



INTERVIEW TRANSCRIPT

DISCUSSIONS WITH WORLD-LEADING EXPERTS

Navigating the Migraine Chaos That Begins During Perimenopause

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Introduction (00:05): Perimenopause and menopause mark one of the most significant chapters in a woman's life. These years are associated with many physical, cognitive, and life changes. And for women with migraine, this can mean attacks that become unpredictable as hormones fluctuate. Many of us feel lost and hopeless during this time, and our symptoms are often not well understood by doctors. Or worse, they're dismissed and we're told it's just part of aging.

Introduction (cont.) (00:36): To help us understand what is actually happening during this time of hormonal chaos and what we can do about it is Dr. Jan Lewis Brandes, a leading headache specialist who is passionate about helping women navigate migraine through every hormonal stage. Dr. Brandes, welcome back to the Migraine World Summit.

Dr. Brandes (00:56): Thank you for having me. I'm delighted to be back.

Wendy Neri (01:00): Well, this is a topic that's very important to many people in our audience, and we do have a lot to cover. So let's dive in. What's happening hormonally during perimenopause, and why does it affect migraine so much?

Dr. Brandes (01:16): Well, the beginning of perimenopause is usually heralded by fluctuations in estrogen — many more fluctuations in estrogen. And we know that during perimenopause, estrogen levels are even higher than they are when women are going through their normal menstrual cycling in their, say, teens, 20s, 30s. When they enter into their 40s in perimenopause, estrogen levels have these fluctuations.

Dr. Brandes (01:44): They're often higher, which means that when they fall for a period, they have a sharper transition. And we know that fluctuation in estrogen has an impact on cortical excitability. So for women who are vulnerable — for women who have migraine — that's a time when those many more fluctuations can exacerbate migraine, leading to more frequent attacks and harder-to-treat attacks.

Dr. Brandes (02:15): And it's interesting, when we think about women, many women in clinical trials have not been separated out. So often in clinical trials, we look at what a preventive drug does, but we're looking at women who are in different stages of their hormonal lives. And so the woman who's in her early 30s — her migraine may behave very differently because the hormonal influence at 45 is considerably different.

Dr. Brandes (02:44): So I think it's really important to think about what a woman's lifetime pattern is and then think about treating her, or at least looking at the hormonal influence on her migraine and addressing what can be treated that is hormonally driven.

Wendy Neri (03:03): OK, so it sounds like it's a matter of fluctuation and not just that the hormone is low; estrogen is low at that time.

Dr. Brandes (03:10): That's right. It's going from high to low, and it's doing it more frequently. So that puts her at more risk for triggering migraine.

Wendy Neri (03:20): OK, and why does migraine worsen for many during perimenopause and then, fortunately for some women, actually improve after menopause?

Dr. Brandes (03:30): Well, it's again that fluctuation. It's the irregularity of estrogen. We know from older studies looking at — Dr. Somerville years ago looked at the drop in estrogen as being the triggering event for menstrual migraine. Well, if you're having repeated drops during perimenopause, that can serve as a trigger. And so women who are having irregular cycles, maybe the estrogen drops enough to trigger the migraine, but not a period.



Dr. Brandes (03:58): Maybe women go for a considerable period of time where their estrogen stays low, then they change. Women are often going on and off of hormonal therapies during that time, sometimes in an attempt to get them under control. I think the thing that is most important to me as I think about working with women who have migraine is to look at the overall pattern.

Dr. Brandes (04:24): Because I think if you look at the overall pattern for an individual woman, that's how you begin to see what their hormonal status is and what you can do that will treat the hormonally driven migraine most effectively. So let's just say if we look at what happens, a woman who has menstrual migraine — we know from a number of studies that those women may be more vulnerable to worsening during perimenopause.

Dr. Brandes (04:56): There's not full agreement on that, but I would say most headache specialists agree with that. But if you look at — some people will point out that when you get to be in menopause and let's say you're not on any form of hormone therapy, your estrogen is low and stable and migraine gets better. Well, that's true for some women, but one may not be in that group.

Dr. Brandes (05:24): The adage about what happens to migraine during pregnancy when the estrogen levels go up and are higher and stable in the second and third trimesters — high estrogen levels — many women with migraine do beautifully in their second and third trimesters. But that's not true for everyone. So I think sometimes migraine with aura starts during pregnancy and it doesn't always start in the first trimester when estrogen is going up. You may see it in the second and third trimesters.

Dr. Brandes (05:54): And for women who have chronic migraine, the migraine pattern may not change very substantially during the pregnancy or it may get a bit worse. So I think that as a clinician, the thing that I think is most important about trying to figure out what you're going to offer a patient, and explain to someone why you've offered it, is to look at what their pattern is. Are they someone who tends to do better with lower estrogen states?

Dr. Brandes (06:23): Are they someone who does better — when I say “better,” I mean their migraine is better — during high estrogen states? If so, that may be the ideal candidate for — if someone is say in their early 50s and they're having vasomotor symptoms, hot flashes, night sweats — that person may do beautifully on hormone replacement.

Dr. Brandes (06:44): If you have someone who always has tended to do better when they were off any kind of hormonal therapy or off combined oral contraceptives, that person may do better in a low estrogen state. So I think we have to look at what the history is. When did they start having migraine? Did it occur around the time of menstruation? What happened if they went on combined oral contraceptives? Did the migraine get better? Did it get worse? What happened if they went on one of the intrauterine devices [IUDs] that has progesterone? What is that pattern? And did they worsen? If you're dealing with somebody later in menopause, did they worsen if they were placed on hormone therapy? And what kind of hormone therapy were they placed on?

Dr. Brandes (07:33): I think it's one of the — in the Women's Health Initiative, which led to the boxed warnings against the use of estrogen in women and really frightened many women and the clinicians taking care of them, many physicians were reluctant to prescribe hormone therapy for women in general, much less those who had migraine.

Wendy Neri (07:56): It sounds to me like you're saying that when you're talking about the overall pattern, that we're looking at: How did they do during menstruation? How did women fare during pregnancy? And then that could tell us how we may do during the later stages. Is that correct?

Dr. Brandes (08:13): Yes, that's exactly right. And I think the important part of that is not only to track it, but [that] how one did in those various stages of one's reproductive life may be the key to



offering the appropriate or the most effective hormone therapy for an individual who has hormonally influenced migraine.

Wendy Neri (08:35): I know from experience that there are many overlapping symptoms between perimenopause, menopause, and migraine, such as hot flashes, anxiety, disrupted sleep, brain fog — that's a big one. How can we tell what's migraine, what's perimenopause, and what's both?

Dr. Brandes (08:56): Well, I think one of the things that's really important is to remember that typically migraine attacks are four to 72 hours. Now, in someone who has high frequency chronic migraine, there can certainly be a blurring of that. But there should be some interictal periods — or some periods between attacks typically — where you really feel normal, where you get back to normal.

Dr. Brandes (08:25): And when that begins to blur with, say, brain fog, that may be a time to really think about: Is there something else going on? In my experience, two of the things — I would say three of the things — that we find as the first harbinger of perimenopause, one is sleep disruption.

Dr. Brandes (09:48): So women with migraine who may have been sleeping fine, they may have been doing very well — all of a sudden they wake up at 2 o'clock in the morning and they can't get back to sleep. And sometimes vasomotor symptoms are part of that. Another thing that can happen to these individuals is that they have a marked exacerbation in their migraine frequency. Sometimes it's frequency and severity.

Dr. Brandes (10:14): Sometimes it's just frequency. So when I see someone who's, let's say, 40, 43, 44, who's been doing beautifully — they're responding to their acute medication, they're not having many breakthrough attacks, they're doing really well and they feel good about their control — and then you get a call and they say, "Can you please see me? Because I don't know what's wrong, but my migraines are just out of control."

Dr. Brandes (10:39): The first thing I think that one should think about in that sign, you have to think about, obviously, other secondary causes for headache. But perimenopause is a secondary cause for headache intensification and in increasing frequency. And then I'd say the third thing that we have seen in our group is that we see a lot of vestibular migraine presenting then.

Dr. Brandes (11:02): So women who start having dizzy episodes, sometimes that vestibular component or vestibular migraine is the first thing we see as someone enters perimenopause. So yes, you're exactly right. The traditional things that we associate with perimenopause: vasomotor symptoms, hot flashes, night sweats, sleep fluctuation, disinterest in sex, lack of libido, energy levels not being what they have been in the past, fatigue — all those kinds of things. And so again, it's important if someone enters perimenopause to be working with somebody who's going to make sure: Is there an issue with one's thyroid, or is someone anemic? What are those other things that can cause some of those symptoms? But if it's also accompanied by changes in menstrual cycling, that may be a key. And so one has to really look at all those patterns.

Dr. Brandes (12:00): But I would say that, in general, the pattern of migraine — with the exception of vestibular migraine — in my experience, the pattern of what happens during an attack really doesn't change. If you had brain fog before you had perimenopause, you're likely to continue to have it. But when you start having a big change in terms of some of those symptoms during your 40s — because that's when perimenopause typically begins — then it's important to try to separate out what's happening with the headache and what's happening with these other symptoms.

Wendy Neri (12:39): And are you saying that even if a woman just has migraine and then perimenopause comes along, could they possibly start experiencing vestibular migraine for the first time?



Dr. Brandes (12:51): Yes, they could. So the pattern of migraine can change. Sometimes women begin having aura when they enter perimenopause. The pattern of migraine can change. Again, there are not any really large studies that I'm aware of looking at specific changes in migraine. Most of the time, what's measured in studies is really frequency and severity, and quality-of-life questionnaires are typically used in those kinds of surveys. But I think one of the issues that we see in a lot of the studies with perimenopausal and some with postmenopausal women is that a lot of those studies are relatively small or they're taken from large databases where whether someone has migraine or not is self-reported. And not everybody really is fully aware of what constitutes a migraine attack.

Dr. Brandes (13:56): So you have a lot of people in those databases who may have had other bad headaches that may not be migraine. You may also have women who've had a history of migraine, but by the time they enter into the study, by the time they're part of that database, they've kind of forgotten about those migraine attacks. They may never have been diagnosed as migraine attacks, but they actually have migraine.

Dr. Brandes (14:14): It's the genetic migraine that we just don't understand completely in terms of the role of estrogen and its impact on women who have this genetic disease or this genetic condition that we know as migraine. So there is a lot of information that gets put out about how everybody gets better during menopause or everybody gets better during pregnancy.

Dr. Brandes (14:44): But what we really could use are some studies that follow clearly well diagnosed, or correctly diagnosed, or International Headache Society [IHS]-criteria-diagnosed migraine — women with migraine — and then follow them over an extended period of time. So there are some newer studies looking at, again, data banks that are in the thousands; then you have data banks that are in the hundreds of thousands. But what happens is that you don't always have the same clarity of diagnosis for all of those women.

Dr. Brandes (15:17): So that's why I think going back to an individual's pattern and then trying to take the data from the largest trials, the best-done trials, the trials where people have really looked at trends [is important]. Now, smaller trials are very important for trends — they tell us things. One that's been done at Vanderbilt recently was looking at a large database to see if there was any reduction in stroke risk if younger women under age 45 were treated with conventional migraine-preventive therapy.

Dr. Brandes (15:48): And they found that propranolol was the one drug that seemed to lower risk for stroke. So that's a big compilation. It's not a huge database, but they've looked at that. So that's a trend that we should think about and that we should design future trials around. But I really would caution anybody who has been told, "Your migraine is going to do this or this or this" — I usually say that migraine does exactly as it pleases. And it's our role as clinicians or our role as migraine patients to try to help figure out: What is our pattern truly like, and how can we partner with somebody who really wants to help us address that component of migraine treatment?

Wendy Neri (16:39): Let's focus on the biggest topic that's at the center of these life transitions, and that's hormone therapy, or what used to be called hormone replacement therapy, or HRT. First, what is the primary goal of using hormone therapy for someone with worsening migraine during these years?

Dr. Brandes (17:00): Well, during perimenopause, it may be to stabilize that estrogen fluctuation. So during perimenopause, that may be an important component. I mean, that doesn't mean that someone doesn't need to be on regular preventive therapy or prophylactic therapy for migraine. But that may be an important way to address it.

Dr. Brandes (17:23): So if someone still needs contraception, it may be that a continuous combined oral contraceptive pill is a really good choice for stabilizing the levels and for ushering someone from



early perimenopause into late perimenopause. That's particularly true if someone needs contraception. A common cause — or I should say result — in one's 40s for late pregnancies is thinking that they've passed into menopause, and they really haven't.

Dr. Brandes (18:06): So it's important that women don't just get hormone therapy, that they get what they need for contraception during the perimenopause. So if a woman still needs — let's say she has not had tubal ligation, or her partner or her husband has not had sterilization, then those women will need something like a combined oral contraceptive. Another option may be a progestogen-only pill, and those may be good for certain women.

Dr. Brandes (18:39): Another option may be an intrauterine device, one of the progestogen intrauterine devices that can be placed and left in. Often after women have been on those intrauterine devices, the IUD — for say, in my experience, as early as three months — they may quit having menstrual cycles, which may help the migraine. And then they also have contraceptive protection if they need or want it.

Dr. Brandes (19:04): So there are many different options within the perimenopausal time frame, but the choice often depends on whether they need contraception or not. If they don't need contraception, then that may be the time when women can be offered things that are more traditionally thought of as hormone therapy. If a woman still has a uterus, though, it's important for her not to be on unopposed estrogen or estrogen therapy alone. So if someone still has a uterus, they need to be on estrogen and a form of progesterone. That's really important. And that advice has not changed. That did not change in the recent relabeling for hormone therapy. So if someone is at the end of perimenopause — and we know that menopause itself, really, you're counted as being in menopause when you've not had a menstrual cycle — you've not had a menstrual period for 12 months. So a lot can go on in that.

Dr. Brandes (20:05): And through the years, I've certainly had patients that had 13 months of no menstrual cycles and then in month 14 had one. So yes, that's usually very concerning to them because they think they're getting there and then they're really not there yet. So during that time, if they don't need contraception, that may be a time, let's say, if they still have a uterus, to use estrogen. The form that we tend to use in our program has been transdermal estrogen.

Dr. Brandes (20:36): So we use the combination of estrogen and progesterone. And we tend to use patches. Gels can be used in that setting. I don't use oral estrogen, which, of course, is what was used in the studies in the Women's Health Initiative. I don't use oral estrogen because of the potential effects that it may have on lipid status. So we don't tend to use those. Absorption can vary.

Dr. Brandes (21:04): And the other thing that we don't use or that I don't recommend — there are many different viewpoints on this, so I want to make clear that this is my perspective on it — I don't use implants. We don't support the use of implants because the release may be variable and the levels can have wider fluctuation, which is exactly what you're trying to get away from — to really stop.

Dr. Brandes (21:29): So those are some of the options that are available. As I mentioned, gel. So you could go through various scenarios. But the formulation for estrogen, whether or not someone needs progestin, those can be fairly low. They can be very useful. And now that we see what's really happened, looking at the data over time, is that estrogen provides bone protection. It helps women with bone protection. It can help their cardiovascular status. It can help with probable dementia, as the black box warning for hormone therapy has been removed.

Dr. Brandes (22:09): And it does not play the role in breast cancer that was originally attributed to it. I think probably the most critical thing to think about with hormone therapy is when it's begun. So when is it offered? When is it begun? In the Women's Health Initiative, the average age of women in that study was 63. So those women were well past menopause. And we know that really the optimal approach for using hormone therapy is to start the hormone therapy early.



Dr. Brandes (22:46): Start it maybe in perimenopause, again, if contraception is not needed. Start it at the beginning of menopause, if the patient is a candidate for it — start it then. What we don't want to see is someone started on hormone replacement — hormone therapy at, say, age 58 because they've been off estrogen since they went through menopause at 48. In general, I'm not aware of any studies that show the perfect time if a woman's been off estrogen and she needs hormone therapy. I'm not aware of a perfect time to begin it. I will tell you that in general, we don't start it if a woman has been through menopause and off hormone therapy for a year, sometimes two years. That would be sort of the upper limit. Because what can happen is that you can have plaque rupture in women who've had an advancement in their cardiovascular disease or in their vascular disease.

Dr. Brandes (23:56): And that's what you don't want to see. That's what we did see in the Women's Health Initiative. So timing is absolutely critical. And that's why I'm so thrilled that programs like what you're doing now raise those questions and increase awareness so that we can think about offering women who have hormonally influenced migraine an appropriate therapy early. For some women, it can really help with their migraine frequency and severity. And it can also help with this host of other conditions that women who are beginning menopause begin to acquire or experience.

Wendy Neri (24:37): Rena from our community says that she recently went back on hormone therapy at 72 years old to help with osteopenia and sleep. And she hopes it will also improve her migraine, which started for her in her 40s. So when is it too late to begin?

Dr. Brandes (24:56): I don't think I can give specifics about something like that. I will say that should really be supervised carefully. I certainly understand why it would have been re-offered at 72. And I think I would only use a transdermal form in that setting. I do think there are some concerns about that. So she needs to make sure she doesn't have any clotting disorder and that all of her stroke risk factors are treated. And that will be a way to do it.

Wendy Neri (25:27): Can you clarify the difference between bioidentical, body identical, and synthetic? If we're talking transdermal, are those bioidentical, body identical?

Dr. Brandes (25:41): Many of those are. And I think one of the things that's confusing is there are so many different terms used: bioidentical, body identical, all these different things. Premarin, you know, was made from the urine of pregnant mares. There are lots of different terms that get thrown around. I think working with a clinician, a physician, another clinician, and working with a pharmacist who really understands the forms is key because using something that most clearly represents what the body produces is the aim for most of the synthetic or bioidentical drugs. I think that's what most of them aim for. So it's really important to look at that. And then also to look at how the formulation's been studied. All of those that pass FDA approval have to go through a formal process. So looking at that can make a difference, too.

Wendy Neri (26:43): And then some evidence suggests that taking hormone therapy reduces migraine frequency. But other studies suggest that it can actually worsen migraine. So how do we sort through that confusion?

Dr. Brandes (26:57): That's where I think looking at earlier patterns. So women who did better during pregnancy or women who did better on the combined oral contraceptive, those may be — we don't have the data to prove it, but those may be the women who do better on hormone therapy with their migraine in terms of when they enter menopause.

Dr. Brandes (27:18): Women who did poorly in terms of their migraine on oral contraceptives, or when they were on estrogen replacement during the days of their menstrual cycle to try to help with menstrual migraine, those women may be the ones that really benefit from a low, stable estrogen and may be the ones who get worse when they're offered hormone therapy in menopause.



Wendy Neri (27:47): Talking again about safety. So you mentioned that the FDA removed the black box safety warnings. How significant was that development for the migraine community? And that was removed in November 2025.

Dr. Brandes (28:00): Well, I think it is extremely significant. I think what we have seen is that many women — since 2002 or 2003 — many women have not been offered or have been told not to take hormone therapy after the Women's Health Initiative was posted and all the concerns came to light. I think what we see is that there were a lot of flaws in that study. And rather than taking them and trying to dissect out what that really meant for women with migraine and for women who were trying to prevent any kind of cardiovascular event or cerebrovascular event — since migraine has an association with stroke — we really did women a disservice.

Dr. Brandes (28:52): And I think the idea that it's almost 25 years later before that gets changed — before the black box comes off — it's really unfortunate because that means that many women didn't have the estrogen that might have benefited their bones, that might have benefited their brains, their hearts, and their vascular systems. So I think again what it speaks to is if someone can participate in a clinical trial to answer some of these questions, please do. And if you read about a clinical trial, read it and try to understand as much as you can about it, and ask the clinician who's taking care of you about it because it's important to really understand what clinical trials show. And these large epidemiologic trials, where there is a statistical association, those lump in a lot of different factors. They try to control for them, they try to approach for them.

Dr. Brandes (29:50): But there's a newer study looking at, is migraine associated with more vasomotor symptoms and are vasomotor symptoms more associated with cardiovascular risk? When they controlled for all those factors in women under age 45, they didn't see an increase in cardiovascular risk. Now, I realize some of this may be controversial from what epidemiologists can say about some of the larger studies. But again, look at what goes in. When you put a lot of patients from a huge database in, your data may not be as specific as if you're doing a really carefully controlled trial where the information is collected, gathered data about someone who has migraine or migraine with aura and what it's like over a long period of time. So I think it's really important to think about those issues.

Dr. Brandes (30:43): I think it's been a real disservice to women and to the people taking care of them. And I think the most recent estimate I read was that 50 million women in the United States have lost the potential benefit or benefits that estrogen might have provided them because of this warning.

Wendy Neri (31:06): I see that in people in generations above me — my mom, my mother-in-law — that they've really missed out on things. And they have issues now that maybe they wouldn't have had. The question of hormone therapy for women with migraine with aura is one of the most common we receive. What do we know about migraine with aura and stroke risk? And when would hormone therapy be a definite “no” for someone who experiences migraine with aura?

Dr. Brandes (31:34): Migraine with aura is the group where there is felt to be an increased association with stroke. That increased association is largely in women who are under age 45. Once women move past 50, once they go through menopause, then the conventional risk factors for stroke really come into play. So that's sort of a break point for women. I would say the one thing that's hard and fast is that women should not be on an estrogen-containing birth control pill if they smoke and have migraine.

Dr. Brandes (32:16): And that's even if they just have migraine and not migraine with aura. But certainly, [for] someone who has migraine with aura, estrogen and smoking is a complete “do not do this.” I think that one has to be firm about making those choices. That's a boundary one really can't cross. I think the other piece for me is that, again, if you look at a lot of the information, the migraine-associated risk for stroke is actually fairly low.



Dr. Brandes (32:47): And some of the data comes from older studies where the estrogen — say the birth control, the oral contraceptive pill — had higher levels of estrogen than do most of the current pills, than do virtually all the pills that are used today. So that's something to take into consideration. The European community and, I would say, the International Headache Society have much stricter, tighter rules about the use of estrogen in women who have migraine with aura.

Dr. Brandes (33:17): In the United States, there's more of a tailored approach to that. And it's not a firm and fast rule except for the one I mentioned in terms of smoking. My perspective on that is, in general, when we look at stroke and women who have migraine or migraine with aura, there is usually what I call "migraine plus" — there's something else that is behind that. So it may be very important for women who have that to have a very careful history taken, make sure they don't have a history of clotting or a clotting disorder in their family, and make sure that all their conventional risk factors for stroke are also addressed. I don't have a — the only hard and firm rule I have about that is really the issue of smoking.

Dr. Brandes (34:09): Again, there's controversy about that. Part of that depends on where you live, and part of that depends on the dose, and part of that just depends on your clinician and whether they're willing to do it. But the real risk, and the area where one has to be extremely cautious, is in younger women, ironically. In older women, you want to be just as cautious, but you're typically dealing with things like cardiovascular risk factors. You're dealing with things like, what is their lipid status? Do they have diabetes? You're looking at those kinds of risk factors for stroke.

Dr. Brandes (34:52): None of us want anyone with migraine to have a stroke. But in my experience, I've had three patients under 50 have strokes that were felt related to migraine. And in each one of those, they had an underlying condition. So it was really, again, "migraine plus" — it was migraine plus an elevated homocysteine level; it was migraine plus antiphospholipid antibody syndrome [APS]. There are ways to pick that up and to make that diagnosis so that you can then use the appropriate therapy in those women.

Wendy Neri (35:27): You mentioned vasomotor symptoms. And that is the hot flashes, night sweats, heart palpitations. Are these more common in women with migraine?

Dr. Brandes (35:38): Well, you can read one study that says they're more common. You can read another one that says they're really not any more common in women who have migraine than women who don't have migraine. So I think that is, in my view, sort of up for grabs.

Dr. Brandes (35:53):

I do think that the help that vasomotor symptoms may have is that [they] may point out if someone is also having more severe and more frequent migraine, that may be a tip-off that they're entering perimenopause. And you really have to think about the hormonally driven pattern and how to help someone minimize their headache severity and frequency.

Wendy Neri (36:16): So if someone is experiencing that and they can't take hormone therapy due to having aura or for other health reasons, what are some non-estrogen options to help with these symptoms?

Dr. Brandes (36:29): Well, there are progestin-only pills. There are progestogen IUDs that can be used. And certainly, one of the things that we always want to remember and attend to are lifestyle and behavioral treatments, [or] nonpharmacologic treatments as they're sometimes termed. So being careful about sleep, being careful about hydration, being careful about diet — not going too long without eating.



Dr. Brandes (37:03): Another thing that we sometimes see and that has been raised as a possibility for women who are having a struggle with migraine and menopause is weight gain. Menopausal weight gain is something that many women experience and many women fear. And now it's being emphasized that that may be an important part of why some women worsen because of the pro-inflammatory state that obesity can render one in. So that's another important point.

Dr. Brandes (37:34): But I think it's really important not to shame a migraineur for any of this because all of us try to do the best we can do in terms of nonpharmacologic therapy. But for most people, there may be, in addition to those, some non-estrogen therapies which can really help. And certainly, as we look at the preventives that are used for medication, it may be really important to have someone on a preventive that also lowers blood pressure. So if they have high blood pressure; to make sure that their bone health is addressed. Again, looking at those kinds of parallel issues that women are going to experience in their 50s.

Wendy Neri (38:16): One of our community members, Alicia, said that the challenges of perimenopause are hard to navigate with traditional doctors. And she wants to know what happens when you're not quite ready for hormone therapy and no doctors can seem to tell you how to handle the slight transition before you go fully into menopause.

Dr. Brandes (38:38): I would say the big question there is, does she need contraception? If she does need contraception and there are no contraindications, she might be a great candidate for a combined oral contraceptive. If she's still having periods, not really through menopause, but she doesn't need contraception, she could have an estrogen-progesterone patch. She'd have a transdermal patch. So those would be some of the strategies that I would think about offering in that time frame.

Dr. Brandes (39:11): And I think she brings up a really good point. I think a lot of headache specialists are very loathe to offer hormonal therapies. That's not how most of us were traditionally trained, and so many people are really reluctant to do that. So if your headache clinician is reluctant to do that, it's really important to also have someone who's very up to date on the hormonal components for treating perimenopause and menopause.

Dr. Brandes (39:46): And if you're looking in your region, it may be that someone who's a member of The Menopause Society — that may be someone who specifically looks at that. They're not headache specialists necessarily, but you might partner within that. So sometimes I may have someone who's exactly in her position, and — if I'm not going to give it — then I'll write my recommendations and give them to the gynecologist or whoever the menopause specialist is.

Dr. Brandes (40:12): But she points out a real issue in the United States. We have — it's really hard, I think, to find somebody where you can have that collaboration. But it's critical to doing well for the last half of one's — let's say the over-50 lifespan.

Wendy Neri (40:35): So moving on to practical management and treatment strategies. Do existing migraine treatments need adjusting during perimenopause? What treatments maybe still work or maybe don't work anymore or aren't safe?

Dr. Brandes (40:50): There's some discussion about the use of triptans past age 65. I think that the triptans have been around for so long that those concerns — again, you wouldn't use them in somebody that has known cardiovascular disease or coronary artery disease or cerebrovascular disease. But I think the real focus should be on looking at: Are they on preventives that can mitigate or manage other comorbidities like hypertension? Are they on something that may be helping with sleep and migraine in terms of prevention?

Dr. Brandes (41:32): So I think it's really this selection of the preventive that's important. So if someone can't tolerate some of the conventional — the older conventional preventive drugs, then they



really should be offered the calcitonin gene-related peptide [CGRP] monoclonal antibodies, of which there are four now. And those drugs do not show — they've not been specifically studied in perimenopause or in menopause. But they don't appear to have any hormonal worsening in patients who are having hormonal fluctuations who've been in those trials. So I think the real focus should be on just trying to — if you can use one drug to treat two conditions, that's really important. But I think the other thing is to be aggressive about both acute and preventive therapy in migraine.

Dr. Brandes (42:27): And if you can choose something that treats another comorbid, as they're called, or coexisting condition, then that's going to be important.

Wendy Neri (42:35): And that goes for gepants as well?

Dr. Brandes (42:38): Yes. The gepants, of course, have not been studied for as long, but they offer a really interesting condition or an interesting state or development in prevention and acute therapy because some of them have FDA approval for both. So I think they're interesting drugs in that they can flip back and forth for some patients as to whether or not they're preventive or whether they are just acute.

Dr. Brandes (43:07): I think the other thing that's really important in terms of that is being aggressive about treating the underlying migraine and then being attuned to the hormonal influence. Because rarely, in my experience, does doing hormonal therapy — whatever it turns out to be — that alone usually does not treat migraine completely effectively. So you need conventional migraine acute therapy and prevention, usually, in my experience. And then it's the hormone therapy that really gives you the level of control that you want for patients who have migraine.

Wendy Neri (43:50): Well, as I'm sure many who are watching this talk can relate to, these years can also come with other challenges like new health issues, poor sleep, plus increased life stress, job changes, kids going away to college, and aging parents. How do these factors influence migraine? And how important is it to address them as part of a treatment plan?

Dr. Brandes (44:14): Well, I think it's always important to think about these kinds of changes. But what's one to do? We know that stress is a trigger for migraine, but very few people are going to jettison their children because of it. And that's truly a joke. Sometimes there are women who've delayed having children, or maybe they've had to go through in vitro fertilization [IVF], so they're having children in their 40s. And then they have little ones and they're also having to deal with perimenopausal issues.

Dr. Brandes (44:49): Again, I think it really gets back to the stigma that continues to follow many individuals who have migraine. Women who have — let's pick something else — women who have endometriosis, or women who have asthma, or women who have rheumatoid arthritis — they go through perimenopause, too. But somehow stress is the thing that migraineurs are responsible for. So I would say giving women with migraine a real break about the stress component.

Dr. Brandes (45:25): And asking for help when you need it. Having a very supportive clinician. Having a supportive family. Teaching people about what migraine is — that it's a genetic, biologic disease. And it's not different if a mother has, or this young woman in her 40s — the older I get, 45 seems pretty young to me but let's say 45 to 50 — if she has a bad attack, how can everybody pitch in and help get through it? Is she getting the right care?

Dr. Brandes (45:56): So I think one of the things is that we can't completely get rid of stress. And goodness knows, all the things that happened to women, that women had to face during COVID, where they were responsible for many different roles. I think that we have to really try to stop blaming stress as the major culprit. Because there are plenty of women who have equal stress, but they didn't get the gene for migraine. So none of us can control whether we get the gene or not.



Dr. Brandes (46:26): And if we have it, we need to — those of us who have it and those of us who treat women who have it — we need to really think about trying to destigmatize the disorder. It's a biologic, genetic disorder. That's what it is. And it has hormonal influences, and it's not anyone's fault. And it is more common in women, but that's simply because they have the hormonal influence that men don't.

Wendy Neri (46:56): Well, I think one thing women really want to know is, is there a light at the end of the tunnel? How likely is it that migraine will improve or even disappear completely once they get through menopause? And if not, where can they find support?

Dr. Brandes (47:12): Well, I think that some of the older data suggests that for women who go through natural menopause, about two-thirds of them who have migraine will essentially have a diminution in their migraine. A third of women who go through surgical menopause will also have a diminution in their migraine. So I think the chances are for many women that that's what they will experience. If they are on the appropriate preventive and acute therapies and hormonal therapies, that may be vastly speeded up.

Dr. Brandes (47:49): And I would say that's what women really need. I think that one of the ways to go about that is to look at things like the National Headache Foundation's data bank of clinicians who are interested in migraine and treating headache. The same is true for academic institutions who have headache programs. The same is true for American Headache Society membership. So look for people who have those things. And then look for someone who also has expertise in menopause.

Dr. Brandes (48:25): If you find that the headache clinician you're working with doesn't have it, get a partnership. Get a team built around that. And then I think the other piece is, if someone tells you something that you feel is intuitively wrong — like if someone says this is not hormone-related — keep a diary so that you can see. Mark down if you're having vaginal spotting, if you're having vaginal bleeding, or if you're having regular periods. Mark down the days you have your cycle.

Dr. Brandes (48:52): Mark down vasomotor symptoms, or when your sleep patterns changed, or when you have brain fog. And mark down what you took. Did you have a headache? It can be a very simple diary — just zero to 10, put down the highest level your headache reached. And then mark how well what you took worked and whether you treated it. And if you change something hormonally — let's say you're on a combined oral contraceptive and maybe you stop having a placebo week. So you move to a continuous dosing regimen. Mark it. Did that change it? If someone adds an estrogen-progesterone patch, did that change your pattern? So looking at that, because it's very hard when you take that to a clinician, and they're looking at it — that's data. When they look at your data, that can really help them make good decisions and can educate you as to what you may need to do.

Wendy Neri (49:51): And what kind of doctors — what's the best approach to seeking treatment when it seems that neither our gynecologist nor our headache specialist, or the doctor we see for migraine, really understands the symptoms of both? We can track, like you said, but what other things can we do to seek the best treatment?

Dr. Brandes (50:12): Well, I do think that The Menopause Society has members throughout the United States that are certified in the management of menopause. And so, again, partnering with somebody who's interested in headache, who's knowledgeable about headache, and someone who's knowledgeable about perimenopausal and menopausal strategies is probably the best way to do that.

Dr. Brandes (50:39): And then asking questions and continuing, because sometimes someone asks a question and that stimulates a clinician to go look it up or to call somebody or to collaborate with someone else. So I think the old adage about not giving up is really important because migraine, from the time I started treating patients 30 years ago until now, is managed very differently. The principles are the same, but they're managed very differently. And we thankfully have bench researchers who



continue to work on understanding the specific mechanisms that let estrogen have its effect on the genetics of migraine.

Wendy Neri (51:28): And how can we ensure that our symptoms are taken seriously and not dismissed as, "Oh, you're just getting older"? Alice from our community would like to know if you have any advice on how to productively discuss symptoms with healthcare providers.

Dr. Brandes (51:45): I think making sure that it's an appointment that is specifically about migraine and other symptoms. Make the appointment specifically for that; don't add it on to a visit. If you're seeing a neurologist for peripheral neuropathy, don't add it on. If you're seeing a primary care person for hypertension and hyperlipidemia, don't add it on to that visit. Make a specific visit to discuss those issues and explain that.

Dr. Brandes (52:18): And then go with a list and stick to your list with your questions. Try to make them straightforward, short — I'm not very good at that — short and very specific about the questions. I think those things help because they focus. If it's when you go to your gynecologist for your Pap smear, that's not the time to do it. Really a specific, focused pattern — fewer anecdotes, more focus on specific symptoms. And sometimes it's helpful to take someone with you. So if you have a nurse friend, a physician friend, or a PA [physician assistant] friend, get them to go with you. That may be helpful. And then make sure that someone will spend more time with you. I had someone in my family just go for a follow-up visit after treatment for a malignancy and we timed it: 90 seconds. The follow-up was 90 seconds.

Dr. Brandes (53:14): So find somebody who will really — and also, I think using one's intuition — I've used the word intuition probably more than I should, but I do think there's still an art in medicine. Yes, we have to be scientifically based, absolutely. But there's also an art to it. If you sense that someone is not interested in you or doesn't care about you or doesn't care about what your outcome is, that's probably not the right person.

Wendy Neri (53:42): And if you could give one key piece of advice or hope to a woman who is currently in the depths of perimenopausal migraine, what would it be?

Dr. Brandes (53:54): Don't give up. Don't give up. Continue. You can find help there. And again, there are many patient organizations. There are many arms. There's the Association of Migraine Disorders that puts out some really terrific information. Again, the American Headache Society, the National Headache Foundation, Miles for Migraine — there are many different organizations that put out a lot of information about headache and about migraine in particular. So don't give up.

Dr. Brandes (54:28): Because there's ongoing research, as we see from this recent change in the black box warning. The FDA has, after almost 25 years, changed that warning. So we want you to be part of that change. Keep pressing for appropriate treatment that really can help you and can change your life.

Dr. Brandes (54:50): I would just add that one of the joys of taking care of women with migraine is that if you get to see them as young women, women in perimenopause, and early menopause, you can really change the last half of life for them. Because you can treat all these other conditions. And by having migraine — sometimes migraine can mean that you get better care in the long run. That's been missed with this 50-million group, but it's not going to be missed in the future, I don't think.

Wendy Neri (55:27): That's excellent. Thank you. Thank you so much.

Dr. Brandes (55:31): Thank you for having me.