[MUSIC PLAYING]

ROBERT KANIECKI: Well, thank you, Janet. And my thanks to the organizers for the invitation to speak. I was walking over, and I thought perhaps a more appropriate title than the one I picked would be Breaking the Stalemate. Pregnant women with migraine, or with headache in general, often face the stalemate out in the wilds of clinical practice, where the neurologist doesn't know a whole lot about pregnancy and doesn't want to do a whole lot, and the obstetrician doesn't know a whole lot about headache and doesn't want to do a whole lot.

So who touched the patient last gets to decide what the treatment is going to be. Well, I can't do it because you saw the obstetrician last. The obstetrician says, you've got to go see a neurologist. So what we're going to try to do is break that impasse that's out there, and starting with, even, before pregnancy.

So pre-pregnancy. Kind of before, during, and after-- that's the way we're going to approach this. I do not like standing behind a podium, but because we're being filmed and this is the only microphone-- you guys can hear me OK? This is the only microphone we have, So we will be standing here for a moment.

So I have some questions for you. First, what is this? Exposure during pregnancy to which of the following agents is associated with fetal congenital heart defects? Is it A, topiramate, B, sumatriptan, C, magnesium, or D, butalbital? So if you want to take a mental note, or because I'm going to give you the answer right away, you have to pay attention to find out what the right answer is going to be. But there are your four answers. We're going to have several other questions.

Number two. Which of the following clinical features provide the greatest risk of a secondary headache presentation during pregnancy? Is it the presence of hypertension, the absence of a prior headache history, seizures, fever, or an abnormal neurological examination? That's a hard one, because you think all of those would probably be connected to a secondary headache, but which one is most likely?

Next. 23-year-old woman in her early third trimester presents with progressive daily headaches for six weeks. She has papilledema on her exam, but her physical is otherwise normal. What's the next most appropriate step in management? Is it head CT, lumbar puncture, brain MRI, or acetozolomide?

Next. 25-year-old woman is nursing, but requires migraines prevention. Her migraines are very frequent. Which of the following agents is most appropriate? A, atenolol, B, topiramate, C, metoprolol, D, sodium valproate?

So hopefully, food for thought as we move forward. Let's talk about pre-pregnancy counseling. So this is ideal. This is when we get to talk to the woman who is thinking about pregnancy, a woman who is saying she's coming off her contraceptive, those who we are embarking upon even the initial conversations about migraine prevention in somebody of childbearing age. So where do we start?

Well, obviously, we want to begin with everything you can do to help yourself. This is risk-free. Now, you might get sore muscles from exercise. But that's about the only trouble you're going to get. Maybe too much magnesium might give you diarrhea, which is another issue. But overall, the natural approaches that we take in migraine prevention are actually very well-tolerated.

We might have to adjust some pharmacologic measures, right? Some of the medicines we are using in some of these patients may not be appropriate for pregnancy in the first trimester. And finally, we need to talk about a couple of things. How does pregnancy affect your migraines? But even more importantly now, as we're seeing increasing evidence, we need to talk about how migraine affects the pregnancy. And is it a risk?

So this is what we do. I don't care if before, during, or after pregnancy, these tenets hold very well. So schedule regulation. The migraines suffer. The migraines brain does much better when it's regulated-- strictly regulated.

So the sleep pattern. Now, this is hard, because often early in pregnancy, or even later there, is a fatigue factor, and naps are often very, very desirable. But the migraine brain prefers you to just keep a stable pattern of sleep. So if you need more sleep, try to get more at night, and sleep the same number of hours per night. Doesn't have to be at precisely the same schedule, but try to sleep the same number of hours.

Screen exposure becoming a bigger deal than it was 10 years ago. And so we advise patients to have their night settings on their tablets, on their phones 24/7. This is probably good rule, again, for all migraine sufferers.

So the blue light, the blue frequency, is clearly more stimulating to the brain. That's why it keeps people up. That's why you turned your night screens on, for those of you who do night screen exposures. So the migraine brain is even more sensitive to that blue light. So if you can just turn it off, that's great.

Eating frequently, small portions. Hyperemesis or nausea early in pregnancy gets in the way of this, but other than that, the control of nausea is actually going to be very crucial. It's actually been shown to be an independent risk factor. Pervasive nausea is an independent risk factor for the conversion of somebody with episodic migraines to convert to chronic migraines, which is nothing we ever like to see. So control of nausea is very important-- not only at this time, but anytime throughout the pregnancy course.

Exercise every day. And it doesn't have to be anything strenuous. Simple walk works. So 30 minutes of exercise.

Hydration. Americans don't drink enough water. We drink a lot of coffee, but we don't drink a lot of water. So water intake should be two to three liters-- so 60 to 100 ounces in the average person. Minimize your caffeine intake. Probably 12 ounces are OK, but other than that, you want to avoid it. Regulate your school and work attendance, and then finally, avoid triggers.

Now, what about magnesium? What about supplements? Well, this is what we usually do. We advise magnesium 500 milligrams per day, and typically, the version of magnesium, patients get tied up. Which one's the best? What brand is the best?

Well, the glycinate and the gluconate and perhaps the citrate are better than the oxide, just in the way they're absorbed, but there's a question mark about magnesium, right? There's been recent data with magnesium sulfate delivery. High doses of magnesium sulfate resulted in bone mineralization in some babies.

So the question is, is magnesium safe at high dose? We know that the IV high dose late in pregnancy was problematic, but we don't know that a standard 500 milligram dose is problematic. So right now, the jury is still out, but I would say that magnesium is probably as safe or safer than most of the medications we could have introduced, so we might as well go there.

Neurostimulators have not been adequately studied at this point. There are a number of them that have been released for migraine and cluster headache, but at this point in time, whether it's the supraorbital stimulator or the non-invasive vagus nerve stimulator or the single pulse transcranial magnetic stimulator, none of them have enough data to say. But they appear to be safe.

Relaxation therapy. Biofeedback's great. We have the shady side group, the complementary health group that can help us with this. The problem with most of these is time commitment and dollar commitment, because insurance doesn't cover it very well. But these natural approaches have clear evidence that they work in migraine. So simplistically, going maybe even to YouTube and finding out how can you best meditate, pray, find ways to wind your nervous system down.

Then we work on the drugs. So a pre-pregnant conversation includes the risk factor, right? What do we know about the acute medications you're going to be using, what do we know about preventive medications? And then some procedures we could do.

So here are the acute medications. So this is basically pre and during pregnancy, right? This is what we need to talk about. What can we use?

And we've got acetaminophen, which is category B, and in a sense, is getting a little bit more of an asterisk, because there has been some questionably good evidence that acetaminophen may result in attention deficit disorder development in. Children if you are exposed, I think the cutoff was 28 days in the pregnancy. It's not a lot. But the studies are very poorly done, so this is not conclusive.

And although, right, this is an outdated scheme. In 2014, the FDA kind of dumped this lettering, BCDX system, and went more to a quantitative-- in a sense of sense of, this is a quantitative listing, or a hierarchical listing. But unfortunately, we still, even with the new labeling, there is no yes or no. That's right. You don't have the yes, this is safe to do, or no, it's not safe with a lot of the information we have available. So acetaminophen looks about as good as it gets.

Ibuprofen-- some books would still like to call it B in the first two trimesters. Most often, I think it's listed as C. And then you'll have late D in the third trimester because of patent ductos arteriosis.

Aspirin-- high-dose aspirin is a D. But not low-dose aspirin. In fact, there was a big study of low-dose aspirin recently for preeclampsia. It was published in the New England Journal in 2017. It was 150 milligrams of aspirin delivered throughout the pregnancy, and it was shown to be completely safe.

Now, the population-- the entire study, it's an easy number to remember. 1,776. So I don't have, necessarily, a mind for that particular trial, but I do remember that number. So 1,776 women in this study, and show no safety concerns. And actually, a reduction in the high-risk population for preeclampsia, which may be covered later in this program, saw that it was helpful in reducing the rate of preeclampsia. And also safe. So that's 150 milligram dose. So a baby aspirin or a couple, probably OK. Half an aspirin is probably not a bad deal.

Then you see otherwise, the triptans are C. We're going to talk a little bit more about sumatriptan and triptan data later. OK? We'll get details on that, because I want to give you the update on those, and you can see the other agents on there.

Preventive medications. Boy, we'd love to have a B. Well, I guess you could put now, in a sense, think about aspirin in low dose as a B. Or as close as it gets. Maybe a C-. No, C+. We got to get closer to B. So a C+ plus or a B-.

So high-dose aspirin? No, but maybe moderate dose aspirin. And then, also, there's recent evidence on the beta-blockers, that they're actually probably safer than we thought. And that was a study published by the Europeans in 2017 that showed, you know, looking at all the data, beta-blocker use during pregnancy does not appear to be problematic. So the beta-blockers, and particularly propranolol and metaprolol.

But you see atenolol listed there as different. So there's something-- and it's just a matter of the data that's out there. But atenolol gets a different label, and so it's going to also get a different label when it comes to lactation and nursing. You'll see later.

What about other things that we can do? Well, this is what we like to do a lot. And so two years ago, when I gave this talk, it had a lot to do with all the bad things that happen during pregnancy, and try to distinguish the bad from the benign, which we'll hit the bad things shortly,

But I want to make this more practical. And one of the practical steps that are really helpful is that top one there. We have the pericranial nerve blocks. So with lidocaine-- not bupivacaine, which is category C, but lidocaine. Imperipheral nerve blocks receives a category B rating. And these are done differently by different specialists, but they're very easy to do, and in fact, later this month, we're going to train all our residents to do the program that we apply, the protocol that we use.

But basically, as we use pericranial blocks. As opposed to just calling it occipital nerve, blocks we call it pericranial blocks, because we don't just block the occipital nerves. We go after the supraorbital, the supratrochlear, the zygomaticotemporal, the auriculotemporal. So all these-- not the cranial nerves, but the pericranial nerves.

And they seem to last for weeks to months. Much longer than the duration of the benefit from the anesthetic, right? The numbness wears off a few hours. But the benefit of the block can last for weeks or months.

And this is very helpful. So we'll do these serially, and sometimes once a month, sometimes once a quarter, for women through their pregnancy. And sometimes we'll start it off beforehand. We need to take you off prevention, we need to take you off topiramate, what we're going to do is do this.

The only issue sometimes is coverage. Aetna doesn't cover them at all. You have to go through a lot of steps, and really, usually dead ends. And United will cover them kind of as trigger points but not necessarily as nerve blocks, so there's some practical approaches in terms of coverage. But they can be enormously helpful, and I would say very, very valuable to learn.

Botox, or onabotulinum toxin A is a really big molecule. And we don't really think it gets across the placenta very well. There's not a lot of data out there. The data that it is out there suggests it is not a significant risk, but you see the numbers are low in the trials and the studies. And the data is generated not from headache, necessarily, which is lower doses than other areas, of which would be, for example, spasmodic torticolllis, some of the movement disorders.

So it's a potpourri of dosing in the reports, where you're seeing the end of 232. But there is evidence that seems like basic-- and even theoretically, it may be safe. But right now, it still carries the category C.

And the new monoclonal CGRP receptor and CGRP antibodies that are now hitting the market-- the first one was approved just three plus months ago, and we expect to two more and a fourth one sometime in the next year and a half through the FDA. This is a new wave of very effective migraine preventive medications used via injection.

And they are also very big molecules. So we don't have a lot of data in pregnancy yet, but because of their molecular structure and their size, it's quite likely that they are going to be safe during pregnancy. Right now, again, listed as unknown risks.

So those are the medicines we're using pre-pregnancy, and trying to transition from tougher ones to easier ones once we get towards the pregnancy. Let's talk about those. So as I said a couple of years ago, we focused a lot on the right-hand side of the slide. Secondary headaches, bad things. And I'm not going to go through. We have lots of cases that we did when it was kind of fun.

But really, what you need to know is not the encyclopedia of all the bad that can happen to pregnant women. Nor do they need to know, mind you, of all the bad things that can happen. But we need to know how do you recognize that something bad might be happening. Right? So that's what I want to do, is kind of focus more on that. Instead, it's the red flags.

So these are true. Headache? Red flags, whether you're pregnant or not. All right? This is we call the nasty nine, I like to call them nasty nine. So the first, worst, abrupt onset headache. These thunderclap attacks are obviously very worrisome to anyone who has them, and to the clinician included. So kind of a no-brainer.

But the number three. Because headache people-- headache women-- who get into pregnant states will say, my headaches are changing. Now often, that's for the better, and we'll discuss that. But sometimes, it's not necessarily for the better. They'll just say it's different. It's longer, it's stronger. I got aura for the first time.

So where do you start to worry? It's of progression or fundamental change in pattern is a red flag. When the woman says, this is new or different, take that very, very seriously. And then also, postpartum. This is new or different. Yeah, I have migraines, doc, but this one's different. It's not like my regular migraines. All right?

New headache and under 5 or over 50, well, typically this is not a population we're talking about today. Maybe a little bit over 50, occasionally. I don't think we're getting any under 5s out there. Not unless medicine has advanced in obstetrics further than I know.

New headache in a high-risk clinical setting. So this typically is listed as cancer, immunosuppression, an immunosuppressive agent, HIV. But pregnancy is a high-risk setting, right? It's a high-risk for a number of neurologic issues.

Headache, with syncope or seizure. These other ones are pretty much no-brainers. Headache that comes on with exertion, sex, or Valsalva. If you got a lot of ones that come on with sex, sometimes you can't get pregnant, so you've got to cover that headache in advance before they get into the pregnancy. Because those, particularly, can be very, very excruciating. Actually, one of our residents just saw one in the past couple weeks, sexually induced headache.

Neurologic symptoms longer than an hour. So this is going to be important. So symptoms longer than an hour. And this is where aura question marks arise in pregnancy. So you start to see, oh, yeah, doctor, usually my vision changes 15 minutes, but now it's two hours.

So where's is the cut-off? The cut-off's an hour where you start to worry. And then an abnormal exam.

Now, I say, new or different headache. 5% of women have a new or different headache during their pregnancy. So this is one out of 20 is going to have that red flag out of the gate. One out of 20 pregnant women will say this. This is new or different. So you already have a 5% rate of worrying when you see a pregnant woman with headache.

Now, acute headaches. This was a study published by Robbins a few years ago. Looked at, OK, if you have a bad headache, and you come to the hospital with a bad headache and you're pregnant, what are you most likely to have? Well, in this study, it was primarily headaches were 65% of them, 2/3rds, and most of those were migraine. Right? Not a surprise. If you're a primary headache person and you're going to come in, it's most likely migraine, and not tension headache.

But secondary headaches. 35%-- so a full one third who came to the hospital for a bad headache had something bad. Now, that's way above the population rate. So if you actually look at all comers to the ED with a bad headache, that rate is 3% to 5%. So there you have again, this is a smaller study than some of these larger ones. But still, it's a big difference from the average secondary headache scenario of 3% to 5% to say it's 35%. And the hypertensive disorders of pregnancy are where you worry.

So which was the answer? When I told you this was one of your questions. What factor is most likely associated with that secondary headache? I bet you wouldn't have picked this one. Maybe you did. Actually, the obstetricians probably did. The neurologists probably didn't. Neurologists probably went with abnormal exam or seizure, or something.

But interestingly, it's hypertension. We got to check the blood pressures every time. Every single time. Every visit. Somebody with headache. And so whether in the headache clinic, the neurology clinic, the primary care office, OB/GYN office, they got to be having their blood pressure checked.

I think this is, for the most part, standard practice. But really take this seriously. The presence of hypertension is actually more likely than these others. The absence of a headache history was actually number two, surprisingly.

All right. So the secondary headaches. These are the ones on the right-hand side we tend to worry about, right? So the vascular disorders of pregnancy. The top three are all that. Intracranial hypertension, idiopathic intracranial hypertension, which actually statistically may be no more common during pregnancy. But we do see it. Is it just a matter of weight gain that kind of tips the balance? So that's something to keep in mind.

We asked the question about the patient who had papilledema. Right? So the answer is going to come up in the next slide. For the patient who had papilledema. In a normal exam, what was our next step? But that's going to come up next.

Tumors. Some tumors grow. Meningiomas, for example, will develop and expand during pregnancy, and there's evidence of perhaps some gliomas do as well. So you have to be attentive to the possibility of tumor. The venous or sinus thrombosis, stroke. Again, a lot of vascular things you see up there. So we're going to have a low threshold for thinking about vascular imaging as we move forward.

So the most appropriate next step in management for the patient who had papilledema, six weeks of progressive headache in an otherwise normal exam, was MRI. So CT, usually, is kind of the first, oh, that head CT. Right? We got to get a head CT first.

Well, head CT is good about ruling out hemorrhage. And that's why you do it in an acute setting. So the Choosing Wisely campaign in migraine, or Choosing Wisely in headache, has suggested that one of the five elements of that is imaging in patients with headache. So if it's acute, CT. If it's subacute or chronic, MRI. So that's the basic rule of thumb. And as I said, you should have a very, very, very low threshold for imaging with MRA and MRV because of the prevalence of vascular disorders in a secondary headache workup.

And obviously, the lumbar puncture in that patient would have been next. Right? We do MRI and an MRV, make sure it's OK. If that's OK, the next step in the papilledema workup would have been lumbar puncture, and then the next step would have been acetazolomide.

So what about imaging? So this was just a study published this year. So to give you a little bit of an update, it was 151 pregnant women with headache, acute headache. 50% underwent imaging. I'm not sure why it was only 50%. But only 50% underwent imaging, and symptomatic pathology was found in a quarter.

So you're seeing a significant subset, whether it's a quarter, a third, of women with acute headache during pregnancy have some bad. And the risk, in this case, of finding something on your scan associated with first trimester headache, the strong pain intensity, the reduced level of consciousness, or a seizure.

A little bit about the diagnostic procedures. For the most part, we're focusing more on MRI than CT, but there is safety data available there in your hand. And then the findings. We get idiopathic intracranial hypertension. So we do do the MRI. Sometimes they are normal.

But they do show some interesting things, and that includes the fact your optic nerve sheath starts to widen. That's the white arrow. The clear arrow the left, top-left, will show the back of the globe being flattened by the pressure up against the optic nerve and the retina, and the partially empty or empty [INAUDIBLE] that you could see with the black arrow. So there are a number of signs of increased intracranial pressure that we can see on MRI that you would not see, for example, on CT scan.

Preeclampsia looks bad, right? I mean, this is-- you want to say that this is just a bad MRI. There's nothing more to say about it. And you have RCVS, which can show vasospasm. So these are vascular disorders. Imaging in pregnancy is crucial to include, because of the high prevalence, again, of a vascular secondary headache in that secondary headache population. MRA and MRV are really widely used.

All right. Well, what about pregnancy and migraine? So migraine affects 25% of women of childbearing age. And although most get better, sometimes the early parts are tough that we have to do. We do have to manage them aggressively. And we'll just go through this. Let me skip this.

So recognizing migraine. These are the criteria in here. The point of this is, don't look for the perfect scenario. Oh, it is one-sided and throbbing, and nausea, and photophonophobia. You're just looking for some of these elements. What you're basically looking for is bad headache that either makes you sick or sensitive to light. All right? Those are kind of the big three. Severity, sensitivity, and sickness. And if you have two of those three, you most likely have migraine.

So there are formal criteria, but don't get hung up on them. And in terms of aura, the only point to make here is that it's not just visual. Well, two points. One, we already made the first, it should be under an hour. Aura should be under an hour. And two, it's not just visual. Sometimes it's sensory. Tingling and numbness. Fingers. Lips. Throat.

So what about the effect of pregnancy on the migraines? So here's pretty much the rule of thumb. If you don't have aura, you're probably going to get better. If you have aura, you might not. Simple as that. OK? So if you don't have aura, you're actually in pretty good shape.

How good? Well, those are pretty good odds when you took a look at first, second, or third trimester, particularly when HCG levels start to drop off. You'll see a change in this headache scenario. Estrogen levels start to climb. And the high estrogen state on a stable nature is usually fairly protective for migraine without aura patients.

But guess what it does? The high estrogen tends to be a troublesome thing for women who have aura. Or this is also the reason we think that aura sometimes happens for the first time.

We already talked about management. So let's get straight to it, instead of natural things. So what do we do? So practically speaking, this is what we do. Acetaminophen, 1,000 with metoclopramide 10, and ondansetron 4. Either one of those. The metoclopramide is much more helpful on the headache side of things than the Zofran or ondansetrn. Although both can help nausea, both are category B, we prefer the top one.

Second-line agents. So sumatriptan. And then prochlorperazine and other non-steroidals and other triptans can be considered. But let's kind of update you on the triptan. First, let's do this.

Emergency department management. I was told that Magee is one of the highest users of acetaminophen IV in the country. So why not, right? So instead of, this is the migraine cocktail without ketorolac, right? So this is the standard migraine cocktail, and you've replaced ketorolac with acetaminophen IV. So 1,000 milligrams of metoclopramide and diphenhydramine and fluids.

But we try to avoid opioids, and the answer to the question of the fetal heart defect was butalbital, [INAUDIBLE] Fioricet. It was published now about four years ago-- data to say that there are congenital heart defects seen in patients, in babies of moms exposed to butalbital. So we tend to avoid them.

Triptans are used commonly. So are they safe? We got 25 years of data. So the triptan registries say probably no problems. This meta-analysis of-- I think it was a total of six studies? Looked at 4,208 exposures. No big deal. OK? So we see pretty good safety data on this.

This is a study published this year. You see 432 pregnant women exposed in first trimester. No problems. Relatively small study. We have another one. Now, not just immediate results, but are there any developmental problems down the road? This is measuring five-year-olds in the population of Norway. So did they have any developmental problems to the age of five? And you can see there that-- well, I'll show you the data. So that's the breakdown. And then there were no neurodevelopmental abnormalities in five years.

But look at this. This was a little sidebar. Triptan-exposed children did have slightly more sociable temperaments. Now, I don't know what that means, but they're nicer kids. So if your moms are looking for nice kids, you just give them triptans. It somehow nicens them up.

And again, we talked about this. Beta-blockers and low-dose aspirin. This is where we now go. Nerve blocks, I already told you about. Sometimes we'll use low dose prednisone to break cycles, category C. And then low-dose amitriptyline.

The antidepressants may be helpful, because if we have partum or postpartum depression concerns, we're going to have to manage that. So then venlafaxine. The problem with baby withdrawal is a big ones. So we tended to lean towards fluoxetine, although its data in migraine is not as robust.

But as we finish the pregnancy part, migraine is a risk factor for problems in pregnancy. And there they are. So the question is now, when we see this state on preeclampsia and aspirin, should frequent migraine sufferers, women who go into pregnancy and continue with frequent migraines, should they be managed with aspirin? Should they managed with aspirin not just for migrant prevention, but should they be managed with aspirin because of line number two?

And then wrapping it up. Postpartum headaches. So is this a big deal? One, within a week of delivering, 40% of women are going to complain of a headache. All right? 10% of these are incapacitating. And the median onset is day two. Oh, yeah, I'm going home. I'm home and ugh, I get this terrible headache.

So just in time for them to call you back. Now that I'm home, day three, four, I need to tell you I have this bad headache. 75% are primary, but a couple studies recently showed that maybe the risk of secondary headache is higher. So we need to be attentive, again-- postural headache is a no-brainer-- but to these vascular disorders postpartum as well.

And then-- well, I'll just skip these, because these are just the cases we did last time. All right. Acute medications. The answer for acute treatment. Ibuprofen over naproxen. I think most neurologists are not familiar with this, that there is a difference in the way those are rated.

And then in terms of the triptan, sumatriptan actually is approved by the American Academy of Pediatrics. The relative infant dose, the amount that actually gets in, is about 3%, I think, somewhere around there, in mother's milk. So it's not a lot. 3% of a maternal dose that's injectable sumatriptan. So not much.

The answer about the lactation question for prevention was metoprolol, because atenolol was also listed, as were topiramate and valproate, but we tend to lean more towards more towards metoprolol. Again, atenolol gets a different rating, both during pregnancy and postpartum. So we tend to avoid in the pregnant woman.

So that's it. I think we're doing questions after both talks, right? All right. So that's it. We'll do questions after Stephanie comes up and does her deal on epilepsy and pregnancy. So thank you so much for your attention.