Why hormones are superheroes when it comes to dementia Transcript

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Introduction and Doctor Gershu2019s Background

Welcome back to the Reverse Alzheimer's Summit. I'm your host, doctor Heather Sanderson, and I'm delighted to have Doctor Felice Gersh here to talk about hormones today.

Doctor received her medical degree from USC School of Medicine and then studied obstetrics and gynecology at the Kaiser Hospital in Los Angeles. There she was honored with the creo G Top Resident award every year.

After graduating, she launched a private practice founded in her passionate belief in holistic women's health care from the earliest years. Way back before it was cool, before alternative medicine was even popular.

Her practice included acupuncture, massage, and Chinese medicine. About 12 years ago, she pursued an interest in holistic healing and graduated with a fellowship in integrative medicine at the University of Arizona and became one of the first dual board certified integrative gynecologists in the United States.

She's also an impressive and sought after speaker, as well as a bestselling author. Doctor, thank you for taking the time and being here with us today.

Oh, it's my pleasure. It's such a wonderful and such an important topic that I'm just beyond thrilled that we get a chance to really delve into this in depth.

You know, there's a lot of confusion out there, but one thing that's clear is that more women than men suffer with dementia. Can you speak to why that might be?

Absolutely. And it is so minimized this big difference. In fact, women have close to three times the incidence of Alzheimer's compared to men. Well, it turns out that females have this built in timeline where we lose our ovarian function.

So it's called menopause, which doesn't actually do justice to what's really going on in the female body, because it's not about just the loss of fertility, ovarian senescence, and the loss of the production of these really critical ovarian hormones.

Estrogen and progesterone changes the very dynamics of how metabolism works in the female body, which is the production of energy. It's really the spark of life, which involves every organ system.

And of course, what organ needs the most energy in the body is the brain. So after menopause, when the ovaries cease to make the key estrogen called estradiol, the brain really goes into a state of estradiol deficiency.

Well, it turns out that estradiol is involved in so many different functions in the body, which we can discuss that this has just enormous ramifications on how the brain functions.

Why Menopause Raises Alzheimeru2019s Risk

It involves, of course, the actual neurons of the brain, the immune system of the brain, and the cardiovascular system, the vascular supply of oxygen and nutrients to the brain.

So virtually every system that supports brain function becomes to some degree impaired after menopause. And this over time, actually has a very huge impact on brain health.

And that involves both cognition and mood. And nowadays, on top of the inevitable effects of menopause, women often enter menopause in a suboptimal state.

I always say it's like you're saving for retirement. So what's your brain savings account? Well, because of our change in circadian rhythm with sleep changes, blue light exposure, environmental toxicants, you know, the ubiquitous endocrine disruptors.

Women spending sometimes their entire reproductive lives without having normal hormones and rhythms because of hormonal contraceptives. And just so many different factors that come into play that they're not really in optimal state when they hit menopause, when they have this big, really huge metabolic impact.

So it's all these forces, like the perfect storm that comes into play that affects women's brain health, which has so many global effects on, of course, quality of life in women.

I heard you say the vascular system, the immune system, right. Pretty much all of the culprits. When we think from a functional medicine perspective, what are the things that affect our cognitive function?

When we take sort of medicines idea of there's 36 holes in the roof, immune system, hormone signaling and vascular supply are up at the top. And the hormonal system, what you're describing is that, oh, and by the way, the hormonal system affects everything else.

So if this piece isn't if we don't have that piece of the puzzle pretty much dialed, then we're going to see a lot of repercussions. Absolutely. In fact, if you create sort of a hierarchy, you know, all those other factors like, well, of course, is effects on detoxification and immune health and, cardiovascular function.

Well, all of those fall under the umbrella of hormones because hormones are the they're the messenger system. They deliver information to the cells. So no cell can function properly when you don't have the proper balance of hormones.

So if you leave out that critical ingredient, it's like you're making a cake and you leave out the key ingredient, you know, yes, every ingredient matters.

But if you leave out the key, the key ingredient which will say, not that I bake cakes, but I think flour, if some cut, some kind of flour is important, or else you end up with a bowl of liquid, right?

So I mean, you can't leave out the hormones and have a functional, healthy body. And of course with the brain at the top. So it's just shocking really, when you think about how minimized the role of hormones has really been in terms of how the conventional medical system has treated hormones and the impact of menopause.

And as well, you know, the different hormonal contraceptives that are being placed into the female body at, you know, very, very early ages now, like 12, 13 years of age when just when they're at the cusp of developing rhythms and hormones, these really young girls are often placed on contraceptives that take away all their hormones and rhythms and and understanding that this matters is just sort of key to understanding how the whole female body works.

So for an aging brain, there's a lot of confusion of this space and really some controversy. I can't tell you how many times I'm having a conversation with a woman who's already experiencing dementia symptoms, and she's terrified of hormones because she's heard from the news media or from a doctor that they have a potential risk.

So I want to, like, get really clear about this. What's the risk? What risk is maybe overblown or misunderstood? And what's the potential benefit? Well, we had this study that of course has left its mark.

And it's like a dirty footprint, unfortunately. And that's the Women's Health Initiative, which was from about 20 years ago now. And prior to that, based on observational studies, there was so much belief that hormones were good for women in every single regard, in every single aspect of health.

But after the Women's Health Initiative, the whole paradigm of thinking about hormones completely went upside down without understanding and even reading the study itself.

Because at the end of the study, it actually says the conclusions of this study apply to what was studied. You know, the ingredients that we used in this study is what really should be applied to the conclusions.

But that isn't what happened. And it just still but I can't get rid of this. It's like it's imprinted. It's like almost like brainwashed people at every in every aspect, whether it's a clinician or a patient.

So it's this is my analogy. If you did a study with strawberry flavored jelly beans and your conclusion was, well, if you eat a lot of strawberry flavor jelly beans, you're likely to get cavities, obesity and diabetes.

But the ultimate conclusion is never, ever eat organic strawberries. And it's like, wait a minute, I don't think that's what you studied. Well, that's as crazy as that sounds.

Hormones, Brain Health, and the Womenu2019s Health Initiative

That's what happened with the Women's Health Initiative in that study, they used conjugated equine estrogens delivered orally. So that meant when you say conjugated, that means it's gone through the liver to be eliminated from the body.

And it's turned from fat soluble to water soluble through this process that occurs in the liver. That means that the pregnant horse came from a pregnant mare, a horse.

The horse doesn't want it anymore. It's like, get it out of me. And it's designed to be either peed or pooped out. In this case, they use the pee and along with these conjugated equine meaning horse estrogens, a whole variety of different estrogens that are never found in a in a human female ever.

There's like a whole array of them. Also, it's not very purified, and it comes along with a lot of other junk like different androgens and so on. That's like testosterone related products and so on that are also conjugated because they're being eliminated from the horse's body through urination.

Now they combine that into a tablet. They dried it up, put it in a tablet. Now, you know, this was like 70 years ago when they first discovered, if you can thought you how to make this product and there was nothing else available.

And if we think back when type one diabetes occurred, before they had insulin, people died. I mean, there was no solution, there was no treatment. And then they started using insulin that they derived from rabbits.

Well, that didn't work out so well over the long haul. And then they developed techniques because, you know, scientists are so brilliant how to make identical insulin to human insulin.

And that's what we've been able to do with female hormones. But they couldn't do that originally. And that became what was used for just suppression of hot flashes.

And it did work for that. Now they combined it in the Women's Health Initiative with another chemical, endocrine disruptor. In other words, this is a chemical never found in a human female body that binds to receptors for progesterone, with different effects in different organ systems.

That's why they called it. Now it's a hormone agonist antagonist. So depending on where it is in the body it either acts as an activation of the receptor or a blocker of the receptor.

And this product called medRxiv progesterone acetate. Well, it sounds like progesterone, but it is not progesterone. It's about as similar as strawberry flavor.

Jelly beans are to organic strawberries. And yet even like researchers from major academic institutions talk about it and they use the word progesterone.

They'll say, well, they used progesterone. No they didn't. They used the drug C, progesterone acetate, which is an

endocrine disruptor for progesterone and agonist antagonist.

But in the uterus it acts as an agonist. So it actually blocks the proliferative or growth effects of estrogens in the uterine lining. So that was the main purpose.

But it has a different effect in the brain and in breast tissue and on immune health and so forth. So you put these two things together, never to be found in a human body.

And guess what? The results weren't even that bad. That's the amazing thing. They weren't that bad. In fact, in this study they found that. And it didn't even go on for very long.

They stopped it initially after about four years, and then the primary and only the conjugated estrogen group continued for another couple of years. So this is really not did not go on for anywhere near the number of years originally intended.

But what they found is in the small group of women who were in their 50s, and that's another whole issue. But in that group, they actually had an all cause reduction in mortality of about 30%.

That means that all the women that got that really like nutty combination of chemical hormones, not ever found in humans, they actually did. They had less death of all causes by 30%.

There's no drug that even does that. So even this bizarre combination actually in younger women under 60 had a really profound benefit. And then when they reanalyzed the data, they did find that women in the group under 60 had benefits from even this group of of hormones.

And that probably aligns quite well with the observational studies that preceded the Women's Health Initiative, where all the data was very pro outcomes.

You know, very favorable outcomes with these hormones because they were not used in women who were older in the Women's Health Initiative. They didn't want women to know what they got.

Of course, they all figured it out anyway because of the symptoms and the side effects, but they didn't want it to be in women who had hot flashes because they knew it would suppress the hot flashes and then it wouldn't be blinded.

They would know what they were taking. So they took women only who had no hot flashes. And so for that they had to go to older women. So the average age was 63.

They had women all the way up to 79. So and they said, well, healthy women. That is not true. When you looked at them, the group, they had high rates of hyperlipidemia, diabetes and all kinds of stuff.

This was not like a pristine, healthy group. I mean, where would you even find that, you know, in women who are in their mid late 60s and 70s in, in the day, right.

So basically it was just an average group of women with all sorts of metabolic issues and, you know, weight issues and so on. And then they stuck them on this group of hormones.

So ultimately the the when once the data was reanalyzed and reanalyzed over the next 20 years, the women under 60 actually did better, but the women older, the average age was 63.

They did not do great even though they didn't do terribly. There was a very slight statistical increase in the incidence of breast cancer. Now, breast cancer takes about 20 years to develop.

So this is obviously a promotional effect, not an initiation effect, because the study only went on for such a little bit of time. But in the women who were only on the and there was actually a slight decrease in the incidence of breast

cancer, not quite making statistical significance.

And what they found was in the older women. And here we're getting to the brain. Oh, there was an increase in dementia. Now how could that be? Because I just told you estrogen is about everything that makes the brain work.

Well, well, it turns out when you take oral estrogen, in this case, the, you know, the conjugated equine estrogen, the brand name was premium that when it goes through the liver, because you're swallowing it, it's converted primarily into estrogen.

So there are different flavors of estrogen. The one that the ovary makes is estradiol. And in the body some of it's converted to estrogen. And then there's estradiol, which is the dominant estrogen made by the placenta during pregnancy.

And they bind differently to different estrogen receptors. Well, it turns out that the brain loves estradiol. It does not love as real as on the whole.

So the brain actually does not have the ability to convert estradiol into estrogen. It's not interesting. Estradiol binds equally and appropriately to the receptors.

It's alpha and beta and a membrane receptor called jeepers. And estrogen primarily binds only to the alpha receptor. Now they're all important. Alpha is not evil.

Beta is not better. They just different. They live in a balanced world. And if you if you have an imbalance, your brain is not going to work right. Turns out the different areas of the brain have different dominance of the alpha or the beta.

And we don't even know that much about the membrane receptor. But that's all out there too. And when you have a dominant up estrogen that is as strong, you're not going to have the benefits on the cerebral cortex, because that is predominantly beta.

And Astron is predominantly alpha. Now, alpha is very much on. That's what's on the innate immune cells. So those are the first line of defense like the mast cells and macrophages and neutrophils.

These these are the immune cells that go out and get the invading pathogen. Whether it's a bacteria virus a fungi parasite whatever. These are the cells that go and out there and protect us.

They have estrogen receptors. The immune system is completely modulated by estrogen. Well it's estrogen receptor alpha. So if you only have alpha you're actually up regulating your innate immune cells creating a state of inflammation.

Well, the process of inflammation, which is lifesaving if you get invaded by a pathogen, if you have trauma, like you're hemorrhaging from a laceration, all of these and the whole inflammatory process gets activated to save your life.

And part of the inflammatory response is to create, blood clotting so that you don't bleed to death. You're going to have platelet aggregation and activation.

Well, if you have predominantly estrogen and you have estradiol is not there. And you're having dominant activation of your innate immune cells through the alpha receptor, you're going to be in a low grade state of inflammation.

And activation of your platelets, hence more promotion of clotting. Well, that is not what happens when you have balanced hormones and you have extra dial, because you're not going to have this overwhelming stimulation of the alpha receptor promoting blood clotting.

So in the group that got the promotion and they were older to begin with, they already had vascular damage. They already had plaque. They already had some degree of inflammation like we call like inflammation in their body, which is what happens with aging and loss of hormones.

With menopause, you get a state of chronic low grade inflammation, which has a huge impact, by the way. Of course, on the neuronal function and health of the brain.

So you now have this low grade state of inflammation in someone who has already vascular disease. And Othello, atherosclerosis. And part of what happens when you have inflammation is you have vascular contractility.

Your arteries are going to constrict to protect you from going into shock. If you have blood loss from hemorrhaging, right. It's all part of our survival mechanism.

So now you have constriction of arteries. You're going to have more hypertension. You're going to have more unstable plaque because you have more inflammation.

That's happening from all of this innate immune cells going into an activated state that leads to ruptured plaque, aka the onset of strokes, heart attacks.

And that's what they found. That is clearly why you would never give that combination of hormones, which is also made worse by the majority progesterone, acetate.

So the conclusions are clear. You should not give older women that combination of hormones. End of story. But that wasn't the end of this story. They then concluded that all hormones, just like organic strawberries, should never be given, and they're all evil and dangerous, and that hormones are harmful to women.

And it it's been my mission in life ever since to get this story straight. It's sort of like the what they gave was like the evil twin, you know, and now the good twin is saying, but I didn't do it.

I didn't do it. And it's like, no, you're innocent, estradiol. You're innocent. It was majority progesterone acetate combined with equine conjugated equine estrogens given orally.

That was the problem. And why it is that so many like, you know, brilliant in quotation marks. You know, academics have perpetuated this crazy story about the effects of hormones on women's health.

It's just beyond me. It's like I can scratch my head perpetually. It's like, why? Why is this happening? You know, it's it's the strangest thing ever.

And I think part of it is that we became so entrenched that the researchers who are all very prominent, the people who were part of that women's health initiative, that for them then to come out and say, you know what?

We were wrong.

Bioidentical Estrogen, Blood Clots, and Safer Delivery Methods

We've created great harm to so many women, and our entire careers were forced. They're just not going to do it. So even though they know, they have to know that this was insane, that this has harmed.

And there have been articles that came out. Doctor Sorelle, who's a brilliant ObGyn, published an article, a number of years ago in a rather obscure journal because nobody would take it.

And they used a lot of statisticians and so on to come up with somewhere between. And this was years ago, 50, and 100,000, you know, women died in the US who early for no good reason other than they went off.

You know, the hormones. And it's, it's really sad. And so I'm so happy that we get the opportunity to try to help

women to understand that hormones never got put in our bodies to harm us.

They don't give us cancer, they don't give us dementia. They don't give us anything but wonderful health and function. And when we lose them, there is a price to be paid.

And it's not just giving hormones as a solution as we know. Like with like Dale Peterson, you know, you can't it's not one thing. It's, you know, you got to do the whole package.

But if you leave out the hormones, I think you're leaving out the most important ingredient. So with that, do we feel clear? My understanding is that there are some good studies about bioidentical hormones, or at least safer topical estrogens, other delivery systems that are safer.

And some of that is from Europe. I believe France and Finland have pretty large data sets that show us that this is safe. So not only can we say, you know, what we what we were doing with the Women's Health Initiative study wasn't safe.

The oral non bioidentical estrogens and progestin. But we can compare that to other literature that shows that this alternative that we have to offer this bioidentical delivery system and delivery systems that make more sense.

They are safe. Is that true? Yes. The Women's Health Initiative was funded through the National Institutes of Health. It cost like, I don't know, like $1 billion.

I'm not sure the exact amount was huge investment and it will never be repeated. They're not going to put that investment in. So the studies that have been done are relatively small scale and short term.

But we have and we all have a ton of animal data too. And but you know, there was a very well done study in France, as you were referring to, that showed that when you give oral estrogens because it goes to the liver, turns into estrogen, which then promotes the activation of the innate immune system, promotes inflammation, has a different effect on the gut microbiome.

It's just very different that when you do that, you increase your risk of blood clotting by about two fold. And that's actually what they also found in the women's Health Initiative that in the average woman, the risk of getting a blood clot was doubled.

Now that happens by the way. And guess what. Like birth control pills. But they ignore that because they say, well, the risk is so low because they're so young.

But of course, as you get old, the biggest risk to getting blood clots is age because of inflammation and loss of hormones, and that inflammatory state that promotes the activation of the immune cells and blood clots.

And, you know, with the platelets and so on. So you end up, having this this problem, if you have a factor of five, Leiden. So you have another factor going on in your body that promotes blood clotting through this genetic propensity.

And then you take oral estrogens that turn into stroke your risk of getting a blood clot, they showed in this study from France goes up fourfold. So you can imagine that's not it's not a rare genetic condition to have a factor of five. Leiden.

So if you have that condition your risk of getting a blood clot is four times higher. If you were just an average person, the risk is doubled and as you age, the risk goes up and up.

So suddenly it's actually not insignificant as a risk of blood clotting. Now blood clots can manifest as a deep vein thrombosis. So it's like a blood clot in the the veins of the leg, which is bad.

Or if the blood clot breaks off and it travels to the lungs, that's a pulmonary embolism, which is definitely a potential

for fatal outcomes, you know.

So that's it could be deadly. Now if you have clots that form and then break off depending on the vessel, if it's in your coronary arteries, that leads to a heart attack, if it's in the arteries that feed the brain, well, that's a stroke actually.

If it's in the blood vessels that feed the intestines, then that's a schematic bowel disease. That's like the equivalent of a heart attack to the intestinal tract, which also can happen in the legs when you have problems with blood clotting and so on.

Then you have peripheral vascular disease. And you can get claudication where you have poor blood flow and oxygen to your leg muscles, and then you get pain in your legs.

So you can have vascular problems throughout the body, where you have blood vessels clogging up and so forth. And blood clots occurring. Now, do most women need to worry about this at this point?

Because are there still I guess I can answer my question because I see it clinically. I occasionally see women come in on oral estrogens. However, for the most part they're doing patches or creams, and if we're doing patches or creams of bioidentical estrogen, is this still the case?

Is this still a concern? Well, that's exactly what they showed in the French study, that it's not because when you take the topical or what we call transdermal application of estradiol, that would remember I said estradiol, the actual name is 17 beta estradiol.

That's the estrogen made by the ovaries, that hormone, that estrogen. When you deliver it through the skin transdermal, it gets absorbed into the bloodstream in the same form as estradiol.

So it's like the same like the ovaries making it and delivering it, delivering it into the blood as estradiol when you absorb it through the skin, whether it's a patch, a gel, a cream, or even a vaginal ring, it's still going to be in the bloodstream as estradiol, and therefore it doesn't have that effect.

It's not just working on the alpha receptor. It's balanced on all the receptors. And it estrogen. When it's estradiol, it's a modulator of the immune system.

What that means is that it turns it on and it turns it off the inflammatory response to modulate it so that it's appropriately, you know, functioning so that if you need activation of your immune system because you're exposed to Covid, you're exposed to another bacteria, you know, strep or, you know, could be any virus, you know, like the flu.

Whatever it is, if you have adequate estradiol, then your immune system will swing into action to protect you by activating an appropriate inflammatory response so that your immune system will do all that it can do to kill off this invading pathogen right at the get go.

And then after it creates this inflammatory response also to damage. We have the dance in the pants. So we have the response of the immune system to pathogens or to injured tissue damage.

And then the estrogen, the extra dial will convert from a pro to a anti inflammatory state. And cause the resolution of inflammation and then promote healing.

Because estrogen in the form of estradiol is all about healing, I can do like the mother it nurtures. It takes care of you. It knows when to step in like you know, like the mother lion and fight off the, you know, the attacker.

But it also knows when to cuddle and nurture and, you know, and give hugs back, you know. So it's really it controls it. But when you only have like one aspect, like the ferocious part and all you can be is ferocious, you can't be the nurturing part.

That's what happens when you take estrogen only in the oral form. And that's not what nature gives us.

Progesteroneu2019s Brain Benefits and Cyclical Dosing

So if you have estrogen coming through the skin, you don't get an increase in blood clots at all. In fact, you could give it to people who've had blood clots.

It's not pro blood clot. It's actually anti blood clot. And that's like a really because your blood was not designed to just clot spontaneously. It's like that's a real problem.

But I mean that's like cancers can do that because cancers create an altered gene expression and altered inflammatory state. You know then. So you should never just spontaneously have blood clots in your body.

Blood clots are life saving so that you don't bleed to death. Okay. So that's what blood clots are form, you know, so that you form this protective clot so that your blood vessel will stop pouring blood out of you.

And estrogen makes sure that you don't clot your blood for no reason. Estrogen controls so many different enzyme systems. For example, the enzyme system that makes nitric oxide endothelial nitric oxide synthase, which controls what we call platelet aggregation so that you actually don't when you have proper estrogen in your body in the form of estradiol, you don't just clot your blood, you actually control your blood vessels so that they the lining stays healthy, that you don't form atherosclerosis.

You don't just suddenly have platelet out platelets aggregating and forming blood clots. Estradiol also controls another hormone system, the process the cyclings, which also prevent just random platelet aggregation.

So after a while actually prevents just random blood clots. That's why young, healthy women rarely end up just spontaneously getting blood clots. If you go on birth control pills and similares, that's a whole different story.

And pregnancy people get very confused about pregnancy because they say, well, look, pregnancy, there's so much estrogen and women in pregnancy are more prone to developing a lot of metabolic problems like pre-eclampsia, hypertension, gestational diabetes, and more blood clots.

That's because pregnancy is a very unique state. When the placenta makes a different estrogen as the dominant estrogen, estradiol and pregnancy is actually a very, very interesting state.

We can say it's actually when women are living on thin ice when they're pregnant because it's actually pro-inflammatory. Now, why would nature create a state in pregnant women that's pro-inflammatory?

Because women who are pregnant, if you go back 20,000 years ago, they lived in a time of food deficiency. You didn't just have food everywhere like we have now for us, not in everywhere in the world. Right?

But so when women were pregnant, it was really critical that they put on fat fast, and they stored it so that they could feed the baby during like the winter, right when if there was not food available.

That's why women who are pregnant can gain weight so readily, even when they don't even eat that much. Because as soon as a woman becomes pregnant, she develops leaky gut.

She developed that altered gut microbiome, which in other times would be considered just biotic or abnormal. So she becomes a little bit pro-inflammatory.

So it's a very interesting state because when you're a little bit inflamed, but remember it's it should be always controlled like sort of like a controlled fire.

Right. Yeah. It's when you're out of control because you're not metabolically healthy to begin with that you get like this, you know, a controlled fire that turns into an out of control forest fire.

That's why pregnancy is now considered a stress test of women. And so it's really you're living on thin ice. If you're not already healthy, pregnancy will put you over the edge because it's pro-inflammatory, because when you're inflamed.

And this, of course, happens when people are obese that you don't diet, they're chronically stressed, and so on. What happens is you become more insulin resistant, right.

So now why would you want to be insulin resistant in pregnancy? Because then you're going to have higher levels of blood sugar to feed the baby and to when you have high insulin, you're going to promote the production of fat and fat storage.

So women will put on fat the baby will get glucose to, you know, grow. And it's just sort of living on the edge. That's what is fascinating. I don't know if it's really different.

That's why I'm anti giving menopausal women as a hormone replacement estrogen to give them estradiol. Because ezreal is predominantly beta. And there's wonderful things that beta receptors do, but it's not balanced.

It's like we want to have what nature created. You know, we're not smart enough to outsmart nature. We tried that with food. It did not work. Right. You're saying so this is really super fascinating about pregnancy.

And I'm sure there's lots of people listening who kind of can remember back to that time when they maybe were pregnant and how it didn't feel like you were on ice.

So on thin ice, they're still in the in a brain that's concerned about dementia, it sounds as if estrogen is really, really important. And it's extra dial in particular now.

Right? I want to clarify. I don't want to give estrogen. We don't want to give an oral estrogen because that's going to turn into estrogen. We don't want to give y'all because that's beta.

And we need alpha in the brain and we need beta. So in the brain the beta receptor is the dominant one on the cerebral cortex. So that's obviously very important.

Also the serotonin neurons. Oh my gosh it's so important. Estrogen in the form of estradiol has receptors on the acetylcholine receptor. They acetylcholine neurons which make the key neurotransmitter acetylcholine which is so critical for cementing and creating memories.

And there are receptors and gene regulation by estrogen on the serotonin neurons. And it's predominantly the beta receptor on the serotonin neurons, which of course, serotonin is such a key neurotransmitter for feeling happy and calm.

And then from serotonin comes melatonin, which is a potent antioxidant so important for sleep and glucose regulation. I mean, melatonin has so many different functions in the body besides sleep.

But of course that's a key one. And of course, it's probably the most powerful replaceable, you know, it's not. You have to keep making it all the time as an antioxidant.

It's so key. And that comes from serotonin. Without adequate estrogen in the brain, you absolutely will not have proper function of your acetylcholine neurons, your serotonin neurons.

These are so critically important. And and this is what you and the serotonin neurons are beta. So if you give oral estrogen you're basically only giving estrogen which is only alpha.

So the the cerebral cortex which is about thinking and feeling that's all beta or predominantly beta. Now the hypothalamus which controls so many of the metabolic aspects of the body and the what how about the whole autonomic nervous system, which is all regulated by estrogen.

So you can't just have alpha, you can't just have beta because you need to have the regulation of the metabolic processes of the body. Also alpha remember is the one on your innate immune cells.

If you only have beta, then your innate immune cells are going to be also become hampered. They're not going to work properly. So we don't want to alter people's ability to fight off infections.

So when you give the proper estrogen in a physiologic amount, you're going to help maintain all of these neurons in the brain, the immune system, both in the brain and outside of the brain.

So it's really important. And I'm sure you have a lot of your listeners have already learned that the brain has its own built in immune system, the, astro glia, the microglia, and these are modified macrophages.

So these come into the brain. They migrate in during the fetal stage of life. Right. When you're in the uterus, you know, you're just being made. And these specialized modified macrophages, which are really key.

They gobble things up. They phagocytes you know, gobble. And they, they put out enzymes that can dissolve like invading pathogens or dissolve damaged tissue.

So then they could be gobbled up, you know, so that you can clean up the mess. And then estrogen, which is like the mother hormone, promotes growth factors and new blood vessel formation and all of these important things called healing.

You know, you get tissue regeneration, like that's why estrogen in the brain, in the form of estradiol, creates neuroplasticity. It creates additional synaptic connections.

The dendrites, you know, of the neurons require estrogen, the immune system of the the brain, the microglia, the astrocytes are critical to maintaining the actual, you know, function and health of the brain.

They're all modulated by estradiol. In fact, estrogen is so key to the brain that the brain makes estradiol, the microglia, the neurons, the astrocytes make estradiol.

They actually also make progesterone, which is also considered a neuro steroid, you know, because these are steroids made in the brain to maintain the health of the brain and men.

I always say my favorite hormone is estrogen, but men's favorite hormone, they think it's testosterone. But it should be estrogen too, because most men I mean, if they don't have adequate testosterone, they're not going to have good brain health.

And, you know, you've got to have good brain health to have a good life because the brain converts circulating testosterone into extra dial in the brain.

The brain is a mega producer. It's called power. Quinn. That's when you make a hormone locally for youth within the organ itself. That's how men get all their estrogen.

They get it by making it from androgens through the enzyme action of aromatase. And the brain is a mega producer of estradiol. The brain doesn't make estrogen, the brain makes estradiol, and it makes it from testosterone.

Now, men should have a lot of testosterone so they can make a lot of estradiol. But after menopause, women do not have very much testosterone, and they're not equipped to turn a lot into estradiol.

And they get most of their estradiol. From where? From their ovaries during the reproductive time. But without that, then their brains. That's why I mentioned earlier their brains have an estrogen deficiency.

But the estrogen of course, is estradiol. So you have all of the cells. Every neuron in the brain has estrogen

receptors. Every immune cell in the brain has estrogen receptors.

Estrogen is like the overlooking overseeing how all these connections work, how all these things fit together to keep the brain just humming along. And then vascular system is all modulated by estradiol.

I mentioned endothelial nitric oxide synthase. That's an enzyme that helps the body to make this incredibly important gas called nitric oxide, which is both a signaling agent and also an antioxidant.

It helps to maintain vascular health. It also maintains heart health, and brain health is also neuronal endothelial nitric oxide. The intake is also stimulated to be produced and activated by estradiol.

To have all of these tissues healthy, well, you can't have a healthy organ no matter what organ it is. If it doesn't get proper nutrients and oxygen. And so in order to have a healthy brain, you need to have a healthy vascular system, which is so key, you know, to having a good life.

And estradiol is essential for heart health. The myocardium of the heart has tons of estrogen receptors. And this is another key thing that has to do with the function of every organ system.

But the ones that need the most energy, of course, are brain and heart. And that is the mitochondria. The energy producing factories of our body are essentially modulated by estradiol.

Without having estradiol, you can't work the whole machinery, you can't have oxidative phosphorylation, you can't burn fat properly without estradiol.

So you will have an energy deficiency. And we actually see this on echocardiograms in women, which is, what we call mild diastolic dysfunction. It's a stiff heart or an energy deficient heart.

Well, that is going to correlate with an energy deficient brain. That's why I love to get echocardiograms, because that is going to give me an idea of energy deficiency state in that woman, which is going to correlate in some matter, you know, reasonably with energy deficiency in the brain.

And in fact, estrogen is so key to the functioning of the mitochondria that even estrogen metabolites like two methoxy estradiol, which is an metabolite of estradiol, has its own receptors to produce energy.

And there are even receptors that we don't even know what they're for. That's called the ligand. What binds to the receptor. We don't even know what it is.

We used to call them orphan receptors. Now you know what they're called estrogen related receptors because we don't know what is needed to bind. But we know that whatever it is, it won't work properly unless you have estrogen.

So that's why they all want it. I want to know a little bit more about progesterone and how progesterone fits into this. We've talked a little bit about balance, about sleep and the importance of all of these things.

And I want I know that estrogen is your favorite. You've mentioned testosterone, but I don't want to lose sight of digestion. Absolutely. So it's very important to talk about progesterone because many women, for all kinds of reasons, don't have a uterus.

And after they have a hysterectomy, they go into menopause if they're going to get hormones. Many doctors say, well, you don't need progesterone because you don't have a uterus.

They think that that's all that progesterone does in the body. That is never true. No hormone has a single purpose. I mean, like that's why, you know, there's issues that may have come up like like antihistamines, like, well, histamine has one function in the nose, but it has a different one in the brain, you know. So you don't want to like, live on antihistamines.

You don't want to live without progesterone in the brain. One of the key things about progesterone is it helps to support the the tissue that's around the nerve.

The myelin sheath. This is so critical. You can't it's like the insulation of the nerves are supported by progesterone. This is very very misunderstood or not recognized that progesterone is essential for maintaining this myelin sheath around the nerves or else you're not going to have proper function of any, any neuron without having proper, myelin sheath.

The other thing is that it's neuroprotective in other ways. It actually does directly help to maintain the health and function of the neurons. What's interesting is the data on seizures and having like convulsions.

So loss of progesterone with aging is related to what they call senior seizures where the seniors get knocked down.

Testosterone, DHEA, and Hormone Balance in Aging Women

These are not seizures like what we call like generalized seizure, like an epileptic seizure where their whole body is like shaking and that these are like more like brief episodes where they just lose the ability to think, you know, it's like absent seizures where their brains just go into the seizure and they, like, just don't remember anything, like what happened for the last few minutes.

Like their brain just went out. And so progesterone deficiency in the brain, that's why the brain actually does make progesterone, but it doesn't make enough as we age.

That's the problem. So but progesterone is made in the brain as well in response to trauma. And there's some research that it's it helps to regenerate neurons as well.

So that for example, the astrocytes in the brain in response to brain trauma will actually make progesterone. Progesterone is neuroprotective and it helps to prevent abnormal electrical activity in the in the brain prevents seizures, these so-called senior seizures, you know, maintaining the integrity of the neurons and regenerating neurons.

So progesterone is no, lightweight. We definitely want to pay homage to progesterone. And another interesting thing about if you're giving hormones to women and in menopause and you're giving progesterone, it's best to mimic nature.

Now, nature takes these hormones away from us and I don't romanticize that. You know, I'm kind of like pragmatic. It's like nature doesn't really like, see the long term purpose, you know, of women after they're no longer reproductive creatures.

In fact, in the animal kingdom, most female animals die when they're no longer capable of making babies. They just that's their end of life is at the same time as their end of reproductive function.

But there are a few animals out there and like elephants and humans that have a length of time of life after reproduction has ended. But it's a time of deterioration.

And I think that we would sort of design for another ten, maybe 15 years and then like, goodbye. But, you know, we do not want that to happen. When they look at burial mounds from ancient times, like 20,000 year old, they do find women that bones, you know, that were in their early 60s.

And that's pretty much when it ended. So that was sort of our lifespan. But we do not like that. We want to live much longer. You know, there are people working to keep us alive for way beyond our what we think is our optimal, lifespan or a maximum lifespan. Now.

But in terms of living well, you know, women live with far more. We know we mentioned Alzheimer's and we've sort of touched on like vascular dementia, because that's when you have the improper vascular system to the brain.

The other thing I didn't mention though, is like the blood brain barrier, which is supposed to keep out environmental toxins, endogenous toxins, so either coming from the outside or from our own bodies, production of toxins, it's supposed to keep it out of the brain.

And that's what they call the blood brain barrier. But, just like you can get leaky gut, you can have leaky brain, you know, turn. And that's why I like to get micro albumin as a, to your intestines.

And if you find these little amounts of excessive, excessive, but little amounts of protein, albumin in the urine, that shows that your vascular system in your kidney is leaky.

Well, if it's leaky in the kidney, it's leaky in the brain. And then toxins are actually, you know, these could be biological toxins, you know, viruses, pathogens.

It can also, you know, fungi, you know, like whatever is circulating. And also it can be of course, toxicants. So chemicals, you know, heavy metals, pesticides, herbicides, you know, all this terrible stuff that we get exposed to and, plastic related things, the le BPA, they get into the brain and estrogen helps to maintain all of these vascular barriers.

So that's, you know, very important thing, having proper blood flow to the to the brain. And progesterone is also part and parcel of maintaining all of these healthy functions.

So and when you give progesterone there is data not a lot because people don't do the studies that if you mimic nature and give the progesterone so that it's pulsed.

So like you give it for 14 days of of the each cycle, remember the lunar cycle is like optimal, you know, like 28 days. Of course there's some human variation there.

But we'll say, you know, the optimal we'll say is 28 days. Then 14 of that is spent in the luteal phase. Post ovulation when progesterone is produced, there is no time in a woman's life other than pregnancy when she has continuous progesterone.

And pregnancy is a very unique time. We're not trying to replicate pregnancy at all. So in a woman's reproductive years, when she's having normal cycles, her progesterone comes and goes.

It's not continuous. And there are a lot of doctors that are giving hormones to post-menopausal women where they're giving continuous progesterone. And there's a lot of problems with that.

There's data that shows that when you give progesterone pulsed, you're and then you stop it and you have that period. So you do get a period, which is good.

You know, you got to say I love being a woman. Having a period is part of being a female. You're not just shedding the crappy cells from the lining of the uterus that are dying and coming out as a period, right?

You're also shedding bad senescence, old yucky, maybe pre-cancer cells elsewhere in the body, like in the breast, so that you're actually going through this purging system, you know, situation.

So you don't want to have continuous progesterone, you want to have it pulsed. And then you want to have that purge. And it's actually some data that it's better for your brain as well.

Like maybe like helping to rejuvenate the brain when you have this sort of purging thing. The other thing is that progesterone and estrogen have this dynamic relationship between their receptors.

So when you have a normal menstrual cycle, which probably is the way to go for hormone replacement, I'm trying to get we're working on starting a study to try to mimic a menstrual cycles, ups and downs of hormones.

Because these ups and downs are not just irrelevant, they actually have purposes. They actually turn on and off tumor suppressor genes and so on. They have many, many different functions in the body besides just create a period.

I mean, that's like really important that nothing is like single purpose in the body. And when you have the spike of estrogen that precedes ovulation, that actually upregulate the tumor suppressor gene, and when you have the peak of progesterone, it also upregulated tumor suppressor genes.

So that's why a menstrual cycle is not pro cancer. It's actually anti-cancer. If you give progesterone all the time, you're going to down regulate your estrogen receptors.

So when you had the peak of estrogen it upregulate the progesterone receptors so that they like welcome. They say hello welcome. Come on in progesterone.

We're going to you know have a party. And then when you have the peak of progesterone it actually down regulates the estrogen receptors. So that estrogen isn't as pro growth or proliferative.

So but if you constantly give progesterone you're going to down regulate the estrogen receptors, which is actually the purpose in the minds of the doctors who are giving it, because they're trying to suppress the growth of the uterine lining so that women don't get bleeding.

But you're suppressing the estrogen effect, not just in the uterine lining, but how about in the brain? How about everywhere? What are you trying to accomplish?

You know, my goal is to try to keep people as optimally healthy and functioning as possible, not to just prevent periods. Okay. So I want to mimic what nature does to keep us optimally healthy.

And there's no time in a reproductive woman's life when she would have a little bit of estrogen, a little bit of progesterone every day. That is not what is going to give you the best brain.

That's not going to give you the best heart, the best anything. And that's why so many studies, because the brain, the the brains of other researchers were brainwashed.

So they think that estrogen, even when they're studying it and trying to show that there's goodness in estrogen, when you give that struggle, they're very confused.

And they still have in their brains that it's bad. So less is better. So they want to keep giving the smallest dose, the smallest dose. Well, you don't ever want to give the smallest dose.

You want to give the optimal dose. And that's why you don't say, why don't you eat vegetables? They're good for you. Why don't you have one bite a month?

You know you'll live. That's the least dose you can get. No, you don't want to get the smallest dose of anything. You want to get the optimal dose, which in terms of hormones is going to be physiologic dose.

You're going to give doses that the body was designed to have. Because when you give physiologic doses remember hormones are messengers delivering information to cells.

The cells will get the right information and do the right thing. So like why don't some of the other things that are so key that estrogen modulates like autophagy.

So autophagy is how the cells like it's like spring cleaning in a cell. They take their old yucky components. They put it in the recycling bin which is called the lysosome.

And then they create amino acids and fatty acids and they reconstruct new cellular components. It's like a total

rehab of the cell. You need estradiol for autophagy to happen properly.

You need to have estrogen for proper apoptosis. When you have proper cell death, you know, and what's called misfolded proteins that are like cancer generating, you know, abnormal proteins that are misfolded.

They need to be gobbled up internally by the cell and destroyed, like this, internal phagocytosis, which is part of autophagy that requires adequate amount of estradiol.

All of the I mean, like we can go for hours. I mean, because I just, you know, read it on and on, but I don't want to like, minimize progesterone. Progesterone has not been as studied as estradiol.

I hope all of our listeners have their notebooks out, because even I am going to go back and listen to this talk again because I, I am learning so much from you right now.

Before you go, I know that you are very busy, but I want to just at least briefly talk about the role of testosterone for women as they age. Well, testosterone has a decline that is different and yet still somewhat connected to menopause.

So they're made by cells that are not part of making estrogen. So if we talk about like how is estrogen made in the ovary, estrogen in the ovary, which is estradiol, all is made from testosterone.

So every bit of estradiol that's made is converted from testosterone to the action of aromatase. Well, in order for that to happen you need to have eggs okay.

But when we run out of eggs we can still make testosterone. But we cannot make estradiol. So our ovaries can make testosterone to some degree like forever.

And that is why ovaries should never be removed. I mean, this is like a really important thing because the doctors say, oh, you don't need it, you're almost in menopause or you just went into menopause, so you don't like, you don't need your ovaries.

That's not true. Have the testosterone in the female body is made by the ovaries. The other half is made by the adrenal gland. And as the adrenals age, the part of the adrenal gland that makes testosterone is called the zona ridiculous.

And just like a lot of other parts of us, they shrivel up so that the zona reticular is shrivels up and our production of androgens from the adrenal gland, the DHEA, sulfate, and the testosterone go down.

Now, the if we take out our ovaries, you know, then we don't we have like a tremendous plummet. So we need our ovaries now. Nature, though, declines our production of testosterone naturally, so that by age 40, the average woman from her ovaries and her greenhouse combined is producing half the amount of testosterone she made at age 20.

Now, you know, I just think that that nature just is thinking from a very practical point of view, like, why would you want a bunch of 40 year old women to have, like, tremendous drive, sex drive and, you know, libido and all that, like, so like, and, you know, we'll just tone it down in those 40 year old, you know, we're like, but when we are 40, we like we've we remember we still want things to feel like when we were 20.

So so testosterone can sometimes be helpful for improving libido and sexual response. But like every hormone for testosterone has only been relegated to being recognized as well for libido and sex.

But it's so much more so. Testosterone is also very important for brain health. And of course, as we age after menopause, the testosterone that we do make from our ovaries and from our adrenal is converted into estradiol in our brain.

So testosterone is also has receptors in the brain in its own right. It's not just being turned into to estradiol, but combined testosterone is also neuroprotective and very, very important.

And testosterone is also an immune suppressor. So it sort of dampens down. It's you know, it's like saying estrogen okay. You know, come a little bit down here, you know, like so it's it's a little bit of an immune suppressant.

That's why men overall by the way have more cancers. You know the non reproductive cancers in women because women have this incredibly robust immune system.

And and testosterone sort of dampens down that effect because it's really takes a lot of energy to keep that immune system of women going. And men need to use a lot of their energy to make sperm and muscle and bone.

So but the thing is that testosterone has many effects throughout the body and including in terms of brain health and vascular health. So and of course, muscular and bone.

And in the brain, testosterone does have an impact on focus and like 3D, like geometry and so forth. So we definitely want to have testosterone and it will go down.

Now there can be a little increase in testosterone. Interestingly, during the Perimenopausal years as women are transitioning their they will have this spiking of their gonadotropin, luteinizing hormone, LH and FSA follicle stimulating hormone because the brain is saying, come on, I want more estrogen.

Well, to make more estrogen, you first have to make more testosterone. So there'll be this little increase in testosterone. It's not a lot, but it's and you're getting a decrease in estrogen.

So the balance is off. And that's why women during the perimenopause will sometimes get adult onset hormonal acne. It's like, what the heck. Like what is with these pimples?

You know, it's because they suddenly of too little estrogen, too much testosterone. But it's not a huge amount. It's just a relative thing. And you have this imbalance type of thing and that sort of quiets down, you know, with age.

But, and as we know, most women as they age will have more hair thinning, androgenic alopecia. And because they don't have so much estrogen to sort of balance it and they get little whiskers.

Have you ever seen like, old women? They have little whiskers. So but we want that's why I would never, by the way, I would never give testosterone without estrogen.

First you give estrogen and then you get that all settled because estradiol upregulate testosterone receptors. So without adequate estradiol, the testosterone isn't even going to work properly. Okay.

So in a woman. So you need to get the estrogen balance.

Circadian Rhythms, Lifestyle, and Where to Learn More

Progesterone balance. Then you add on the testosterone. Now if I measure testosterone levels I use serum levels because that's where we have the most data.

And if you get total testosterone, you can also look at free. But it's not the most accurate in women because the master is so tiny. You can also look at sex hormone binding globulin, which binds these hormones.

And if a woman spent most of her life on, hormonal contraceptives like birth control, sometimes she'll have really high sex hormone binding globulin, which never goes down, which means that you'll have deficiencies of these hormones, which we don't even know what the heck we're doing.

You know what? What? That all means. But it's not good, you know, because we want nature to be properly self-

regulating. And now we're taking that away from the body to properly regulate itself.

But I like to have, I'm a very I'm a moderate, so I like to have my testosterone in sort of like the middle range. So if the range is like, say, three, you know, you and you'll get a reference range, you have to understand what that means.

It means 95% of all the random people tested had from the bottom number to the top number. And that's 95% of all the people tested. So 2.5% scored below the bottom number, 2.5% scored above the top number.

That's not a normal range. They call it normal. It's not normal to reference range. And as the population gets more unhealthy, the reference range has got to get more weird, you know, because you know like, you know, it's a reflection of who you're testing.

So say the reference range and it varies from lab to lab is say 3 to 50 okay. That's not uncommon. That's a pretty big range. So does that mean that 3 or 4 is as good as 49 or 50.

Of course not like that. That never makes sense. So I like, you know, like we don't even have quite the best data on like what is optimal. So I figure you know, split the difference.

So like how about 20 something, you know, so what if you have a level that's like seven. Well that's pretty low. Like you're scraping the bottom of the barrel.

So I offer my patients recognizing limited data, limited research. But you know, but there is some data and it's mostly about hyperactive sexual desire.

You know, it's like that's all they ever study. They're not looking at it. That's good stuff. They look at it more in animals. We know more about rats and humans when it comes to this, but I will offer it until later.

I have to understand it's off label. It's all compounded. We don't have any products that are, you know, commercial products for testosterone for women in the US.

And, and a lot of women feel better, you know, they just have more energy. It's better for their bones, for their brains. But I never overdose. I am a total, anti these people who are giving super high physiologic, super physiologic doses of testosterone, against pellets because you cannot control the dosing with pellets and you always get crazy levels like would be good for a man, you know, like you always get these really super physiologic levels.

So I just do small amounts, I give compounded creams and I also use vaginal DHEA cream, which has also been shown to restore vaginal health and also improves sexual response and sex drive.

And so that's kind of a nice thing. And DHEA which we didn't, I talk about, but that's another hormone that is very important for women as well. In fact, DHEA has been shown to help maintain ovarian function in the Perimenopausal years for women who are trying to get pregnant, as they're like in their, we'll say sunset years of reproductive function, DHEA can help prolong the life and function of ovaries.

So, you know, definitely something to look at as well as another, another hormone and another neuro steroid as well. And as you mentioned, the a good alternative vaginally for vaginal dryness as opposed to the ezreal, which also gets used.

But you said you prefer to avoid well, vaginal estradiol is not going to. It's in such tiny amounts it's not going to be absorbed very much systemically.

So I don't really have a problem. I don't really use a lot of it because the FDA really, you know, you got to be careful with everything you do in life.

You know, those of us who have a medical license because the the medical boards of most states, say, and the FDA, they really took a negative position, whether it's like it's not logical, but, you know, but because all there is actually some interesting data.

So because it really binds predominantly to beta receptor which down regulates alpha, so that you doubt if you have a lot of beta down regulates alpha.

There's some data that came out initially from UCLA that, it can potentially be a therapeutic for multiple sclerosis because the, the high and if you give a lot of the beta, it will down regulate the alpha and the alpha.

What the innate immune cells are the ones that make the inflammatory cytokines that are out of control in a lot of, you know, the autoimmune especially like with Ms..

So there may be some therapeutic value to using astral in it used to be used as a breast cancer treatment before like tamoxifen came down the line because breast cancer happens to be alpha receptor positive.

But estrogen is not. When you have natural hormones they do not give you breast cancer. I mean, it's like it actually helps prevent breast cancer with the rhythms and the, you know, the the, purging of abnormal breast cells.

But when you have chronic inflammation because, I mean, people are so afraid of breast cancer, I just have to mention this, you know, because they'll say, well, you know, I want to have a brain, but you're going to give me breast cancer. No.

When you have chronic inflammation that goes along with menopause, the inflammation when you're not making estrogen, you're not properly modulating the immune system.

You end up with a despotic gut microbiome. You get leaky gut. This happens in all women who are not on hormones in the menopause. You then have leaky gut.

You're going to have this dysregulated system. The sort of default system of the body is in a pro-inflammatory state. You're going to have what they call the renin angiotensin aldosterone system, which is part of the regulatory system of the immune system and the vascular system.

It goes into a sort of a chronic state of on like all in pro-inflammatory. So menopausal aging is all pro-inflammatory. And this is, you know, really, you know, horrific.

And you get inflammation in the breast tissue as well. You get inflammation everywhere including in the breast. Chronic inflammation promotes DNA breakage and instability.

When you break DNA and you get end up developing cancer. The breast itself, just like I mentioned, the brain can make estrogen because it's so important for brain health.

The brain makes estrogen. The breast also is a paraquat organ. It can make estrogen as well. So it will make estrogen. And the reason that the breast makes its own estrogen is that if a woman is breastfeeding and she gets an infection, a mastitis, it's so important for the local estrogen to be produced because a woman who's breastfeeding doesn't have ovarian function typically, right.

Her ovaries are suppressed by the prolactin so that she's nursing. Right. So that's why women often don't get periods back for months after they have a baby.

So they don't have the estrogen coming from their ovaries. So the breast will make it itself to help modulate this inflammatory response, to keep it from going too strong or too weak.

It just like makes it just right so your body can fight off a breast infection. Well, that took the tools to make estrogen in the breast maintain themselves are still there.

When your post-menopausal but so but the they wasn't designed for chronic inflammation. It was for an acute infection acute inflammation. And then it's resolved end of story should be resolved.

But when you have chronic ongoing inflammation because you have inflammation, you're not getting younger yet. There's no reason for this inflammation to ever clear up.

It's not like from an infection. It's just from a dysregulated immune system creating chronic states of inflammation. So now you have chronic inflammation.

And so you can have upregulation of the enzyme aromatase to make estrogen in the breast. That's why on a mammogram if you see dense breasts in a postmenopausal woman who's not on hormones, that's considered a risk factor for breast cancer.

What that really means is that she's an inflamed woman, her breasts are inflamed, and her body's response is to make estrogen in the breast as to try to control this inflammation.

But it's a losing proposition when you're inflammation. So you have chronic estrogen being produced in a chronic state of inflammation. If the inflammation causes DNA instability and breakage and you get cancer, the estrogen that's being produced was not designed evolutionarily to deal with cancer.

So it's designed to nurture and heal. So part of nurturing and healing is promoting tissue growth. New blood vessels because that's part of how we heal damaged tissue.

So the brain interprets the cancer as damaged tissue. And the estrogen produced in the breast is now supporting the breast cancer, which has estrogen receptors like all the other cells of the body.

So it's not the estrogen that's causing the breast cancer, it's this chronic state of inflammation, which, by the way, is ongoing in the brain as well.

That's why when they talk about, oh my God, we can't believe this. We just discovered this amazing thing. There's a link between women who get breast cancer and dementia.

Oh, there's a link between women who have osteoporosis and breast cancer. Oh, there's a link between colon cancer and dementia. That's because it's inflammation everywhere in the body causing tissue breakdown.

I mean, our DNA, damn it. I mean, it's like all one body. We sink or swim as a unit, and it's just a different people may manifest differently with how their inflammation sort of focuses like whether it's in the breast and you get breast cancer, it's in the colon. Yeah.

Colon cancer, it's in the brain and you get dementia, you get osteoporosis, you break your bones or you get all of the above. Right. So but if you maintain proper physiologic levels of these hormones, these critical hormones that modulate all these systems that keep everything humming properly, you won't get into a state of chronic inflammation.

You won't have inflammation, neuroinflammation, bone inflammation, which is what osteoporosis is, breast inflammation, which leads to breast cancer. So we must not blame estrogen.

Estrogen is trying to put out the flames in the breast. It just can't. The inflammation wins. Breast cancer occurs. And then the estrogen becomes sort of a unwitting facilitator because it's designed genetically to facilitate growth and healing.

And it sees breast cancer as damaged tissue. And it's promoting growth and healing. But it's breast cancer. So poor estrogen is taking the blame and it doesn't deserve it.

Really. It's the hero of our story I think it's a male hero. Okay. Let's hear some of the themes here. Have been

about balance. And just so I think you and I share this reverence for how there's a lot that we don't know, and that when we affect one thing over here, we're affecting something else over there.

And we want to, I definitely am a natural Catholic doctor. Right. So this idea of supporting the natural rhythms, the natural, the the all intelligence of the system, you know, I am so glad you mentioned that.

I just have to throw this one thing into. Our rhythms are critical for every organ functioning, including our brain and our immune system. So it turns out that once again, I know sounds like a broken record for those of you who remember records so that the brain has a master clock.

It's called the super Quiet somatic nucleus. It's a group of neurons. It sits atop the optic nerve and gets fed signals from the back of the eye, from the retina that, you know, along the optic nerve so that the brain can register whether it's day or night.

Well, it turns out that this clock is critical to maintaining all the organs working in synchrony. Everybody has to be on the same beat, okay? You can't have one organ who thinks it's in the eastern time zone, and another one that's in Pacific Time zone.

No, you got to all be in the same time zone while working together. And estrogen estradiol has receptors on the master clock, the super charismatic nucleus.

And after menopause, the master clock becomes off the beat, which is like drifting. It's drifting. And so you become dis synchronized with your organ systems, including in the brain.

And that's why it's so important not only to have hormones, because right now we can't like, replicate. I can't turn anyone into a 25 year old. I do not have that power.

I have, you know, we do the best we can, but we're not turning. And, you know, a 55 year old into a 25 year old. I don't have that ability. We just do better, right?

We do better. And but that means we have to use all the tools. So like bright light is like amazing, I know. I hope people are talking like light as therapy.

Light as medicine. So light will help you get back your, you know, back on track. And, it's so important. But because recognizing that without adequate estradiol in the brain, you're going to have this drifting of your circadian clock and you're going to be like in different time zones, in different parts of your body.

So you know it. Absolutely. Everything is linked in this beautiful web of life, you know, and, you know, I think of estrogen and all the other hormones as like the glue that keeps everything working together.

Otherwise everything's like drifting apart towards chaos. Right? And so, you know, it's just once you realize it, it's like, so simple. I think I'm, like, very simple in my thinking, you know, like, you just need to give the body what it needs and it will do what it should do, that I can't micromanage the body.

I'm not that smart. I can't manage every peptide and every lipid signaling age. I can't do that. But I'm going to try to use a macro view like give the basic nutrients the lifestyle, the sunlight, the fitness, the sleep, the love, the nurturing and keep those basic hormones imbalance.

And guess what? Your cells don't know how old you are. Your cells will do what they're programed to do if they get what they need. How incredible. Doctor Grace, you are an inspiration.

Really a mentor of mine. I look up to you so much, and I'm so impressed by what you have done in your career and just how impactful, how many, how many people's lives you have personally made better because of this information, because of changing the narrative.

You've done a really good job of that with hormones. And now I hope that we can do a similar thing in the world of dementia, that this is reversible, that there are things that we can do.

I want to make sure that every one of our listeners who I know are inspired and better informed now than they were an hour and 20 minutes ago. I want to make sure that they know where to find out more about you, how they can find your books, your clinic, how they can personally benefit a little bit more from this information.

Well, that's very generous. I have, I'm a very old fashioned doctor. I still have a brick and mortar practice. I my office is in sunny Southern California.

Irvine, California. It's called the Integrative Medical Group of Irvine, and I see patients there every single day. I do some telemedicine. I do lots of in my off my office, and I do hands on care, you know, touch people and examine them.

We do all kinds of different imaging. And I have like a great support team with, a gym in my office. We do fitness medicine, we do nutrition and stress control.

So I try to cover the gamut of what people need to optimize their health through every stage of life, with a focus on on females. And I also have an Instagram Live, which I haven't done for just a little bit, but I'm getting right back to it.

And I put on shows and it's also archived on YouTube. So my Instagram handle is Dr.. Period. Make sure you put the period in Dr.. Period. Felice Gersh and my my I have a website which you can look up and it's integrative mgi.com for my group.

And you know has a lot about my practice. And I would love to help individuals and I do have a new book that will be coming out in the fall on menopause that doesn't have an official name yet, but, you know, keep an eye out for it.

And my other two books on polycystic ovary syndrome, which are really lifestyle oriented, so they're actually appropriate for anyone with or without PCOS, are available on Amazon and other online booksellers.

Thank you so, so very much for your time and for your expertise and wisdom in this space. You have decades of wisdom to share, and we are so grateful for the download today.

My pleasure.