Upgrade Your Brain As You Transition Through Menopause Transcript

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Introduction to Dr. Louann Brizendine

– Welcome back to the Reverse Alzheimer's Summit. I'm so excited to introduce to you to Dr. Louann Brizendine. She has completed her degree in neurobiology at UC Berkeley.

Graduated from Yale School of Medicine. And did her internship in residency at Harvard Medical School. She's also served on both the faculties of Harvard University and the University of California at San Francisco.

She founded the Women's Mood and Hormone Clinic at UCSF. You can see why I'm delighted to have her here today. Her New York Times Best Seller, The Female Brain and its follow up, The Male Brain, continue to be read around the world.

And her brand new book, The Upgrade: How the Female Brain Gets Stronger and Better in Midlife and Beyond was released today. Now as the Lynne and Marc Benioff endowed professor of clinical psychiatry UCSF, Dr. Brizendine continues to speak, write, research, and consult.

Thank you so much for joining us today. – Thank you for having me. What a great summit and what a great topic. Just amazing that you're doing this. I really appreciate this on women's behalf.

(Dr. Brizendine laughs) – I mean, thank you for showing up today because it's a busy day. Your book is being released and you have spent decades of your life really dedicated to understanding the role of hormones in the brain and why menopause creates this big shift in how the female brain works.

We know that dementia affects women at double the rates of men. And so let's dive in to what happens in our brains as the estrogen fluctuations are taking place.

– Okay. What's important to know is that all of our life from the beginning, from when we're born, the female brain has estrogen in it. And until we die, we have estrogen in it.

So it's not like we have no estrogen, but of course it fluctuates and starting at the puberty time, when we start our periods roughly about age 12, plus or minus two years for women, that fluctuation starts to come out of the ovaries and the estrogen will go up for the first two weeks of the cycle.

And then, it will dive down as the progesterone comes up when the egg is ovulated. So we have this rolling up and downhills of estrogen and progesterone in our brain through the cycle every four weeks, actually every day, it changes a bit.

And what we know happens from working back in the 1990s is that estrogen stimulates lots of areas of the brain, but particularly we look at the hippocampus and those of you in this field know that the hippocampus is a really major, major memory area in the brain.

And it causes all of these little boutons and synapsis to sprout almost like a really bushy tree in the spring.

How Estrogen Shapes the Female Brain

Everything grows like crazy and it starts to touch the other neurons and make synapsis during the first two weeks of that cycle, when the estrogen is really pumping out like crazy from the ovary.

And so that is what we're used to. It then gets torn back down at the end, last two weeks of the cycle, 'cause progesterone reverses what estrogen does.

So that's just what the female brain is used to during the menstrual cycle years up onto what I call in my book, I've called it the transition, which starts between age 40 and 50.

I call those the transition years, AKA perimenopause. So that's when we call, or are called the sputtering ovaries syndrome. When the ovaries are starting to make less and less estrogen as we go up towards the cessation altogether of our estrogen.

– And so when we lose estrogen, what's happening cognitively? – So that's sprouting and that stimulation of nerves and in the brain, the neurons and the synapsis are all stimulated.

Also, so the other things that estrogen does in our brain that you need to know about is that estrogen also protects the brain. It's called a neuroprotective agent for many reasons, but let's just name a few.

So it helps to keep the blood-brain barrier healthy and intact. And what the blood-brain barrier does, it's a really cool filter. It doesn't let toxic stuff into the brain to damage the brain, but when it gets like little mothy in holes in it, you know, if it's not working properly, it will let bad toxins from the blood into the brain.

And you know, we don't want that. So estrogen helps keep that nice and intact. Estrogen also stimulates what we call the little, every little cell in your brain in your body has a little powerhouse, lots of little powerhouses in each cell.

I call them like, they're called mitochondria. I had to call them like the mighty mouse powerhouse, (Dr. Brizendine laughs) 'cause it's really what makes the energy in your body and in every cell, estrogen stimulates that and keeps it working.

And when you get the estrogen decrease in the perimenopause and menopause, that can go down by about 50% studies show. So it's a big decrease in kind of the powerhouse energy in the brain and all over the body.

So estrogen is quite powerful in things other than just sprouting those dendrites to make synapsis. So you can just see it's got all of these activities in it that really help our brains and our bodies be their best.

– And then let's go into, because you've established, this is really important. So before we skip it, I wanna talk about progesterone because a lot of the emphasis is put on estrogen, but what about the other female hormones?

– So let's think about progesterone and when it comes into play. Now we always have, even men, we have a small amount of progesterone that's made by our adrenal glands, all of our lives.

So there's a small, like a little bit of amount. But in females, the major progesterone, the word progesterone, gestation, gesterone means gestation. It means pregnancy and holding a pregnancy, progestation.

So the function of progesterone is to maintain a pregnancy. So of course, now we call day, let's go back to the menstrual cycle for a minute. Day one of bleeding is called day one of the menstrual cycle, so the first two weeks of the menstrual cycle is when the egg is first starting to be developed and usually eight or nine eggs start to develop at the same time.

And they have a little race during those two weeks about which one's gonna be first and which one's gonna be the best and which one's gonna get ovulated.

So all that time in the first couple of weeks of the menstrual cycle is when these eggs are developing and there's lots of estrogen being made in the follicles to help to develop the egg.

So as the estrogen climbs and climbs during those first two weeks, a couple of days before ovulation, you get more flirtatious, more sexually. It has a lot of behavioral effects in the brain, the hormone of estrogen going way up, but it also makes the egg pop out of its little sac where it's been developing down into your fallopian tube.

And the little sac it leaves behind becomes a hormone producing engine to make progesterone, 'cause it needs to keep progestation. It keeps the whole lining of your uterus really plump and just keeps it ready to be there for the egg in case it gets fertilized.

So it really helps the egg implant if it gets fertilized. So that's what the progesterone is needed for. And that doesn't start until the egg pops out on, let's say day 14 on average.

So day 14 when the egg pops out is when the progesterone starts to really climb and what's happening in the brain at that time is quite interesting. So those last two weeks of the menstrual cycle, week three and four are the weeks when the progesterone is the highest.

What they found is that all of those beautiful sprouting of all the dendrites and synapses in that big forest, the estrogen has like fertilized to grow.

Progesterone actually about three or four days after it starts pumping out, it actually acts a little bit like weed killer or Roundup. And all of a sudden, it shrinks back all of this overgrowth.

So it comes in and it prunes everything back a lot. So you can just imagine about all this action that's taking. If you lift up the hood, look under the hood into your brain, this is what's going on on the weeks of your menstrual cycle.

The last two weeks is when all of those little synopsis and branches are being cut back and the weed color is being put on. So progesterone has that effect in the brain, which doesn't really have that much to do in some ways with our fertility and what's going on in your uterus, getting ready for the implantation of the egg.

And remember, the last couple of days of the menstrual cycle right before bleeding starts are the days we call the PMS days. In my clinic, we always call it the crying over dog food commercials days, (Dr. Brizendine laughs) which is the sensitivity that the decrease, it drops quickly.

Progesterone drops like a rock or like taking a table cloth from a table and just yanking it out. It drops very quickly and it can make your brain more tearful.

It acts a little bit like, you know, Valium in our brain, progesterone dies. And so when it drops quickly, it's like you're in withdrawal. You're in progesterone withdrawal, makes you more irritable, more easily angered, more tearful, just your emotion increases.

And I don't think that there's anything useful that Mother Nature made (laughs) it to happen like that. But anyway, my clinic is certainly full of my wonderful patients who suffer from things like bad PMS happens at that time.

So that's kind of a just an overview of what happens during our fertility years. – And then with menopause, what changes as progesterone drops, as our ovaries are less able to produce that adequate progesterone?

– So of course what happens as, (clears throat) so we are born with about a million eggs and then actually they start dying off from right after we're born.

When we're little girls, we're losing a whole lot. By the time our period starts, we actually lost half a million eggs before we even start ovulating them.

So that's just kinda the way it works, but our 1 million eggs are issued at the time of birth. And then by the time of menopause, you'd like run out of your eggs.

So that's kind of the time that the eggs have stopped. And why that's important is that as the eggs start to become running out and less of what we call viable, 'cause they have maybe too many mutations, you know, women in their 40s have babies with more birth defects.

You all, everybody knows that.

Progesterone, PMS, and the Menstrual Cycle

So the reason is, because there's a lot of mutations in those leftover aging follicle eggs. And as that happens, it's producing the little follicle when the egg jumps out at ovulation, the little follicle left behind sometimes doesn't make quite as much progesterone.

And actually what happens, more and more during the stage of that perimenopausal, the transition of those years between like 45 and early 50s is that many of your cycles don't have any ovulation at all.

It'll start and build up, the follicle may meek some estrogen, but the egg doesn't develop enough to be ovulated. So it's just like, there's no ovulation and we call it an eggless cycle.

The reason that's important is there's no progesterone if there's no ovulation. So that matters because it means that your uterine lining is gonna build up more and more and more and not flush out like it needs to at the end of your cycle when progesterone drops, 'cause you haven't had any progesterone.

So that's why a lot of women start to have really heavy bleeding at the, you know, in their mid 40s to mid 50s during this transition. So progesterones are important.

Progesterone starts to get less and less and less as you go through the transition. – My clinical experience has been that as people transition, mood irritability, and like you mentioned, it's like a drop in progesterone or maybe not even having enough.

And you also mentioned that progesterone can be like Valium, right? (laughs) It helps us to sleep. And so both moods symptoms where estrogen is kind of more that like the hot flashes and maybe the vaginal dryness, the progesterone shows up as that irritability and the lack of sleep, which then of course makes us more irritable when we're not getting good sleep.

So do you see that as well? – Yes. So, the symptoms, I just want this, that's the basic background of what happens in terms of your biology and, you know, progesterone in the brain actually converts into a compound that actually hits the receptors that are like the Valium receptors in our brain.

– The GABA receptors. – The GABA receptors, it hits all the GABA receptors and it metabolizes into a drug we kind of for shorthand, we call it ALLO. So if you have progesterone in your brain, it'll start making this metabolite called ALLO.

That's the one that goes and attaches to all of the receptors that we call your endogenous or your own Valium receptors in your brain. And of course that makes things more calm and makes you much less irritable in the middle of the last three or four weeks of your cycle.

And then of course, when that starts to drop quickly, the ALLO starts to drop 'cause the progesterone is gone, that's when you get the irritability from having a drop in your progesterone.

So a lot of women do a little bit better on a little bit of progesterone replacement during these transition stage for two reasons. One is that you get much more, (clears throat) it modifies your uterine lining and doesn't let it build up so much from just having too much estrogen.

And it also can make you calmer. But there's a caveat to that. A lot of women who come to my clinic, they almost have what we call progesterone X, almost like psychiatric poison.

The progesterone is really hard for them to take for some reasons and it can make them more depressed. That's about maybe a fifth of women, 20% of women have a big sensitivity to progesterone.

So you have to, if it's fair, this is a very individual custom-made one woman at a time, (Dr. Brizendine laughs) you know, helping each woman through their own transition.

– Yeah. I think the theme becomes balanced, right? And in individualization, what's best for you? And I almost imagine, menopause, its transition is like, you're on a magic carpet ride, but the second you figure it out, everything gets ripped out from under you and you have to just like hang on for the ride and be working with a really good clinician who can help you to troubleshoot these symptoms as they keep coming up, whether it's heavy bleeding or hot flashes or whatever comes next.

– Absolutely. So I think that it's important for each woman to have permission. I really encourage women. And like in my new book, in the appendix, I give a lot of like little tips on how to track certain things and how to track things and specific things to bring into your doctor, so you can work together.

You really need what I call a medical partner during this time of your life. You need a medical partner. You don't do this. It's not just any doctor or anybody that does hormones that will do.

It has to be someone you trust as to be your medical partner and to listen as things change, 'cause you know, things can change every couple of months during this time, just because that's what the biology is.

It's not that you're nuts. (Dr. Brizendine laughs) Medical profession doesn't usually deal well with things that change so fast as the perimenopause, menopause transition.

– So let's jump into hormone replacement. What effect does replacing hormones have on our brain? We kind of understand what's happening biologically and symptomatically as the hormones are dropping.

Now, what if we support them? What happens? – So if we are able to give women estrogen replacement, I'll just focus for the minute on estrogen just because we know the most about it.

And of course if you do have a uterus, you have to take progesterone as well during the transition, but let's focus on estrogen replacement. So finding a good balance in your estrogen replacement can be really helpful to your bones, your heart, your brain, your blood vessel, you know, lots of the cells in your body.

And the cool thing about brain health that I love is that if you've got all these other organs functioning well, it always adds to brain health. And even estrogen helps your microbiome in your gut, be at its healthiest with the best flora in your gut.

That is really important also for brain health and keeping your inflammation in your total body down because the brain does not like inflammation. And if there's inflammation in any part of the body, it will feed back to the brain, especially if there's inflammation in your gut.

So estrogen will help with like all of those things. So it's important to remember that that's the good news. And if you're thinking about brain health and cognition and dementia issues, studies have shown that, you know, estrogen does not treat dementia.

Estrogen does not treat Alzheimer's. And that over the age of 60, if you start taking hormones, that may actually make your dementia and cognitive symptoms worse, according to the study.

So if you're gonna take it, it's really important to start taking it during what we call the transition years, between the 40 and 50 group. Remember, 7% of women will go through menopause before age 45.

So there's a whole group that goes through early. So if you're one of those, it's like important to just, you know, it is what it is, and just get help earlier than that.

And the majority of women will go through between like 45 and 55. And then a tail into women, in 5 or 6% will go through after 55. So that's kind of the spectrum of when women are going through this and that's the time, it's not necessary.

As a matter of fact, it's probably, if you're gonna take estrogen, it's not advantageous to wait until you've stopped

your periods to start taking it.

It's probably best to start taking it in the late transition or if you can just kind of think of the bracket of your age group somewhere between 45 and 50.

If you're gonna take estrogen, that's the best time to really take it in terms of your cognitive and overall health. And, you know, that's a tough one because we'll talk about the doctors not wanting to go that direction for various reasons.

Right now, it hasn't become as understood and robust in area as we hope that it will become, right? (laughs) – Right. Well, let's go there because there are a lot of women, certainly who I interact with clinically who have a lot of fear of estrogen replacement.

And a lot of these, I think was from the women's health initiative trial that was ended early. There were a lot of variables there. I think looking back as people have looked at the data again, there are some clarifying assessments that have been made or adjustments to the interpretation.

So would you dig into that? – So let's talk about the WH5 just for a minute, because actually it's 20th birthday just happened. It's been 20 years. And in my book, I go into a little discussion, a short discussion of this, just to help people get a snapshot of what it was, what it is and where we are now, because things have changed a great deal.

So the thing to be remembered is that the women that were given the hormone replacement were an average age, when they started giving it to them, average age of 60, 64.

And remember what I just said about, if you start giving women over 60 hormone replacement, you can actually make their cognition worse, so there's that piece.

But also the women in the study, the divisions of women that got the hormones, actually, there were slightly more smokers in that group, there were more women who already had a heart attack or a stroke in that group.

So the data was really messy. And also very importantly, they did not weed out women that had genetic family history of breast cancer.

Perimenopause and Hormone Decline

So they didn't take the women out with the BRCA, one or two genes that we now know are the one category where we still do not recommend, women take hormones.

If you have the BRCA gene mutation, which means you'll have a 70 or 80% chance of getting breast cancer. There's all kinds of great things to do for that.

And there's the other things we can help you with if you're in that category. So don't worry that there's nothing to do, but other than that, so they didn't take those women out in the study.

So you can see there's all kinds of big troubles with it. And then when they released it, they have a small amount in the women taking estrogen plus progesterone group.

There's a small increase in breast cancer and the media took it and really ran with it, and it exploded. And within a few months, doctors were all, you know, and they immediately alarmed all the doctor and things just shut down, whammed very quickly.

I still remember hearing an interview from the person, the woman that was the editor at that time of The New England Journal of Medicine, you know, was on a radio show basically saying, oh, you know, we just have to stop giving all women this.

And I have stopped taking it myself and it, you know, so it really went down, and by the year 2008, there were only 5% of women taking hormone replacement therapy, where it happens.

– My understanding as well was that, that was not bioidentical hormone replacement. So that's one of the other variables. I'm curious, your take on that.

– [Dr. Brizendine] Yes. – And then also a lot of it was oral estrogen, which it feels pretty clear. My understanding of the literature is that we shouldn't be taking estrogen orally.

It should be topical or through other routes of administration. Is that accurate? – So let's do a deeper dive into the other aspects of that. So the selection of the women, you know, was not a very pristine study, it was a mess.

And if you went to what they gave them, so there's an old-fashioned synthetic progesterone called medroxyprogesterone. And actually it hasn't been given for over 30 years in Europe, they stopped giving it to women of having all kinds of problems.

So that's the progesterone that was given in this combination. So, this thought that that may have had a big factor when giving it also with what's called CE, which is conjugated estrogen.

Also, remember the pregnant horses have a lot of estrogen and that's the major compound, before they knew how to synthesize it, that's where we got hormone replacement, it's from pregnant horses, pregnant mares' urine.

The companies put it in a little pill called Premarin and which still exists today. And it's not a bad thing. It's just that, that was combined with this other thing called medroxyprogesterone.

That combination probably had a lot of nefarious effects in the women that ended up taking it. And some of the results, particularly for heart disease and for the breast cancer seem to have caused a slight bit more.

Now the women only on estrogen, even though it was Premarin, well, the conjugated estrogen, even though it was that estrogen, actually had a less amount of breast cancer in the big study.

So you can see that it was a fairly messy study. I can't say that all the things that had been debunked, but we know much more about it. So the bottom line about the breast cancer now is that if you take the hormones, if you take HRT for 5.6 years, it's how they've measured it so far, they've measured up to their, you only have a 0.1% chance of having breast cancer and that's considered almost an insignificant difference from the other group.

So basically, five or six years of taking it during the transition for your hot flashes, your sleep, your bones, whatever it is. And even for cognition, it's been shown that even if you take it for that five or six years, you will have long term better effects for your cognition.

We don't entirely understand why. So women, it's kind of been expanded to being a nine or 10 year block of time that most doctors are feeling comfortable prescribing HRT to women right now.

Tell me what we missed, anything. (laughs) Did I drop a stitch there that we needed to talk about? – The oral estrogen versus topical, I'm curious about your thoughts there.

– Oh, so important. So important. So like me, I take the patch, I'm on the estrogen patch and I've had a hysterectomy. So I do not need to take progesterone, which I am very grateful for.

So we'll talk about that for just a minute. The patches or the non-oral. So to take an oral pill of estrogen, basically it stimulates your liver and that's not a bad thing necessarily, but it causes it to make all of these, what's called these very sticky big binding proteins that can decrease or change a lot of other, either drugs or hormones in your body.

So something about the oral gives more chance of clots and strokes, at least that. And it will also, because of those big sticky proteins it makes, it'll make your own body's testosterone and other hormones go down very low, even

your thyroid hormone.

So if you're a woman that's taking thyroid hormone, if you start to take oral estrogen, so the pill that was the amount of your thyroid hormone may need to be adjusted upwards because you've got all these extra binding globulins that the estrogen is making.

So the cleanest way to do it is to give either topical, or patch type, or vaginally. There's a few other ways to take it. And even the implants are, you know, anything that's not going through your stomach is considered the safer way to take it at this point in time.

– And so you talked a bit about who should not take estrogen, and this is like a BRCA positive, somebody who's clearly at risk for breast cancer, probably also people who have a personal history of breast cancer.

So if you've already had it, then you wanna avoid taking estrogens. – [Dr. Brizendine] Absolutely. Yeah. – And then, who else can kind of firmly be in the camp?

Like it's just not worth the risk. – So, you know, if you have a clotting disorder of some kind that runs in your family, where you're going to end up throwing clots to your lungs, your brain having stroke, that kind of thing.

If you have a clotting disorder which, you know, doctors don't want, I mean, it's very, very important to not take it if you have a family history or you, yourself are affected by a clotting disorder, it's one of the other reasons not to take it.

Hormone Replacement Therapy and Brain Health

Also if you have different types of cardiovascular diseases, it's good to check with your cardiologist about whether it would be helpful to you. Sometimes, estrogen is very helpful and cardiologists do recommend that their women patients take it for actually being more helpful for cardiac disease.

So it's something that you have to really discuss with your doctor, depending on what other underlying diseases you have. – Like osteoporosis as well.

– Well, osteoporosis is like, it's a miracle. Estrogen builds strong bones, and it's what keeps your bones strong. And there was in the 1980s and 90s, actually that protocol for giving women with thin bones or with age 78, they recommended was the ideal time for women to start taking estrogen to help them have prevention for having their bones considered to deteriorate.

So at 78, it feels like the magical time where you would have the fewest side effects for the most benefit, which was, of course we don't do that anymore, but it just kind of gives you a little snapshot of course, how medicine changes, but that the age at which your bones really start to deteriorate and cause you problems can be in your mid 70s.

But if you've been taking estrogen all along, which I plan to continue doing, (Dr. Brizendine laughs) you know, your bones will stay the healthiest they can stay.

And so I feel very badly for all the women and in the last 20 years that didn't have access to estrogen, that got ripped off their estrogen and now in their 70s have osteoporosis.

I think it's criminal. I feel very badly about that. – They could have been prevented. It's so challenging as a clinician, right? To see like the ramifications of yeah, when things get misconstrued.

So what tests exist? So like how can we, again, you and I are both clinicians, so like, what tests can we run? What labs can we run to understand and help our patients understand where that risk benefit analysis lies for that individual?

– So let's see where we could go with that. You may have something particular in mind, like the APOE4 or the, I mean, just thinking about like if you wanted to do a risk profile for yourself, let's say cognition, and maintaining cognition and preventing Alzheimer's is your goal.

Particularly if you have a family history of it. So if you're in the category where your mother, your grandmother, your aunts, or uncles have Alzheimer's, one thing you might consider doing to help yourself is to get a test for whether you have the APOE4 variant or not.

And I don't recommend that for everybody. And I describe that in my book about who should and who shouldn't, because if you don't have a lot of Alzheimer's in your family, and you're not at risk, getting that test and finding something out that you don't wanna know may not be the best for your brain.

But if you're in the category where you have a family history of it, and you find out that you are APOE4 variant positive, either you have one or particularly if you have two.

About two or 3% of the population has the two, which means you're in the highest risk group for getting Alzheimer's on the basis of your APOE4 variant.

If that is you, and you don't have any other contraindications to taking HRT, taking estrogen, then I would get yourself to a doctor and get yourself on HRT because that's one of the things including, remember, you know, three or four times a week, getting moderate cardiovascular exercise, having the Mediterranean diet with very healthy fats in that, as well as eating the low carbs.

And there's a lot of dietary and exercise getting the best sleep you can get. Remember, sleep is critical to brain function. So all of the other things that you have in your control to do, and this is one of them, even though you get the test and you find out you're APOE4 positive, then you have action that you can do, and one of those actions is to be taking estrogen replacement.

– And then I hear you're a bit cautious about progesterone, and yet progesterone really helps a lot of women get better sleep, which like you mentioned is so critical for brain health.

– [Dr. Brizendine] Yes. So where's the risk benefit analysis from your perspective there? – Well, so the progesterone, you know, so, by the way, a lot of women will get a compounded formula for their cream, for their estrogen replacement.

And the compounding pharmacy will put everything in one. They'll put the estrogen in it, they'll put the progesterone in it. And if you're gonna be on either testosterone or DHA, they'll put that in it.

And those are hormones that will help your, the DHA and testosterone, your muscle power, and also your libido. But they may put it all in there together once.

And you may be slapping it on first thing in the morning. And the progesterone is in that, which may make you a little more sedated, but you would rather have them separated because taking progesterone before bed, and oral progesterone doesn't seem to have much of a problem.

I mean, a lot of women would rather take it on a cream, but it's great to take it at night before sleep, because it will help you get better sleep. It relaxes you and helps you get sleep.

So if you have a uterus, you have to take progesterone. You might as well just take your progesterone as a sleeping pill. So you get a two for one there.

(Dr. Brizendine laughs) – It works amazingly well for so many postmenopausal women, but it sounds like, I mean, you mentioned that you were glad that you didn't need to take it.

So as a clinician, right? I'm learning from you and I don't have the same concerns, but maybe I should. What is the

risk there? – Okay. So remember in the big studies, the estrogen plus progesterone together, those two.

(hands clapping) Taking estrogen alone seems to have more beneficial effects in all the longer term studies, if you don't have to take progesterone. And I think, I don't know what it is in the country at this point, but it's kind of roughly in a lot of areas about 25%, 20, 25% of women that have had hysterectomies, because I had mine because of big fibroids that were pressing on my bladder and it was like, (Dr. Brizendine laughs) you know, it was either get them out soon or have them get too big.

And I got to have them taken out vaginally, luckily. If you don't have to have the abdominal surgery, that's also good. It's just that I think a little bit of progesterone for bedtime and that kind of stuff.

Even for women, sometimes who've had hysterectomies, it can help them, they feel better. – Because what we understood about that increased risks, that was with the medroxyprogesterone, right?

So do we know if the same risk would be there if we're using like an oral micronized progesterone? – So the natural progesterones that we have now available either, you know, by compounding pharmacy or by prescription are fine.

And there's probably a small bump in some correlations with things, but it's very small. So we're not worrying for women who take the, remember, the word bioidentical is an important word to know about.

It basically means that the molecule is the same as the molecule that's made by your ovary, but it's also synthetically made in a factory. So that molecule is synthetically made in a factory and it's called bioidentical, 'cause it's the same exact shape, and as the ones that are made by your ovaries.

So that's what bioidentical means. And of course, when your ovary is making it, you're not taking it by mouth, you're not putting it on a patch or cream, and that kind of stuff.

So the bioidentical is important to remember, that it's not somehow magically made from somebody's ovaries. (Dr. Brizendine laughs) It's made in a factory just like the synthetic ones are, but that synthetic progesterone, the synthetic hormones have a different shape than the ones in your body.

So we really try if we can possibly, and you know, each woman needs to test try these. I've had some of my patients do a little bit better on certain synthetic ones because they're not doing well on the bioidentical ones.

So you can switch back and forth and find out what's worth or best for you, but I think as a kind of a basic approach, I like to start with the bioidentical ones and use it either as a cream or a patch form.

I think that's a much safer way to go, and the natural progesterone of course. – The way I explain it to patients, it's like if you have a cell that has a receptor for those estrogens or progesterones, then if you have the exact same thing sitting down on that receptor site, then we have some way, we can approximate the natural system.

And we can anticipate what the cascade of biochemical events in that cell will be. Versus when we something with a different molecular structure, it sits down on that same receptor site, but it's less predictable in terms of how the cell is going to respond or what cascade or flood potentially of estrogenic events or progestogenic events are going to happen next.

And is that sort of how you think of it as well? – Yeah, the receptors in our bodies, and of course you think about all kinds of other things that we use, like antibiotics, all kinds of other drugs, they're all made to fit certain receptors that we already have.

So even the synthetic ones, you know, will fit certain receptors, but in a slightly different way. But the way to keep balance and harmony in a system at its best (laughs) is to use what's already like, it's already used to, it's already got the receptors for, and you're not gonna jiggle other things.

There's 17 different types of estrogen in Premarin, for example, and the one that comes from the horses. And

there's three in that humans don't even make.

So by taking that, you've got, but coincidentally, some of the doctors who do cognition research found that those three are more powerful for cognition (Dr. Brizendine laughs) in the brain than our own natural ones.

So who knows what the future will hold with that. But yes, you're absolutely right that the receptors that we already have that are made for those, why not just start there and see how you do with the ones that are gonna keep you in the most harmony, the best balance.

– So we talked a little bit about sleep and exercise, but I'm curious from your perspective, what other preventive or brain healthy measures should women be taking as they approach the menopausal transition or even maybe after the menopausal transition?

– So I think, just to pause for one beat on the sleep issue, because I think we can't emphasize that enough. And one of the things to know about that is that we have these really, you know, we used to think that the brain was like mostly made up of neurons and there were more neurons in the brain than anything else, but actually there's a competing type of cell that's actually as many or more than neurons in the brain that are in the category called glial cells.

So they're called astrocytes and microglia. And those are the technical names for them, but they're really important to make friends with these guys because they are the ones that keep the blood-brain barrier intact.

They're the ones that go around at nighttime. So at nighttime when you sleep and this is the issue about sleep. So the cells during the day are all puffed up, they're communicating with each other and the synapses.

And as they're firing, they're making all these sort of gunky proteins, you know, proteins, they're making a lot of trashy proteins, and that's the garbage that needs to get taken out at night when you sleep.

So those cells, the astrocytes and microglia help to garden and clean out those and take out the trash at night. The cells actually kind of shrink back a little bit from each other at night.

And there's this big river of lymphatic tissue of the cerebrovascular fluid that flushes all that trash out when you sleep. So if you're not sleeping, you're not taking out the trash in your brain to have it refreshed the next day.

So I just wanted to really do a deep dive on why sleep is critical to your cognition and to your healthy brain. – And then are you also aggressively referring to sleep medicine and getting people to treat sleep apnea?

– So, so many people end up with sleep apnea, and the combination of drinking alcohol at night and sleep apnea is a very bad combination because I know for myself, I don't do well anymore since the menopause (laughs) with alcohol or at night, because it will actually maybe put you to sleep, but then it kind of wakes you up in the middle of the night if you're drinking alcohol, like say after 6:00 PM.

Risks, Candidates, and Testing for Treatment

So if you're gonna have a glass of wine, do it really early, four hours or so before you go to sleep. Yes. So I'm thinking about that other question you asked, what was it again?

(Dr. Brizendine laughs) I was thinking. – Oh, it was sleep studies, and aggressively treating sleep apnea. – So important because what happens of course is you don't wanna starve your brain at night of oxygen.

And that's what happens if you have sleep apnea. So that's why your throat basically kind of, it closes up and if you're like choking, coughing, or your partner says you're really snoring a lot at night.

If you're a snorer and you really need to get yourself and your sleep looked at and assessed by a sleep medicine or a sleep clinic, because it will end up depriving your brain of oxygen at night, which you really need to have it

rejuvenate.

So yeah, sleep apnea is a very common diagnosis. I don't know how patients with it, but the snoring is the number one, but you know, you don't usually know this, it's your partner who knows.

And maybe your partner's snoring too and they don't know, but there's all kinds of little apps that you can wear now or things that you can figure out whether that you're snoring or not.

And so get it treated because it's such an easy thing to have better cognition if you've got sleep apnea and to get it treated. And then all those little cells and the rivers can flush out all the trash from your brain (laughs) while you're sleeping.

So you can wake up with a refresh oxygenated brain. – We screen essentially everyone in my clinic, if they're having any sort of cognitive decline, because I think we think of the classic sleep apnea patient is overweight and male, and that's part of why they have sleep apnea is because, you know, they were punched in the nose when they were 16.

And so they've got a deviated septum and they're overweight now and they can't breathe at night. But so many of my thin women also have sleep apnea and they don't realize that they snore.

And so just getting that assessment either through a watch or we use watch pad right now, which is an at home sleep study that's relatively good, getting them into sleep medicine, doing what we need to do to really understand if that's part of the equation, because as you said, it's just so, I mean, all of these pieces are critical, but sleep is really critical to getting that good cognitive function back.

And what we see is such great, quick change as well, just feeling rested during the day. I mean, you and I, I certainly can relate to being sleep deprived.

I have a child and like those years of sleep deprivation, when she was a newborn. My brain, I had like half capacity and then getting sleep back like you turn back on.

And so I think no matter what stage of life, we can all relate to that lack of really sharp cognitive function in the morning if we haven't gotten good sleep.

– [Dr. Brizendine] Exactly. – And so figuring out why, and then treating it is so crucial. – My best girl friend and I went to this little store, we went to a spa together and we shared a room.

We did a double room, whatever, you know. And I'd known her for, you know, forever. We did our training and stuff together, and she was from Albuquerque and I'm from the Bay Area.

And we flew together and like, the first night, she's snoring like crazy. And I thought, oh my God, I can't do this for a week. I'm, you know, whatever.

And I didn't have my earplugs with me. I thought, oh my God. And I said, Adrian, do you know that you snore? She goes, really? I do? Bob's never said, I mean, she's been married for 50, you know, for whatever number of years, she said, Bob never said anything about me snoring, whatever.

And I had to get a separate room, but she never knew until that point that she snored. And then she got worked up. And of course, you know, she had the sleep apnea, which is, you know, sometimes you don't know, and your partner, she says, well, he snores too, and whatever, you know, (laughs) so yeah, you may not know.

– And rather than writing off snoring is something that's normal. I mean, this is something that we ask everyone in my clinic is, do you snore? Do you know if you snore?

And at least if you do, don't write it off as normal, make that the trigger that makes you get a sleep study or at least

makes you wear a watch that tracks your O2 sats at night, so that you have a sense of whether or not this is something contributing.

– Absolutely. I mean, that's Cognition 101. So if you do, let's say that you're gonna get your APOE4 variant measured, 'cause your family has a, you're gonna figure out your sleep apnea status, whether you snore or not, get the watch that measures your O2 sats all night long.

Just take a look at that. You know, your exercise and you're eating a Mediterranean diet. You get your microbiome in good shape, meaning that you eat a lot of healthy fibers.

I mean, you don't necessarily need to load up your body with a lot of, you know, fancy, pre and probiotics, unless you've had a lot of antibiotics. For some reason, you need to rebuild it again, but rebuild it with your own diet and maybe taking a few supplements for the probiotics and the fibers may help depending on your individual situation.

So get everything from the inside, out, really buffed up and get your sleep up, and over the counter medications. Can we talk about that for a minute?

'Cause I find, that can be a cognitive killer and people don't realize it because it's not a prescription medication. The doctor, you know, it's like we take them a lot.

You take antihistamines, you can take over-the-counter sleep medications. And you know, Benadryl, let's talk about just Benadryl. And I talk a lot about the Benadryl in my book, 'cause I have had a few patients come in.

I talk about my patient stories in the book and one who came in and she was, you know, she was basically having word finding problems and you know, she was really not following and tracking stuff at work very well.

And also she was in the transition in the perimenopause. And so everything was happening at once. But come to find out, she was taking 50 milligrams of Benadryl in, you know, she was taking Tylenol PM or Advil PM, you know, on a couple of those a night before she went to sleep.

And so, those are what they do. So let's talk about the basics of why those are bad, bad, bad for your cognition. So there's a really important, wonderful chemical in our brain called acetylcholine.

It's a long name, but acetylcholine, (Dr. Brizendine laughs) you should make your friend because it helps with cognition and memory. And any medicines that are what called anticholinergic.

They block that. And so you can't use your own memory neurochemicals for your brain power. So things like Benadryl and the antihistamines, many over-the-counter things.

Look at them, if it has diphenhydramine in it, which is the generic name for Benadryl. Read your labels because it may have something in it that's gonna be causing you cognitive problems.

I don't know if you find that in your practice or not, but I'm just. – Yeah, absolutely. I'm so glad that you brought this up. A lot of people are familiar with the acetylcholinesterase inhibitors when we're talking about dementia.

These are the medications that are typically used by neurology. They're questionably helpful, but basically what they do is they enhance the amount of acetylcholine in those synapses.

So where there's neurons connect. And when we reduce the amount of acetylcholine in the brain, we have, in fact, this is where some of those medications came from, is they were studying people who had cognition issues and what they saw is that they had low acetylcholine.

And so when we maintain more of this in the synapse, you get sometimes an improvement in memory, at least temporarily with those medications. Now, if we are unintentionally doing the opposite, by taking an antihistamine that also has anticholinergic effects, we are reducing cognitive function, especially if it becomes habitual and you're

taking it over and over again.

Sleep, Lifestyle, and the Benefits of Midlife

So probably a little bit less risky than like the benzodiazepines and how they affect cognition, but still an important consideration. So if we can, you know, if our list of sleep support is progesterone, antihistamines that have anticholinergic effects or benzodiazepines, we probably wanna reach for the progesterone if that's an option.

– Absolutely. And I think, isn't it interesting though, how we've discovered, I mean really, Dr. Sandison, we in this area for our clinics find that the sleep issues are the way in which people get stuck on these benzodiazepines like Valium or even the other ones like the Ambien and the, you know, no dozer over-the-counter sleep medications that really hurt your cognition over time.

So it's like a double whammy, you're not sleeping, but you're taking these sleepy medications, you're decreasing your cognition. So I feel like, you know, the real one of the cornerstones of cognitive medicine has to be the sleep assessment in the clinic.

– Yeah. And prioritizing sleep. You know, society is set up to make us overstressed and eating late at night and not getting enough exercise. And then the blue lights, of course, it's easy to watch TV or watch something stressful, the news.

And then we're not protecting the quality of our sleep. So kind of having conversations, like you said, with a medical partner who can help you identify like sleep hygiene strategies and get you that higher quality sleep.

I think again, absolutely crucial. – So yeah, I give a tip in the book on, I call it Louann's sleep program. I give them my own sleep program. So one of the things that I saw basically, you know, you get bright light in the morning when you first get up and you see, I mean, if you really wanna be clean about it, you basically stop using caffeine because that, especially in the female brain, will even affect you 12 hours later trying to get to sleep.

So you get some bright light in the morning, you get a certain amount of exercise before three o'clock in the afternoon where you're feeling enough exercise to make you sort of tired.

And you decrease your alcohol preferably to zero because alcohol with hormones increases your risk of breast cancer just by itself. So that's a whole nother issue.

So if you can drop it all together, that's really wonderful. And you don't take the sleep medications, 'cause those will really mess you up. (Dr. Brizendine laughs) Taking your hormones.

And you know, basically not eating too close to dinnertime is really also important. – There's a bedtime, right? Like allowing three hours between that last bite of food and then going to bed.

– Yeah. I mean, there's a whole lot of things that you can actually do for yourself that you may not be able to do it all at once. I mean, it's a big, it was a real slug for me to get over to the not taking the caffeine, but I had to do it for some, I was starting to have some stomach problems as well.

And so they told me I had to get off the caffeine for that. (Dr. Brizendine laughs) So I actually. – What about a green tea? A green tea or matcha, I feel like every time I read any study about green tea, there's another reason, it's bone health, you know, the EGCG is good for cognitive function.

Do you have any thoughts about, is there some form of caffeine, especially as someone's maybe transition from coffee. – There's about 75 milligrams of caffeine or something in green tea in that kind.

And in a big strong cup of coffee is about 150 milligrams. So it's about half what's in a cup of coffee or something. So, you know, so it's not nothing.

And you know, the issue of like there's a whole lot of areas in cognitive health where they're actually using caffeine, they're actually using nicotine.

Nicotine is one of the best things for cognition that they've used. So, you know, there's some stuff that we kind of think of as being bad, bad, bad that may turn out in a lot of clinical studies to be better.

So I would say, my message to people right now is, do everything that we know now works, but stay tuned because there's a lot coming down the pipe. And the issue of taking estrogen for dementia prevention in women is the jury is still out.

And there's a new big study that just started. And probably in the next four or five years, we'll have some evidence about if estrogen taking it at the transition will help prevent onset of dementia or Alzheimer's.

So stay tuned for that. But right now, we know that it's good for your bones, it's good for your brain, good for your cardiovascular system. And in all likelihood, it's good for your cognition.

– This is so hopeful and you're right, we're at this really exciting time in Alzheimer's research and in women's health research as well, where I think there's a lot of reasons to be very hopeful, and optimistic about what the future holds and what the science holds.

– That's why I call it. That's why I call my book, The Upgrade, because there's so many cool things that happen in your brain once you get out of that cycling hormone thing, and you basically get very consistent and stable.

You get more direct, you can, you know, really embrace your authentic self and really take very good care of yourself. So there's a lot of really good things that come and you start to get more focused, 'cause you discover you can't do multitasking your several things at once, 'cause your brain won't allow you.

So you get really focused and you can become more direct, stop being so much of a perfectionist and a people pleaser. You know, there are lots of really, really good things that are coming on with your brain after 50, shall we say?

So take hope, ladies. Take hope. (Dr. Brizendine laughs) – How exciting. Well, thank you so, so much for being here today. I want everybody to know where they can find your latest book and you're still working as a clinician.

So if someone wants to become a patient of yours, is that an option? Is there an online? – Well, right now, I'm mostly supervising. So I've moved up to the more of the kind of administrative level.

So there are lots of people that are really working in this area and we refer people all the time to, all of my former students. I've in training students for the last 25 or 30 years in the Bay Area.

So there are many of my students that are out there wonderfully practicing in the area of psychiatry. And they've learned about psych, the brain, and hormones in a way that most doctors are not trained.

– And your book is called The Upgrade, and is available by the time this goes live, will be available everywhere. Books are sold. And so head online, and I want to just spell your last name.

So first name is Dr. Louann, L O U A N N. Last name, B R I Z E N D I N E. Dr. Louann Brizendine. And again, The Upgrade: How the Female Brain Gets Stronger and Better in Midlife and Beyond.

So it's such a contribution to what we know and breaking it down so that women understand it in the context of like we've been talking about, sleep and exercise and life and making sure that our brains are turned on for those that sunset of our lives.

– Yes, the second half is the best half. As far as I'm concerned, (Dr. Brizendine laughs) it's really definitely an upgrade. So I'm wishing all the listeners to go out there and get ready for your upgrade.

(Dr. Brizendine laughs) – Oh, how wonderful. Thank you again. – Thanks for having me. (bright music)