Introduction and Dr. Gersh's Background

Welcome Felice. I am so, so glad that you agreed to be part of the M. S. and Neuroimmune Summit and would like to have you do is introduce yourself explain your area of expertize and then we'll get right down to two hour to our conversation.

Well, I am Dr. Felice Gersh. I am board certified in obstetrics and gynecology and integrative medicine. So I call myself an integrative gynecologist.

I take care of women at all stages of life, and my goal is to help them to optimize their health. Now, I would like to talk about pregnancy and let's have a conversation.

We certainly have had many of our patients in our study. Patients tell us when they were pregnant, they feel great. They have fewer symptoms, they have more energy, more mental clarity.

And we've had some women that want to have just stay pregnant all the time because they felt so much better. Can can you explain to our listeners what's going on?

Why why does pregnancy feel so good to the most patient? Well, pregnancy is such a unique it's a unique state for women.

Why Pregnancy Improves MS Symptoms

And it's a time when the immune system has to walk a very thin line between protecting the women from infectious agents and pathogens and so on, and also keeping the immune system at bay to some degree so it doesn't attack and kill this little alien.

Really, it's a different entity than the woman who's carrying the baby so that the immune system doesn't reject it like it would, you know, a transplanted organ.

So the first thing to recognize is, is that estrogen, which is talked about in such a loose way, it's not a hormone, it's a family of hormones. And this really comes into play in great measure during pregnancy.

So there are three main types and there's another one which we won't go into, which is really of fetal estrogen. But the three main types EE one, which is estrogen, which is the dominant estrogen in menopausal women and also in women who have a lot of metabolic dysfunction, a lot of obesity.

Then there's e two, which is the estrogen made by the ovaries during the reproductive years called estradiol. And then there is e three that estriol that's the dominant estrogen of pregnancy made by the placenta.

And there are different estrogen receptors and the different estrogens e one, two and three have a different propensity for binding to these different receptors.

E Two binds in a sort of balance fashion with the different receptors. E One predominantly alpha and. E three ester feel the dominant one in pregnancy is the beta receptor.

So this is not an accident. Nature has everything worked out just perfectly when things go right. So what happens in pregnancy is that you have both you have all the estrogens in balance, but with the dominant one being estriol.

So what you're doing is you're activating more than would ever be another time in a woman's life. The beta receptor. Well, it turns out that when you have a high amount of beta, it actually downregulate or makes less

effective the alpha.

Well, as it turns out, interestingly enough, the innate immune cells, we call them the attack animals, and you all know them. I'm sure by now the macrophages, the mast cells and neutrophils, they are predominantly, not exclusively, but predominantly alpha.

And then B the B cells that make the antibodies are predominantly but not exclusively the beta. So when you have a lot of the beta agonists, the estriol present, what you're doing is actually acting as an immunosuppressant, just like there are many pharmaceuticals now available that act as immunosuppressants that work to downregulate the production of these pro-inflammatory cytokines that you've heard of, like, you know, interleukin seven and tumor necrosis factor alpha.

So those are made by those innate immune cells. All of that is downregulated by estriol. So it's designed to keep those immune cells from killing off the fetus, but has a side amazing benefit for women who have M. S.

It acts as an immunosuppressant and downregulate them a lot the way different pharmaceuticals do to actually reduce this inflammatory process, which becomes a benefit.

But of course, it's a limited time benefit because pregnancies will end with this. Just form cells. So so the estriol and that does that climb during the whole pregnancy.

So it just shows up immediately and it's high all nine months until delivery. Well, it's interesting. The massive benefit, the most benefit comes in the third trimester of pregnancy when you do have higher levels of both progesterone, because that's also a key player here, too, which we didn't touch on yet and in estriol as well.

And so were lowering the symptoms of M. S. in, let's say, because this is the neuro immune summit. So with people with inflammatory bowel disease, rheumatoid arthritis, lupus and other autoimmune diseases affecting the peripheral nerves.

Would the estriol be beneficial for those people as well? The most data that I have come across is really involving M. S.. However, once you understand the mechanism, absolutely.

There's no question in my mind that this would be beneficial all along with progesterone. And I don't want to downplay the benefit of estradiol either e too, because that is what creates this balance of all the receptors being activated.

But estriol, because it is so prevalent in pregnancy and it really down regulates that alpha receptor with all of that beta receptor. And so it really does reduce that inflammatory cytokine production.

But of course is another cost to be paid pregnant women have a higher adverse outcome if they do get infections, for example, with COVID during the COVID pandemic, or if they had chickenpox or the flu.

So everything, of course, comes with a certain price to be paid. And of course, we know that these the pharmaceuticals that are immune modulators, they all have risen.

You know, don't take this. If you have active tuberculosis or if you get a fever, call your doctor because it does downgrade, regulate those innate immune cells, which are so critical for, of course, activating the inflammatory response, which is designed to fend off and help us to deal with pathogens that try to get into us.

Okay. Now, everyone who's listening, I am aware that there are a number of studies that have used estriol and they have been able to show that the addition of estriol was estriol plus Copaxone, that arm had lower numbers of enhancing lesions, fewer relapses.

Estriol, Progesterone, and Autoimmune Disease

And I certainly know some integrative physicians are now having their women take estriol in addition to their disease modifying drug treatments. But you'd also mentioned progesterone.

And can you review for us when does progesterone show up? When I'm menstruating, having my cycle and then when I'm pregnant. So there's a beautiful dynamic at play all the time between the different hormones, estradiol and progesterone in a menstrual cycle.

You have two distinct phases that one is called in terms of looking at the uterine lining, proliferative. So that's the time. The first two weeks, if you have a 28 day cycle, which is sort of like the theoretical ideal, if you have a 28 day cycle, the first 14 days are the proliferative phase.

That's when you have just estradiol being produced from the ovaries and that we're not going into testosterone here right now. But that's a precursor by the way.

Testosterone is made in the ovaries. That is the precursor to all estradiol. So all estradiol, the estrogen produced in the ovary comes from testosterone production.

Okay, so. The. Atom did come first and then Eve came because you have to have the testosterone to make the estrogen. Well, that's so fascinating that you said that all testosterone is testosterone is required to make estradiol.

But what's so interesting is they've gone back and they found that the first steroid receptor that they've been able to identify, like 500 million years ago was estrogen receptor.

So even though testosterone existed as a precursor to estrogen receptors for estrogen pre and to date the receptors for that well. So we win. Okay. Okay.

But but so in the ovary, during the first half of the menstrual cycle, you have just estradiol being produced. We call that proliferative because estrogen has many, many functions, one of which is growing things.

It stimulates growth factors. And one of that result is it grows the uterine lining. But then you have this miracle, this incredible miracle, where you have this spike of estradiol that leads to a spike of luteinizing hormone from the pituitary, which triggers ovulation.

And then after as soon as ovulation is occurring, you have a transformation in the ovary and it turns into a corpus leading producer. So it makes this little structure that makes progesterone.

So then in the second two weeks of the menstrual cycle, you have both progesterone and estradiol being produced. And this is so amazing because the progesterone actually down regulates the receptors of the estrogen and estrogen in the first half of the cycle.

Upregulates the receptors of progesterone. So essentially having the first two weeks of estrogen enhances the way that progesterone can work in the body.

And then when you have progesterone, it downregulate sort of like quiets down the receptors. So the estrogen is a little bit quieter in its effect in the body.

And this is so amazing how it interplays with the immune system as well. And in fact, one, I don't know if you talked about it all in the summit is it's a complex subject, but it's the endocannabinoid system.

And this is a whole different system. This is the system that cannabis works on, which is another whole thing that they discovered that cannabis works in the body, but they didn't know how.

And then later they discovered it works on our own system that has receptors for cannabis. But you know, that's a plant. But our system, they then named endo for within ourselves cannabinoid after cannabis.

But it turns out that the endocannabinoid system has receptors in many different organ systems, including on the immune cells. So it's like an amazing thing where as the extra dial up regulates the endocannabinoid system, progesterone down, regulates it, and it sort of cons things down.

So progesterone is very anti inflammatory and that's really important because remember, the menstrual cycle is all about creating a pregnancy. And so when you have this new embryo, it's assuming fertilization occurred.

You don't want the immune system to attack and kill it. So you have progesterone acting as a very anti inflammatory agent and as well and it shifts your.

RF You talked about this from like T 1 to 2, so it's actually down regulating again those attacks animals see the innate immune cells as well. And when you have that spike, spike, spike of estradiol in the menstrual cycle that precedes and then triggers helps to trigger through the ovulation.

Hormones Across the Menstrual Cycle

When you have that really high level of estradiol that is the most anti inflammatory time of the menstrual cycle once again, so that the sperm which are totally alien right to the female body that the sperm coming in will not be attacked so that ovulation can occur, that you don't attack with your own immune system and kill off the sperm.

And then when you have that embryo, so now the whole immune system is downregulated by the progesterone combined with the estradiol so that you don't attack and kill your little developing embryo within you.

So it's just an amazing system that works with the immune system. I want to talk a little bit more about progesterone to the audience. I know in the traumatic brain injury arena, there are more people that are using progesterone to help protect the brain and that they get progesterone orally and it works very well.

Calming the brain is very protective. I don't know of any studies in the EMS world. However, I do know integrative physicians who are giving women estriol.

I often combine that with progesterone. Can we talk a little bit about is that the optimal strategy from your point of view? Phyllis Well, just a word on progesterone.

Progesterone actually has been shown to be, like you mentioned, in traumatic brain injury. It is produced in the brain, what we call that a neuro steroid.

Right. So it's not only produced by ovaries, but it's produced in the brain in response to trauma. And what's interesting is progesterone has its own beneficial direct effects, like it lowers the production of inflammatory cytokines.

It also helps with re myelin ization, actually helps to promote the neurons to get myelin on them. And it actually upregulates in the brain. It stimulates the production in the brain of estradiol, which then acts to also work to heal because not only remember estrogen is also promote growth, but growth is not just about growing big, it's also about rejuvenation, regeneration.

And so it helps to heal. So estrogen is essential for the process of healing, promoting brain derived neurotrophic factor, for example, that's actually stimulate these brain growth factors by estradiol.

And so it's amazing this interplay in the brain in response and in terms of giving hormones to menopausal women, this is a very tricky thing. Now, I personally only give estradiol and I know that a lot of people are giving this, you know, this blended product that's called biased, which has estriol in it.

Now, there's no really clear data of if you're going to do that, how much would you give? How would that work? So I'm very simple in my thinking, and I do love giving women menopausal hormone replacement.

I really believe in that because I don't think that women can really be really well-served if they are deficient in these. I call them life hormones. I've gotten rid of the name sex hormones and I call them life forms because they have they have effects in every single organ system.

So of course, in the neurological system. So we have many people listening who may be thinking, okay, I'm perimenopausal or menopausal, maybe I should be asking for these life form hormones.

How how would the people who are listening find a practitioner who feels comfortable using estrogen, perimenopausal or postmenopausal? Well, in terms of perimenopause, I actually do believe that we should start.

We now know menopause, of course, is not like you cross the finish line. If that we have to stop thinking of it that way, that you have to do conventional definition 12 consecutive months without a spontaneous bleed of whatever lead that is.

That is an arbitrary, made up definition. It's a process of ovarian aging and we know that a lot of negative things happen several years before that so called less period when you have official menopause, including on the brain like word finding, word recall becomes really impacted in women in the perimenopause.

They've shown that over and over mood changes when women are transition running into the menopause, a huge percentage of them are put on anti-depressants because they have mood changes.

And we know that menopausal transition, not just the full blown end of the line, actually increases the risk of anxiety and depression by two fold in women who've never had a history and fourfold.

In women who've had a history of like postpartum depression or severe PMS or other anxiety depression situation. So I believe in starting hormones as a supplement in the perimenopause.

And that's, you know, sort of touchy feely. You have to look at each woman as an individual and then to give it in the in the menopause. And I don't have the solution to how to find the perfect practitioner, because there's still this unfortunate legacy from the Women's Health Initiative from over 20 years ago where they studied women who were on the older side, the average age 63, and they gave them a different kind of hormonal combination, which would never be found in any human female ever in the history of humanity, using horse urine from a pregnant horse that they dried into a tablet and they called it Premarin.

But that's after a pregnant mare. But the the real name, so to speak, would be conjugated equine. That's horse estrogens and it's not human. It's very different when you take that orally.

Progesterone, Brain Protection, and Menopause Care

Then having estradiol given through the skin and they use medroxyprogesterone acetate, which is not progesterone, even though it kind of has its name in there and it's modified, it has a totally different effect in the body, most of which is quite negative.

And based on that study, the mantra that developed, which is still so pervasive, is as if you're going to give any hormones, give the smallest dose. Okay?

So unfortunately, many people keep, you know, practitioners. So there are a lot a lot of folks that are going to be nervous. The old, old physicians like me, because I was taught now that that mantra, which I have since unlearned, by the way.

So I'm thinking we look for younger people that may be helpful. You know, I'm old. You are. You're enlightened, my friend, and I'm enlightened as well.

So we're looking for gynecologists integrative. Gynecologists integrative physicians, asking them how open they are to hormone replacement. So I think to asking those questions, I call it whoever it is and hopefully someone who

has a functional, integrative background.

But just say, are you in favor of more physiologic like trying to get to a physiologic level or are you into very tiny doses? So that will at least tip you off right at the get go.

Is this doctor kind of living in the past from 20 plus years ago or kind of really in the present? Okay. Yeah. So you're very fond of estradiol. Do you give progesterone as well? Always.

And that is another key point that a lot of women have had hysterectomy. And the conventional approach is, well, if you don't have a uterus, you don't have to give progesterone because they are so limited in their view of progesterone.

They think progesterone is only in a woman's body to prevent overgrowth and then potentially cancer of the uterine lining. And that is absurd. There is no hormone.

There was no enzyme there. There's no neurotransmitter. There's nothing that has one function. Everything is a multitasker. And progesterone has receptors also all over the body, including in the brain and on the neurons and in the bone.

And it's like so you need progesterone for a host of functions. And they it works together in a beautiful balance as well. Progesterone can actually down and regulate cancer potential by but when you think what I'm very much in favor of having cyclic progesterone to somewhat mimic the menstrual cycle.

It's not the same, but you purge tissue when you have that period. You're not just purging the uterine lining. You're also helping to promote programed cell suicide like that.

The dead, ugly, yucky senescent cells will kill themselves off. That's part of the cycling of of menstrual cycle. And so you like to give progesterone a couple of weeks each month and then a couple of weeks off in.

Did I hear correctly that estriol is not part of your. It is not. I'll tell you why. There are actually some published studies that show that when you give est or a dial to a postmenopausal women, to the skin transdermal estradiol, it will convert naturally into estradiol in the body at very good levels.

So the human female in the reproductive years has estriol in her body. It's one of the byproducts of it's made from estradiol. It's a estrogen also comes from estradiol but that's bi directional.

Estrogen can turn into estradiol as your dial can turn into estrogen. And then when everything is right, nature makes it so it has the proper balance.

And estriol comes from estradiol, but it only goes in one direction. Once you make it through estradiol, you don't go backwards to estradiol, but the body controls it.

It makes to happen as needed. So I rely on giving all the right things. Hopefully, you know, food and sleep and stress control and control, endocrine disruptors in your body.

I try to do the best we can with lifestyle medicine and then give the body the foundational hormones that it had during the healthiest years of life, the reproductive years, and then let the body self-manage.

How much estriol it's going to make, because you can't forget that estradiol down regulates to this variety of mechanism involving the receptors that it down regulates the activity of the innate immune cells, which is has its really good points.

But it also is a concern because what if you have a woman now who is like 55, 65 and she's on a significant amount of estriol, and you're not treating M. S., you're not.

It's just being given for hormone therapy. And now you're down regulating the innate immune system, and then she has a sepsis event or she get you know, she gets infected with a pathogen like pneumonia is one of the biggest killers of people as they age.

So you want to downregulate your immune system's initial response, which is to create that inflammatory response to try to kill and destroy that invading pathogen.

You're down regulating the body's ability to fight off an infection. And I have great concerns as women are aging, that if we would do that, I would rather give estradiol just like you would give in a healthy 25 year old and let the body itself self manage the production of estriol.

Because I do not want to create a problem where they can't have a proper, optimal functioning immune system as they age and they are presented with pathogens like pneumonia. So.

So you're giving this or you're giving it topically, are you giving it virtually or it's just through the skin? Well, when I give it for systemic, you know, like I'm trying to get healthy total body levels, I give it to the skin if I'm trying.

Also specifically, sometimes some women need that extra boost to the area around the in the vagina and the bladder. So that's a very big problem called genital urinary syndrome of the menopause, which incorporates all the bladder problems, all the vaginal problems that a little boost extra in that area can can be really very helpful.

Yeah. And of course women with M. S. and Norman issues we often have bladder issues and we are dealing with overactive bladder.

Finding the Right Hormone Practitioner

So I can see where this might be super helpful, but, you know, absolutely. We haven't talked has spoken at all about testosterone. Do you include any topical testosterone in your practice or is that really not so much?

I don't do it universally like I would with estradiol and progesterone. So testosterone is made by the ovaries forever. I mean, that's an interesting it's like a different skill set in the ovary to make extra dial and progesterone versus testosterone because the ovary cannot make estradiol and progesterone if it doesn't have any eggs, you have that.

And when the egg supply is gone, you cannot make those other two hormones. But you don't need eggs in the ovary to make testosterone. So testosterone is made for life.

It does decrease as a woman gets older to a certain degree. But around the menopause, sometimes the production of testosterone from the ovary actually goes up.

And that's because the pituitary gland puts out more of the stimulating hormones to the ovary to make testosterone. Because remember, testosterone is the precursor to estradiol.

The brain has sensors for estrogen. And it says when the production goes down, the brain says, I want more estradiol. So it puts out the signal to the pituitary, puts out its signal luteinizing hormone.

LH and then also FSA, but LH Luteinizing hormone stimulates the ovary to make testosterone, so. LH goes up and the ovary makes more testosterone and we.

All go in here. Yes, that's exactly. So a lot of perimenopausal women say what is happening? I'm getting acne. What am I? I'm getting facial hair and my hair is thinning is I'm I going through some weird aging plus puberty at the same time.

So that's not the group you want to give testosterone to, but so you have to watch over time because it goes down. The other thing to know is testosterone in the body of a reproductive aged, healthy woman, 25% of testosterone in the body comes from the ovary, 25% comes from the adrenal gland.

And the other 50% comes from adrenal gland. Androgens like DHEA is DHEA that get converted through the action of the enzyme aromatase that's located in many organs of the body that not the ovary, but like fat tissue in particular.

So that tissue can also make testosterone and then also estrogen. So the the so the estrogen is with the enzyme aromatase. And then there are other enzymes that can convert the precursor androgens into the more potent testosterone as well.

So it's confusing and it's not universal that testosterone needs to be given to all post-menopausal women and the problem as well is measuring blood levels or even celebrate any kind of level that's going through the body of testosterone doesn't necessarily tell you what the tissue level is because these androgens that are circulating that are coming from the adrenal gland can be converted directly into testosterone and the more potent form of testosterone dihydrotestosterone in tissues like the brain, like in skin.

And so it's not circular aiding. So the circulating blood level doesn't always reflect the tissue level. So every case has to be evaluated independently based on symptoms plus levels plus physical findings.

Okay. Now, I did want to touch briefly on the pregnant symptoms go down and then the woman is lactating breastfeeding.

Estradiol, Progesterone, and Testosterone in Practice

And do you have thoughts about breastfeeding for people with M. S and neuro immune conditions? Well, breastfeeding is so wonderful for both the mother and the baby.

But of course, you do have to watch. This is a special these are special populations. So we know that when these hormones, these life hormones, estradiol and progesterone are low, which happens post partum.

So that's why you can have flares. In fact, when you talk about autoimmune diseases, some of the most prominent times in a woman's life when she may be diagnosed with an autoimmune disease, can be postpartum.

Them, particularly women can turn up with Grave's disease and Hashimoto's postpartum and that or it can flare. So we have to look at we have to watch closely.

We have to watch for that and then look at each individual case because you have to look. Everything in medicine is always risk benefit ratio. So we always have to look at that.

Now, eventually, and sometimes sooner than later, the hormones will come back in. Women who are breastfeeding and they'll get their cycles again. So it's also possible to give women, if they are starting to have any kind of a flare while they're breastfeeding, you can give them small doses of hormones, of bioidentical hormones that will help perhaps to regulate their immune system so that they can sort of slow down or somewhat downregulate the flare as it happens.

So it's really great if they can breastfeed and then if they don't if they do have a flare, then we have to look at, well, what can we do to help maintain breastfeeding?

And it may be just a small amount of hormones can do it for them. Yeah, the neuro group here or neurology group has a little project on breastfeeding for most patients and they're actually very excited.

There's much more recent finding that if you breastfeed, you do you minimize that rebound, relapse for if you if you deliver and you bottle feed those women seem to be at a higher risk of a flare.

Well, I'm glad to hear all that, because one of the things, if you look at what happens when a woman the hormones that happen with with breastfeeding, there is an increase in oxytocin and oxytocin is a very important neural steroid.

Or, you know, you can it's like on the border between a peptide and a hormone and it has a host of benefits and it's very calming and it's just helped some women with bonding.

And so I'm so happy to hear this news, this new data. And it's interesting, the neurodevelopmental kids with autism difficulty socializing. They're are now giving oxytocin nasal sprays to those kids.

So I think that's super interesting. What I think is happening, this is my theory when you're talking about this is as we talked about, that progesterone estradiol or neural steroids are also made in the brain where, of course, oxytocin can be made in the brain.

And a lot of these tend to come from they all can come from adrenal precursors. So I think what's happening is that and once again, when you look at blood levels, they're very low for these important hormones.

But if you look at tissue levels, they can be very substantial.

Breastfeeding, Postpartum Flares, and Oxytocin

So by having the conversion, there's probably things that we don't even understand yet that are happening postpartum, that are up regulating the enzymes that help promote the conversion of these precursor hormones from the adrenal gland into the these hormones that are so critical, the progesterone, the estrogen that are in the local tissues, the neurons, the brain and so on that are impacting in a very beneficial way the immune system in postpartum women who are breastfeeding.

You know, I think everyone who's listening, one of the key messages that I'm hearing and please correct me if I don't have it right. Hormones are vital and we need estrogen.

We need progesterone. If we breastfeeding, we need some oxytocin. But everyone's individual, if you have a perception that things are not going well after delivery, by all means you back in to see your physician to have a hormonal evaluation, because things still could be going wrong.

You could be having a thyroid that's overactive, underactive, that's part of us. And so very occasionally can have a massive pituitary insufficiency and have major, major hormone problems.

Occasionally post-delivery this has been complicated. Everyone, you may have to listen to this talk a couple of times. But Felice, you want to give us what you think is the one really big message that we want all of the listeners to remember from our conversation.

I have to go around protecting and defending estradiol and progesterone everywhere I go. And so the takeaway is these vital life hormones, estradiol, the ovarian, produce, estrogen and all of its other.

We'll take cohorts like estradiol and progesterone, which is the other hormone made by the ovary that's so critical for pregnancy and immune function that these are life hormones and they are neuroprotective, that estradiol estriol, progesterone are neuroprotective.

And by the way, so is testosterone neuroprotective. Yeah, this has been wonderful.

Key Takeaways and Where to Find Dr. Gersh

I so appreciate the work that you were doing. I could you tell our listeners how they would find you? Well, I'm right now in one of my exam rooms in my office.

So I have a brick and mortar practice. I'm very traditional in that respect, although do also do telemedicine. It's called the Integrative Medical Group of Irvine.

I'm located in Irvine, that's Southern California. Okay. What? Thank you for this. This has been wonderful. My

pleasure.