detail. But we have a couple of key themes. We've got the hypothalamus, GnRH. We've got the pituitary with LH and FSH, and those hormones travel to the ovary. The ovary has eggs in a vault, basically immature eggs in a vault. Some of those are activated by the presence of FSH and LH each month. And one of those eggs will be selected and will

ovulate. The remnants of the follicle and egg that are not selected, the chromosomes that you don't need disappear in the polar body. And the corpus luteum gives rise to progesterone and sets in motion the second half of the ovulatory menstrual cycle, which is the luteal phase, which is essentially the potential for that fertilized egg to embed in a nice, nourishing environment. And of course, we should all be thinking, if the egg is fertilized and then it lays down in the nice, comfy uterine lining that's been prepared by progesterone in the corpus luteum, well, then everything's fine and good. But what if fertilization doesn't occur? Well, we all know what happens if fertilization doesn't occur. If fertilization does not occur for whatever reason, that uterine lining is going to shed. And that's actually what's referred to as the period. It's the actual removal-- or the departure, rather-- of the thickened endometrium lining of the uterus when fertilization has not occurred. And of course, if that happens, we need another ovulatory menstrual cycle. So how does that happen? Well, the hormone inhibin is also made by the corpus luteum and doesn't go quite as high as the hormone progesterone. But it kind of tracks that increase in progesterone that occurs in the second half of the ovulatory cycle. But then, if fertilization does not occur, inhibin levels start to drop. And what I haven't told you is what inhibin does. Inhibin, in concert with other hormones like estrogen, feed back to the hypothalamus and prevent the further release of follicle-stimulating hormone and luteinizing hormone. If you have an egg that gets fertilized and can implant, well, then you don't want more eggs to mature. You want to hold on to the ones in the vault. You don't want them to mature. And hormones like inhibin and, again, working with other hormones are going to prevent the secretion of things like FSH and LH. Now, typically, people are not getting pregnant every month. In fact, that's not possible. And part of the reason it's not possible is that if the fertilized egg implants, there are a number of different hormone cascades that shut down the production of things like GnRH, FSH, and LH in ways that prevent further maturation of follicles and a follicular phase. But in the instance where fertilization doesn't occur and menstruation occurs-- and I should mention that the duration of menstruation, the actual bleeding, typically is anywhere from one to five days. The, quote, unquote, "heaviness," the lightness or heaviness of that bleeding will depend on-- you guessed it-- the amount of progesterone that is secreted from the corpus luteum. That's one of the key players there. And if menstruation occurs, well, then inhibin levels also drop. Progesterone levels also drop. And when that occurs, there's a positive feedback signal up at the level of the pituitary. The pituitary literally can register how much inhibin and progesterone and estrogen is present in the bloodstream.

And if those levels are sufficiently low, well, then GnRH gets secreted again, FSH gets secreted again, and LH gets secreted again. And the first half the follicular phase of the menstrual cycle initiates all over again. It's hard to overstate how beautifully orchestrated this entire system is-- The number of feedback loops and feed-forward loops. I think if you can just generally understand that the first half of the menstrual/ovulatory cycle is marked by the maturation of the follicles and FSH and that the second half is marked by the accumulation of progesterone and the thickening of the uterine lining should fertilization and implantation occur, I think that you will certainly understand

00:58:14 Ovulation & Libido; Luteal Phase & Malaise; Individual Variability

the female reproductive cycle better than most people out there. It will also help you understand a number of things that are sometimes associated with the female reproductive cycle. For instance, there are data showing that, in many, not all, but in many women, in the four to five days prior to ovulation, there is a dramatic increase in libido. That dramatic increase in libido is triggered by a number of things, but some of those things include the spike in FSH that occurs, the spike in LH that occurs, and some associated increases in androgens, things like DHEA and testosterone, which, just as in males can be related to libido, in females trigger libido. You can imagine why this would be an effective mechanism to have in place in females if the goal, as it were, certainly of the egg, perhaps not of the woman as a whole, but if the goal is to fertilize the egg-- so increases in libido just prior to the onset of ovulation. There's also been a lot of discussion and interest and, frankly, data exploring the malaise that it can occur at certain portions of the menstrual cycle. And there's a lot of misconception about this. A lot of people have focused on the malaise that can occur around the time of bleeding. But there are actually stronger data to support the fact that some, again, some, not all women experience a kind of malaise sometimes associated with anxiety, sometimes not, that's associated with the mid to second half of the luteal phase of the ovulatory/menstrual cycle. And that, despite what people commonly think, is not associated with elevated levels of estrogen. It's actually associated with the depletion in estrogen levels that can occur during certain portions of that second half of the luteal phase of the menstrual cycle. So again, this is highly variable. For some people, they might not experience any malaise at any point during their menstrual cycle. Other individuals also, for instance, might not experience any variation in their libido at any

point during their menstrual cycle. Again, highly variable, and yet there are some statistically significant trends that have been observed that tracked very specific hormonal components within the menstrual cycle. Again, this will all be very contextual. And of course, this can play out in a number of different ways. So for instance, some women experience very heightened levels of sensitivity to caffeine at certain portions of their menstrual cycle. Other women experience more cramping than others at different portions of their menstrual cycle. Tremendous variation from individual to individual. One of the-- I view it as an advantage. But one of the things that many females can really do and experience because they have cycles that occur every month that are fairly dramatic in terms of their levels of hormones-- so for instance, a more than 1,000-fold increase in progesterone during the luteal phase of the menstrual cycle and, I should also mention, a 200-fold increase in estrogen during the period just prior to ovulation. That's why they always say estrogen primes progesterone. That's what you learn in kind of basic endocrinology when you're learning the menstrual cycle. Estrogen in the first half of the menstrual cycle primes progesterone in the second half of the ovulatory/menstrual cycle. Well, those estrogen increases just prior to ovulation are in part responsible for the increases in libido. But it's also the presence of increased androgen just prior to ovulation. So there's a lot of complex interplay. I think what we will do is we will reserve the discussion about libido, per se, and some of the other aspects related to sexual differentiation that we were talking about earlier for a future episode. But hopefully now you have in mind what the ovulatory/menstrual cycle is. It is a signal from the brain, from the hypothalamus, which then triggers a signal from the pituitary, an endocrine gland, which then signals the release of hormones that travel to the ovary and that control two things, maturation of eggs and the identification of one egg in particular and then preparation of the milieu, the environment in which that fertilized egg could potentially land and mature into a healthy embryo and child. So if you have that framed up in your mind and even if you just extracted maybe 10% to 15% of the hormones and different aspects that I described up until now, I would consider you far more knowledgeable about this entire process than 99% of people out there, certainly not the OB/GYNs and urologists, but the 99% of individuals out there. It also frames up for us the second half of this whole story about fertility and fertilization, which is the generation of sperm and how the sperm eventually arrive at the egg and how certain sperm are selected to potentially fertilize that egg, whereas others never really stand a chance. So next we're going to talk about sperm. We're going to talk about what sperm are, where they are

generated, and how they are generated, and how they need to travel both within the male

01:03:14 Inside Tracker

and within the female in order to allow fertilization to potentially occur. I'd like to take a brief break and thank our sponsor, InsideTracker. InsideTracker is a personalized nutrition platform that analyzes data from your blood and DNA to help you better understand your body and help you reach your health goals. I've long been a believer in getting regular blood work done for the simple reason that many of the factors that impact your immediate and long-term health can only be analyzed from a quality blood test. The problem with a lot of blood and DNA tests out there, however, is that you get data back about metabolic factors, lipids, and hormones and so forth, but you don't know what to do with those data. InsideTracker solves that problem and makes it very easy for you to understand what sorts of nutritional, behavioral, maybe even supplementation-based interventions you might want to take on in order to adjust the numbers of those metabolic factors, hormones, lipids, and other things that impact your immediate and long-term health to bring those numbers into the ranges that are appropriate and indeed optimal for you. If you'd like to try InsideTracker, you can visit insidetracker.com/huberman and get 20% off any of InsideTracker's plans.

01:04:18 Sex Chromosomes, Sperm

That's insidetracker.com/huberman to get 20% off. So we've covered the ovulatory cycle in females. And I confess, it was a lot of information with a lot of biological nomenclature. But I promise you that many of those same themes and indeed the same names and nomenclature will show up in the discussion that we're going to have now, which is about the generation of sperm. Now, sperm are similar to eggs in the sense that they are part of the germline. They are these protected cells, protected in the sense that the activities of an individual are not going to change the genetic makeup of those cells. Now, again, there are instances in which mutagens, such as chemicals, could disrupt the genomes of the germ cells in males, just as it could in females. But in general, the activities, the things that we do, the experiences we have, doesn't tend to change the genome of those cells. However, there are a lot of lifestyle factors-- dos and don'ts, nutrition and

supplements and prescription drugs, et cetera-- that can indeed modify the quality of the sperm. And we'll talk about what sperm quality means. But the point is that the sperm cell, much like the egg cell, are both germline cells. They are not like somatic cells. They are unique populations. And let's just remember what the job of the sperm cell is. The job of the sperm cell is to deliver the genetic material from the father and to do that in the form of a haploid cell. So that means 23 chromosomes, 22 autosomes, one so-called sex chromosome-- again, not sex the verb, at least not in this case. Sex, the verb, is a discussion we're going to have in a few minutes, but sex the noun. The sex chromosome can either be an X chromosome or a Y chromosome. So 22 autosomes and then one sex chromosome is going to be contained within the sperm because it's a haploid cell, not a diploid cell. Remember, the egg was diploid, then it became haploid. The sperm cells are cells that are created through the division of other cells. But after that division occurs through a process called meiosis, the sperm cell is going to contain 23 chromosomes, consisting of 22 autosomes and one sex chromosome. And the sperm that manages to deposit its DNA contents into the egg, to fertilize the egg, will either have an X sex chromosome or a Y sex chromosome. And the Y sex chromosome has a number of different genes on that chromosome that will suppress, for instance, the development of the female reproductive axis. One good example would be the Müllerian-inhibiting hormone, or MIH. The gene for Müllerian-inhibiting hormone, which is a hormone that prevents the formation of the Müllerian ducts, which is part of the female reproductive structure, well, that gene controls the prevention of the development of the female genitalia and in doing so promotes the development of the male genitalia. And there are other examples of genes that are on the Y chromosome that give you a what we call male phenotype. You have genotype and phenotype. By the way, in case you haven't heard this in a while from your high school biology-- or if you never heard it, no big deal-- karyotype is the complement of chromosome-- XX or XY. And there are individuals out there that are XXY or XYY, a discussion for our episode on sex differentiation. That's karyotype with a K. Then there's genotype, which are the genes that you have. And then there's phenotype, spelled P-H-E-N-O-T-Y-P-E, phenotype. And the phenotype is how the genes, which then code for RNA, which code for protein, how those are expressed in terms of things like eye color. So eye color is a phenotype. Height is a phenotype. Hair color is a phenotype. So you have karyotype, genotype, and phenotype. Well, what we need to do is we need to bring together that sperm, which is haploid it contains those 23 chromosomal strands-- with either an X or a Y. Sex

chromosome is the 23rd chromosome. We need to get that cell to the egg. And so when we talk about spermatogenesis, of course, we are talking about the generation of sperm cells. But what we're really talking about is the generation of cells whose job is to deliver the genetic material from dad to the egg within the female in a way that increases the probability that not only will that egg be fertilized but that it will progress in a healthy way with each set of chromosomes from mom and from dad-- each set of 23 chromosomes, that is-- will progress in a healthy way, will implant in a healthy way, and will maintain and grow in a healthy way to a healthy embryo and child and eventually adult. That's the job of the sperm. So as we talk about spermatogenesis, let's just remember that and why they're there in the first place. Now, a few things about sperm that are interesting, besides the fact that they're haploid and besides the fact that, as you all know, they swim. They have a head and a tail. They actually have a head, a mid region, and a tail, and that mid region turns out to be very important. It's something we'll come back to again and again. That mid region is really key for the ability for sperm to engage in forward progression to swim forward. It involves the activity of mitochondria, which are involved in generation of ATP, which is involved in all aspects of energy and all cells. But let's just remember that the sperm are swimming cells. And in order to create a really good swimmer or set of swimmers, you need a couple of things. First of all, within the testes is where the sperm develop. And unlike in females and unlike in the ovary, there's no vault of sperm. The sperm are continually being generated. It takes about 60 days for sperm to be born from their parent cells-- because cells actually give rise to other cells, that's the way it works-- to be born from their parent cells and then matured to the point where they can be a really good swimmer. Now, that doesn't mean that a bunch of sperm are made on day one, and then 60 days later, all those sperm are deployed in the form of ejaculate, and then the cycle starts over again. So it's a little different than the ovulatory menstrual cycle. Rather, at any given point in time-- like right now, if you have testes, you have some sperm in your testes that are immature and cannot swim, cannot deliver those contents to-- those genetic contents, rather-- to the female egg. And you have some sperm that are mature, and you very likely have some sperm that are so mature that they are dying off or that they're dead. Almost certainly, also, regardless of your age, you have some sperm that are healthier than others, that are better swimmers than others. This is just the way the system works. Now, the process of spermatogenesis involves a couple of things, but a lot of the players are the same as the process of developing the so-called oocyte, the immature egg. We've got GnRH from the

hypothalamus. That's going to be a player. We have FSH, follicle-stimulating hormone, although the name's a little bit of a misnomer in the context of spermatogenesis, because in the context of spermatogenesis, there is no follicle. What we're really talking about is FSH for stimulating the maturation of the sperm cell, so not egg follicle but sperm cell. But we still have GnRH, FSH, LH, and rather than the ovary being the target of those hormones,

01:11:40 Tool: Testicular Temperature & Fertility

it's going to be the testes. So most everybody should know that the testes and the ovaries are the so-called gonads. The testes, of course, reside outside of the body. There are instances where the testes fail to descend during development. Certainly, if the testes don't descend on time, that's something that doctors need to be made aware of, the pediatrician should be made aware of, because that can prevent fertility. Why would that be? Well, it turns out that the testes reside outside the body in the scrotum because the temperature conditions under which spermatogenesis can occur and under which healthy sperm can be maintained are very restricted and is approximately 2 degrees cooler than the rest of the body. This is very important. I think this is something that used to be discussed a lot more but isn't discussed so much these days. But keeping the testes cool enough-- doesn't necessarily mean keeping them cold, although there is a place for using cold exposure, deliberate cold exposure, to improve sperm quality and number and perhaps even testosterone levels. We'll talk about that a little bit later. But keeping the testes about 2 degrees cooler than the rest of the body is absolutely key. If sperm get too hot, they die. And if spermatocytes, the cells that give rise to sperm, get too warm, well, then oftentimes the sperm that develop are not healthy, not healthy in a number of ways. Either they can't engage in fast forward progression-- that is, swimming-- or they will lack the ability to deposit their DNA contents within the egg. So again, whatever is contained in the ejaculate is going to be a mixture of different sperm qualities. And sperm of different ages will impact the quality, but also the temperature under which those sperm developed is going to impact their quality. And so we're going to get into tools a little bit later, as I mentioned, but just to give you a simple takeaway. If you are hoping to conceive in the next 90 days-- the spermatogenesis cycle take 60 days, but then the sperm actually have to migrate from the testicle into the so-called epididymis, which is a related structure, and then into the

vas deferens and then into the urethra, where it can be part of the ejaculate. In order for sperm to do all that properly, undergo that maturation and then exit in ejaculate in a way that's healthy or that the sperm is healthy, if you plan to conceive children or to try and conceive children in the next 90 days, you definitely want to avoid exposing your testicles-- that is, your scrotum-- to elevated temperatures. So that means definitely avoiding hot tubs, definitely avoiding hot baths. Now, a brief hot bath or hot tub or hot shower isn't going to be a problem, although if you're really interested in conceiving, I would avoid hot tubs and hot baths as much as possible. Hot showers are probably fine. But if you're going to go into a sauna, for instance, you might want to rethink that decision. And if you do decide to, you almost certainly would want to bring a cold pack in that you could-- well, hopefully put some material between the cold pack and the scrotum so you don't get a cold burn. But put something there, but keep the scrotal tissue cool. Keep it cold to cool because heat exposure can really mutate and disrupt the developing sperm, and it can kill sperm. And so, again, that would be for an entire 90 days leading up to your attempts to conceive. Again, we'll get into more tools later, but a number of people also have probably heard of the boxers versus briefs controversy, I guess it is, or whether or not people call it going commando with no underwear of any kind-- boxers, briefs, briefs, or otherwise rather. It turns out that the data on that point to the fact that there isn't really a big difference in terms of sperm quality if people wear boxers or briefs or don't wear anything under their jeans or shorts at all. The scrotum has the ability to move the testicles far enough away from the body in order to achieve lower temperatures if it needs to. It achieves that through a muscle called the cremaster muscle, which is a really interesting muscle, believe it or not. I was reading up on the biology of the cremaster muscle, something I never thought I'd spend too much time on but that I ended up spending far too much time reading up about. And it's really fascinating. What you have is a muscle that is a smooth muscle tissue, unlike skeletal muscle, which is striated muscle, that is temperature dependent. So it has certain nerve endings, and it has certain receptors on it that allow it to respond to local temperature and then to relax in order to essentially let the testicles to descend further from the body or to contract and bring the testicles closer to the body in order to try and maintain the optimal temperature range. And it turns out the cremaster muscle can achieve that whether or not people are wearing boxers or briefs. Although it stands to reason that any kind of-- there's no other name for it-- undergarments-- you know, I don't know why that word just seems kind of antiquated-- but undergarment that allows some movement of

the scrotum and the testicles should be sufficient to allow these temperature variations to occur and keep things in range. That said, a little bit later, we'll go into some detail, really-- because it's important-- as to why, for instance, if you are somebody who has big thighs, believe it or not, that it actually can lower sperm count substantially, whether or not the big thighs occur because you're very muscular or the big thighs occur because you are overweight. It can increase the temperature. If you're sitting a lot, increases scrotal temperature, for sure. And there are some other things that can increase scrotal temperature, seat heaters in cars, for instance-- terrible idea, just terrible idea if you're hoping

01:17:22 Sperm Production, Seminal Fluid, Vasectomy

to conceive in the near future-- and again, hot tub, things of that sort. So temperature modulation of spermatogenesis and sperm quality and function is key. That relates a little bit more to tools. But what happens? How does the actual sperm develop? Well, contained within the testicle, you have the cells, the so-called spermatogonia, which differentiate into so-called spermatocytes. You don't have to remember all this. And the spermatocytes undergo this process of meiosis. Meiosis is a form of cell division, which reduces the chromosome number to those 23 individual strands as opposed to pairs. So it makes them haploid as opposed to diploid. Very, very important for reasons that we talked about earlier. And the meiosis process in these primordial sperm cells, these immature sperm cells, is similar to the meiosis process that occurs in eggs when the chromosomes segregate in that it involves these spindle-like structures within the cell. Now, why do I keep bringing up the spindles? Well, it turns out that the function of the spindle in the egg and the sperm is heavily dependent on mitochondrial function. And later when we get into tools for improving egg and sperm quality, you're going to hear about a lot of tools for improving mitochondria. And it's not just because the mitochondria are involved in energy-demanding aspects of cell biology. But it's also because the mitochondria in this context are very, very important for the removal of or the separation of one set of chromosomes to give you these two sets of haploid cells, the egg and the sperm. And this is so important because many failures at fertilization, many failures at implantation, many, many miscarriages, and many birth defects that do survive after birth that are very detrimental, such as trisomies and things like that, occur because the spindles don't effectively pull apart the chromosomes in typically the egg, but it can also

occur in the sperm. So the spindles and the fact that mitochondria are rich on the spindle are very important for generating these haploid sperm-- again, 23 individual strands of chromosomes. That's occurring inside of the testes. So there's not as much long-distance migration of the spermatocytes and the sperm cells as there is the egg just when you think about the overall architecture of the uterus and the Fallopian tubes compared to the testicles, but there's still a lot of movement. So within the testicle, if you were to look at the testicle in cross-section-- and I prefer to call it that rather than cut the testicle in half. Any time you talk about anatomy, you actually talk about slicing things. That's what you would do with a cadaver is what I teach and we do in my laboratory and, frankly, in biological laboratories all over the place. But when you talk about it, you talk about if you were to take a visual cross-section through the testicle, what you would find is that there are a lot of different little tubes, a lot of ducts, D-U-C-T-S, ducts. Those are pathways. And the main ducts that are important for this discussion are called the seminiferous tubules. So it's a mesh-like or network structure of tubes in the testicle. And the immature sperm sit on a little compartment along the edge of those tubes. And as they mature, they move towards the center of those tubes. And then when they are mature enough, those sperm cells actually drop into the hollow of the tube, and then can travel through those tubes to a structure that's along the side of the testicle called the epididymis. The epididymis, again, is a series of ducts. And then the epididymis converges with something called the vas deferens. I think in high school, we all remember this by thinking about it's the vast difference. I don't know who came up with that. I think it was a young girl sitting to the left of me that was like, oh, it's like the vast difference. I never forgot that. I don't know. Maybe it was the topic matter. Maybe it was her. Maybe it was some combination of the two. But in any case, the sperm go from the seminiferous tubules to the epididymis and then to the vas deferens and then are contained in the ejaculate, along with seminal fluid. Now, the seminal fluid is the carrier fluid for the sperm themselves. This is important because it turns out that a lot of things that can both negatively or positively impact the quality of the sperm relates not just to the sperm cells themselves and the temperature of the environment that they were matured in, but also to the semen quality. For instance, if you are a heavy drinker, if you are a smoker, or if you are a regular user of cannabis, especially if you smoke cannabis or vape cannabis, you create a lot of reactive oxygen species that disrupt the chemistry of the seminal fluid, which disrupts the sperm cells. So it's not a direct action always on the sperm cell itself, although it can be. So for instance, in the form of smoked tobacco

or cannabis, there are a lot of carcinogens and mutagens that actually mutate the DNA, can cause DNA fragmentation, and debilitate sperm. But there are also a lot of things created by smoking in particular, regardless of what's being smoked, that can create elevated reactive oxygen species and disrupt the seminal fluid that the sperm are contained in in the so-called ejaculate, the semen. Now, this will also become a relevant conversation later when we briefly talk about vasectomies. Vasectomies are literally a cutting of the vas deferens, which leads to a situation, provided the surgery was done correctly, where men can still achieve all the other aspects of intercourse. They can still achieve erection. They can still achieve orgasm. They can still ejaculate. But when they ejaculate, the seminal fluid is released, but there are no sperm contained within the seminal fluid. And it turns out that vasectomies are a very effective form of birth control. And they always check to see if zero sperm and confirm that zero sperm are being released in the ejaculate. They are reversible. And that is, vasectomies are reversible, but not always. There are a subset of cases where it's not reversible, in which case if people still want to have children, you have to go in and actually surgically extract sperm from the testicles. But it's a process in which the vas deferens is altered or severed in a way that the sperm can't actually exit the testicle. They can get into the epididymis, usually, but not into the vas deferens and so on and so forth. So if you've ever wondered what a vasectomy is, that's what a vasectomy is. And I mentioned vasectomy now because it illustrates the difference between the seminal fluid, the semen, and the sperm that the semen contain. So 60 days to generate the sperm, another two weeks or so for the sperm to travel through the various ducts

01:24:07 Sperm Cells, Mitochondria & Motility, Intercourse Frequency & Fertilization

to the point where they can be contained in the ejaculate. Let's talk about the sperm cells themselves. The sperm cells, again, have these 23 pairs of single-strand chromosomes. They're haploid. They have either an X or a Y sex chromosome as the 23rd so-called sex chromosome. And as we all know, they have a head. The head tends to be oval in most cases. The head contains very important enzymes and proteins that are designed to fuse with the much larger egg and to actually take the membrane of the sperm cell and combine to actually mesh with the egg cell's membrane and then deliver the genetic contents to the egg cell, in other words, to fertilize the egg cell. Now, just behind the head is a region called the mid region. That mid region is a slightly thickened region. And

here, of course, I'm talking about healthy sperm cell morphology. Morphology simply means shape. A mid region-- that mid region has a bunch of things related to cell motility and to the forward progression of the cells. First of all, it is chock a block full of mitochondria. In fact, if you were to look just behind the head of the sperm, what you'd see is that it is completely surrounded by mitochondria. There are mitochondria elsewhere in the cell, but most of them are contained in this mid region compartment just behind the head of the sperm. And that thick region is where the tail movement of the sperm, the flagellation back and forth, is actually generated from. Much like if you were to hold a rope, like a battle rope in the gym, and you were to whip the battle rope, the whip at the one end of the rope is what allows for the sort of-- let's just call it what it is-- the curves in the rope, the oscillations, the rising and falling of the rope all the way out to the end. It is the force of the whip right at that end that with the battle rope you're doing with your hand-- and with the sperm, that is occurring just behind the head of the sperm-- that is actually going to dictate how fast and how well that sperm can swim. And indeed, the sperm has to swim very far. How far? Well, on a relative scale-- and again, these are estimations because they're going to be-- how should we say? There will be differences in the distance from the head of the penis and where the ejaculation occurs to the cervix, depending on the relative size of the vaginal canal and the penis that delivers the ejaculate to the vaginal canal. But once the sperm arrive at the cervix, which is at the back of the vaginal canal just at the opening to the uterus, once the sperm arrive there, the distance from the cervix to the egg, of course, will vary depending on where that egg is in its ovulatory trajectory, its pathway. But it is akin, if you scale for size, to the distance between Los Angeles and San Francisco, which is many, many hundreds of miles. So those sperm have to swim very far. Now, of course, if the sperm are delivered in the vaginal canal somewhat further away, they will have further to go. If they're delivered right at the cervical opening, they will have less far to go. The very effective swimming sperm swim very fast. So they are able to accomplish that distance in just a few days. And this relates to a discussion that we will get into in a lot more detail later as to how often couples should have intercourse if they're trying to conceive. Many people might think, well, it's every day. However, the more frequent the ejaculation, the lower the concentration of sperm in each ejaculate. So this is not a discussion about how often to have intercourse depending to your preferences, for pleasure or bonding or whatever reason. This is a discussion about how often to have intercourse in order to optimize the probability of fertilization of the egg. There's some general rules that, of

course, come to mind, which is ejaculations close to ovulation-- both before, during, or sometimes after-- are obviously advantageous. But you will also hear OB/GYNs and urologist suggesting intercourse every other day leading up to the day of ovulation, starting about three to four days out

01:28:31 Sperm Production, GnRH, FSH, LH & Testosterone

from the day of ovulation. So we got a little bit sidetracked, albeit I think appropriately so, in focusing on fertilization. But what we were talking about right up until the point of that is the anatomy of the sperm itself, which is the head, the mid region that contains all those mitochondria, and then the tail. Now, what we haven't discussed is the actual generation of the sperm. So if you're a male or if you're a female, I think it's really important to understand how spermatogenesis works. Spermatogenesis works in much in the same way that the generation and maturation of eggs work, although, as I mentioned before, it's going to occur ongoing throughout the cycle of the male's life after puberty. We already talked about puberty, and I'll just cover this in two or three sentences as it relates to males. And it's essentially the same thing. The hypothalamus, up until the point of puberty, is providing suppression of the release of gonadotropin-releasing hormone. Then some biological clock, which is still not clearly understood-- it's probably not leptin coming from body fat. Again, unlike in the female, it's probably not leptin coming from body fat. But some other signal arrives to the hypothalamus, removes that inhibition, and GnRH, gonadotropin-releasing hormone, is now released onto the pituitary. A bunch of hormones are deployed from the pituitary as a consequence. The two most important ones for the context of this discussion are follicle-stimulating hormone and luteinizing hormone. Follicle-stimulating hormone and luteinizing hormone travel to the testes, and they're going to do two main things. One, they're going to trigger the production of testosterone. And they're going to trigger the production of the sperm themselves. They're going to set in motion, for essentially the rest of the life of the male, the production of sperm. They're going to initiate the spermatogenesis cycle, and that cycle is going to be ongoing at various stages for different sperm for the rest of the man's life. This is very different than the triggering of development of oocytes and eggs in females, where there's an existing vault. That vault can be depleted to the point of zero where it can't occur again. Men can generate sperm their entire lifetime. Of course, there's a diminishment of sperm production in very, very late age, say, 80s and 90s or

100s. But believe it or not, there are still sperm being produced. The quality of those sperm is another question. So everything we're going to talk about now is essentially puberty onward. Prior to that, testicles are present, but they're not generating sperm. Ejaculation isn't possible, or if it is possible, it's very unlikely and unusual, and it's not going to contain sperm. Everything we're going to talk about now is puberty forward, so puberty onward to the rest of life. And luteinizing hormone secreted from the pituitary acts on the testes and on a very specific cell type in the testes called the Leydig cells, or Leydig cells, L-E-Y-D-I-G, the Leydig cells. The Leydig cells of the testes are what produce testosterone. Testosterone is going to have two major effects. And here I mean really major because it has many, many hundreds of effects on different tissues of the body. In fact, that's the definition of a hormone, really. It's a substance that acts in an endocrine fashion. It can act on the very tissue that generated it. So for instance, testosterone made by the Leydig cells within the testes will act on the testes, as we'll talk about in a moment. But it can also act on other tissues. It can act on the pharynx and larynx and deepen the voice, as it does during puberty. It can act on the hair follicles and generate facial hair. It can act on the musculature and generate protein synthesis and development of muscle, bone, et cetera, all the things we associate with puberty and with testosterone typically. Restricting the conversation to the effects of testosterone on the testicle itself and on spermatogenesis, the Leydig cells make testosterone. And keep in mind that some of that testosterone will travel elsewhere in the body and do its thing for gene expression and the more acute effects of testosterone on the brain included. But the testosterone within the testes is at extremely high concentration. In fact, the concentration of intratesticular testosterone is at least 100 times higher than the concentration of testosterone anywhere else in the body, even though it's being secreted into the rest of the body. And that's because there are a number of different so-called binding proteins and enzymes that sequester the testosterone within the testes. So the Leydig cells are making testosterone, and a lot of that testosterone is acting on and is restricted to the testes. And that turns out to be very important because testosterone within the testes acts in concert with a different biological program that starts with FSH, follicle-stimulating hormone, that also travels to the testes and acts on a very specific set of cells that are called supporting cells or, more specifically, the Sertoli cells. The Sertoli cells are the cells that generate something called ABP, or androgen-binding protein. And it is the combination of testosterone from the Leydig cells and ABP from the Sertoli cells that is necessary for spermatogenesis. It's necessary for those spermatocytes to

become what will eventually be healthy, mature sperm that have really nice shaped oval heads, have a mid region, chock a block through mitochondria, and can generate a fast whipping motion of the tail to swim from the cervix, or up the vagina into the cervix, and from the cervix to the egg to fertilize the egg. So it's really a basic set of chemical players that are involved here and so basic, in fact, that if you were to disrupt any one of these chemical players-- either the luteinizing hormone, the FSH, the testosterone from the Leydig cells, or androgen-binding protein-- you would observe pretty marked disruption in spermatogenesis or the elimination of sperm entirely. We'll get into a few deficits in sperm development and sperm number and sperm function a little bit later. But just keep in mind-- or I should say, maybe sit back and just appreciate that the exact same players generate from the hypothalamus, which causes luteinizing hormone and follicle-stimulating hormone released from the pituitary, which travels to the gonad, which in this case is the testicle, which triggers the release of testosterone from Leydig cells, which triggers the action of the supporting cells, the Sertoli cells, which make androgen-binding protein. Testosterone and androgen-binding protein combine and create a chemical and actually a structural milieu in which those little spermatocytes can go from the walls, from literally the walls of the tubes of the seminiferous tubules, can mature into healthy, well-developed sperm, and can hop into those ducts, those little tubes, and then head off to the epididymis, where they will reside-- the epididymis is the tissue nearby the testicles or surrounding one portion of the testicle-- and then eventually fuse with the vas deferens, can combine with or be contained with, rather, the seminal fluid, and then can be ejaculated via the urethra into the female, where then they can swim very quickly, effectively the distance, for them anyway, from Los Angeles to San Francisco, over the course of a very short period of time, and fertilize the egg. So that's the process of spermatogenesis, the maturation of sperm, which is ongoing throughout the lifespan from puberty onward. And in doing so, we talked about some of the hormonal elements-- coming from the hypothalamus and coming from the pituitary, and within the testes themselves the Leydig cells, which produce testosterone, the Sertoli cells,

01:36:21 Ejaculate Quality, Sperm Counts, Fertilization, Ectopic Pregnancy

which are the support cells that allow spermatogenesis to occur. With that in mind, next I'd like to think about what's actually contained in the ejaculate in terms of numbers of sperm and what's really being selected for in terms of the sperm that actually

successfully fertilizes the egg and what sorts of elements come into play in dictating whether or not fertilization will or won't occur. And the major themes that we're going to discuss are frequency of ejaculation, but really that's just kind of a proxy for talking about maximizing sperm concentration and quality of sperm arriving at the egg-- because, remember, ovulation and the menstrual cycle are really about creating the opportunity for fertilization. And we are also going to talk about how the vaginal duct, the vagina, and the milieu around the cervix and some other elements within the female herself contribute to and support the sperm in their journey to the egg and in the likelihood that they will fertilize the egg. So really what we need to talk about first is sperm quality. And we should also probably talk about ejaculate quality, because, as odd as that theme might seem, really the ejaculate quality, which has a number of different parameters, including the number of mature sperm that are not so mature that they're swimming slower or are dead, but also quality of sperm. They have, for instance, one tail. It's not entirely uncommon to see sperm with two tails because they just didn't form properly or sperm that are not moving very much. In fact, sperm motility is scored along a scale of 0, 1, 2, or 3, 3 being the best, fast forward progressing. 0 is not moving at all. 1, they're actually called twitchers. Twitchers are sperm that sort of just twitch in place but don't undergo forward progression. 2 is somewhere in between 1 and 3, not surprisingly. Different clinics, different OB/GYNs, different urologists will throw out different numbers. But in general, it is hoped that more than 50% of the sperm should be motile in some way or another, so not scoring a 0, but a 1, or 2, or ideally a 3. The concentration of sperm-- of course, if it's higher within the ejaculate, the total number of sperm per milliliter of ejaculate, if that's higher, then there's a higher probability that one of those sperm will fertilize the egg. One thing I didn't mention before when discussing the production of eggs and ovulation-- and I probably should have, so I will now-- is that most often only one ovary gives rise to an ovulating egg. It happens, but it's somewhat rare for two mature eggs, one from each ovary, to be deployed during a single ovulation. There's a name for that when it occurs and both are fertilized. It's called fraternal twins. If a single egg-- that, of course, comes from a single ovary-- is fertilized and the egg splits-- and that's something that happens further along in the process of fertilization and differentiation of the embryo-- well, then what you get are identical twins. There are other instances that are quite uncommon in which you can get fraternal twins through other circumstances. But in general, that's the way it works. But essentially what happens is one egg from one ovary-- that's the most common occurrence. The sperm, once

ejaculated into the vaginal duct, are going to pass through the cervix and then are going to swim toward the egg. The egg could be at varying locations along the female reproductive axis. Now, this is actually a very important thing and actually gets right down to the safety of both the potentially developing embryo and the mother. There is something referred to as ectopic pregnancy, and that's when the pregnancy actually occurs within the Fallopian tubes. So the precise location in which fertilization between the sperm and the egg occurs can vary somewhat. But ideally, the fertilized egg implants into the endometrium or the endometrial lining of the uterus and develops there as opposed to within the Fallopian tubes, which is so-called ectopic pregnancy. Now, where the sperm and the egg meet exactly can vary, as I mentioned before. But in general, the faster swimming sperm and the more far along the ovulatory trajectory the egg are, the higher the probability of a successful fertilization because of the proximity to the implantation zone of the uterus. So basically it's all a probabilities game. It's a probabilities game related to the number of sperm cells that encounter the egg and where the egg is in terms of its ovulatory cycle and also its position where it is in the ovulatory cycle. The sperm parameters-- or I should say the semen parameters-- and ejaculate parameters that most clinicians want to see, if you were to give a sperm sample, would be somewhere in excess of 15 million sperm per milliliter of ejaculate. Now, there's a lot of discussion nowadays. It seems to be a very popular news theme to talk about diminishing sperm counts, the idea that 100 years ago or maybe even 35 years ago, the typical male ejaculate contained 100 million sperm per milliliter, and nowadays it's down to 15 to 20 or 50. And indeed, sperm counts do seem to be declining. And the exact reasons for that are not clear. I confess I'm a little bit reluctant to talk about this because there have been a lot of back and forth discussions about the safety of EMFs, of electromagnetic fields, and it's not exactly what we're talking about here. But there are some excellent data contained in meta-analyses and reviews that I will provide links to and that we'll talk about in more detail in a minute that correlate the advent of smartphones and in particular carrying of smartphones in the pocket with diminishing sperm counts. Although there are certain to be other factors that can explain diminishing sperm counts as well. Dr. Shanna Swan, for instance, has done beautiful work describing how the phthalates and the BPA's and so-called endocrine disruptors might be disrupting some of the milieu of the seminiferous tubules. So this would be reductions in testosterone and/or disruptions to the Sertoli cells and androgen-binding protein brought about by endocrine disruptors such as phthalates contained in pesticides

and contained on printed receipts and things of that sort. There are some data that that is negatively impacting sperm counts. How much so is still debatable. There are also quite good data pointing to the fact that both the heat-related and the non-heat-related impact of smartphones and laptops contained on the lap are impacting sperm count and in a negative way. Again, there's going to be tremendous variation in the concentration of sperm from one individual to the next. It will vary according to age and a number of other factors that we'll talk about a little bit later. But in general, if somebody is wishing to conceive, then clinicians like to see an ejaculate volume of more than 2 milliliters. So ejaculate volume can be anywhere from 1.5 to 5 milliliters. And that will strongly be determined by how frequent ejaculation is occurring. There's a lot that goes into evaluating the quality of ejaculate and sperm. But basically these huge variations that are observed of anywhere from 15 million sperm per milliliter or, in some males who are not producing sperm for whatever reason-- we'll talk about those reasons in a little bit-- as low as 5 million sperm per milliliter, all the way up to 100 or maybe even 200 million sperm per milliliter. Huge variation-- the cause of which is not always clear but is certainly determined in part by the frequency of ejaculation. So because there are so many variables impacting why one male versus another male or even the same male across the lifespan

01:44:14 Tool: Sexual Intercourse Frequency & Fertilization

might have variations in his concentration of sperm within the ejaculate, let's talk for a second about frequency of ejaculation as it relates to the goal of fertility, per se, because that's really what today's episode is all about. So what I'd like to talk about next is how people can increase the probability of a successful fertilization, focusing both on the components from the male side and from the female side. And I'm mainly going to couch this discussion in the context of the so-called natural method of sexual intercourse and ejaculation in vivo, within the female. But I will also touch on some parallel themes as it relates to in-vitro fertilization and intrauterine insemination. So the idea here is that we want the maximum number of high-quality sperm-- that is, rapidly forward, motile sperm that are of the correct morphology-- that is, shape. That's going to require a lot of mitochondria in the mid region, a well-shaped head-- so it's going to be an oval-shaped head. The tail is going to be a single tail, not multiple tails. These aren't going to be the twitcher type of-- or immotile type of sperm that are either twitching in place or aren't

moving forward. All of those components are going to be essential for increasing the probability of fertilization. But of course, there's the female side of it, too, which is that ovulation occurs on just one day during the menstrual ovulatory cycle. And that egg will be available for fertilization for approximately 24 hours. Now, keep in mind that the sperm can survive within the vaginal duct and within the area around the cervix and within the uterus and along the female reproductive tract for anywhere from three to five or it's even been described as up to seven days. But generally, it's going to be about three to five days. Now, most women can figure out the day of their ovulation by counting the total number of days of their typical cycle. And this is where it's really useful to have a cycle that's of more or less regular duration or, rather, of more or less regular length. So as we talked about earlier, if somebody's cycle is 21 days or 25 days and it's 21 or 25 days consistently or even 30 days consistently, that's going to be a far better scenario to favor fertilization than if it's 20 days one month and then 21 days the next month, but then suddenly 30 days and then suddenly 35 days. Those varying durations of the ovulatory cycle make it very hard, obviously, to time and understand when ovulation is going to occur. So regular duration ovulatory cycles are the ideal circumstance, and they're the ideal circumstance, because even though the egg is only available for fertilization for a few days, those sperm can survive for some period of time, which leads to the issue of how often should couples be having intercourse. And here, I'm referring specifically to intercourse with ejaculation. How often should couples be having intercourse around the time of ovulation if the specific goal is successful fertilization of the egg and the creation of a baby? This is leaving aside all issues, which, of course, are interesting issues, related to how often people are having intercourse, whether or not there's ejaculation every time they have intercourse or not, for sake of pleasure or for sake of pair bonding and pleasure or for sake of any number of other potential goals of intercourse. Here I'm only referring to intercourse as it relates to the goal of fertilization of the egg. So knowing what we know about spermatogenesis and the fact that ejaculate is going to contain a certain concentration of sperm but that within that ejaculate some of the sperm will be older and less healthy and some will be optimally mature and some might even be a little bit immature-- although there's a tendency for the immature sperm to not have yet exited the seminiferous tubules, gone into the epididymis and vas deferens. But given that the ejaculate contains sperm of varying ages and therefore varying quality and given that with each successive ejaculation in a short period of time there's going to be a decrease in the concentration

of sperm per milliliter of semen, of ejaculate, we can make some good arguments as to how often couples should have intercourse with ejaculation around the time of ovulation if the goal is to fertilize. If ovulation occurs on, for instance, day 14 of a cycle-- and here we're using the kind of standard average of 28 days of the cycle. But for some people with a 30-day cycle, it could be day 15, or with a shorter cycle, it could be day 12, for instance. But given a 28-day average cycle, let's say ovulation occurs on day 13 or on day 14. And typically, it would occur on day 14 of a 28-day cycle. Well, then, given how long sperm can survive inside of the woman, you might think that the optimal strategy would be to have as much intercourse with ejaculation in the three or four days leading up to ovulation, hope that those sperm have swam as far as they possibly can and will encounter the egg just as soon as possible after it ovulates. It turns out that's not the optimal strategy. The optimal strategy is really to maximize the concentration of healthy sperm within each ejaculate and to really center that around the day of ovulation. So what this involves generally and what the typical recommendation is is to abstain from intercourse with ejaculation about two or three days out from ovulation and then, on the day prior to ovulation and on the day of ovulation, to essentially introduce as much semen and ejaculate into the reproductive pathway of the female as possible. Now, that's the general recommendation that the OB/GYNs and the urologists that I spoke to gave. But you will also hear a different strategy. It's only slightly different. But the different strategy involves trying to maximize the concentration of healthy sperm within each ejaculate with the understanding that, with each subsequent ejaculation over about a 24-hour period, that there's going to be a dramatic reduction in the concentration of sperm. What that means is that if a couple, for instance, were to have intercourse with ejaculation many times on the day prior to ovulation, yes, that will introduce a lot of sperm into the reproductive pathway of the female, but what it means is that, on the day of ovulation if they were to have intercourse, the number of high quality sperm that will be available to the egg will be greatly diminished. And if none of the sperm that were introduced in the day prior managed to fertilize that egg, well, then essentially chances are off that there will be fertilization or they're greatly diminished. Rather, if they're having intercourse with ejaculation once or twice on the day prior to ovulation and then a maximal number of times with ejaculation on the day of ovulation, that itself can maximize the probability of fertilization. So which strategy is optimal? Should couples have as much intercourse with ejaculation on the day prior to ovulation and on the day of ovulation? Or should they have intercourse on the day prior to ovulation but not so

frequently that it diminishes the concentration of sperm and then allows for intercourse with the maximum number of ejaculations on the day of ovulation? You really hear it both ways. And what this really boils down to is, frankly, that nobody knows. And the reason nobody knows is that there's tremendous variation among males in terms of the absolute concentration of sperm per milliliter of ejaculate and the amount of sperm per milliliter of ejaculate within a given time frame. But what everyone agrees on is that a period of abstinence ranging from 48 to 72 hours prior to an ejaculation increases the concentration of high-quality sperm within that first ejaculation to occur after the abstinence period. So again, to reiterate, if one's goal is to fertilize the egg, you want to take into consideration that most often there is going to be a dramatic decline in the concentration of sperm per ejaculate any time those ejaculations are occurring within a short period of time, say, within 12 to 24 hours of one another. Now, all of this, of course, also relates to the female biology and the extent to which the woman can precisely identify the day and timing of her ovulation. Some women feel as if and indeed are very accurate at estimating their time of ovulation to within a couple of hours or some women even report being able to feel their actual ovulation, whether or not they are feeling the ovulation itself, the deployment of the egg or not, isn't clear. I certainly wouldn't know. I've never produced eggs, nor have I ovulated, and I'm certainly not going to contest the idea that women can do that. I mean, it makes sense that some people have a very keen so-called interoceptive awareness, an awareness of the sensory events within their body. And while, of course, the ovaries are not thought of as an organ that we want to be able to sense what's going on in there in terms of feel, there are sensory endings within the ovary. And so the notion that one could literally sense changes within their ovary, including the deployment of the egg, is not outside the bounds of reason and, in fact,

01:53:24 Tools: Tracking Ovulation, Libido, Lubricants

could likely be the case. Now, that said, there are a number of different ways that women will track their ovulation. One is the temperature method. So they'll actually measure intravaginal temperature. They're looking for changes in temperature that are consistent around the time of ovulation. We're going to have an expert guest on, an OB/GYN, who can tell us a lot more about the details and nuances of the temperature method. You'll see a lot of information about this online, but there's a lot of misunderstanding about it, as well. Other women will use apps that take into account

either the temperature information if they're acquiring temperature information-- that'll be entered into the app-- as well as marking the onset of menstruation, the onset of bleeding, therefore, the start of the ovulatory cycle, because, of course, as we mentioned earlier, that marks day one of their cycle. And then, again and again, you can see how regularity of cycle duration or relative regularity of cycle duration really favors this whole process of being able to predict when one ovulates. And fortunately, if the goal is fertilization, there are some margins for error that are introduced by the fact that the sperm can survive within the female reproductive tract for some period of days, thereby reducing the need for absolute certainty about the time of ovulation and so on. In fact, it's pretty well known that around the time of ovulation a couple of things happen. Earlier, we talked about one thing, which is there's an increase in libido just prior to ovulation. This relates to, in part, an increase in some of the androgens, things like DHEA, but also testosterone and some related androgens that can increase libido both in males and females and changes to the reproductive pathway, the female in particular, a change in the pH-- that is, the relative acidity versus basic nature of the mucosal lining near the cervix and also vaginal secretions, such that, around the time of ovulation, the entire milieu of the vagina and the cervix and the locations in which fertilization can occur and certainly in which the sperm are swimming towards the opportunity for fertilization is shifted to support sperm motility and health. In other words, one of the best environments for sperm to survive is going to be within the female reproductive pathway itself. And as long as we're talking about vaginal secretions and mucus, it's important to point out that a number of commercially available lubricants can actually be detrimental for sperm health, even if they don't contain spermicide. So this is something that you'll want to discuss with your OB/GYN or, certainly if you're male, you could also discuss this with your urologist and your partner's OB/GYN. A lot of the commercially available lubricants contain chemicals that, while they may favorably change the consistency or the viscosity of the vaginal pathway for purposes of intercourse, certainly may not be the most favorable for maintaining the health of the sperm and the motility of the sperm. So again, here we're talking about intercourse only in the context of trying to maximize fertilization. And I should mention that there are certain lubricants that are more conducive to the sperm environment. But it's something that you'll really want to talk to your OB/GYN about or at least read up about if your interest is

01:56:42 Fecundability: Egg Quality & Woman's Age, Cumulative Pregnancy Rate

in trying to fertilize and develop an embryo. So we covered the optimal strategies for how often couples should have intercourse with ejaculation around the time of ovulation in order to maximize the probability that successful fertilization and ultimately pregnancy will occur. What we haven't covered yet, however, is how long couples should apply that method over time in order to achieve successful fertilization in pregnancy. Now, of course, if a couple decides that they want to conceive and they apply that method or any other method, for instance, and they achieve fertilization and a successful pregnancy the very first month that they try, well, then there's no other work to do, at least until that child is born and if and only if they decide they want to have more children. However, many couples find that they do not conceive in the first month of trying, even when they apply the optimal methods and even if their age and every other factor related to egg quality and sperm quality is optimized. Now, I think it's the rare instance in which egg quality and sperm quality are optimized. In fact, the word "optimal" and "optimization" and "optimized" is a little bit misleading in general because no one really knows what that is. But of course, there is an ideal. There's a perfect standard to which everyone would like to achieve. But of course, we all enter the picture with genetic variables, environmental variables, and so forth, many of which we'll talk about because you can, in fact, adjust them in the direction that you would like to improve sperm and egg quality. But most people simply will not succeed in achieving a successful fertilization the first month that they try. Now, there is a truth that governs how many tries it ought to take in order to achieve successful fertilization and ultimately pregnancy. And it's very age dependent. And in particular, it's dependent on the age of the mother, because the age and quality of the egg, while it's not the only factor, is certainly one of the most determining factors in whether or not successful fertilization occurs. And as women age, the quality of the eggs tends to diminish over time, largely due to changes in the mitochondrial function and the spindle that pulls the chromosomes apart, although there could be other factors involved as well. Now, before continuing any further, I just want to acknowledge that this whole language around egg quality and sperm quality is not the greatest language because it's entirely subjective. And yet the word "quality" in these instances is really there to explain a broad variety of factors that can, in fact, be measured, things like the number of follicles that are deployed each month in a woman's ovulation or the number of motile sperm or the number of morphologically-- that is, correctly shaped sperm in the male and so forth. So when we talk about egg quality or

sperm quality, we're really referring to an amalgam of different features related to the different aspects of ovulation leading to successful fertilization or the different aspects of sperm related to whether or not they can arrive and deliver their DNA contents and so forth. So I will use the words "egg quality" and "sperm quality" just as general themes because that's what a lot of the clinicians use. But I do understand that it's a little bit of a loaded term in both instances, and it doesn't relate to any one specific parameter, per se. So getting back to this issue of how long couples should try according to the age of the female and perhaps also the age of the male. Well, most of the data that have been collected relate to the age of the female, as I mentioned before. And what we're about to discuss is, within the scientific literature, described as what's called fecundability, which is the amount of time over which a given couple needs to attempt to conceive-- of course, by having intercourse with ejaculation-- around the time of ovulation. It assumes that all the other things are being done correctly. And what we know is that there's a strong age-dependent effect that largely rests on the age of the egg-- that is, of the female. And what we know is that for females 30 years old or younger, if they have intercourse with ejaculation around the time of ovulation, say, on the day before and on the day of ovulation-- and there could be other intercourse with ejaculation around that time as well-- on average, that will result in a successful fertilization in pregnancy about 20% of the time on the first month of attempting, the first ovulation cycle. Now, if fertilization and pregnancy occurs, great. There'll be at least a nine-month lag until they decide whether or not they want to try and conceive again. However, most couples, even if the woman is 30 years old or younger, will not successfully conceive on that first attempt. And that's because the probability is not 100%. It's 20%. So 80% of the time, they simply will not conceive, which means that they hopefully will try again the very next month. And if they successfully conceive, great. And if they don't, then they ought to try again the next month, the next month, and so forth. Now, the typical advice that an OB/GYN would give you is that, for a woman 30 years or younger-- and leaving aside the age of the father but still assuming that egg quality and sperm quality are sufficiently high to achieve fertilization-- that the couple should-- or if the woman is trying to have kids alone, the woman should attempt to conceive over the period of six months. Why? Well, if you think about it, if there's a 20% chance in the first month and it's unsuccessful, well, then on the second month, there'll also be a 20% chance. On the third month, also a 20% chance. What I'm describing here is what obviously is independent probabilities. That is, if you were to flip a coin and the probability of getting heads is 50%, the

probability of getting tails is 50%, of course. You don't expect that the previous flip had anything to do with the result that you'll get on the subsequent flip. That's what independent probabilities are. However, when it comes to fecundability, we're really talking about something which is called cumulative pregnancy rate, which is not really independent probabilities. Now, why would that be? Why would it be that if you did not successfully conceive in the first month of trying that, by simply trying again and again and again, the probability of conceiving would increase? Well, the reason for that is that this whole business of fertilization is not just about what's happening with the egg. It's also about what's happening with the sperm. So there are a number of different events related to the biology of the egg and the biology of the sperm, which you are now very familiar with from everything I've talked about up until now. And there a bunch of chance events, for instance, that the sperm won't actually arrive at the egg in time or that the egg won't arrive at the sperm in time, because, of course, it's a bidirectional migration of those two cell types, or that, for whatever reason, fertilization won't occur. So what we're really talking about when we talk about the cumulative pregnancy rate over time is the fact that there are multiple probabilities at work. And yes, those are somewhat independent in the sense that the biology of the sperm doesn't really strictly depend on the biology of the egg, at least not until they meet and fertilize. But the likelihood of pregnancy depends on those independent probabilities, which makes this a cumulative pregnancy rate. Now, if any of that is confusing, what it basically means is that for the egg and the sperm to meet and to fertilize, a number of different events that carry some intentionality-- the sperm swims towards the egg and so forth. The egg doesn't have a personality in there, at least not yet. But it, quote, unquote, "wants" to be fertilize. It is, in principle, receptive to fertilization. Well, in order for that to happen, there are going to be some events related to chance that could limit the ability for that to happen, and there'll be other events dictated by the biology of those two cell types that are driving that event to happen, that are biasing the event to, yes, happen. And so what we're talking about when we talk about cumulative pregnancy rate is how much of the biology of the woman is skewed towards fertilization to be likely to occur. So to make this very simple, all we need to know is that for women 30 years old or younger, because the probability of getting pregnant on any one attempt to conceive is 20%, well, then if that doesn't occur the first time, then she should simply repeat that at least five and probably six times before deciding to go to an OB/GYN and conclude that there's something going on either with the egg or, of course, it could be with the sperm because 20 times 5 is 100. So

we're talking about cumulative percent-- so 20, 40, 60, 80, 100. And the six month there would take you to 120%, which is a different thing altogether. But in general, that's why OB/GYNs will tell their female patients, look, if you're setting out to conceive, try for about five or six months, and if you're not successful, come back and see me. Now, for women who are age 31 to 33, the probability of conceiving in that first month drops to about 18%. So women in that age range and their partners should certainly try and conceive naturally over a period of six or seven months in order to get to that 100% cumulative probability. And then for women who are age 34 to 37, the probability of conceiving in that first month of trying and certainly every month thereafter is about 11%. So when the age of the woman starts extending out to about 34 or 35 years old, then the typical advice of the OB/GYN is going to be to attempt to conceive over a period of about nine months to a year before deciding to take some sort of medical intervention. And then, of course, as the age of the woman increases, so too does the quality of the eggs go down. Now, that's not true for every woman. There are many women who, in their late 30s and 40s and even early 50s, have successfully conceived healthy children, although the probability of that-- the likelihood of it drops substantially. So for instance, for women who are age 38 to 39, the probability of a successful conception by natural conception-- intercourse with ejaculation-- is going to be about 5%. So it's really dropped to a quarter of what it was when that woman was 30. Again, these are averages only. What does that mean? Well, it means that if you are age 38 or older, chances are that you should probably go to your OB/GYN right at the outset of your desire to conceive and ask what you can do to improve egg quality. Otherwise, if you were to extend the math out, we know that if you're age 30 or younger, 20% chance in any one given month. That means about four to six months of trying. Well, you can simply multiply that times four or five for someone in their late 30s or early 40s. And so what you're really talking about is several years of trying. And of course, what's happening during those several years? The woman is getting older. And as a consequence, the quality of the eggs is declining even further. So if you are 35, 36 years old, it might not be entirely unreasonable to talk to your OB/GYN right at the outset of desiring to conceive, but you could also just take the approach of trying to conceive naturally for about a year or a year and a half before deciding to do that, keeping in mind that all the while you can't stop time. So biological time and aging is going to occur in the backdrop. But hopefully this description of cumulative pregnancy rate makes sense. Again, the idea is that while it's true that every single month there's an independent chance of the woman getting pregnant and that

chance is dropping from about 20% at age 30 over time to about, really, 1% to 3% for women 40 or older, there's also this notion of cumulative probability, which involves multiple biological events in both the egg and the sperm that have to converge in time and space in order for successful fertilization to occur. As long as we're on this topic, I

02:08:17 Miscarriages, Chromosomal Abnormalities

think it's only fair to address the issue of miscarriage. And miscarriages can arise from a variety of sources. They can arise from genetic defects. They can arise from issues in the milieu view of the uterus. They can arise from issues with the sperm, for that matter. We really don't want to put all the weight and all the responsibility on the egg. This is always an egg/sperm dynamic. And when I say egg/sperm dynamic, now hopefully that calls to mind the huge library of information that we've been covering up until now about chromosomal segregation and the coming together of these different cell types and their genetic information. Any number of different steps within the process of fertilization leading up to pregnancy can lead to miscarriage. However, the probability of miscarriage greatly increases as a function of the age of the egg. And the basic numbers on this are that for women who are 35 years or older, about 25% of successful fertilizations lead to miscarriages. Now, when those miscarriages occur during pregnancy can be highly variable. Sometimes it's within the first trimester. Sometimes it could be later. But the probability is about 25%. That probability increases greatly over time, such that by the time women are in their early 40s-- so 40 or older-- the probability of miscarriage after a successful fertilization is going to be about 50%. And this could be due to a number of factors, as I mentioned before. But one common reason is that there can be chromosomal abnormalities. And that could be related typically to the segregation of the egg when half of the chromosomes in that egg are removed, taking it from diploid to haploid. If you recall, there's that little polar body, which is the removal of the chromosomes that's ejected from the egg that will eventually ovulate. And sometimes not all the chromosomes that were supposed to be ejected in that polar body are ejected. And as a consequence, there are multiple chromosomes or duplications of chromosomes, things like trisomies. Sometimes too many chromosomes move away and there are actually removal of entire chromosomes, meaning both strands, so that you have chromosomal deletions. And in that case, typically fertilization won't occur. But there are instances in which fertilization will occur. So a woman will get a positive

pregnancy test. Her periods will stop. And the couple will think that they're advancing along the steps to a successful pregnancy, and then there will be, sadly, a miscarriage. Many, many times those miscarriages are the consequence of the fact that, when there are extra chromosomes there or there are too few chromosomes present, that embryogenesis can simply not progress in a healthy way. There are some instances in which all of the chromosomes and all the chromosomal arrangements are perfectly normal and miscarriages can still occur. I'm going to do a future episode about pregnancy and embryonic development where we will get into this more deeply. But just understand that the frequency of miscarriages increases dramatically after about age 34 and then continues to increase dramatically, extending well out until the 40s. Now, a very important consideration

02:11:23 Female Fertility: Age, Follicle Testing & Anti-Mullerian Hormone (AMH) Testing

in terms of understanding and predicting fertility and fecundability, this word that describes the probability of getting pregnant on a given try and over time, is trying to address how, quote, unquote, "fertile" a woman is and, importantly, how, quote, unquote, "fertile" a male is. And we'll talk about the male side in a moment. But when trying to address how fertile a woman is, of course, age is going to be one of the major factors, but just one factor. We already talked about how age determines the likelihood of a successful pregnancy if the intercourse and ejaculation is being carried out at the correct times and with viable sperm capable of fertilizing eggs. And then, of course, there's the issue of egg quality. But in general, most women would like to know how fertile they are as a function of their age. And I actually think this is one of the most important topics in this whole space around fertility that isn't often discussed or at least isn't often discussed until women are in their late 30s or 40s, when oftentimes they will look back and wish that either they had frozen their eggs or they had frozen fertilized embryos, which is a whole thing unto itself. And we can talk about that when we have an episode on in-vitro fertilization in more depth. But there is a fairly straightforward way or set of ways that women can determine their basic level of fertility. Leaving aside a lot of the detailed issues about the quality of eggs and so forth, one thing that you already learned is that there's this vault, there's this reserve that we call the ovarian reserve, and that each month a certain number of follicles leave that reserve, and there's the opportunity, based on the ovulation of a single egg, to fertilize that egg and for the woman to get pregnant.

Now, one thing that we know for sure is that the size of the population that's released from that vault each month has a very strong positive correlation with the size of the reserve in the vault itself. So the way to think about this, perhaps, is that the vault is like a bank account. It has a certain amount of money-- in this case, eggs-- in it. And you could imagine, if someone's reasonably logical, that if they have more money in their bank account, then they're going to withdraw a larger amount each month than if they have a small amount each month, if the idea is to make that vault, that bank, of eggs available to them over the longest period of time. And indeed, biology is pretty smart. It doesn't deploy or release half the follicles in one month and then just slowly trickle out the remainder of follicles. No, that's not how it works. What you find is that, of course, in younger women-- so, say, in their late teens, 20s, and 30s-- the ovarian reserve in the vault is going to have more eggs in it, and the number of follicles and eggs that leave that vault each month is going to be quite high. So one way to evaluate how, quote, unquote, "fertile" you are-- again, just one way-- is to go to your OB/GYN and say that you would like to know how many follicles you have in a given month. And of course, they'll look at them on both sides, in both ovaries. And for instance, if a woman has just two or three follicles that are out each month, well, then the assumption-- again, it's just an assumption-- but the assumption that's pretty good-- because there is this positive correlation that generally occurs-- is that that ovarian reserve-- that the number of eggs in the vault is fairly low compared to someone who, say, has 20 follicles or 30 follicles each month. And that's the typical trend. Again, these are averages. And it's very important to not get attached to any one number here. Again, these are averages. So for instance, there are women who only deploy five follicles and eggs each month out of their ovarian vault but who find themselves to be very fertile. And there could be a number of different factors to explain that. Other women will have 20 or 30 eggs and follicles that leave that vault, the ovarian reserve, each month. And they will have a harder time getting pregnant for any number of different reasons. But in general, the more eggs and follicles that leave the vault each month, the higher number of eggs that are still in reserve, meaning the greater amount of time over which a given woman could still attempt to have successful fertilizations. Now, this small collection of follicles and eggs that are released each month actually has a name. They're called antral follicles. These are small follicles. They tend to be about 2 to 9 millimeters across. The way these are analyzed or measured is woman will go into the OB/GYN office, and by ultrasound-- typically there's some local anesthesia, but it's not often a general anesthesia, but by

local anesthesia or sometimes no anesthesia-- they will essentially count the number of follicles that are present in each side, on ovary on the left and the ovary on the right, and give a woman some sense of how many follicles she has. And typically this is done over a series of months to determine how many eggs are leaving the ovarian reserve each month and therefore how many eggs she is likely to still have in the ovarian reserve. Now there's a noninvasive way to do this, as well. Although, typically, an OB/GYN will do both what I just described with ultrasound and measure something called AMH, which is anti-Müllerian hormone, which is a hormone that is released by that antral follicle population, the population of follicles and eggs that leave the ovarian reserve each month. So one is a blood draw measure of a hormone, AMH. The other is a structural imaging measure of the antral follicles directly. Again the typical trend is for the number of antral follicles to decline over time. So one might expect, for instance, that a woman in her 20s or 30s might have 20, 30, maybe even 40 antral follicles that are exiting the reserve each month. And again, that's the total across both ovaries. Again, these are just averages. These are going to be distributions. There will be people with far fewer. There will be people with far more. But that over time, regardless of where a woman starts out, from one decade to the next half decade and decade and so on, that the number of antral follicles will decline and the amount of or the levels of AMH will also decline. So what does this all mean? What this means is that if you are a woman who is in her 20s or 30s or 40s, whatever your age, if you are interested in conceiving in the future, it's very likely a good idea to go to your OB/GYN and get either your AMH levels measured or your follicle count measured and to do that several times in a given period. And I don't mean a menstrual period. I mean given a period of time across several months to determine what is the average number of follicles, what's your average AMH level, thereby giving you some window into how many eggs you are likely to still have in your ovarian reserve. I cannot tell you how many women that I've spoken to and how many OB/GYNs-- more importantly, because they speak to many more women about this than I ever have or ever will-- wish that they had done this earlier. They think, oh, well, I'm in my 20s, so I'm likely to have a ton of follicles, or they got pregnant once before, and so they're not so concerned about the number of follicles or their AMH levels. But over and over again, I was told in researching for this episode that the earlier and more frequent that women do this procedure of measuring AMH and measuring their follicle count, the higher the probability that they will eventually have a successful fertilization and pregnancy when they seek to do so.

02:18:51 Male Fertility: Sperm Analysis, Age

Now, the mirror image of all this, of course, is the sperm. And there's a kind of common misconception out there that, you know, the sperm, you only need one. And indeed you only need one. But actually, you need many, and it's only one that's able to successfully fertilize the egg. So this whole concept of you only need one is both dismissive of the sperm but more importantly dismissive of the biology of the sperm and the egg. It only takes one successful sperm and one successful egg, but that's sort of like telling a woman, hey, you only need one egg. You need one egg of sufficient quality in the right time and place, and you need one sperm of sufficient quality in the right time and place in order to get successful fertilization and hopefully pregnancy. But you need a lot of sperm in order to get a high probability that that one sperm will be able to successfully fertilize the egg. So we have this image of sperm as these dumb operators that just sort of swim mindlessly towards anything. And if they bump into an egg, then they fertilize the egg. And that's really not the way it works. As I talked about earlier, the sperm-- with its head, its mid region, its tail, chock a block with mitochondria in the mid region-- is really an active motile cell that indeed will just swim forward, if it's a healthy, forward progressing sperm. But many males out there just simply do not have any knowledge of how many quality sperm that they happen to have. Now, given the fact that sperm analysis is relatively inexpensive and also the fact that freezing sperm is relatively inexpensive, I think it stands to reason that most men should at least get some window into the number and quality of their sperm. Now, it's a fair assumption to say that if someone is in their late teens or early 20s or 30s that they probably have high-quality sperm. But again, as with the egg and the importance of measuring AMH and follicle count across time, men should really evaluate the quality and number of their sperm. And we talked a little bit earlier about some of the parameters that urologists and OB/GYNs like to see when evaluating sperm. There's a minimum number or concentration of sperm that they'd like to see if a couple is going to use IVF, in-vitro fertilization. And typically that's going to be about 15 to 20 million per mil of sperm or semen. And typically they want to see somewhere between 2 and 5 milliliters of semen, overall, in a given ejaculate after a 72 to 48 hour abstinence period, because, of course, the more ejaculations, the smaller the volume of the ejaculate in a short period of time. But after 48 to 72 hours, you more or less maximize the volume of ejaculate. And then,

of course, they want to see 50% but typically 60% or more of motile sperm in order to get IVF, but more is better. And of course, there is an enormous range, as I mentioned before. Some males will have anywhere from 10 to 20 million sperm per milliliter of ejaculate, and some men will have 100 to 200 million. But just because they have 100 to 200 million doesn't mean that all of those sperm are of high quality and can fertilize eggs. Sometimes more than half will be twitchers, and some will be immotile, and so on and so forth. So it's very straightforward what I believe most people should do and what the urologists I spoke to in advance of this episode said to do, which is to simply do a sperm analysis. Refrain from ejaculation for 48 to 72 hours. Give a sperm sample. Have that sperm sample analyzed. The cost of the sperm analysis is not typically that much. And considering that conception and healthy conception and fertilization is an expensive process if you have to go the in-vitro fertilization route, it stands to reason that the cost is pretty well justified. You also have the option to freeze sperm over time. There is evidence that the age of the father and therefore the age of the sperm can dictate whether or not there's a higher incidence of problematic pregnancy or developmental outcomes, including autism. That is true. You've probably heard that if the father is 40 years or older, the incidence of autism is increased significantly. That is true. Although the overall probability of having an autistic offspring if somebody-- if the father, that is-- is 40 years or older is still quite a bit lower than you would imagine. It's not as if the probability suddenly skyrockets. So we'll have an episode on autism and genetic and non-genetic influences on autism and other aspects of the autism spectrum. But the point is this. I believe and the urologists I spoke to who are interested in fertility and male health and sexual health suggest that men get their sperm analyzed at least once every five years and certainly, if they're going to want to conceive children in the distant future, that they consider freezing their sperm because that, too, is fairly nominal cost in order to freeze sperm at a younger age. And of course, if you can freeze and use sperm from the time in which you were younger, why wouldn't you, right? I mean, you can still opt to go for natural pregnancy later if that's what you want to do. But having that in reserve is generally a good idea. And I discussed some of the parameters that are looked for. And perhaps most importantly, there is the possibility of an underlying issue whereby, for instance, there is very little sperm in an ejaculate. As I mentioned earlier, the seminal fluid in the ejaculate could have zero sperm in it, but the volume of ejaculate could appear completely normal. So just because your ejaculate volume is normal to you or is in that range of 2 to 5 milliliters, well, then that doesn't necessarily mean that there are

any sperm there or that there are very few sperm there and the few sperm that are there or the many sperm that there are functionally motile. So get this analyzed. It's really worth doing. And again, it's not something you have to do every year. It's something that you want to do probably every five years, at least until the point where you've conceived as many children as you ever want to conceive. So the basic takeaway here is that, if you're a woman,

02:24:52 Fertility & Hormone Analysis, Age

to get your egg count-- your antral follicle count, that is-- and therefore your reserve of eggs, indirectly measured, and of course also get your AMH levels measured, and if you're a male to have a sperm analysis and to do that relatively early. In fact, another incentive for doing that early is that you have a comparison point so that, for instance, if you are in your early 20s and you're not thinking about having kids at all or you're thinking that you might someday have kids but it's a really someday, someday, far off in the future, well, it's wonderful to have a reference point from which to compare your biology in your early 20s to your biology in your mid or late 30s or 40s when you might happen to be interested in conceiving. And if that doesn't provide incentive enough, I should mention-- and this is important to point out and that I think both males and females are not aware of-- is that one in five couples that have issues with fertility, the issue ends up falling on the biology that is the quality of the sperm or a lack of number of sperm. So I think there's a misconception that when fertility is an issue it's always an issue with the eggs and this age-dependent decline in the egg quality-- again, it's the best language we have available to us at the moment-- this age-dependent decline in egg quality is often to blame, but not always. One in five couples that have challenges conceiving it turns out that it's going to be an issue with the sperm. And of course, there are a number of different sperm analyses that, should all the other parameters of sperm appear normal, now, for instance, you can get a DNA fragmentation analysis. You can see whether or not the DNA of the sperm are somehow disrupted. Urologists these days are excellent at figuring out, for instance, if a male has lots and lots of sperm, everything looks great, but the shape of the head of the sperm isn't quite right-- if it's not oval enough and it's too rounded, that could be a genetic defect under which conditions there is zero probability of the male ever naturally conceiving, regardless of who the female partner is. Believe it or not, males can have a ton of sperm, but if they carry a certain

genetic defect, those sperm will be incapable of depositing those 23 chromosomes into the egg. However, there are ways in which that sperm can be coaxed or forced to fertilize the egg and deposit its genetic contents by in-vitro fertilization and then implantation into the female. So again, lots of reasons to have an egg reserve analysis by ultrasound and AMH for females and lots of reasons for males to have a sperm analysis. And of course, typically with a sperm analysis and an ovarian reserve analysis will be a hormone analysis. And I'm a very strong believer in people getting an insight-- that is, a window-- into their hormonal composition, not just when they encounter problems but starting at a pretty early age, even if it's only done once every five years or so, having a reference point to your 20s and to your 30s and mid-30s for when you felt a certain way. Maybe, as in the case for many people I know, they actually feel better in their 40s than they did in their 20s because they're doing a lot of things to support their health. That is possible. But in many cases, people start feeling not as well or their fertility seems to be dropping off or any number of different parameters that we've discussed today were related to vitality and longevity seem to be dropping off over time, and they want to get an insight into what could be the issue. And hormones are sometimes, not always, but sometimes involved in those underlying issues. And there is nothing as valuable as having a reference point from a time in which things were going well to evaluate the, for instance, levels of hormones, not just testosterone but also estrogen and progesterone and so forth. So you need a comparison point in order to determine what really needs to be changed. So all of this is a strong push for people to use your insurance, if you're able to put it on insurance-- oftentimes people are-- and if not, to try and find a reasonable or reasonably priced way to do a sperm and egg analysis and to ideally do a hormone analysis as well. It's really going to set you up for the maximum probability of being able to conceive children when you want to and also to avoid a bunch of other health-related issues that involve hormones and reproductive health and, in general, to support your mental health and physical health. So I've been talking about a bunch of things to do.

02:29:07 Fertility Effects of Sleep, Cortisol/Stress, Cannabis/Nicotine & Alcohol

There are a couple of things to be mindful of to actively avoid if your goal is to be and remain fertile. And that's regardless of whether or not you want to conceive children in the future or not. Now, in the context of this discussion, the same things that we've heard

to be true for other aspects of our health turn out to also be true. So let's just start with the basics. Everybody should be getting approximately six to eight hours of sleep every night. That should be quality sleep. Optimizing your sleep is fundamental to balancing your hormones. Now, balancing your hormones is kind of a catch phrase for all things related to proper hormone regulation. Sleep is the fundamental layer of mental health, physical health, and performance of all kinds and, believe it or not, fertility. When people are not sleeping well or enough, stress hormones, in particular cortisol, shift to peaking later in the day, and those elevated cortisol levels later in the day cause a bunch of different problems in both males and females, many of which impact fertility. So controlling cortisol starts with controlling your sleep. It also impacts testosterone and estrogen levels. So of course, the proper ratios of testosterone and estrogen will vary from males to females. But in order to get those right or as right as they can be without other interventions, you want to make sure you're getting enough quality sleep. How much sleep? Most people need about six to eight hours of sleep per night. Waking up once, maybe twice per night in the middle of the night and going back to sleep is not such a big deal, but six to eight hours of solid sleep would be ideal. Some people need a little bit less in order to function-- five hours. Some people need a little bit more. Developing teenagers and babies and kids need a lot more. People who are sick or recovering from injury need a lot more. We've done multiple episodes on sleep. We have a toolkit for sleep available free at hubermanlab.com. You go there. You don't even have to sign up for the newsletter, although you can if you want. Just go to a Toolkit for Sleep under the menu, and you'll be able to download that, or you can even just view it on the screen if you don't want to download it. It has lots of tools. We've done an episode called "Perfect Your Sleep" that has a lot of tools. They're all timestamped for you. We've done a "Master Your Sleep" episode, so lots of tools to get your sleep right. Get your sleep right if you are wishing to conceive and/or to simply have healthy biology, to be fertile, or otherwise. That's just fundamental. Now, there are other things to not do. And those, again, fall into the somewhat obvious categories, but I think a lot of people aren't aware of just how striking an effect these certain behaviors that you want to avoid can have in diminishing your fertility for both males and females. So let's talk about those. The first one is smoking. And when we talk about smoking here, we're talking about smoking nicotine and we're talking about smoking cannabis. And indeed, there are strong data-- and I will put a reference to one of the better larger analyses of these data. There are strong data showing that cannabis reduces fertility. Now, I can already hear the screams

from the back, although they're probably fairly drawled out screams, from the back of people saying they smoke cannabis and they had no trouble conceiving. Certainly, there will be exceptions. But whether or not you're male or female, smoking cannabis is a bad idea if you want to conceive a healthy child. Can you still conceive a healthy child while smoking cannabis? Probably certain people can. Many people will greatly decrease the probability of a healthy fertilization and pregnancy by smoking cannabis. There are excellent data to support that. As well, nicotine, both smoked or vaped, is going to disrupt the process of fertilization and can disrupt pregnancy dramatically. So just avoid it altogether. How does this happen? Well, it turns out that smoking increases what are called reactive oxygen species. This greatly disrupts the quality of the egg at the level of the spindle and mitochondria and a number of other features. And in the sperm, turns out that smoking doesn't necessarily disrupt the sperm directly, although it can cause DNA fragmentation, which can cause all sorts of abnormalities, can prevent fertilization, can lead to birth defects in the offspring. But more importantly, it increases what are called reactive oxygen species in the seminal fluid, in the semen that contain the sperm, this very, under normal circumstances, under healthy circumstances, beautifully orchestrated chemistry of fluid that allows the sperm to thrive in their trajectory and attempt to fertilize the egg and lead to a healthy pregnancy. So if you are a smoker and you want to conceive, the best advice I can give you is to quit smoking. And yes, that includes cannabis as well. Now, I am not somebody who believes that cannabis across the board is not useful. There are medical applications and other applications. I talk about that in an episode all about cannabis for health and disease. And notice, health was in there too. So you cannabis smokers, don't come after me with-- I guess, whatever it is-- with bong and pipes or whatever it is that you want-- or with vapes. The point is that, while it can be beneficial for certain populations, it's certainly bad for others. And if you're trying to conceive, it is bad for fertility and for a healthy pregnancy. Now, that's smoking-- and vaping, by the way. Vaping is included there. Now, the next category of don'ts relates to alcohol. Now, everyone has heard that drinking during pregnancy is a bad idea. You may have heard and some people have talked about the fact that there are cultures in which they allow, if you will, or even condone, sadly, one or two drinks while pregnant, provided it's just champagne or something of that sort. That is a terrible idea. I did an episode all about alcohol, both its potential health effects, of which there turned out to be zero. And yes, that includes red wine. It is far better to not drink at all. And if you're going to drink, the limit-- if you're a healthy adult who's not trying to

conceive, not pregnant, and you don't have issues with alcoholism-- is probably two drinks per week total. That's right, two drinks per week total. And that's the level that you really should consider if you're a drinker if you're somebody who's trying to conceive. However, for a woman who becomes pregnant, the total number of drinks that you should allow yourself per week while pregnant and breastfeeding is indeed zero. There is absolutely no evidence that one can, quote, unquote, "get away" with drinking during pregnancy. And people say, well, I had a perfectly healthy child. But, of course, you don't know what the health of that child would have been had you not drunk at all. Now, I'm not here with any generally strong stance against alcohol. I myself am somebody who has a drink every once in a while, although I don't consider myself somebody who has a strong proclivity for alcohol. And of course, at this moment, I'm not trying to conceive children and I'm certainly not pregnant. So that's safe for me. But frankly, I haven't had a drink in a very long time. And so I don't miss it. And that's me. But I do realize that a lot of people enjoy alcohol, and so it's that two drinks per week limit that really sets the upper limit and threshold beyond which you start running into issues with cellular mutation. You start running into issues of oxidative stress, greatly increase cancer risk, in particular breast cancer risk. All of that's covered in the alcohol episode that we did. You can find it at hubermanlab.com and timestamped if you want to navigate to specific topics and so forth, find out all about the data supporting the statements that I'm making, so on and so forth. Now, if you're somebody who's seeking to conceive or you fall into this category that some couples describe themselves as we're not trying but we're not not trying-- meaning they're not using birth control, they're kind of letting chance run its course-- well, then you should definitely be aware of the data showing that even just one bout, one bout of so-called binge drinking, which is five to six drinks in a given night or half day, in a 12-hour period-- one bout of five to six drinks, if you're a woman or you're a man, greatly increases both the likelihood of mutations in the embryo that would result from a fertilization and at the same time, for reasons that should be obvious to you based on all the biology we've talked about, a greatly reduced probability of fertilization. Now, that absolutely does not mean that you should use the ingestion of five or six drinks as a method of birth control. That is not what I'm saying here. What I'm saying is that, if you go out on a given night and you have five or six drinks and you happen to become pregnant, the probability that that pregnancy will be disrupted in some way is greatly increased. What the exact consequences are, no one can tell you. But also, if you're somebody who is interested in conceiving a child, well, then you absolutely should

abstain from ingesting drinks more than one or two during the time in which you're trying to conceive, and ideally it would be zero. And you certainly would want to avoid drinking multiple drinks per night. And so this idea of going out and having three or four drinks or four or five drinks in a given night at a time in which you're also trying to conceive children, the biology tells us, the epidemiology tells us that this is just a terrible idea. It's going to reduce the likelihood of fertility and successful pregnancy. And if there is a successful pregnancy, the word "success" needs to be in quotes, right? I mean, I think every parent-- every species, for that matter-- wants to increase the probability of having healthy offspring. And so, to my mind anyway and to the OB/GYNs and the urologists that are focused on fertility that I spoke to, everyone will say, try as hard as you can to avoid these so-called binge drinking episodes. And again, these episodes are one night of consuming five to six drinks. Now, another important thing to remember in this context is that the negative effects of consuming five or six drinks in a given night extend over many weeks following the ingestion of that alcohol. If you're a male, what that means is that's going to impact the quality of your sperm and greatly decrease the likelihood of successful fertilization and/or healthy pregnancy over the period of that entire spermatogenesis window, which is, as we talked about before, 60 to 90 days, 60 to generate the sperm and then some additional time for the sperm to be transported to the point where they could be ejaculated. If you're a woman and you have five or six drinks on a given night, well, then you are going to disrupt the quality not of just the egg that eventually ovulates but indeed the entire pool of follicles that leaves the ovarian vault in reserve and from which the one egg will be selected. In other words, you are reducing the quality of all of the eggs that you happen to deploy that month. Now, some of you who were really following the biology earlier might say, well, what if I have those five or six drinks during the time in which I'm menstruating, just in which there's bleeding present? And therefore, I haven't yet ovulated. Ah! But if you remember the biology we talked about earlier specifically, there is a subset of follicles and eggs that leave that ovarian reserve quite a bit before that one egg is selected for and ovulates. And of course, there are all the different hormonal cascades and the general milieu of the ovary which are important and are being regulated by different hormones. And yes, indeed, the regulation of those hormones is strongly impacted by alcohol through a number of different pathways, through the regulation of the neurotransmitter GABA up in the brain-- it's actually a lot of GABA and GABA receptors in the hypothalamus, the very region from which gonadotropin-releasing hormone, our old friend from a couple hours ago in

this discussion, going to disrupt GnRH secretion. You can disrupt pituitary function with alcohol. Again and again, what we're seeing is that consuming more than one or two drinks per week of alcohol is really detrimental to the entire process of fertility and the entire process of healthy pregnancy. And that's true from both the male side and the sperm, and it's true from the female side and the egg. So my simple advice on this is if you are wishing to have a healthy fertilization and pregnancy, the best thing to do would be avoid alcohol altogether and, if you are going to drink, to really limit that drinking to one or two drinks per week maximum. So those are the major don'ts. Really avoid excessive stress. And I should mention, excessive stress is not just best avoided by getting enough quality sleep at night. Although that is the primary way. There are other ways to avoid stress. We've done entire episodes about this, and we have a toolkit related to reducing stress with very simple, zero-cost tools. Again, you can find all that at hubermanlab.com. And I should mention, if you want to find any episode or topic or timestamp, that website is keyword search available. So you can just go to hubermanlab.com, put into the search function "stress tools," and a bunch of different links will pop up related to those topics, likewise with sleep, likewise with any number of different topics you might be interested in. So get enough quality sleep and thereby reduce stress and also directly buffer stress with real-time tools to buffer stress that I've talked about in the episodes that you can access. And there are ways to greatly reduce your overall level of stress, to limit any cortisol that's released to early in the day, which is when you want cortisol released, and not have it late in the day and so on and so forth. So reduce your stress. And as I just told you, by all means, do not drink more than two drinks per week. And zero is better than two. If anyone tells you, oh, well, there's all this resveratrol in red wine, and that's good for us, the data simply tell us there's not enough resveratrol in red wine to really have any positive health benefit. The data around resveratrol and health benefits itself is under question nowadays. Zero alcohol is better than any alcohol. Two drinks per week is the limit. Also, limit or eliminate or avoid nicotine and ideally cannabis, smoking and vaping, at the time in which you are trying to get pregnant. And certainly, if you are pregnant, avoid all of the things, as best you can, that I just described a moment ago. Now, there are a couple of other don'ts that are really important.

02:42:40 Fertility, Sexually Transmitted Infections (STIs), Viral Infection & Cystic Fibrosis

One of the most important don'ts relates to STIs, or sexually-transmitted infections. Everyone who is sexually active should get an STI check. In fact, if you go to a fertility clinic or you go for sperm analysis or you go for egg analysis, almost always they will do an STI check, even if you happen to be in a monogamous relationship, even if you happen to be not sexually active and you're somebody who is seeking to use IVF with a sperm donor or something of that sort. Why would they do that? Why is there so much concern about that? Is it about avoiding giving birth to a child that has something like a herpes infection or HIV? Well, certainly that's one reason, but that's a down-the-line reason, because at the time when someone goes into the clinic for one of these sperm or egg analyses, that's well in advance of any pregnancy, right? The reason is there are a number of STIs-- in particular chlamydia-- for which it greatly increases the probability of miscarriage. So chlamydia is one of those very insidious and cryptic STIs because a lot of people, both males and females, don't even realize that they have chlamydia, and then they can carry chlamydia at the time in which they conceive, and then that can lead to ectopic pregnancies and/or miscarriages. So by all means, get an STI check if you are somebody who's seeking to conceive children or evaluating your fertility generally. Chlamydia can also have damaging effects on the epididymis and on the various other aspects of male reproductive health. In the future, we will do an episode all about sexual health. This is not the time for that. But get an STI check if your goal is to conceive a healthy child. Now, the other thing that can have a very negative impact on fertility and healthy pregnancy is a viral infection. For instance, if a male has had a severe viral illness-- and this could be any number of different viral illnesses, from flu to cold or any number of different viruses. Pick your favorite virus-- in the previous 70 to 90 days, that can greatly diminish the number and/or quality of sperm. So that's really important. This is also important if you're going to go in and do a sperm analysis and you had a viral infection in the previous 70 to 90 days. Well, then you need to be aware of that because it could greatly impact the parameters of that sperm analysis. Likewise, for women, if you've had a serious viral infection in the previous 30 days, does that mean you should not try and conceive? Not necessarily, but you should talk to your OB/GYN about that. There are data showing that viral infection-- in particular of influenza-- in the mother in the first trimester of pregnancy has some correlation-- it's not 100%-- but some correlation with negative mental health outcomes of the offspring sometime later, including schizophrenia. This is some of the work that was done at Caltech a number of years ago and other laboratories, as well. Those data are still being built up over time.

Again, it's not one-for-one. It's not causal. So if you did get an influenza or a cold or other kind of viral infection during the first trimester or any trimester of pregnancy, I don't want to cause alarm, but you should talk to your OB/GYN about this. The goal, of course, is to avoid viral illness at any time when you're trying to conceive or have a healthy pregnancy. But of course, sometimes people will get ill, and the children can turn out to be perfectly normal and fine. But it is something that you want to avoid. And it will impact your egg analysis, and it will impact sperm analysis. And one thing I found really surprising in researching this episode was that 1 in 25 men carry a copy of a mutation for cystic fibrosis. Now, some of you are probably familiar with cystic fibrosis as a condition that can cause issues with the lungs, the accumulation of fluid in the lungs or other tissues. Cystic fibrosis, in order to express that way of accumulation of fluid in the lungs, you really need two copies. You need two mutant copies or you need two copies of the cystic fibrosis gene. 1 in 25 men will carry just one copy and therefore will not have any symptoms of cystic fibrosis. But those 1 in 25 men will have defects in the architecture of the vas deferens, the duct through which the ejaculate needs to pass in order to eventually be ejaculated out of the urethra. And so what that means is that these men can have what appears to be normal semen volume but that they won't have normal numbers of sperm. And that's not because of a deficit in making the sperm. The testes can function just fine. The brain and the pituitary are communicating with the testes just fine. But that literally the passageway by which those sperm arrive within the seminal fluid and are eventually ejaculated is disrupted by the cystic fibrosis gene. Luckily, if somebody has just one copy of the cystic fibrosis gene and they're male and this is the issue, the vas deferens either can be repaired by a urologist who's expert in the surgical repair of vas deferens or sperm can be extracted from the testicle directly, which might sound like a painful procedure, but I believe nowadays, in talking with various experts on this, it turns out that it can be done with a minimum of discomfort. And certainly, if the goal is to have a healthy child, you're going to need those sperm, so you're going to want to get them one way or the other, regardless of the discomfort. Now, before getting into some of the things that you can do in the positive sense to increase your fertility, we do

02:47:42 Tool: Testicular Temperature & Fertility

need to touch on just a few other things that you want to avoid in order to avoid

diminishing your fertility. And this mainly relates to males, but it will also be relevant to females. And of course, when I say also relevant to females, I'm referring to the fact that, if it's a woman and a man who are trying to conceive, then she, of course, is going to be interested in her egg quality but also the sperm quality. And of course, there are women who are conceiving by way of sperm donor, through IVF or IUI or otherwise. But in any case, the need to understand and maximize the quality of both the egg and the sperm is paramount. So in order for men to maximize the quality of their sperm, as I mentioned earlier, does not seem to be a big difference whether or not they use boxers or briefs or whether or not they, quote, unquote, "go commando," they don't wear any boxers or briefs of any kind. However, it is important to keep the testicles cool enough. They need to be about 2 degrees cooler than the rest of the body. And there are a number of different ways to do that. As I mentioned before, avoid going in hot tubs during the period in which you're trying to conceive children. You should also avoid going in saunas during the period in which you are trying to conceive children. And if you do go in the sauna, you can bring an ice pack there and you can put it on the testicles in order to offset the heat of the sauna and keep the testicles cool while in the sauna. The other thing that you'll definitely want to do is avoid putting a laptop or any other hot device directly onto your lap. There are a number of different devices that you can put on your lap. You could put books or a box or there are these devices that are designed to dispel the heat from the laptop. I would say, if you're trying to conceive, just keep the laptop off of your lap. Just put it on a table or standing desk or whatever. Just keep it off of your lap. Also, there are some really interesting data showing that the amount of time that men spend sitting, regardless of whether or not they sit with their ankle on their opposite knee or with knees spread, the classic man spread stance, or any other kind of seated stance is going to increase the temperature of the scrotum for reasons that are somewhat obvious if you think about the architecture of all this. I think both men and women, if you put enough thought to it, you go, oh yeah, that would increase the temperature. Obviously avoid seat heaters in cars or otherwise. But reducing the total amount of time that you spend seated is really important if you want to keep the temperature milieu of the scrotum optimal for sperm quality and fertilization. And as I mentioned earlier, it's going to be important to make sure that your legs are not really big to the point where they are creating a hotter than is healthy environment for the scrotum and testicles. So a hotter than normal environment for the testicles can be caused by legs that are very large, upper thighs that are very large due to obesity or due to those

upper thighs being too muscular. So by all means, don't skip leg day. But be aware that if you're somebody who's trying to conceive, you want to do whatever you can to reduce the temperature of the scrotum or at least not let it get too hot for too long. So I can think of all sorts of reasons now that men are going to come up with to do the man spread stance of their knees really far apart, even further if they have large legs. That's not a discussion we want to have here, and that's not really what today's discussion is about. Really the principle is what's most important, which is to keep the temperature of the scrotum and testicles lower than the rest of your body. There's a direct blood flow from the body to the testicle that provides blood flow. It's designed in a way that that blood pathway should be outside the body and as far away from the body as possible in order to get the temperature milieu of the scrotum and testicle correct for healthy sperm quality. Now, a topic that is sure to be a bit controversial--

02:51:26 Tool: Phones & Sperm Quality

but it really shouldn't be because the data, at least to me, are very clear-- is this issue of phone use and sperm quality. Now, this can open up a whole array of issues related to things like EMFs, and you've got people out there who have ideas about 5G and all of this stuff. That is not what this discussion is about. The discussion I'm about to have with you relates to the fact that the electromagnetic fields and the heat-related effects of smartphones can indeed have a detrimental effect on sperm quality and, yes, indeed, on testosterone levels as well. I'm going to refer you to a paper. We will link it in the show note captions. The title of this paper is "Effects of Mobile Phone Usage on Sperm Quality. No time-dependent relationship on usage. A systematic review and updated meta-analysis." This is the paper that came out in 2021 and talks about the fact that phones emit a radio frequency electromagnetic waves, which are called RF, radio frequency, EMWs, electromagnetic waves, at a low level between 80 and 2,200 megahertz that can be absorbed by the human body-- we know this. This is not controversial-- and have potential adverse effects on brain, heart, endocrine system, and reproductive function. That has been established. Keep in mind, there is basically no controversy that radio frequency waves and EMFs can have a negative impact on biological tissues. The question is, how intense are those radiofrequency waves and EMFs, and how detrimental are those on those biological tissues? It's a matter of degrees. But there is very little controversy as to whether or not they have an effect on

biological tissues. And I'm aware of absolutely zero data showing that they can have a positive effect on biological tissues. Since what we're mainly talking about now are smartphones, we want to separate out the heat effects of smartphones from the EMFs related to the fact that they are Wi-Fi smartphones or they're using cellular towers and Wi-Fi, one or the other or a combination. So there are a number of different things in the phone that could be detrimental. We need to separate those out. Why? Well, because you might have heard that carrying your phone in your pocket can reduce your testosterone levels and sperm count. And guess what, that is true. The data contained within this meta-analysis and other meta-analyses clearly point out that it can reduce sperm count and maybe testosterone levels significantly, but certainly sperm count and motility significantly. It reduces sperm quality. So should you avoid putting your phone in your pocket, certainly your front pocket? I would suggest yes, if you are somebody who is seeking to conceive. I'm not somebody who is going to stop using my smartphone. I don't expect anyone's going to stop using their smartphone. The question is, should you carry it in your front pocket if you're a male? I think, to be on the safe side, the answer is probably avoid doing that too much of the time. Ideally, don't do it at all. Then people will say, well, what if I turn off the Wi-Fi or I turn off the cellular access? Then is it still a problem? Well, it's a problem due to the heat-related effects. And then people say, well, I don't actually feel the heat of the phone. It doesn't get that warm. But the temperature effects of the phone, it turns out, are enough, even under conditions in which people don't report it to be uncomfortably warm, that it can change the temperature milieu of the testicle in ways that can diminish sperm quality. How much and how that relates to fertility and healthy pregnancy, not clear, but since we're talking about things to avoid, if your goal is to have a healthy fertilization and pregnancy, well, then, by all means, just don't carry it in your front pocket. Then people say, well, what about back pocket or what about backpack? Look, it's very clear that avoiding being too close to the phone is probably better for your sperm quality than putting the phone very close to your testicles or anywhere else on your body. But it's also the reality that most people are going to carry a phone nowadays. It's just the reality. I think the current estimates-- and it's discussed in this paper-- that 90% of the human population has a smartphone-- 90%, which is incredible-- the adult population, of course. Although a lot of kids have them, as well. So this paper goes on to detail a number of different studies and outcomes from studies. But basically what they find-- and here I'm paraphrasing-- is that the data indicate that sperm quality declines when people start using a mobile phone. So from the

point they start using a mobile phone, regardless of the usage time-- this is important. It used to be thought that it was four hours a day or more of holding your phone or having that phone close to your body was going to diminish sperm quality. It turns out that it's not related to usage time. That's even the title of the paper. It's just the fact that people are using mobile phones is reducing sperm count and quality. That's the reality. Is it entirely responsible for all the reductions in sperm quality and maybe even the reductions in testosterone levels that we're observing from decade to decade going forward? I doubt that's the case. Is it likely to be one of the major players? I've got my bet on the fact that it is based on the data that I've observed. And so if any of you would like to peruse the data in this meta-analysis, they're quite good. This study looked at 18 studies that include 4,280 samples. They were able to separate out the radio frequency versus the heat effects, and they were able to eliminate this time of usage variable, that previously we thought if you were exposed to a lot of cell phone contact, then it was far worse than if you were exposed to a little bit. Turns out, if you're exposed to any at all, you're going to diminish sperm quality. What does that mean? Does that mean that no matter what you do, if you own a smartphone, that you're going to diminish sperm quality? I think the short answer is yes, but that you can mitigate it. What might you do? Well, keeping your phone away from your groin or as far from your groin as possible if you're a male who's wishing to conceive and maybe even a male who's wishing to maximize his testosterone levels because it does appear that radiofrequency waves and the heat from the phone-- so both of those factors, independently and together, of course-- can disrupt the Leydig cells of the testes and the production of testosterone, and intratesticular testosterone is important for sperm production. The exact biological variables leading to all of these changes isn't exactly clear. But if you're like me, you say, OK, probably not a problem for most males to carry their phone. But probably best to not carry it in the front pocket. Maybe even avoid carrying it in the back pocket as well. Again, in the future, we will have an episode all about Bluetooth. We'll talk about various aspects of EMFs. It's a super interesting data set. And it's a data set for which there's a ton of controversy. It's really interesting, however, and there are more and more quality data coming out all the time. And I think, going forward, we are going to see that, indeed, there are some negative effects of smartphones related to both the radio frequency transmission and the fact that they generate heat. And in general, heat is not good for biological tissues. So any discussion about heat and sperm

02:58:06 Deliberate Cold Exposure & Fertility, Testicular Temperature, Cortisol/Stress

and how heat is detrimental to sperm has to raise this issue of whether or not cold is good for the testicle. OK, well, now there's a lot of data starting to come out about the positive effects, the positive biological effects, of deliberate cold exposure on different aspects of brain biology, such as the release of dopamine and norepinephrine, and on the biology of the body, to some extent metabolism but more so the impact on brown fat stores, which are good for us, so-called brown fat thermogenesis. There's a lot related to deliberate cold exposure, and we've done entire episodes on deliberate cold exposure. Again, you can find that at hubermanlab.com. We did a guest episode with an expert on the use of cold for health and performance with my colleague Craig Heller from Stanford Department of Biology. We also have a toolkit on how to apply deliberate, cold exposure for health for both females and for males-- for sports performance, cognitive performance, mood, sleep, et cetera. You can find all that, again, at hubermanlab.com. Totally zero cost. Just go into the menu, go to newsletter, and scroll down, and you'll find those. When thinking about sperm quality, we want remember that excessive heat is bad. Now, does that mean that deliberate cold is good? Well, it turns out that one of the major causes of lowered sperm count and overall reduced sperm quality that's quite common is the presence of what's called a varicocele. A varicocele is kind of like varicose veins of the veins that innervate the testicle. And what it essentially does is it means that blood will pool in the testicular region. It can't circulate back to the body quickly enough. And therefore, the temperature of that environment increases. There are some other things that varicoceles do which can be obstructive at the physical level. So they're not just temperature related. It's pretty clear that using deliberate cold exposure can be healthy for the sperm because of the ways not that cold directly supports testosterone or sperm quality but rather because cold reduces heat. So you will find available online-- I think they're actually called-- forgive me, but that's what they're called. I didn't name them-- called snowballs. These are-- they're sort of like gel pack cold briefs that you can buy and men will wear for some period of time. I don't think you wear them all day. You wear them for some period of time. A lot of people are now using cold showers and ice baths and circulating cold baths or going into a cold ocean or lake for any number of different reasons I talked about earlier. I, myself, start every day with either a one to three-minute cold shower or a one to three-minute immersion up to my neck in a cold bath, cold water, circulating water, or a cold shower. I do that mainly for

the psychological effects related to the long lasting increases in dopamine and epinephrine. But there are other data starting to come out showing that that sort of approach or similar approaches can increase testosterone levels and maybe even sperm counts, can reduce cortisol late in the evening if the cold exposure is done early in the day, so on and so forth. So a lot of interesting data coming out in really good journals that are peer-reviewed and so on-- in humans, I should mention, those studies are done in humans-- to support the use of deliberate cold exposure. But again, if you're going to use deliberate cold exposure to improve sperm quality, can it work? Yes, indeed, it can work, either indirectly by increasing testosterone or directly by improving sperm quality. But both of those effects are likely to be indirect by virtue of reducing the temperature of the testicle overall, not because there's any sort of magic effect of cold on the testicle. Now, I have to imagine that a number of you, in particular the females listening to this, are going to say, is deliberate cold exposure-- and for that matter, is deliberate heat exposure, like sauna or hot tub-- good or bad for the ovary, for eggs, and for fertility? Now, there are fewer data to look to, unfortunately. But what we do know is that deliberate cold exposure done in the way that I just described-- one to three minutes a day, ideally early in the day, through cold shower or immersion up to the neck-- doesn't have to be an ice bath. It could be cold circulating water or even non-circulating cold water. And people will say, well, how cold? I should have mentioned that before. How cold? There is no way I can tell you exactly how cold the water should be, because for some people, 60 degrees Fahrenheit will be exceedingly cold. For other people, 40 degrees is going to be more appropriate. How cold should you make it? If you're going to embrace these practices, you want-- according to the literature, what you want to do is make it uncomfortably cold such that you really want to get out, but safe. You don't want to go into 30-degree water immediately. You can actually have a heart attack and die if you do that. So you want to progress gradually into the cold. So you don't want to shock your system too much. Although it is the adrenaline evoked by that [GASPS],, that quickening or shortening or elimination of the breath for a short period of time when you get into uncomfortably cold water that correlates with or is actually the reflection of-- would be more accurate to say-- the release of adrenaline and then dopamine and so forth, which has been very well documented. So uncomfortably cold, but safe to stay in. And I cannot tell you an exact number that is uncomfortably cold but safe for you. It's going to differ person by person. You want to figure that out. Just like I can't tell you how much weight that you should squat in order to achieve some effective resistance training

for the legs, it's going to differ depending on your strength and your prior experience and so forth. So ease into it. Be safe. But it does appear that both for men, for reasons I talked about a few minutes ago, and for women that deliberate, cold exposure can be beneficial for fertility and for hormone production, but in particular for females in terms of regulating cortisol and for hormone production. Now, you might say, OK, getting into cold is stressful. How can that be helpful for regulating stress? Well, it turns out, when you get into the cold, you get a big surge in adrenaline and then dopamine, which is very long lasting, provided that's done in the early part of the day. So I would say, not too close to sleep. Then what you do is you restrict your maximum cortisol release to a period earlier in the day that buffers-- reduces, that is-- the likelihood that you would have excessive amounts of cortisol later in the day, which not only can disrupt sleep but is correlated with a number of other hormonal effects that are not good for us and therefore not good for fertility. So here what I'm describing are positive yet indirect effects of a cold on hormone levels both in males and in females. So for men, we talked about increased testosterone, improved sperm quality that was indirect. You're reducing the temperature of the testicle. But it's not that cold itself is positively impacting those things. Does that make sense? Heat is bad. Therefore, reducing temperature is good. Likewise, with females, deliberate cold exposure can be good for the overall fertility process, not because cold is good for the ovary or being cold is good for the ovary or for luteinizing hormone or for follicle-stimulating hormone or anything else like that, but rather that using deliberate cold exposure as a way to restrict stress in a deliberate way to a particular time of day increases the release of cortisol, then, and indirectly reduces the amount of cortisol that's released at other times along the 24-hour cycle. So these are positive yet indirect effects. So if you're a woman who really is interested in exploring deliberate cold exposure or who enjoys it or is already doing it and you're wishing to conceive, great. Explore it. Do it safely, of course, but explore it and continue to do it. However, if you're somebody who just hates the cold and doesn't want to go anywhere near it, there's no reason to think that you absolutely need it, provided that your stress, your sleep, and other factors are all being carried out properly. The next things that we'll talk about in terms of positive things or things that we can do in order to maximize fertility for both females and males are the things that you also generally hear about elsewhere.

Right along with sleep and avoiding alcohol and avoiding nicotine and avoiding cannabis, avoiding excessive heat for the testicle, avoiding excessive stress, is that you want to try to get enough exercise. Why would exercise have anything to do with any of this? Well, exercise-- and that is both a combination of resistance training and cardiovascular exercise-- is going to improve the health of the mitochondria-- in particular, cardiovascular exercise. And I realize that for you fitness experts out there, any time someone says "cardio," people kind of roll their eyes, like, what is that? There's endurance training. There's interval training. There's HIIT training. There's sprints. There's all sorts of different things. Some of those overlap. Some of them are separate. Indeed, that's the case. But we can use a general rule of thumb here, which is that, for most people, getting anywhere from 30 and ideally 45 to 60 minutes of exercise per day for six days per week, maybe even seven-- but most people like to take a day off or need to take a complete day off each week-- six to seven days per week is going to be good for mitochondrial health and function. It's also going to impact all the other things, like quality sleep, mood, reducing stress, and so on and so forth. So exercise we can handle pretty quickly by just saying everyone should be doing it. Now, when people are pregnant, they might have to, of course, change the amount of exercise or the type of exercise that they're doing. There are varying opinions on that, but certainly the type of exercise and the amount can vary when people are pregnant. But if you're seeking to conceive, getting enough exercise is good because it's good for the mitochondria. The mitochondria are present in that mid region of the sperm. And mitochondria are critical for chromosomal segregation and the spindle and other aspects of the formation of a healthy egg, ovulation, and fertilization in the female. One thing that I know a lot of people are interested in nowadays is so-called intermittent fasting or time-restricted feeding. I mean, let's be fair, everybody is restricting their feeding time because hopefully everybody is sleeping at some point in the 24-hour cycle, and nobody is eating while they are sleeping. That said, many people are employing a so-called eight-hour feeding window or a 10-hour feeding window or a 12-hour feeding window. And indeed, there are some data to support the idea that that can be a good thing for a number of different biological and health parameters. However, there are also a lot of data, especially recently, pointing to the fact that your overall number of calories and the quality of your food sources is going to be the most important variable. And some people simply find that time-restricted feeding-- intermittent fasting, as it's also called-- is just a convenient way to ensure that your total intake of calories is not excessive for what you

need. Now, with all that said, there is evidence that I've covered in a solo episode and will soon have an expert guest on showing that time-restricted feeding can have certain positive outcomes for various aspects of organ, cellular, and tissue health. This is somewhat controversial, but there is growing evidence that, by restricting your feeding window to, say, 8 hours or 10 hours or 12 hours, that it is better than if you were to eat over a longer period of each 24-hour cycle. But again, the data are still incoming. The reason we want to talk about time-restricted feeding, intermittent fasting is that a lot of people do use it because they find it easier to not eat at certain periods of their 24-hour cycle than to restrict calories. But again, keep in mind, you have to restrict calories if your goal is to maintain or lose weight, a discussion that we've covered in that episode on intermittent fasting and in the episode with Dr. Layne Norton and that we will cover in other episodes in the future. So refer to those episodes at hubermanlab.com if you would like to learn more about intermittent fasting, per se. For sake of this conversation, a number of people are probably asking, if I restrict my feeding to a certain window each 24 hours because that's what's convenient or because I'm excited about the potential positive effects of intermittent fasting, is that going to disrupt the likelihood of fertility and thereby a healthy pregnancy? And the short answer to that is, if you are a female and you are having regular menstrual cycles that is a fairly consistent duration-- so maybe it's 21 days, maybe it's 35, or anywhere in between, but it's fairly consistent from month to month-- and you are following intermittent fasting, time-restricted feeding, well, then chances are pretty good that it's not disrupting your fertility and likelihood of fertilization and a healthy pregnancy. Of course, during pregnancy, you need to talk to your doctor and make sure that you're eating in a way that's supportive both of you and of the developing fetus. That's extremely important. I am not aware of data exploring, in a regimented way, time-restricted feeding during pregnancy. So please, please, please, if you're pregnant, do not jump on a time-restricted feeding, so-called intermittent fasting diet. Talk to your OB/GYN. Talk to your doctor. Talk to multiple doctors, for that matter, before doing anything like that, because, of course, you're now eating for two, or if you have twins in there, you're eating for three. Very important. If, however, you're not yet pregnant and you want to be fertile, get pregnant, or simply maintain a fertile potential and biology and you're following intermittent fasting, it's going to be the regularity of those periods and regularity of cycle length that will tell you whether or not that's a good idea or not. Keeping in mind, of course, that if your total number of calories is too low, your periods will cease. That's a well-known effect. But of course, stress can also induce

cessation of menstruation. And there are other factors that can induce cessation of menstruation as well. Some of them start with changes in the brain, literally, in the hypothalamus. Some occur in the pituitary. Many lifestyle factors can do that. But most typically, it's going to be excessive caloric restriction or it's going to be a caloric deficit brought on by excess physical activity. So even if someone's eating a lot, if they're not eating enough to offset their physical activity or they're not eating enough of, in particular, fats, the essential fatty acids and protein, but also carbohydrates, well, then menstruation can cease. And of course, if menstruation is ceasing, chances are, almost with certainty, that you're not getting regular ovulations. Now, in terms of males and whether or not intermittent fasting is going to disrupt spermatogenesis and testosterone production, there's essentially no data we can look to. But we can look to the general logic around the relationship between body fat, testosterone, and spermatogenesis. And this was something that was covered in a discussion I had on optimization of hormone health for males that I had with Dr. Kyle Gillette, who's a medical doctor and obesity specialist. Again, you find that episode at hubermanlab.com if you want to learn all about hormone optimization in males. And essentially, the story is as follows. If a male is excessively overweight, he's carrying too much body fat in particular, not too much muscle-- although that can be an issue too, but too much body fat is typically the issue-- so more than, say, 20% body fat-- well, then losing body fat is going to be the primary goal for maximizing testosterone, sperm health, and spermatogenesis. If, however, a male is already lean, well, then actually increasing calories will increase testosterone. So it's a bit of a complicated story, although not so complicated that none of us can understand it. Basically, if you're overweight, you should focus on losing weight in order to maximize sperm quality and health. If you are very lean, well, then restricting your calories to the point where you are starting to lose weight or you're dropping even more body fat is unlikely to increase your testosterone further. It doesn't necessarily mean it's bad or that you shouldn't try and go, for instance, from 15% to 10% body fat. I'm not saying that that's bad and that will reduce your testosterone. But in general, if you're already very lean-- so 10% body fat, 5% body fat-- and you start restricting calories further, your testosterone levels will drop. So in the context of intermittent fasting, it's really not an issue of whether or not your feeding window is 8 hours or 12 hours. It's really an issue of whether or not you're getting enough calories to offset the physical demands and activities of your life, whether or not you're on a maintenance diet to maintain your weight. And of course, you have to put all that in the context of whether or

not you're overweight or lean to begin with. The simple thing to take away from this is, if you're a male who's using-- because you like it-- intermittent fasting, so-called time-restricted feeding, and you're following an eight hour or maybe even a one meal per day type approach-- although I don't really recommend that for a number of reasons we could talk about separately. If you're eating over the course of 8 or 10 or 12 hours per day because that's what works for you and you are ingesting enough calories to maintain your weight if you're already lean or you are ingesting fewer calories than you are burning in order to lose weight because you are already overweight and you want to lose body fat, you're probably optimizing for all the things that you need to do in order to improve sperm quality and testosterone levels. Now, also in that episode that I did with Dr. Kyle Gillette on optimizing hormones for males, we talked about testosterone replacement therapy. It's not a topic I want to get into in any detail right now. But I will say this.

03:14:46 Testosterone Replacement Therapy & Sperm Production; Supplements

Remember earlier when we were talking about spermatogenesis and the fact that in order for sperm to be generated consistently every month ongoing from the time of puberty until essentially the time that a man dies, you need two things. You need testosterone production from the Leydig cells of the testes, and you need spermatogenesis to be supported by that androgen-binding protein coming from the support cells, from the Sertoli cells. So you need testosterone, and you need androgen-binding protein, and you need the Leydig cells and the Sertoli cells active. When men take exogenous, meaning from outside the body, testosterone, either by cream or by patch or by pellets or more typically by injection-- the most typical TRT approach nowadays is testosterone cypionate, which is biologically identical to the kind of testosterone you would make. Well, because of negative feedback loops, which you also learned about earlier, the testicles themselves shut down their own testosterone production. Why would that be? OK, so you're taking testosterone in by syringe or by patch or any other method. So the circulating testosterone and the amount that arrives at the testicle is going to be hopefully clinically appropriate, not super physiological, but it'll be somewhere in the healthy reference range, maybe a little bit higher. Nowadays, some people are going a little bit higher. So we're not talking about full blown, quote, unquote, "anabolic steroid use," keeping in mind, of course, that estrogen is a steroid.

Testosterone is a steroid. But when we think about steroids, we mean like performance-enhancing drugs, so super physiological doses. We're talking about within physiological or near physiological ranges. So if someone's taking their testosterone in from an outside, exogenous, source, the levels of circulating testosterone will be sufficiently high that the pituitary will register that and will stop making luteinizing hormone and generally follicle-stimulating hormone, as well. And as a consequence, spermatogenesis is vastly reduced or eliminated. In other words, for men who are on TRT or who are taking testosterone from an external source, the number of sperm that they're going to make is going to be dramatically reduced. There are things that they can do to offset that, like taking hCG, human chorionic gonadotropin, which is just kind of a mimic for luteinizing hormone to stimulate the testes to continue to make testosterone. And some men will also-- or instead-- take FSH to stimulate the Sertoli cells to support spermatogenesis-- excuse me-- or both or some combination. Some people take clomiphene, Clomid. There are any number of different ways to bypass or offset the sperm-reducing effects of taking exogenous testosterone. This is a conversation that was covered in a fair amount of detail in that episode with Dr. Gillette. But just keep in mind that if you are taking testosterone from an exogenous source, your sperm counts will dramatically be reduced, unless you do something to offset it. So if you are wishing to conceive, you need to think about whether or not you're going to offset the testosterone replacement therapy or whether or not you're going to come off it entirely. So you'll need to talk to a urologist endocrinologist about that. And again, a number of these different themes and ways to go about tapering off TRT were covered in that episode with Dr. Kyle Gillette. So if you're on TRT or you're considering taking it and you're interested in having children, not just now but at any point, you really want to take these things into consideration. Now, I do want to point out that, for the number of you out there who are taking supplements, some of which we've talked about on this podcast and I've talked about in other podcasts, such as tongkat ali-- it turns out that there are a lot of men and women taking tongkat ali to reduce sex hormone binding globulin levels, to increase testosterone and estrogen, in some cases, libido and so forth. Those approaches, meaning supplement-based approaches, to increase testosterone or free testosterone or some related hormones, are not going to shut down your own endogenous testosterone production and reduce the number of sperm that you make or, at least as far as we know, disrupt ovulation in any kind of way, provided that the dosages are within normal ranges. Again, supplementation to support your hormones should not disrupt ovulation or

spermatogenesis or testosterone production. Quite the opposite. It should enhance it. What I just described around TRT as taking exogenous testosterone, that itself is an entirely different beast. Now, with all of that said, there are some supplements out there that include testosterone as an ingredient that's been snuck in to various formulas that include blends and things of that sort. You want to be aware of that. And we did an episode about how to develop a rational guide to supplementation. I highly recommend listening to that episode. Again, it's timestamped, available free at hubermanlab.com in all formats. Because it talks about which supplements are likely to be "clean," quote, unquote, to contain the things that you expect them to contain, there's more and more evidence coming out that a lot of supplements, including some-- for instance, supplements that contain testicle or the extracts of testicles can contain testosterone. Whether or not they can shut down your own endogenous testosterone production isn't clear. No one's really explored that in detail. But based on everything we just talked about with TRT, it stands to reason that it might either reduce it or shut it down. It's just never been explored yet. So by all means, make sure that what you're taking if you're taking supplements. But again, the major point here is that, for both females and males, taking supplements to support healthy hormone production, including things like tongkat ali, is not the same as taking hormones or bioidentical hormones, which indeed can shut down your own endogenous production of hormones and thereby reduce both egg quality and the chance of fertilization and healthy pregnancy and sperm quality and the chance of fertilization and healthy pregnancy. Any time there's a discussion about fertility and pregnancy, there seems to also be a parallel discussion about sex determination.

03:20:36 Sex Determination in Offspring, In Vitro Fertilization (IVF), Sperm Fractions

That is, what factors can influence whether or not the child that's born is male or female. That is, whether or not it has double X chromosomes-- so one X chromosome from mom, one X chromosome from dad because the egg was fertilized by a sperm that had an X sex chromosome, that 23rd chromosome-- or whether or not the offspring is male, whether or not it has the X chromosome from mom, because it's always going to be the X chromosome in that egg, and a Y chromosome from the sperm that fertilized that particular egg. Now, of course, there are instances out there of people that have XXY chromosomes or XYY chromosomes. But the vast majority of people out there are going to have either an XX chromosome-- so we call that a female karyotype. This is different

than genotype and phenotype, but a female karyotype would be XX-- or a male karyotype, which would be XY. Now, despite the fact that it is the egg and the sperm and the chromosomes that they carry that are going to determine the chromosomes, there's a lot of lore and discussion about the factors that can bias which sperm will fertilize the egg and thereby whether or not you're going to get an XX, female, or an XY, male, chromosome and therefore offspring. Now, not only is the lore around this whole issue of sex determination rather prominent, but it is also somewhat unusual and perhaps even interesting. So for instance, Aristotle himself proposed that if a man is thinking about himself and his own pleasure more than his partner and her pleasure at the point of ejaculation, then the offspring will be male. Aristotle also asserted that if a man is thinking more about his partner and her pleasure at the point in which he ejaculates, well, then the offspring would be female. And of course, we have zero reason to believe that there's any truth to Aristotle's theory. There are no data to support that. In fact, I'm not even sure how you would run that experiment because you can't really look at people's thoughts. You'd have to rely on honest self-report. And even if people were to faithfully report what they were thinking about at the moment of ejaculation, this would involve, of course, bringing people into the laboratory and somehow measuring or analyzing their thoughts or gathering their thoughts during the sexual intercourse at the point of ejaculation, then figuring out which biological sex was the offspring, et cetera. Just near impossible and probably not the most important experiment to invest our time doing. Nonetheless, there continues to be a lot of lore about what determines the sex of the offspring. Most notably, there's a lot of lore and discussion and rumor about the idea that particular sexual positions at the point of ejaculation during intercourse can somehow bias the likelihood that a pregnancy will be either resulting in male or female offspring. Now, again, there are zero data to support this, and yet this whole notion of sex determination is a really interesting one that people seem to be somewhat obsessed by, so much so that, again, if you go online or if you were to talk to people in the sort of let's call it holistic or peripheral health spaces related to fertility, there is discussion about, OK, well, you take this sexual position at the point of ejaculation to get a boy and you take that sexual position at the point of ejaculation to get a girl or you do this in the early part of the day or the later part of the day. Again, all for which there is zero data to support any kind of systematic relationship between what I just discussed and the biological sex of the offspring. That said, there are now emerging methods that people are using in order to separate out the sperm that will indeed give rise to a male offspring

versus a female offspring. Now, this, of course, is done in the context of in-vitro fertilization. We haven't talked too much about in-vitro fertilization. But in-vitro fertilization involves, as the name suggests, taking an egg and taking a sperm, pairing them in a dish. This can be done a number of different ways. But just to briefly describe the IVF procedure, IVF involves administering supra-- meaning greater than normal-- supraphysiological levels of follicle-stimulating hormone and luteinizing hormone during the follicular phase of a woman's cycle. What that causes is the maturation of not just one egg that would be ovulated but multiple follicles and eggs. And then ovulation itself is suppressed also through the administration of exogenous hormones. And then, under ultrasound guidance, an OB/GYN goes in and collects the mature eggs and follicles, puts them in a dish, and then sperm are delivered to that dish, and those could either be sperm that were frozen previously, or more typically or ideally, it would be live sperm collected that day that are washed through a very straightforward procedure. And then those sperm either are allowed to compete for those eggs and fertilize those eggs and allow them to advance to very early embryo stage before those embryos are frozen and eventually implanted into a woman in order to have them be carried to full term, ideally. Or there's a procedure in which specific sperm are selected because they have the best morphology, motility, and so forth. And in a process called ICSI, I-C-S-I, in which the sperm themselves are literally forced to fertilize that particular egg. Now, under those conditions, typically a couple or a woman, if she's doing this on her own with a sperm donor, will get multiple fertilized embryos that are carried to a multicellular stage so that it's clear that they could grow into a child if they were implanted into a viable host-- sometimes the surrogate, sometimes the woman who wants the child herself. And under those conditions, it is possible to look at the genetic makeup, including the karyotype, of those early nascent embryos, in which case people really can select the sex of their offspring. That is, they will have some embryos that are XX, some embryos that are XY. It's very likely, also, that they will have some embryos that have karyotypes or genotypes which are not ideal in that they would potentially lead to a miscarriage or some other genetic defect. And so, typically, people do not select to implant those embryos if they have the option to implant embryos that are of either XX or XY karyotype and the normal chromosomal arrangements for obvious reasons. So the whole point here is that sex selection is possible, but only using in-vitro fertilization. The other thing that is becoming clear to us in more recent years is that sex selection is actually possible at the level of the sperm even prior to fertilization. This is an emerging data set, and this is largely

happening in clinics outside of the United States. But there are some clinics that have figured out methods in which they can take a sperm sample and they can spin that sperm sample in a centrifuge at a rate that separates out the sperm into what are called different fractions. So for those of you who've done a little bit of biology with centrifuge, it's when you spin any kind of substance that includes multiple things in it of different weights. When you spin them, the things of different weights segregate out into different fractions along the depth of the tube. And then you can take out one fraction or the next simply with a little pipette. You take out the top fraction, the middle fraction, and so forth. And what these clinics have figured out is that if they spin the sperm sample at the correct spin rate that the sperm that will give rise to male offspring and the sperm that will give rise to female offspring segregate out into different fractions, allowing them to take each of those fractions separately and to apply them to eggs, if it's in-vitro fertilization, and give rise very reliably, certainly much more than chance, to either male or female embryos. They also, of course, can choose to do this outside the context of in-vitro fertilization. So some people are now opting to have their sperm samples spun out in this way, separate out the sperm that give rise to male or female offspring, and then to only use the fraction that they are interested in-- so if they want a boy, they'll use one fraction. If they want a girl, they'll use different fraction-- and then to use those fractions in the context of what's called IUI, or intrauterine insemination, which is, as the name suggests, rather than having the man deliver the ejaculate with his penis and the sperm with his penis, they have a device. The devices are now commercially sold. Believe it or not, they're sold over-the-counter and on the internet, so people will even do this at home. And so what they're doing is they'll take the sperm, and they'll do IUI in order to bias the probability that they're going to get a male or a female offspring. Again, this is something that's now emerging. It's not commonplace. Most of the time, people simply roll the dice, as it were, by having either intercourse and just hoping for or not caring if they get a male or a female offspring or, in the instance of IVF, selecting male or female offspring, sometimes largely on the basis of the chromosomal arrangements. So of course, some people might prefer to have one or the other biological sex as their offspring. But of course, the healthy chromosomal arrangements are going to be paramount for getting a healthy child. And as I mentioned before, unhealthy chromosomal arrangements or abnormal chromosomal arrangements often lead to miscarriage and/or birth defects. So selecting for healthy chromosomal arrangements is always paramount, but some people are selecting for biological sex. And indeed, some

couples who can conceive naturally are opting for IUI in order to be able to select biological sex because of this ability to spin out the sperm samples to different fractions and select the male or female sperm. That is, the sperm that would give rise to a male or female offspring. So this is a rapidly emerging theme, believe it or not. Who knew? And of course, it has nothing to do with Aristotle's assertions about what people are thinking about at the point of ejaculation, nor does it have anything to do with body position at the point of ejaculation. But I do find it rather interesting that, even in this day and age, people seem to be continually pursuing new and different ways to understand why one sperm or another sperm happens to fertilize the egg. And when that information is not available, because, frankly, it's not available yet-- we don't know why a sperm containing a Y chromosome or a sperm containing an X chromosome is more likely to fertilize an egg. And there are some ideas, for instance, that older fathers tend to have more daughters as opposed to sons. But when you really look at the data, it's pretty mixed. So if you've heard that before, it has a particular nickname that I'm not going to describe on the podcast. You can look it up online. But if any of you are aware of any other kind of ideals or lore, no matter how ridiculous or crazy, please put them in the comment section on YouTube. I'd be very curious to learn about those, mostly out of interest and curiosity. But, look, sometimes these outrageous stories, such as notions of body position and how they influence biological sex, even though they turn out not to be true, turn out to be interesting for other reasons. And in fact, next, we're going to talk about how body position during sexual intercourse can, in fact, influence fertility and pregnancy. So another common theme around fertility and pregnancy that you'll hear about is that, for couples that are trying to get pregnant, that during intercourse they

03:32:23 Postcoital Female Position & Fertilization, Sperm Quality

should do whatever it is that works for them, but then after the man ejaculates that the woman should try and position her ankles above her head or somehow otherwise tilt her pelvis back in order to increase the rate and/or probability that the sperm swim toward the egg, as opposed to the other direction. Now, I talked to a couple of different OB/GYNs and urologists that are focused on fertility about this topic, and it turns out you get pretty mixed answers as to whether or not there's any validity to this idea that the woman's body position after the man ejaculates inside of her can somehow influence the probability of pregnancy. One group of experts told me that there is no reason for a

woman to need to continue to lie down, elevate the ankles, or in any way tilt her pelvis back in order to increase the probability of successful fertilization. The other group suggested that indeed there is a strong reason to believe that tilting the pelvis back, maybe even keeping the ankles elevated, and having a woman lie on her back for about 15 minutes with the pelvis positioned at about 20 degrees back is ideal for optimizing fertilization. I mean, they were really specific about the recommendations. So I find this interesting that, within the cohort of extremely well trained MDs, OB/GYNs and urology fertility docs, and OB/GYNs, you see a split. It has nothing to do with whether or not the physician was male or female or their training or their institution, none of that. There just seemed to be a sort of even split between the two. Now, granted, it wasn't the largest sample size that I could have obtained. And yet I do find it interesting that there's this split in the opinion about this. One group, the group that said, no, pelvic position doesn't really matter, don't worry about it, it's not going to influence the rates of fertilization, argued that the sperm swim very quickly and that if they are released near the cervix they're going to swim very quickly toward the egg in order to fertilize it regardless of pelvic position. The other group said, well, yes, sperm swim quickly and even if they're released right at the entry to the cervix that the sperm still have a long distance to go. Again, if you were to scale this according to the size of the sperm versus the size of a human body, an entire human body, what you'd scale it to is the distance between Los Angeles and San Francisco. And it needs to undergo that basically within 24 hours or so. Although, as we mentioned earlier, sperm can survive quite a while inside of the woman's body-- maybe three or five days at least. So in both cases they acknowledge it's a long distance. But on the one hand, you have a group of experts that are saying the sperm more or less know what to do and are going to do it regardless of the position of the woman after ejaculation inside her and the other group saying, no, we want to do everything we can to bias the likelihood that the sperm will fertilize the egg. Well, setting aside the basic argument that tilting back at the pelvis and lying stationary or so for about 15 minutes after sexual intercourse and ejaculation is not an expensive endeavor, although it requires a little bit of time. And it forces people to remain motionless or close to motionless, and they're not up and around and moving about. Aside from that, it's a relatively low investment. So one argument is, well, if it could bias the likelihood of fertilization at all and people want to get pregnant, why wouldn't they do that? So that's a reasonable argument. But it doesn't really point to the mechanism. The arguments that point to a potential mechanism are that-- if you recall what we were talking about when

we talked about sperm quality, sperm quality involves a bunch of different measures, like concentration of sperm per milliliter of semen, morphology of those sperm, how many are forward motile. It turns out that in any one ejaculate sample, the total number of forward motile and yet fast forward motile sperm that are also of the highest quality morphology is actually quite low. And so the idea here is that you want to get as many sperm of the highest quality swimming toward the egg because those sperm stand the highest probability of fertilizing that egg. And in fact, this relates to some of the discussion we were having earlier about behavioral dos and don'ts for sake of increasing the probability of fertilization.

03:36:57 Cannabis & Sperm Motility, Libido, Pregnancy

And the one that is most important here is cannabis. It turns out that the data on cannabis really do support the idea that some of you may have heard from parents and teachers-- I don't know, I did hear this from parents and teachers-- that cannabis can disrupt the swimming styles of sperm in ways that are not supportive of fertilization, that it can turn more of the sperm into twitchers. Although when I learned about this, I was not informed of the word "twitchers." What I was told is that, if you use cannabis, that the sperm don't know which direction to go, that they're confused, almost implying that the sperm themselves are high on cannabis. Well, that's certainly not the argument that I'm making here. But it does seem to be the case that people who use cannabis, even once, the sperm that are generated during that particular month or two months during which or after which they use cannabis have less forward motility and possibly altered morphology, as well. I want to be very clear, I did not say that if you use cannabis once you are forever disrupting the motility and morphology of your sperm. I did not say that. What I said is that if you use cannabis once, then the sperm that are generated in the 60 days after that cannabis use are going to have a higher incidence of disrupted motility and perhaps morphology as well. Remember, sperm are continually generated every 60 days or so. And so if you use cannabis once, you are not forever disrupting your sperm. But if you are using cannabis and then you are looking to conceive in the next 60 days, you are going to be reducing, we think significantly so, the number of quality forwardly motile sperm. So the simple takeaway from this is avoid cannabis use. Although if you are going to use cannabis-- and again, there are medical uses of cannabis and beneficial uses of cannabis for certain populations. It can be bad for other populations.

We talked about that in the Huberman Lab podcast all about cannabis. But if you're going to use cannabis, you should try and abstain from cannabis in the two months prior to the attempt to fertilize and get pregnant. Now, I'm not aware of any data on how cannabis use by the woman can influence the likelihood of fertilization and pregnancy. And I want to couch this whole discussion around cannabis under the umbrella of something that came up in the episode that I did on cannabis, which is that, for about half of people out there, male and female-- so here we're not distinguishing by biological sex. About half of people that use cannabis report it as an aphrodisiac. It makes them want to have sexual intercourse more than if they don't use cannabis. And for the other half, it actually has the opposite effect by way of an influence on a hormone called prolactin, which suppresses the dopamine system, the testosterone, and the estrogenic system. And so this whole idea that cannabis is an aphrodisiac seems to be true for about half of the human population and not for the other half of the human population. So I mention that because I know a number of people use cannabis as an aphrodisiac. They like to use cannabis before intercourse. It was actually very surprising to me to discover when I researched that cannabis episode that approximately 15% of women who are pregnant continue to use cannabis during pregnancy. And that's a very alarming statistic. And everything we know is that the use of cannabis during pregnancy is detrimental to the health and particularly the brain development of the fetus. So that's a real concern. I highly recommend women abstain from cannabis use during pregnancy. Talk to your OB/GYN about it if you're using it all or considering using at all. So based on what I told you earlier about the fact that cannabis use is not good for egg quality and the fact that cannabis use can disrupt the motility of sperm and therefore is not good for sperm quality and it can disrupt the patterns of swimming in sperm in ways that reduce the likelihood of fertility, I think the take-home message is clear, which is that whether or not you want to be a cannabis user or not, if you are going to try and conceive and certainly while you're pregnant, you're going to want to avoid the use of cannabis. And that is smoked cannabis and vaped cannabis. And during pregnancy, the consumption of cannabis even in edible form or in tincture form is also going to be detrimental to the developing fetus. But of course, we started this conversation in the context of body position, in particular at the point of ejaculation, in determining the sex of the offspring and/or the likelihood of getting a successful fertilization in pregnancy. And I think that given that the tilting back of the pelvis-- so again, this is elevating the pelvis by about 20 degrees-- I don't think it has to be exact, exact-- but about 20 degrees for about 15

minutes post-ejaculation inside of the woman-- or I suppose if people are using IUI, intrauterine insemination. Since that seems to be the consensus among those experts that believe that pelvic tilt backward can be beneficial for increasing the probability of fertilization and given that it involves no cost but a little bit of time seems to me that, if you want to get pregnant, that that would be the right thing to do. And as far as I know, there's no information nor was I able to obtain any recommendations from experts about what the ideal body position of the male is after ejaculation if the goal is to increase the probability of fertilization in pregnancy. So we've been talking about behavioral interventions, some dos and some don'ts that people can do to increase their fertility, and the likelihood that any fertilized egg will be carried to term successfully.

03:42:33 Acupuncture, Fertility & Pregnancy

And soon we'll also talk about things that people can take to improve their fertility. Now, keep in mind that this entire discussion is about fertility. But also remember, as we discussed at the beginning of the episode, trying to increase your fertility is one of the best ways to think about trying to create and maintain optimal physical health. So for people that are trying to conceive and for people who are not trying to conceive, optimizing your fertility status, whether or not you're male or female, is one of the best ways to target those approaches. And there are now a lot of data supporting the idea that acupuncture of all things can be very beneficial for improving both female and male fertility and, should a woman get pregnant, for improving the quality of outcomes-- that is, the likelihood that there will be a successful pregnancy that is carried to term, not premature, and so on and so forth. Now, for some of you out there, you might think, oh, of course, acupuncture, acupuncture has been known to work for thousands of years. And therefore, it's not surprising that it would assist with fertility and pregnancy. For many of you out there, however, probably thinking, acupuncture, that seems kind of like fringe science. But what I can assure you is that there are now quite a few clinical trials funded by government agencies, like the National Institutes of Health, showing that acupuncture is a very effective treatment for a number of different things, including fertility and pregnancy, but for hormone status, for stress relief, even for chronic illnesses of different kinds, including autoimmune illnesses. So this is no longer considered fringe science. In fact, one of the best laboratories in the world working on this is a laboratory out of Harvard Medical School run by a guy named Qiufu Fu. Qiufu's lab has really been

exploring in a mechanistic way how the different stimulation sites that are used in acupuncture-- so where the needles are inserted-- tap into neural pathways that link the different organs of the body. So for instance, they've found that stimulation of a particular site on the lower limb can reduce inflammation dramatically throughout the body by way of neural pathways that originate in the lower limb and extend to areas such as the kidney and the pancreas. So all these, quote, unquote, "ancient maps" of the human body as they relate to acupuncture are now being parsed at the level of mechanism, which I think is wonderful because it not only is showing us that so much of what has been purported and reported in the landscape of acupuncture actually has an underlying mechanistic basis, and with additional mechanistic understanding, of course, always arrive new and better practices. That's the idea, to evolve these fields of acupuncture, to evolve the fields of mechanistic understanding of our biology and health. And so the issue of whether or not acupuncture can assist in getting pregnant and in carrying a child to term and for that child to be healthy are really starting to emerge in a major way. And rather than go into all those data in detail, what I can tell you is that there are clinical trials and data supporting the fact that female fertility itself can be supported by acupuncture through several mechanisms, one of which is the balancing-- and I realize that's a somewhat tricky term, and I'll define it better in a moment-- the balancing of hormones across the ovulatory/menstrual cycle, including regulating levels of FSH so that they're not too high nor too low and restricting the FSH to the follicular phase of the menstrual cycle, as well as using acupuncture to improve things like blood flow and the health of the ovary itself and other aspects of the female reproductive axis. So acupuncture can operate at the chemical level, impacting hormones. It can act at the mechanical level, impacting the different tissues through which the egg has to pass and so on and so forth. Likewise, on the male side, acupuncture has been shown to improve semen volume, quality of sperm, sperm motility, et cetera, and in large part through changes in the neural pathways that innervate the very tissues and vascular input to the scrotum and testicles, because, as we learned earlier, temperature regulation of the scrotum and testicles is so vital for getting healthy sperm and increasing sperm quality. In addition, there are good data to support the idea that acupuncture can increase levels of testosterone, free testosterone, and the sorts of hormones that are going to support healthy hormone production and sperm production in males. And this is distinct from applying testosterone from an exogenous source. So when we're talking about acupuncture and increasing levels of testosterone, we're talking about increasing levels

of endogenous testosterone. So those Leydig cells can support the Sertoli cells, and the Sertoli cells can make that androgen-binding protein, and you get enhanced spermatogenesis. You can find evidence for all of these different features, both changes to the chemical milieu-- that is, the hormones-- and changes to the mechanical milieu, including, for instance, improvement of the pathways leading from the seminiferous tubules to the epididymis to the vas deferens, basically clearing out the plumbing so that more quality ejaculate can be delivered, which, of course, is going to increase the probability of fertilization. So when you hear that acupuncture can improve the likelihood of pregnancy, that's an accurate statement for which there are now increasing amounts of mechanistic data. If you want to learn more about how acupuncture can be used to contribute to improved fertilization and pregnancy, there are a number of different excellent reviews on this, both as it relates to females and as it relates to males. One of the best papers that I happen to like is one that we'll provide a link to in the references entitled "Acupuncture and Herbal Medicine for Female Fertility, An Overview of Systematic Review," so a review of reviews. This was published recently in 2021. We'll provide a link to that. And there's also going to be a link to a review that relates to acupuncture for male fertility and hormone augmentation. I should just mention briefly that if you're going to look at scientific papers, one thing that you'll want to consider is also looking at the references that they reference. Now, of course, papers tend to reference a ton of references, in particular in reviews. So what you'll want to do is look for the references that are showing up most often in the introduction. Those references often are going to be the most prominent recent reviews or the most important findings in recent years. That's not always the case, but that's often the case. So if you read the first couple of paragraphs of these papers-- and these are openly available as full text, by the way, online if you go to these links-- you'll be able to access the best papers, the most relevant papers, in the context of acupuncture supporting female and acupuncture supporting male fertility and hormone status. Now, I'd like to discuss things that both men and women can take in order to maximize their fertility. And again and again, when we're talking about fertility,

03:49:25 Fertility Supplements: L-Carnitine & Allicin, Coenzyme Q10

we're talking about people who want to conceive and have children, but also we're talking about a basic measure of overall health status. So if you're somebody who does

not want to conceive children, I still encourage you to think about whether or not you would want to do certain things or not do certain things in order to maximize your fertility as a means to maximize your vitality and longevity, because that's really what maximizing fertility is about for a lot of people. That said, I know a lot of people would like to conceive children, perhaps not right away but in the future. And what I'm about to describe are some tools and interventions that is things that one can take in order to improve their hormone status but also, in particular, the quality of their eggs and the quality of their sperm in the short and long term. The first on the list of things that people can take in order to improve egg quality or sperm quality is L-carnitine. L-carnitine is present in various foods, in particular in red meats. But again, it's going to be very hard to get sufficient levels of L-carnitine to improve egg quality and sperm quality, the unless you're going to take it in supplement form. The typical recommendation, based on peer-reviewed studies that have shown significant improvements in egg quality-- that is chromosomal arrangements, that is the likelihood of fertility-- or pregnancy, rather-- the likelihood of sperm being forward fast swimmers as opposed to twitchers or immotile and having proper morphology-- all those measures has been demonstrated to be significantly improved by the ingestion of L-carnitine. How much L-carnitine? Well, that depends on how you're obtaining the L-carnitine. If you're obtaining it in capsule form, 1 to 3 grams per day of capsule form L-carnitine is what's been suggested to improve egg quality and sperm quality. Now, 1 to 3 grams per day can be taken all at once or spread out throughout the 24-hour cycle. It can be taken with or without food. It does not seem to matter. And when taken for a period of 30 to 60 days, it does seem to significantly improve all the parameters that have been discussed for egg quality and sperm quality. Now, the mechanism for that effect is pretty clear. L-carnitine is involved in the processing of lipids, fats, in terms of mitochondrial function. And as we talked about before, mitochondria are vital for the organization and action of the spindle that pulls apart the chromosomes, taking that cell within the female from diploid to haploid, which is essential. You really want just the 23 individual chromosomal strands. You don't want chromosomal repeats. It's also involved in the actual fusion of the egg as it exits the ovary and enters the ovulation cycle. Mitochondria are also important, as we talked about before, for the forward motility of sperm because of the enrichment of mitochondria in that mid region just behind the head. They cause the whipping flagellation of the tail, allowing for forward movement, as well as other aspects of cellular morphology. So it makes a lot of sense as to why L-carnitine supplementation would be

beneficial. Again, it's 1 to 3 grams per day over a period of about 30 to 60 months. If you're hoping to conceive in the upcoming months, recommend taking it for at least 30 days prior to that. Of course, based on the data we talked about before-- cumulative probability, fecundability, et cetera-- there's no reason to not continue to try for pregnancy before taking L-carnitine, but L-carnitine is going to improve egg and sperm quality. And so you might actually take the stance that, even if you don't have any problem getting pregnant, wouldn't you want to maximize the quality of the egg that gets fertilized and the quality of the sperm that fertilizes that egg? So that's additional rationale for taking L-carnitine. One important note-- if you are going to take L-carnitine in oral form, in capsule form, it can increase something called TMAO. TMAO can cause stiffening of the arteries. You don't want TMAO levels to go too high. One way to offset the increases in TMAO caused by oral L-carnitine is to take 600 milligrams of garlic per day. I suppose you could eat cloves of garlic. That would work just as well because garlic contains something called allicin, which can offset the increase in TMAO. But 600 milligram capsules of garlic are going to be-- or garlic extract, rather-- is going to be the most probably cost effective and simplest way to do this. And also, they are going to create that garlic smell. Some people like the smell of garlic. Some people don't. So if you're going to take oral L-carnitine, I suggest also taking 600 milligrams a day of garlic extract. And you can do that at any time throughout the day. It doesn't have to be with the L-carnitine. The next item on the list of compounds that have been shown to improve egg quality and sperm quality-- and quite robustly so-- is coenzyme Q10. Coenzyme Q10 is something that you can actually measure levels of in your blood. Most physicians will say that they want to see your levels of coenzyme Q10 to be somewhere between 0.5 and 2.5. It's going to depend on the units. Most people, I realize, are not going to run off and get their CoQ10 measured. It's not included in most standard blood tests. But if you were to measure your CoQ10, that's the range that you want to look for. That said, many people opt to supplement with CoQ10. And you'll find that many fertility docs, OB/GYNs, and urologists that are trying to assist their male patients with fertility will suggest CoQ10 because, again, it supports the health of mitochondria. Mitochondria are so vital to so many aspects of the formation and fertilization of the egg and sperm that, of course, fertilizes the egg. The coenzyme Q10 dosages that are most often suggested and that you'll observe in the peer-reviewed research literature-- on humans, I should add-- is 100 to 400 milligrams per day. And the coenzyme Q10 is taken generally with a meal and ideally a meal that contains fat. And there's even some idea that taking

coenzyme Q10 with your dinner, assuming that dinner includes some fat-- you don't have to add additional fat-- is going to be more advantageous than taking coenzyme Q10 early in the day, although that's probably a detail that's getting a little too far down in the weeds. So again, 100 to 400 milligrams of coenzyme Q10 per day, whether or not you're a man or a woman, for improving the likelihood of fertility by way of improving egg and sperm quality. And again, if you're somebody who just doesn't have any problem getting pregnant or if you're already producing many sperm of quality morphology, this is another case in which you could take a step back and say, well, why wouldn't I want to further optimize the quality of the egg and the sperm, because the quality of the egg and the sperm ultimately are going to determine not just whether or not you have a successful pregnancy but are going to determine, admittedly in ways that will forever remain cryptic to you-- but nonetheless are going to be important in determining the qualities of the brain tissue and body tissue of your offspring. The third item on the list of compounds which are commonly suggested or prescribed by fertility docs nowadays for men and women wishing

03:56:18 Fertility Supplements: Inositol, Omega 3 Fatty Acids

to conceive and/or optimize their fertility as a basis for general vitality and health is inositol. Now, inositol has many uses. So you'll hear about the use of inositol for reducing anxiety or improving mood or even for the treatment of depression. We talked about inositol in previous episodes of this podcast. For instance, I talked about inositol and in particular taking 900 milligrams of myo-inositol prior to sleep, which is something that I do, along with the other supplements that I take and recommend for sleep, such as magnesium 3 and 8, apigenin, and theanine. If you're curious about those, you can see our newsletter on sleep or our "Perfect Your Sleep" episode or the "Master Your Sleep" episode. It talks about behavioral and supplementation-based tools for improving sleep. But myo-inositol is not just suggested for or prescribed for people that are wishing to get pregnant and for general health. But myo-inositol is often recommended for people that want to improve egg and sperm quality because of the way that it can positively impact insulin sensitivity. Insulin sensitivity might sound like a bad thing to people out there. But it turns out that you want to be insulin sensitive. The last thing you want is to be insulin insensitive. Insulin insensitivity is associated with type 2 diabetes, with obesity, and even for people who are not challenged with obesity, you want your cells to be insulin

sensitive. You don't want a lot of insulin floating around in your system with your cells unable to use that insulin. That's really what insulin insensitivity is about. Myo-inositol, at dosages of 1 to 5 grams per day-- that's pretty high, 1 to 5 grams per day, keeping in mind that 1,000 milligrams is 1 gram-- has been suggested to improve egg quality and sperm quality. Now, one point of-- I wouldn't say caution-- but of note is that myo-inositol can reduce anxiety, and it can be a slight sedative, which is why some folks, including myself, take almost a gram, 900 milligrams, prior to sleep. If you're going to take 5 grams of myo-inositol, you would want to restrict that to the late evening or second half of your day. And I don't suggest starting that high. I would start with 1 or 2 grams and then working your way up, seeing what you can tolerate in terms of the level of anti-anxiety and drowsiness that it produces. 1 to 5 grams per day of myo-inositol is what's suggested for both men and women wishing to improve egg health and sperm health. But for women, it's also often suggested to include also-- so to take myo-inositol, but to also take D-chiro inositol. D-chiro inositol has elements in it that can be both pro and anti-androgenic. Androgens are things like testosterone and related molecules. There are a number of different causes of infertility and disruption to egg quality, age being the most significant factor. But another significant and very common factor, even among young women who are of fertile age, is having too many androgens and as it relates to something called polycystic ovarian syndrome. We'll do an entire episode about menopause and PCOS and a number of other things that relate to fertility because it's an entire and very interesting other discussion that we need to have. But the recommendation is that women take 1 to 5 grams of myo-inositol but also D-chiro inositol because of the ways that it can balance androgens and offset some of the negative effects of polycystic ovarian syndrome or even for women who do not have polycystic ovarian syndrome because of the ways that D-chiro inositol can balance androgens in ways that are beneficial. The dosages of D-chiro inositol that are recommended tend to be 1/25 to 1/40 of the myo-inositol dose. So you'll have to get out your calculator. Remember, 1,000 milligrams equals 1 gram. So figure out, if you're taking 1 gram of myo-inositol per day or 2 grams, you're going to want to convert that to milligrams. So let's say you're taking 2 grams of myo-inositol per day. That's 2,000 milligrams. Then you'd want to divide that by 25. And that's how many milligrams of D-chiro inositol you would want to take, as well. Or you could go with the lower end dose and divide it by 40 and take that number of milligrams of D-chiro inositol along with the inositol. Again, probably taking it later in the day is going to be good. And it's not clear at

all that taking it with food or without food makes any difference whatsoever. So I would suggest you do either. Keep in mind, as I'm discussing these recommendations, I may call them prescriptions. But none of these are prescription drugs. And of course, you should always discuss any supplements that you're planning to take or stop taking, for that matter, with your physician. I don't say that to protect me. I say that to protect you. Any time you're going to add or change something in your overall health regimen, you want to discuss that with your trusted health care professional, typically, I would hope, a board-certified MD. The fourth item in the list of commonly suggested supplements for men and women wishing to optimize egg and sperm quality, respectively, is omega-3 fatty acids. And now, here, we're talking about something that could be obtained from food and can be obtained from food. So if you're consuming fatty ocean fish, things like sardines, anchovies, salmon with the skin, chances are you're going to get some quality omega-3s. Omega-3s are also available in plant-based sources. It's also available in krill, for that matter. But most people find it difficult to reach the threshold required for optimizing mental health and physical health that is the threshold of the EPA essential fatty acids. And so for that matter, I've suggested before on this podcast-- and many fertility docs will suggest-- that their patients take omega-3 fatty acids in supplement form. It could be taken in liquid form or in capsule form, but enough of those that you're getting at least 1 gram per day of the EPA form of omega-3, so at least 1 gram per day and as high as 2 or even 3 grams per day of the EPA form. So you'll need to look at the packaging because oftentimes it'll say high potency omega-3. It'll say 1,500 milligrams of omega-3s. But that's not 1,500 milligrams of the EPA form. You look on the back of the label, and it'll say, each serving contains 750 milligrams of EPA. You want to get above that 1 gram dosage per day and as high as 3 grams per day of the EPAs. The most cost-effective way to do that is going to be liquid-form omegas, but that's a little bit inconvenient for many people, and some people don't like the taste. That's why they rely on the capsule-form omegas. And of course, there are compounds that can impact fertility status, quality of eggs, quality of sperm, not by adjusting mitochondria

04:02:50 Supplements for Hormones: Tongkat Ali, Shilajit, Zinc

or insulin sensitivity or creating a general milieu of support for the egg and the sperm production and function, such as the compounds that I just listed off do, but rather compounds that influence the hormones involved in the generation of sperm and the

generation of the eggs, involved in the ovulatory cycle and the spermatogenesis cycle, that is. Now, these are going to come in different forms. And I want to just emphasize that the supplements that do this, that adjust hormones in these ways that can be beneficial, are distinct from hormone therapy or bioidentical hormones, distinct from hormone therapy or bioidentical hormones, because, as we discussed earlier, when you take a hormone like testosterone or even estrogen, for that matter, from an exogenous, an outside source, you're going to disrupt the feedback pathways inside of your body, and you're going to shut down your own endogenous production. The supplements I'm about to describe do not do that and yet can adjust levels of hormones in more subtle ways that can be beneficial for the process of maximizing fertility for males and for females. The first of which on this list that I'd like to discuss has been discussed in previous podcasts as well, which is a substance called tongkat ali. Tongkat ali also goes by other names. But when taken at 400 milligrams per day, sometimes separated into two dosages but typically taken as once a day early in the day because they can be a little bit stimulating, although not anxiety provoking-- I've never heard of that. It can be a little bit stimulating. But 400 milligrams a day of tongkat ali has been shown to increase free testosterone by way of reducing something called sex hormone binding globulin. It's also been shown to increase luteinizing hormone, the net effect of which has been described as a subtle but significant increase in libido and some of the other parameters associated with increased androgens, like free testosterone in males and females. So a number of people out there are taking tongkat ali in this way-- 400 milligrams per day, restricted to the early part of the day, with or without food. People always ask, do you need to cycle tongkat ali? I'm not aware of any need to cycle tongkat ali. In fact, it tends to work better, meaning the effects on libido and some other hormone profiles tend to increase over time. Again, tongkat ali is an option. Certainly, none of these things are requirements. We're simply listing off options. But many people, both males and females, seem to benefit from and like tongkat ali, even if they're not seeking to conceive. There's no reason to think that tongkat ali directly improves sperm quality. Except in males, the increase in androgen created by tongkat ali supplementation can indeed lead to improved spermatogenesis. So there's a growing amount of data in the research literature on tongkat ali. Many people find it beneficial. And so it's something that both men and women wishing to conceive and/or optimize their fertility just as a general health parameter might want to explore. The other supplement that's been shown to improve both egg quality and sperm quality-- and there I'm referring to a

number of different parameters related to egg quality and sperm quality-- as well as to increase libido fairly substantially is a substance called Shilajit. Shilajit, spelled S-H-I-L-A-G-I-T-- Shilajit is actually a compound that's used in ayurvedic medicine, but there are some really good research studies exploring the supplementation with Shilajit at about 250 milligrams twice per day. And this has been looked at in males and in females. And it does seem to significantly increase two hormones. One is testosterone, and the other is follicle-stimulating hormone. And for that reason, Shilajit is often considered a tonic that people use both as an aphrodisiac to increase libido as well as to increase fertility. Now, one note of caution, if you're a woman and you're considering taking Shilajit in order to increase testosterone and follicle-stimulating hormone, keep in mind that the ovulatory cycle is this very tightly regulated cycle in which you want low but elevated levels of follicle-stimulating hormone early in the follicular phase, then it peaks right before ovulation, and then low levels of follicle-stimulating hormone in the second half of your cycle. For that reason, using Shilajit chronically around the entire course of your ovulatory cycle could be a little bit risky, and I'd recommend that you talk to your OB/GYN prior to doing that or if doing that at all. For males, it's a little bit less of an issue, because, as I mentioned earlier, sperm are constantly being generated, and the presence of FSH is going to increase spermatogenesis. Now, Shilajit is not FSH itself. Shilajit stimulates the release of FSH. And it stimulates the release of testosterone. So again, there's no reason to think that it would shut down your endogenous testosterone or FSH production. Although there are limited amount of data that really explore that in detail. Many people use Shilajit in order to increase their testosterone, FSH, their libido, and various aspects of sperm health. Again, the dosages of Shilajit are about 250 milligrams, two times per day. One issue with Shilajit is it often comes as a tar, which is a little hard to measure out the dosages. Yes, a tar. It's this kind of thick, gummy substance that you're supposed to dissolve in water. And the recommendations are you take a little bead and dissolve it in water. It is available in capsule form where the ability to control the dosage is made a little bit easier. But of course, as with any supplement, I recommend starting with the lowest possible dosage. So you might want to start with a very small bead of Shilajit dissolved in water, taken once per day, and then increase the dosage as needed in order to obtain the effects that you want. Things like Shilajit start to bring us into the realm of what can only be described as a little bit unwieldy, right? Here we're saying you can't really control the dosage. Now you're talking about hormones that need to be tightly regulated, at least for females across the ovarian cycle. For males,

yes, it has been shown to increase testosterone and FSH, improve sperm motility and sperm count pretty significantly. No reason to think that you couldn't do that chronically with Shilajit. And yet, I do want to acknowledge that Shilajit, as this black tar substance, contains a lot of different things. In fact, it comes from a mineral pitch. What is that? It comes from literally the dirt and plants that have been compressed by rocks in the Himalayas. So that's pretty esoteric stuff when it really comes down to it. But the biological effects of Shilajit, in both males and females, seem to be related to the fact that it is highly enriched in something called folic acid, and folic acid is involved in a lot of different cellular processes, not the least of which, at least in this context, is the transport of molecules across cell membranes. And for hormones to have their effect, they need to cross cell membranes on the outside and the inside of the cell. So maybe that's how it's having its effect. Again, the mechanisms of exactly how Shilajit increases testosterone and FSH and thereby libido, egg quality, and sperm quality aren't entirely clear. But for the more adventurous of you out there who want to experiment with Shilajit, whether or not you're trying to conceive or not, it might be something to consider. But of course, do talk to your physician. The next compound that I want to discuss is zinc. And this discussion mainly pertains to males, although I, of course, should point out that females should get the recommended daily allowance of zinc each day. Males, on the other hand, seem to benefit from having additionally high levels of zinc intake. Now, that can be obtained through foods. You often hear, oh, oysters are enriched in zinc, and oysters are an aphrodisiac. I don't know who's doing the marketing for oysters, but it's really terrific. I think that seems to have persisted. And maybe it's true. Oysters are enriched in zinc. What does zinc do for fertility? Well, in males, we know, based on a really nice set of studies, that zinc dosages that are pretty high of about 120 milligrams taken twice per day-- that's quite a lot-- with meals can significantly increase testosterone and dihydrotestosterone. And this probably shouldn't come as a surprise to us. It turns out that zinc is highly enriched in human testes and in the testes of other animals, including fish and other mammals. And it was actually in 1921 that it was observed in fish that zinc levels skyrocket in the testes of fish during their breeding season. So zinc is correlated with increases in breeding, but you never know which direction that correlation is running. It turns out that zinc in both animals, including fish, other mammals, and in humans, strongly impacts the enzymatic functions in the testes, including the function of androgen-binding protein. So it seems that high levels of zinc can increase spermatogenesis and testosterone levels very significantly. This was explored in a really

nice study that I'll provide a reference to. It's an older study. But I really like. It's called "Effect of Zinc Administration on Plasma Testosterone, Dihydrotestosterone, and Sperm Count." This is but just one study among many now. This dates back to 1981, but there have been studies subsequently that point to the fact that supplementation with zinc at those high levels can really be helpful in terms of increasing sperm count, testosterone, and even testicular size, of all things. So one important point about taking zinc-- this 120 milligrams of zinc two times daily definitely needs to be done with meals. If you've ever taken zinc on an empty stomach, even if you just take 15 or 30 milligrams of zinc, you can feel very nauseous, not well, for a few hours. So make sure that you're taking zinc with full meals. So this would mean that you're taking in at least two full meals per day. I should also mention that zinc supplementation did not appear to impact gonadotropin-releasing hormone or prolactin. So it seems to be a fairly targeted effect on the testosterone and related pathways in males. As far as I know, there have not been systematic explorations of the effects of high levels of zinc administration on females. I would hope that those studies would soon be done. But meanwhile, if you're a male and you're interested in improving sperm quality and your testosterone levels overall for whatever reason, zinc likely is a good candidate. And that pretty much summarizes the compounds that men and women should take in order to maximize egg quality, sperm quality, and fertility. And then, of course, we start to enter the landscape of other things that men and women can take

04:13:02 Fertility & Prescription Medications

in order to improve fertility, and those other things generally are prescription drugs. And so I just want to mention what a few of those are. But of course, these are things that you would absolutely have to obtain prescriptions for from your MD, and your MD, without question, would want to take blood tests prior to prescribing these things. So for instance, if men have been taking exogenous testosterone through the use of anabolic steroids, like performance-enhancing drugs or even testosterone replacement therapy, their endogenous testosterone levels are going to be very low, and their sperm counts are going to be very low, unless, for instance, they are prescribed and taking something like hCG, human chorionic gonadotropin, which mimics LH and would stimulate the testes to produce testosterone and through some indirect pathways rescue spermatogenesis, although not to the same degree as if people are not taking

exogenous sources of testosterone. Some men, even if they've never touched TRT or exogenous testosterone of any kind, will be prescribed to take hCG because of its ability to stimulate the testes to produce more testosterone and sperm. So they're just taking hCG alone. Other men will take-- or will be prescribed, rather-- FSH in order to stimulate spermatogenesis, or hCG and FSH, or clomiphene, which can regulate all sorts of things in the both testosterone and estrogen-related pathways at the level of brain and pituitary and gonad, testes. Likewise, for women, if they're low in FSH, they might be prescribed FSH. If they are low in luteinizing hormone, they might be prescribed hCG. If they're low in testosterone, they might even be prescribed testosterone. And if their testosterone is too high and they're dealing with PCOS, they might be prescribed anti-androgens and androgen blockers and on and on and on. There are so many different hormones that can impact the different aspects of the ovulatory and the spermatogenesis cycle that the OB/GYNs and the urologists focused on male fertility nowadays really have an excellent handle on which levers and buttons and threads to pull and push and so forth in order to set in motion a proper ovulatory cycle and a proper spermatogenesis cycle. Everything we talked about up until now and in the early phase of this episode, especially, about how the brain commands the pituitary and the pituitary commands the gonads and then the gonads, the ovary, or the testes send feedback signals to the pituitary to then influence the pituitary, all of that incredible orchestra, that dance, is so tightly regulated in a way that really provides the OB/GYNs and the fertility docs concerned with male fertility exceptional tools to, for instance, figure out if a man is not producing any sperm but his testosterone levels are well within normal range, well, then there are some very clear sets of explorations and potential treatments. Some of which are mechanical, making sure the epididymis and vas deferens are clear, allowing the sperm to enter the ejaculate and the ejaculate to enter the urethra and obviously to enter the female, as well as for a woman who's not ovulating to adjust her levels of FSH or maybe even to apply acupuncture in conjunction with supplementation and various prescription hormone therapies to adjust fertility and ovulation and the probability of successful pregnancy. So there's a vast landscape of prescription drugs and surgical interventions of varying degrees of invasiveness. And some are, for instance, outpatient procedures. Some require general anesthesia, et cetera, in order to maximize male and female fertility. What I've tried to do today is to provide you with a deep dive understanding of the ovulatory and menstrual cycle. We talked about the brain, the pituitary, the ovary, the Fallopian tubes, and, in fact,

04:16:44 Human Reproduction & Fertility

the whole female reproductive axis as it relates to fertility and reproduction I also describe the male reproductive axis as it relates to the brain, the pituitary, the gonad, the testes, and the various ducts, the pathways, out of the testes that allow the sperm to be enriched within the semen and then the semen and the ejaculate to exit through the urethra. I did all that as a way to frame the various tools and interventions that can really assist in increasing fertility, egg quality, and sperm quality. So when we discuss mitochondria in the context of the development of an egg or the development of sperm and its ability to swim quickly forward, now it should make sense as to why give an intervention, whether or not it's L-carnitine or whether or not it's exercise or whether or not it's getting enough sleep and limiting stress, why all that should matter and why, in fact, mechanistically those interventions can work. Because, indeed, there are many interventions that we can all do and use to support our fertility. And again, as a more general theme today, I really wanted to, A, teach you about the human reproductive axis-- I do find the biology of the ovulatory and menstrual cycle and spermatogenesis to be absolutely fascinating to me. And again, if you're somebody who's interested in conceiving or if you've already conceived children and even if you don't want more children, this is really the aspect of our biology that allowed us to be here. It's the aspect of our biology that determined whether or not we are male or female. It's the aspect of our biology that determines so, so much, and yet I think that most of us generally are not taught this in school or at least not at the depth that we discussed it today. So hopefully that information was in and of itself interesting and perhaps useful as well. And I do think that even if people are not wishing to conceive more children that the information related to fertility and optimizing egg and sperm health is of value in the sense that optimizing egg and sperm health can be used as a proxy for optimizing our body and brain health generally. In other words-- and here I'm admittedly taking words out of the mouths of the various wonderful doctors, the OB/GYNs and neurologists that helped inform me in anticipation of this episode-- what is good for the woman is good for the egg and for fertility and for pregnancy. And what's good for the man is good for the quality and production of sperm and for fertility and pregnancy. Put differently, whether or not we are male or female, the things that we can do to optimize our fertility are the exact same things that we should all be doing to optimize our vitality and our longevity. And I realize

today's episode was so much the deep dive and fairly broad, as well, that it ended up being fairly long and extensive. And yet we still have not touched on any of the important themes that I know a number of people want to know about-- so, for instance, menopause, andropause, PCOS, and other themes related to hormones and reproductive function and biology. And I promise that we will have episodes, both solo episodes and episodes with expert guests, in the future to cover all of those topics in detail. Meanwhile, the information discussed in today's episode should serve as a basic foundation for those discussions going forward and hopefully were of interest to you in their own right. If you're learning from and/or enjoying this podcast, please subscribe to our YouTube channel. That's a terrific, zero-cost way to support us. In addition, please subscribe to the podcast on Spotify and Apple. And on both Spotify and Apple, you can leave us up to a five star review.

04:20:12 Zero-Cost Support, YouTube Feedback, Spotify & Apple Reviews, Sponsors, Momentous, Social Media, Neural Network Newsletter

If you have questions or comments about the podcast or guests that you'd like me to bring on the Huberman Lab podcast, please put those questions and suggestions in the comment section on YouTube. I do read all the comments. In addition, please check out the sponsors mentioned at the beginning and throughout today's episode. That's the best way to support this podcast. During today's episode and on many previous episodes of the Huberman Lab podcast, we discussed supplements. While supplements aren't necessary for everybody, many people derive tremendous benefit from them for things like sleep, hormone augmentation, focus, and much more. The Huberman Lab podcast is now partnered with Momentous Supplements because, as I mentioned at the beginning of today's episode, Momentous Supplements are of the very highest quality, they ship internationally, and they have single-ingredient formulations that allow you to develop the most biologically-effective and cost-effective supplement regimen for you. If you'd like to see the supplements discussed on today's and other Huberman Lab podcasts, please go to [livemomentous](https://livemomentous.com)-- spelled O-U-S-- so livemomentous.com/huberman. If you're not already following us on social media, please do so. We are Huberman Lab on Instagram, Twitter, Facebook, and LinkedIn. And at all of those places, I discuss science and science-related tools, some of which overlap with the contents of the Huberman Lab podcast, but much of which is distinct from the

content of the Huberman Lab podcast. So again, it's Huberman Lab on all social media platforms. And if you haven't already subscribed to our newsletter, we have a zero-cost newsletter. It is called the Neural Network Newsletter. And each month, it includes things like podcast summaries and toolkits for things like sleep, focus, dopamine optimization, fitness, and so on. You can sign up for the newsletter-- again, completely zero cost-- by going to hubermanlab.com. Go to the menu. Go to the newsletter. You provide your email, and we do not share your email. And again, the newsletter is completely zero cost. Thank you, once again, for joining me for today's discussion all about the biology surrounding this incredible thing that we call fertility, including the ovulatory cycle, spermatogenesis, fertilization itself, and all the events leading up to pregnancy. And last but certainly not least, thank you for your interest in science. [MUSIC PLAYING]