CURE Webinar
Epilepsy, Pregnancy and Contraception
(Transcript)

Dr. Laura Lubbers:	00:00	Welcome everyone to today's webinar. I am Laura Lubbers and I'm the Chief Scientific Officer for Citizens United for Research in Epilepsy or CURE. I would thank all of you for joining us today. Today's webinar is entitled Epilepsy, Pregnancy and Contraception. Pregnancy and contraception can be a difficult subject for women with epilepsy to discuss with their doctors. However, it is critical for the reproductive health including 1.1 million women with epilepsy of childbearing age. This webinar will focus on the research surrounding epilepsy and pregnancy, as well as provide strategies to help minimize risks for both mother and baby. This is the first installment of our 2019 Leaders in Epilepsy Research Webinar Series.
Dr. Laura Lubbers:	00:51	We are grateful to the BAND Foundation for sponsoring this, as well as the rest of the webinars this year. CURE's mission is to find a cure for epilepsy by promoting and funding patient focused research. CURE's robust grants portfolio has led the way to advancing epilepsy research across areas as diverse as infantile spasms, post-Traumatic epilepsy, Sudden Unexpected Death in Epilepsy or SUDEP and genetics. Today's presenter is Dr. Elizabeth Gerard, who is an associate professor of neurology at Northwestern University Feinberg School of Medicine. Dr. Gerard's clinical practice at Northwestern Memorial Hospital focuses on the care of women with epilepsy.
Dr. Laura Lubbers:	01:34	This includes contraceptive and pre-contraception counseling, as well as the management of epilepsy during pregnancy. She is the current site principal investigator of the MONEAD trial, which is a clinical trial examining maternal outcomes and neurodevelopmental effects of antiepileptic drugs. A very important trial in our community. She's also interested in the use and understanding of continuous EEG monitoring in the critically ill and is the site principal investigator for the critical care EEG consortium. Before Dr. Gerard begins, I'd like to encourage everyone to ask questions. You may submit your questions anytime during the presentation, by typing them into the Q&A tab located at the bottom of the Zoom panel and clicking sent. My colleague from CURE, Brandon Laughlin will read them aloud during the Q&A portion of the webinar.
Dr. Laura Lubbers:	02:30	We do want this webinar to be as interactive and informative as possible. However, to respect everyone's privacy, we ask that you make your questions general and not specific to a loved one's epilepsy. I also want to mention that today's webinar as well as all previous and future webinars will be recorded and

are available on the CURE website. So with that, I'll turn it over to Dr. Gerard.

Dr. Elizabeth Gerard: 02:54 Thank you very much. It's a real privilege to be here and giving this webinar. I want to thank Dr. Lubbers for organizing and Brandon for organizing this and inviting me to be your first speaker. It's been really great to work with CURE and the families that are involved in CURE over the years. I'm going to talk today about an area of epilepsy that's very important to me and in my clinical practice, which is helping women with epilepsy understand how epilepsy and their seizure medications can affect them and the reproductive choices about pregnancy and contraception. As Dr. Lubbers mentioned, I have a clinic that specializes on the care of treating epilepsy and women with a lot of attention to these reproductive issues.

Dr. Elizabeth Gerard: 03:44 Just by way of disclosures before this talk, I have given similar talks in China sponsored by UCB to travel there to speak to patients about pregnancy and epilepsy. I've been involved in clinical trials sponsored by Sage Pharmaceutical and Sunovion. And as Dr. Lubbers mentioned, I have research support from the multisite trial with the maternal outcomes and neurodevelopmental effects of antiepileptic drugs, where the lead PIs are Kim Meandor and Paige Pennell. And that is a very important study to the kind of things we're talking about here.

Dr. Elizabeth Gerard: 04:34 So the issues that I'm going to talk about today are ones that are sometimes difficult for patients to talk about with their doctors. And if the doctors don't necessarily bring up this conversation, patients have indicated in prior research that it can be hard to bring up. A lot of patients get the understanding implicitly from either doctors or their family members that they shouldn't really be talking about having children or thinking about having children because of their epilepsy, and so it's really important to get this information and bring it out and have frank conversations with it. Patients may want to know, "Can I have healthy children? Will my seizure medications be okay when I want to get pregnant?"

Dr. Elizabeth Gerard: 05:14 So just a couple of overview points where I always start in my clinic is that for the most part, women with epilepsy should not be discouraged from carrying children because of their epilepsy. The majority of women with epilepsy will have normal, healthy babies and pregnancy and epilepsy, those should be planned well in advance to try to re reduce risks to both mother and baby. It's possible to choose medications with lower risk for pregnancy, and we recommend thinking about that even when

you're a teenager, not necessarily planning your pregnancy, but asking how will these possibly affect a future pregnancy.

Dr. Elizabeth Gerard: 05:50

So what I do in my clinic and what most epileptologists do when they're seeing women who are considering pregnancy is they try to balance risk of seizures with the risk of medications. We all know that seizures can be dangerous obviously to both mother and baby, it can lead to personal harm to the mom. There's a risk of SUDEP for untreated seizures. And so in general, we do feel that it's really important to continue medications for patients who need medications to control their epilepsy. But what are the risks of the medications? What do we know about them and how do we explain them to you? These are the things that in our community we've worked pretty hard on, and I have to say that, although there's a lot more research that needs to be done, we know a lot about the medications that we use to treat seizures in pregnancy, in some cases, even more than over the counter medications, because we've been studying them for about 20 years now in very rigorous ways.

Dr. Elizabeth Gerard: 06:43

So when you do research, you have to focus on an outcome point. So I'm going to talk about the outcomes that have been looked at the most in the research studies that we have. The main thing that has been examined in research studies of women taking seizure medications during pregnancy are major congenital malformations. Major congenital malformations are fetal malformations which affect physiologic function or require surgery. I'll show you some examples of these. These are the best studied outcomes to date. It's important to understand as I talk about them, that these malformations occur in the general population.

Dr. Elizabeth Gerard: 07:16

So people without epilepsy and not taking any medications, also have a risk for these malformations. And we'll talk about how the risk differs in women with epilepsy taking seizure medications. Historically when people first started looking at the children born to women with epilepsy, they focused on what we call minor congenital malformations, just slight irregularities with finger or the face that don't require surgery. These are not common. They've been reported with some of the older drugs, and it's not something that we have a lot of data on, really the risk for this. The new phase of research in the last more like 10 years for women with epilepsy is trying to understand how the seizure medications affect the cognitive development of the children who were exposed to the medications during pregnancy. And so I'll touch on that as well. This is one of the focuses of the trial that I'm involved with.

Dr. Elizabeth Gerard: 08:14 So here's some examples of major congenital malformations. These are some of the more common major congenital malformation. They're not all of them. And when I say common, I don't mean they commonly occur, but of those that occur. One of the most serious ones is spina bifida. Spina bifida is the picture up in the left hand corner here. I don't know if you can see my mouse, but the one up here is a outpouching of the spinal cord. There's a range to the severity of spina bifida. It can be mild and cause neuropathy in the feet or weakness in the feet or it can be more severe associated with brain development abnormalities and many other illnesses as well.

Dr. Elizabeth Gerard: 08:56 Other malformations that we see are abnormalities in heart development. So abnormal connections between two chambers of the heart, which can require surgery. Cleft lip and cleft palate is another malformation that can be seen. These are where the lips did not fuse together completely, or the top of the pallet did not fuse. It can affect feeding. And so these also would need to be surgically fixed. Hypospadias is another malformation. This is in male penises, the outpouching where the urine comes out can be farther back, and that can be fixed surgically as well.

Dr. Elizabeth Gerard: 09:35 Important thing to know about malformations is that if these occur in a pregnancy, they start to occur very, very early. So things that affect the spinal cord, the spinal cord forms 28 days after conception, which is about six weeks of pregnancy. So, that means that when the woman first finds out that she's pregnant any risk in terms of spinal cord development has already occurred. So a strategy, which is, "Oh, I'll fix my medications or change my medications once I'm pregnant," is not a good strategy. Ideally, you want to make any adjustments or any preparations for pregnancy well in advance of the pregnancy.

Dr. Elizabeth Gerard: 10:14 A lot of the data that we have in terms of the risk of seizure medications, in terms of major congenital malformations is from large pregnancy registry. So there are registries throughout the world that have been tracking women who are pregnant over the last 20 years. The one in the United States is run out of Massachusetts General Hospital. It's the North American Pregnancy and Antiepileptic Drug Registry. If you are pregnant, you can self-enroll yourself in that registry at the information that I put there. So this is a summary slide of some of the drugs that we know the most about. I keep track on an annual basis of what these registries are publishing and try to keep track of the risks related to malformations from each of the registries.

Dr. Elizabeth Gerard: 11:04 And the registries don't do their studies exactly the same so there's slightly different numbers in different registries, but looking at them across the board is very useful. Because then you can see what the range is and what you can see for the seizure medications is that consistently valproic acid, which is also known as Depakote or Depakene, is associated with the highest risk of major malformations. So these malformations across the registries, the risk ranges from about five to 14%. So while that is much, much higher than the baseline risk of about one to 3%, it might not be as high as what some people have in their mind, but it is definitely much higher than other seizure medications.

Dr. Elizabeth Gerard: 11:48 Topiramate is a medication that also seems to have an increased of malformations, although the numbers of the individual studies are still smaller. So about three to 9%. Topiramate has been associated specifically with cleft lip, cleft palate, and that's one of the reasons why the FDA gave it a higher rating in terms of risk in pregnancy than other medications. Carbamazepine, we consider sort of a medium risk drug or low to medium risk. And I still think it's a very reasonable option for women who need to be on carbamazepine. And for lamotrigene and Levetiracetam. These are the two drugs that have consistently had the lowest risk in terms of the risk of major congenital malformations. In some studies, not too different from the general population and some studies slightly elevated compared to the general population

Dr. Elizabeth Gerard: 12:41 For most of the seizure medications, the recent research is showing that the risk seems to increase the higher, the dose of the medication. Now, dose may not be the main issue. It may actually be people's blood levels, but the information we have available is based on dose. So we try to keep doses lower when we can at a dose that best controls a patient's seizures. Often taking more than one medication during pregnancy may increase the risk of malformations, especially if one of the medications is valproic acid. There's also some recent research from the Australian Pregnancy Registry showing that if Topiramate is part of a polytherapy combination, that that also are two drug combination or three drug combination that also seems to increase the risk.

Dr. Elizabeth Gerard: 13:24 But it's less clear that if all combinations of seizure medications increase the risk of malformations, we used to think that was the case. It's starting to seem that it's really about the drugs that are in the set of combinations. And moreover, very recent research has actually shown that perhaps not only is it the type of drug that's in the combination, but the dose of that drug as

well, that is really driving the risk of malformations. So these are things that we're continuously looking at. There is generally a trend, and we can see this in the MONEAD Study sometimes to use combinations of drugs that have lower risks to avoid using a drug with higher risk.

Dr. Elizabeth Gerard: 14:07 Cognitive development. We talk a lot about malformation risk and in general, guidelines on whether a drug is safe or not when you ask about, for example, Tylenol and stuff, or other things that you might ask about, a lot of it's driven by data on malformations. But of course, parents are also very appropriately concerned about the effects on cognitive development. That's something that's newer to the table, and that has taken a while to get really good studies looking at that. But there have been several good studies recently looking at the risk of exposure to seizure medications and the effect on the cognition of the child who was exposed to them.

Dr. Elizabeth Gerard: 14:41 So again, consistently valproic acid or Depakote has been associated with poor cognitive outcomes in children whose mothers took this medication during pregnancy. On average, there seems to be a decrease in IQ points by about 10 IQ points lower than what would be expected or lower than in children who are exposed to other medications. And there does seem in some good studies to be an increased risk of autism or autism spectrum disorders in children who were exposed to valproic acid in pregnancy. That doesn't mean that if you're taking valproic acid during pregnancy, your child will have autism. The numbers are still low just like the malformation numbers, but there is an increased risk.

Dr. Elizabeth Gerard: 15:23 And these effects on cognitive development do also seem to be dose-related. So we see more of the effect in higher doses. That doesn't mean that there is a safe dose of valproic that doesn't have these risks, but if you do need to take valproic acid, and there are some patients where that is the only drug that works for them, we recommend trying to figure out if you can be on the lowest dose possible. Other drugs and their effect on cognitive development and behavior and autism risk is still being studied. So far IQ does not seem to be significantly affected in children exposed to Lamotrigine or Levetiracetam. So that's Lamictal and Keppra. But there's definitely a lot more research that needs to be done and that's one of the main points of the MONEAD Study that we're involved in is looking at the cognitive development of the children who are on these medications and other new medications.

Dr. Elizabeth Gerard: 16:12

So what can you do to prepare for your pregnancy? Talk to your doctor early on, even when you start taking a medication, even before you're thinking about getting pregnant about how the medications might affect a future pregnancy. If possible, once you're thinking about getting pregnant or even before, change to a medication that's known to have a lower risk of pregnancy. The best medication for you is still the medication that best controls your seizure. So we don't want you to switching to a medicine that doesn't work for you just for the sake of pregnancy, but we definitely want to give a lot of thought in terms of risk reduction and what kind of changes might be made.

Dr. Elizabeth Gerard: 16:47

It is recommended to take folic acid, and the American Academy of Neurology recommends taking folic acid for all women of childbearing age, and definitely when they're planning pregnancy. What is not known as what's the appropriate dose of folic acid. So we use folic acid because traditionally exposure to folic acid has decreased the risk of neural tube defects in women in general. The data for its effect in women with epilepsy taking seizure medicines is mixed. However, there is some nice research showing that it does seem to be associated early taking of folic acid with higher IQs and reduce risk for autistic behaviors.

Dr. Elizabeth Gerard: 17:25

So we do recommend taking folic acid early on and before planning pregnancy. The recommended dose is anywhere between 0.4 to 4 milligrams a day. Folic acid 1 milligram can be given by prescription in the United States, which is helpful because if you tried to buy it over the counter, it tends to be either in a form of 0.4 or 0.8. It will say 400 micrograms or 800 micrograms that's 0.4 and 0.8. So it's helpful if your doctor gives you a prescription. Most epileptologists who work in this field recommend taking between one and 4 milligrams of folic acid when you're planning pregnancy or during early in pregnancy. And most OBs would recommend that as well, and we do also recommend a prenatal vitamin.

Dr. Elizabeth Gerard: 18:12

So what else can you do to prepare for pregnancy? And again, this is a process that ideally starts even years before you plan to get pregnant. But one thing to ask is if you're still having seizures, should you better understand that? Should you do epilepsy monitoring to understand what's the cause of your seizures, are your medications right, and might you be a candidate for actually epilepsy surgery? The picture on the right is a patient of mine who came to me on three seizure medications with frequent seizures, and we worked hard to evaluate her and have a temporal lobe surgery, which was

successful, and she is now doing extremely well with a... now her daughter, I believe is about four and a half years. We just saw her recently and she's part of the study.

Dr. Elizabeth Gerard: 18:56 She was able to reduce down to just lamotrigene for pregnancy and stay seizure free. So by doing that surgery, we wanted to improve the quality of her life, but we also helped her plan a safer pregnancy. Another thing to think about is talk to your doctor about, do you understand the cause of your epilepsy? If you guys are following CURE webcasts and CURE in general, you probably know a lot about the boom in genetic testing that's available for patients with epilepsy and our dramatically increased understanding of the genetics of epilepsy. Adult epilepsy genetics is another focus and area of interest for me recently because of the overlap of what I do here.

Dr. Elizabeth Gerard: 19:39 Not every patient needs genetic testing before they get pregnant and we'll talk about that, but there are a couple of syndromes where it's important for you and your doctor to recognize that understanding whether there's a genetic cause might have an implication for your child and for planning pregnancy. It's important also to understand that most people, these days or a lot of people get offered prenatal genetic testing with a genetic counselor by their Obs, and that is not the same as neurogenetic counseling. So that training, which looks for common diseases that can exist in certain ethnic populations is not the same as genetic testing that focuses on epilepsy or that cause of epilepsy.

Dr. Elizabeth Gerard: 20:22 So just by way of example, the scope of genetic testing for adults with epilepsy is quite large. But this is an example that has compelled me and really started my career focusing on looking at genetic testing for patients with epilepsy. This is a patient, a woman with epilepsy who has periventricular nodule. So if you look at the MRI here, those of you are familiar with MRI. MRI is gray matters on the outside, and this darker color is white matter. This patient has these little nodules that are lining the ventricle, that are not typically there. And that's not a common cause of epilepsy, but we see it in epilepsy centers, not infrequently in women.

Dr. Elizabeth Gerard: 21:05 In some cases, this can be explained by a mutation in a gene called Filamin-A. And so this is an excellent mutation that patients can have and they can pass on to their children. So a woman who has a Filamin-A mutation like this patient, will have a 50% chance of not passing the gene on at all. She'll have a 25% chance of passing the gene on to a daughter who will have similar symptoms to her, and unfortunately she has a 25%

chance of passing the gene on to a boy and in many cases, if that gene is passed on to a boy, it has a more severe phenotype where the child will die during pregnancy or shortly after.

Dr. Elizabeth Gerard: 21:44 This is just one of those cases that really stands out is the importance of you and your doctor recognizing what's the cause of your epilepsy and does it need to be worked up before you plan a pregnancy? These are not common, but it's just important to recognize. For most patients, we can be pretty reassuring about the risk of passing on epilepsy or passing on something serious. If you are the only member of your family who has epilepsy, if you don't have a lot of other abnormalities on your brain, MRI or other things, your risk is probably not that high of passing on epilepsy, and so this is what we know from epidemiologic studies, which look at large groups of people. Some epidemiologic summaries that in general, the risk of epilepsy is about 1% of the population.

Dr. Elizabeth Gerard: 22:32 And the risk of epilepsy in a child of a mother with epilepsy is interestingly between three and 8%. For a reason that they don't completely understand, mothers are more likely to pass on epilepsy than fathers. For a father to pass it on, it's between one and 3%. But in general, again, without other risk factors for a genetic or heritable epilepsy, the risk is overall not that increased. But this is really important thing and where we are right now with genetic testing, an important thing to talk to your doctor. We here at Northwestern are starting a epilepsy genetics clinic to help people try to find the genetic diagnosis for their epilepsy when it's appropriate.

Dr. Elizabeth Gerard: 23:10 Another thing about pregnancy and epilepsy, that's both interesting and makes the management a little bit more complex is that anti-seizure medication levels can drop significantly in pregnancy. This has been best documented with lamotrigine or lamictal. Lamotrigine levels can drop significantly, even in the first few weeks of pregnancy and throughout the pregnancy. It's been shown that if this drop is not recognized and managed, patients may have worse seizure control. Other drugs that have been associated with changes in pregnancy are levetiracetam and oxcarbazepine, Keppra and Trileptal. And these can change significantly too, but it's not limited to these drugs.

Dr. Elizabeth Gerard: 23:50 Doses of seizure medications should usually be adjusted in patients whose levels are falling. So what we typically do is before a patient gets pregnant, we check and establish what we call a baseline seizure medication level in her blood, and set that as a goal level for when she's doing well. And then during

the pregnancy, we'd follow it about monthly to make sure the levels are staying stable and make adjustments if they're not. When I started doing this, a lot of my patients had gotten messages that were interesting. They said that they had been told that they could get pregnant, but they just couldn't breastfeed. And fortunately this perception is changing. But in general, most of us who treat women with epilepsy are very much in favor of breastfeeding even though you need to take seizure medications.

Dr. Elizabeth Gerard: 24:39

Some of the seizure medications do get into breast milk, but there hasn't been any evidence that this is harmful for the baby. And it depends on what medication and how much is in breast milk and it's definitely something to talk to your doctor about, but in the most part, seizure medications are considered safe in breastfeeding and the benefits of breastfeeding, which include better bonding with the infant, decreased risk of diabetes and ear infections, and just in general better immune system, are thought to outweigh any kind of potential risks of the medications being in the breast milk. The NEAD study which is the precursor to the study that I've been mentioning had shown that actually the babies who were breastfed had higher IQs and verbal abilities than children who were not breastfed when they were taking one of these four medications.

Dr. Elizabeth Gerard: 25:26

So I'm going to switch to birth control. One of the things about planning a healthy pregnancy and a successful pregnancy is making sure that you do it when you're ready and that it's not unplanned, but many pregnancies throughout the world and in America are unplanned and that's true for women with epilepsy as well. So some of the questions that you might want to ask is, "What kind of birth control is right for me, and can my medications affect my birth control or can my birth control affect my seizures?" So it's always a good idea to discuss contraception early with your doctors even if you don't need it yet, contraception might be indicated for women with epilepsy for many reasons, obviously, to prevent pregnancy and for some women need it to regulate menstrual cycles, to control acne or symptoms of polycystic ovary syndrome, which can be more frequent in women with epilepsy or to control heavy periods.

Dr. Elizabeth Gerard: 26:16

So this is from the CDC. This is just an overview of contraceptive methods that are available to us, and we'll talk about a couple of them. You can see that the less effective methods around the bottom, which include condoms and barrier methods. These are effective methods, but they are better with other methods alongside them. The next level here are hormonal treatments.

Hormonal treatments fail about 9% of the time on average. On the top is a Nexplanon implant, which I'll talk about in the IUD. There's also surgical options, but those are not reversible. So that's really for people who do not want to have children anymore.

Dr. Elizabeth Gerard: 26:58

So what's important to know is that the majority over half of our seizure medications that we have available are what we know as enzyme inducing seizure medications, and these enzyme inducing seizure medications can make hormonal forms of contraceptive less effective. So that includes carbamazepine, clobazam, eslicarbazepine, felbamate, oxcarbazepine, phenobarbital, phenytoin, perampanel and topiramate. The ones with stars next to them, and oxcarbazepine have research to suggest that the effect is more at higher doses of these medications, and so some people argue that with lower doses, it's safe to use hormonal contraception. And my perspective on that is you're either pregnant or you're not, and so I try to recommend to use additional forms of contraception rather than just hope that a low dose is not an issue.

Dr. Elizabeth Gerard: 27:48

So with those enzyme inducing anti-seizure medications, the following forms of hormonal contraception are really less ideal. So that would be any kind of hormonal pill, hormonal patch or hormonal ring. The shot depo-medroxyprogesterone known as Depo-Provera has a very high dose of hormone. And so the CDC and the World Health Organization think that this is still an acceptable form with anti-seizure medications that are enzyme inducing. Not all of our medications, by the way, are enzyme inducing. The levonorgestrel implant. This is a progesterone implant that gets put in the arm. This one may be okay with enzyme inducing seizure medications. However, there were a few pregnancies reported. The World Health Organization says it should work. Again, I advise caution with that combination. And then we're going to talk about the intrauterine device, which is a highly effective form of contraception.

Dr. Elizabeth Gerard: 28:48

So the levonorgestrel IUD is a little plastic device that gets inserted by a doctor into the uterus. It's appropriate for women of all ages. So we used to think the IUD was just for after you gave birth, but now actually the American Academy of Pediatrics advocates for it as a form of contraception for teens. And so we can certainly use it in women before they get pregnant. It releases progesterone locally. So it doesn't really act like these hormonal contraceptions that affect that throughout the body. And so a lot of times people ask me, "Well, my OB said, I can't have this progesterone IUD because it interacts with my seizure medications."

Dr. Elizabeth Gerard: 29:27 So, that's not true. So we still think that the progesterone IUD is fine if you're taking any kind of seizure medication. It may make your period stop and it can help relieve painful periods. There's three kinds that are available and they can last between and five years. There's also a copper IUD, which has no hormones, and this lasts up to 10 years, but periods often get heavier with this type of contraception. So the intrauterine device, I'm hoping they'll make a purple one like this in honor of epilepsy. It's very effective for preventing pregnancy. It does not however treat symptoms of polycystic ovary syndrome, and it does not protect against sexually transmitted diseases. So people who are using this for contraception should also be using condoms as well. `

Dr. Elizabeth Gerard: 30:12 This is data from the Epilepsy and Birth Control Registry, which is run by Andrew Herzog in Boston. He's been collecting data on patients with epilepsy who report themselves about their experience with different forms of contraception. And so it's a very worthwhile thing to contribute to... What he has demonstrated similar to what you might expect is that the IUD and women with epilepsy has a very low failure rate. He quoted 3%, that's slightly higher than in other women, but this is a self-reported study. There was a medium sized study in the UK looking at this, and the failure of the IUD was just similar to or slightly hired, like 1%, one and a half percent, I believe.

Dr. Elizabeth Gerard: 30:58 Barrier methods like condoms were exactly what we would expect. Just like in the general population, about 12%, but the effectiveness of hormonal contraception was lower than you would expect and women not taking seizure medications and not too different from the withdrawal method, which we know is not very effective. So what to know about birth control and seizure medications? Most seizure medications can make hormonal forms of contraception less effective.

Dr. Elizabeth Gerard: 31:25 Again, that's not all. It's more than half. There are seizure medications that are not enzyme inducers and are fine with hormonal contraception. But when we actually looked in our group, one of the things to think about is that as you start your treatment plan with your doctor, your medications may change several times. And so we found that the majority of women in our clinics that we followed, even though they didn't start on a medication that would make hormonal contraception less effective, they often ended up one that would interact with it. The other thing to know is that hormonal contraception that contains estrogen can make certain seizure medications less effective. So this is a letter from a patient who contacted me. She was a patient who started having epilepsy as a teen, and

she was doing very well, when she finally got to a good dose of lamotrigene that was working for her.

Dr. Elizabeth Gerard: 32:20 And then when she went to college, she was started on a birth control pill, and after that she had three seizures. She had just gotten her driver's license and so this changes thing, she asked her OB at the time and her neurologist, if it was the birth control pills and she was told no. So it was actually her initiative to say, "I think there's something here." And she found me based on a podcast like this, I had done many years ago and said, "I think there's a connection here," and she was absolutely right because the birth control pills had essentially cut her lamotrigine levels in half. So it was as if she was taking half the dose that she was taking previously.

Dr. Elizabeth Gerard: 32:56 So lamotrigene can actually affect birth control. I didn't put it on that original list. It's a very mild effect. It only affects the progesterone component of birth control, but that is one thing to be aware of can make that less effective and birth control affects lamotrigine. So in summary, we just talked about that, that birth control methods that contain estrogen can lower lamictal levels. If you start any of those methods, while on lamotrigene, your doctor needs to know about it in advance and what we do for our patients, who need to be on birth control pills, because many of them do not just for contraception, but they also want to be on it for, like we said, some of the symptoms, polycystic ovary syndrome. And so we will adjust the lamotrigene dose for them. We'll say, the day you start your pill, you increase your dose by this much, and then you stay on it.

Dr. Elizabeth Gerard: 33:41 The people who take a placebo week will find that their lamotrigine levels will fluctuate. Let's say they're at a number of five during most of the month. They can go up to an eight or a nine when they're on their placebo week. So one that's just something that's been very aware of. We have patients who sometimes call and say, "All of a sudden, I started having symptoms of double vision or dizziness, which are lamotrigene toxicity symptoms. It can be because they're on their placebo week. One way we can avoid that is asking the OB, if they're willing to prescribe the birth control pills throughout the month without a placebo week skipping the placebo pack going from pack to pack.

Dr. Elizabeth Gerard: 34:16 So I mentioned that lamotrigene may affect how well the progesterone part of the birth control works. For most people think that, that's not an issue with the birth control pills or with many of hormonal contraception available, but I usually do recommend using condoms as well if you're using that

combination. And again, the hormonal containing IUD will not interfere with lamotrigene. So what can you do about epilepsy and birth control to make sure you're heading in the right direction? Talk to your doctors about how your medication will affect your birth control and vice versa, discuss what your needs are and your concerns about birth control. So it's very different if you're on birth control, because you're trying to avoid pregnancy and different if you're trying to use it to control your symptoms.

Dr. Elizabeth Gerard: 35:00 Consider notifying your doctor in advance, if you would like some time alone to discuss. So a lot of times patients come in with their mothers, so it might be good to let them know in a busy clinic that you can send a message now through the portals, or I'd like a little bit of time alone to talk to the doctor and then they can navigate that. And then if you're sexually active to use condoms in addition to hormonal contraception or birth control or an IUD. So I think I'll stop there for questions.

Dr. Laura Lubbers: 35:28 Great. Thank you, Dr. Gerard. We'll now go to the Q&A session. I thought that was terrifically informative. Thank you so much. Again, participants if you have any questions, please submit them via the Q&A tab located at the bottom of the Zoom panel and click send, and Brandon will go ahead and read them out loud.

Brandon Laughlin: 35:49 Sure. Actually our first question, Dr. Gerard, touches on a slide that you presented earlier. Are there a lot of known genes, like filamin-A where you have a 50% chance of actually passing on that particular mutation to your child?

Dr. Elizabeth Gerard: 36:04 Yeah, there are. There are a growing number of genes where we know that they can be passed on what's called an autosomal dominant form. So the one that I showed was an X linked form, but there is a growing number of autosomal dominant genes that can be passed on. One of the ones was actually a CURE... There was a CURE email today about the SCN1A gene. That's a very complicated gene because you have a 50% of chance of passing it on, but the symptoms in somebody who inherits it can vary. So somebody who can inherit it could be very normal with just febrile seizures, and another person who inherits it could have a more severe epileptic encephalopathy known as dravet syndrome.

Dr. Elizabeth Gerard: 36:51 So that's an example of an autosomal dominant gene, where you have a 50% chance of passing it on, and it's also an example of what makes it very difficult to do genetic counseling and genetic testing pre-pregnancy. There are growing number, still

small, but a growing number of genes that are autosomal dominant, and I typically look in an adult population that can be passed on. So one of the ones is the LGI1 gene, which is associated with focal temporal lobe epilepsy with auditory features. So a lot of patients will hear symptoms before their seizures. It's traditionally a pretty mild syndrome. Then there are the gator complex genes.

Dr. Elizabeth Gerard: 37:31 So DEPDC5, NPL3, NPL2. These are just some examples and I don't have a specific number for you at this time of the number of autosomal dominant genes, but it's growing. And so that's an important thing to look at. Signs that you might have an autosomal dominant gene in your family, although it could always start with the individual who has epilepsy, but signs that it might be in your family are if you have several close relatives, usually first degree relatives in your family. And that would be one of the things that would, if patients see me elevate my recommendation to consider genetic testing.

Brandon Laughlin: 38:09 Great. Thank you. The next question actually is also a follow up question on one of the slides you presented earlier, and that was if you're no longer looking to become pregnant, what are the reasons to stay on folic acid?

Dr. Elizabeth Gerard: 38:24 That's a really good question. You know, we traditionally recommend to all of our women who might get pregnant to be on some folic acid. Again, how much varies for patients who are still of reproductive age, before menopause, I usually have my patients on one milligram, although if they're not really planning pregnancy, we can usually go down to the lower amount that's in a women's multivitamin or prenatal vitamin. Some people feel it's good for hair and nails and stuff like that, but there's not really any strong evidence to treat the epilepsy or other symptoms that a woman needs to continue on folic acid, other than planning pregnancy. We just traditionally continue it. We don't usually continue it after menopause.

Brandon Laughlin: 39:10 Thank you very much. Switching gears a little bit, the next question came in and wanting to know about the strategies for women with epilepsy during labor or are C-sections more recommended or more common?

Dr. Elizabeth Gerard: 39:25 That's an excellent question. So we actually do not recommend C-sections for women with epilepsy. There isn't any indication that just because of having a seizure disorder or having epilepsy that you need a C-section in our MONEAD trial, they're looking at this data, but they're very few in academic centers who know this information. It's very rare to have C-sections done for

purposes of epilepsy. So we don't consider it a risk for C-sections. There have been studies that have shown in our country and other countries that C-sections are more commonly done for patients with epilepsy, but we suspect that this is more of just providers thinking that they need to do that rather than any kind of clear indication that needs to be done.

Brandon Laughlin: 40:15 Great. So the next question actually came in and it actually deals with a model that this woman follows called the Creighton Model. And she wanted to know if there are studies being done on this methodology and it's used as a better understanding women in epilepsy.

Dr. Elizabeth Gerard: 40:30 I'm not familiar with the Creighton Model. I'm not sure if I can answer that. Maybe if I have any more details on that or...

Brandon Laughlin: 40:40 It was just the Creighton NaPro Model. Actually helps understand the cycle and whether there's the correlation between seizures and cycles.

Dr. Elizabeth Gerard: 40:50 Oh, I can speak to that. I don't know the Creighton method per se, but I can speak to the issue of what's known as catamenial epilepsy if that's the question, but I'm not sure about the Creighton Model. It's long been known that epilepsy can respond to hormonal fluctuations. So I had a few slides on that, but about 30% of women with epilepsy will find that in some way, their seizure frequency syncs up with their cycles. Usually in my experience, not exclusively that, but if you have more seizures during certain periods of the month, often it's a few days before the period leading into the few days afterwards. I may actually show something. I had a couple extra slides. Let's see.

Dr. Elizabeth Gerard: 41:40 So there's a couple of different periods that people seem to be vulnerable to seizures. Again, 30% of women and those tend to be about ovulation or towards the end of the cycle. These patterns have been designed by Dr. Herzog. And so yes, for many of my patients, there's different ways. This is an ovulation tracker that you can follow your period. This is actually a way we used to do in our clinic where we followed temperatures. And your temperature goes up when you ovulate and through the end of the cycle. So you can see for this patient, this is her temperatures. This is likely where she ovulated, and this is where her periods started and she had more seizures. This is the period here. She had more seizures, both around the time of ovulation and then leading up to her period.

Dr. Elizabeth Gerard:	42:32	Treatment for hormonally sensitive epilepsy. I'm not a believer that hormones cause the epilepsy, but that it's one of many triggers that can trigger people's epilepsy, just like sleep deprivation or alcohol or stuff like that. And so recognizing these kinds of patterns, I'm not sure of the Creighton method, but any other method can be very useful for women first just to identify the vulnerable periods of the month, and then there's other strategies that are usually add-on strategies to try to control catamenial seizures. So this is my patient's seizures here. I like to stress that I don't think that hormonal treatments or approaches to hormonal modifications typically replace standard epilepsy treatments.
Dr. Elizabeth Gerard:	43:16	We still do first line treatments, anti-seizure medication, surgery if appropriate, but sometimes there are hormonal treatments that are given in addition to standard therapies. The evidence for this though is very limited. And then the other thing you can do though, and that I often do is that if you can recognize the pattern, which may be the participant was asking about, you can often give time to extra medications at the vulnerable periods of the cycle, and that can be very useful as well.
Brandon Laughlin:	43:42	That's great. And actually you were able to answer two additional questions that I had come in as well. So, that was fantastic. The next question is, for women with epilepsy, what resources are available that can help them really track their seizures and track their menstrual cycles?
Dr. Elizabeth Gerard:	44:01	So seizuretracker.com, I know that they have been developing... it's a great way to track your seizures and you can share with your doctor. There's also the ability to put in your periods as well. Many of my younger patients just find that period tracker apps, there's a ton of them available. They just do that and you can put symptoms in there as well. But seizure tracker is nice if you are in a computer. I know they were working on it, I don't know if you can yet actually put the information in on your phone. That's the only limitation for your periods, but they were working on developing that and right now on a computer, at least you can put in your periods as well as your seizures, and you can print out that information and provide it to your doctor.
Brandon Laughlin:	44:51	Wonderful. Thank you. And then actually the last question that we just had come in, so we have time for one more question. Why is PCOS more common in women with epilepsy?
Dr. Elizabeth Gerard:	45:05	Not completely known. There's some interesting research on that, but one of the reasons that we feel is actually early exposure to valproic acid or Depakote. So women who are

exposed to valproic acid or Depakote in their teens are much higher risk of having a polycystic ovary syndrome, but there's some other research in animals that there may be something to the epilepsy itself and to the frequency of seizures that may predispose to polycystic ovary syndrome, not just the valproic acid explanation and some of it is may be because seizures, particularly temporal lobe seizures involve the temporal which is right near, it gives feedback to the hypothalamus and pituitary, which then regulate ovulation. And so there are some theories about that, but there may be a direct effect on hormonal function that may lead to it. But those are the two main theories. One is valproic acid and then the other is this regulation of cycles.

Brandon Laughlin: 46:03 Great. Thank you so much, Dr. Gerard.

Dr. Laura Lubbers: 46:10 Yes. Thank you so much, Dr. Gerard for your presentation and to the Band Foundation for sponsoring today's webinar and our entire webinars series. So this concludes our webinar on Epilepsy, Pregnancy, and Contraception. I'd like to thank our audience as well today for your engagement and asking some great questions. If you have any additional questions about the topic or wish to learn more about any of CURE's research programs or our future webinars, please visit our website at www.cureepilepsy.org. Or you can email us at info@cureepilepsy.org.

Dr. Laura Lubbers: 46:46 I also encourage you to check out some of CURE's other programming including our newly launched Seizing Life Podcast, which is being hosted by Kelly Cervantes. We also have a number of CURE Day of Science events that are coming up across the country. So please stay tuned for those as well. So with that, I'd like to thank you all again. I hope you will join us on April 25th for our webinar discussing, transitioning from pediatric to adult epilepsy care. Thank you.