

Seizing Life, episode 91
Rare Epilepsy: Collaborating for Advocacy, Research, and Community
Guest: Yssa DeWoody
(Transcript)

- Kelly Cervantes: 00:00 Hi, I'm Kelly Cervantes, and this is Seizing Life, a biweekly podcast produced by CURE Epilepsy. This week I'm pleased to welcome Yssa DeWoody to the podcast. Yssa is the mother of a daughter with Ring 14 Syndrome, a rare genetic epilepsy caused by a mutation in the 14th chromosome. Yssa is the co-founder and director of research for the Ring14 USA organization. She is here today to talk about rare epilepsies, what they are, how they are diagnosed and treated, and what the particular challenges are for those families impacted by rare epilepsy. Yssa, thank you so much for joining us today. So excited to get into this conversation. A lot of people don't know how common epilepsy as a whole is. However it is made up of all of these rare epilepsies, so many different types of epilepsies. And so many of them are rare. What makes one of these epilepsies rare?
- Yssa DeWoody: 01:16 Well, I mean, so the definition of a rare epilepsy is really just a rare disease where the dominant feature is epilepsy. So in the United States, the definition of a rare disease is less than 200 case... 200,000, pardon me, 200,000 cases in the United States. And so definition then of a rare epilepsy is that definition. But on top of that, epilepsy is going to be the dominant feature of that rare syndrome.
- Kelly Cervantes: 01:50 And how many rare epilepsies are there, or are, I guess the better phrase of that question should be, are known?
- Yssa DeWoody: 01:57 Sure. And you would think that that would be an easy answer, an easy question to answer, but it's actually, it's actually quite tricky. And I tried to do in my homework, really nail down on what this number was. But what we know is that there's over a thousand different genetic disorders. And we know that there's an excess of about 130 of those where the dominant feature is epilepsy. But if you try to find a citation, it's a moving target. Because new genes are discovered every day. And so it really comes down to, it's not enough just to have a gene. It's kind of, you have to have a clear presentation of a syndrome or a disease along with, or without, really an etiology. So we think it's somewhere in the ballpark right now of 130 to 150.
- Kelly Cervantes: 03:00 And what are some of those, the names of some of those syndromes that people may have heard of that are either more common within the rare epilepsy world, which sounds like an oxymoron? Or are just more well known?

Yssa DeWoody: 03:16 Sure. So a couple of them come to mind. One is Dravet syndrome pretty well known, definitely in the epilepsy circles. That's actually kind of associated with the gene, a couple of genes, but the most common gene is SCN 1A. And then another pretty common one would be LGS syndrome or, or Lennox Gastaut syndrome. And actually this is kind of different than the other one, because this is actually like if epilepsy progresses to a certain state, then you develop LGS. But so it's kind of like a bucket diagnosis.

Yssa DeWoody: 04:01 And then inside LGS are all these different ideologies or genes associated with it. But if you say LGS, a lot of people tend to understand or kind of have a vague idea of what that is. That it's really severe epilepsy syndrome with developmental impairment and a certain EEG signature. But there's a lot of them. I mean, this is kind of like alphabet soup after that. So you've got things like SCN-2A. You've got KCNQ-2. So these are all names of genes. But these turn out to be really common in the epilepsy world. And so they give rise to kind of more common, rare epilepsies. But for every one of these, there's like 10 other genes that not so many people have heard of

Kelly Cervantes: 04:59 Now are all these rare epilepsies genetic?

Yssa DeWoody: 05:03 So we think that about 80% of them are genetic in origin, but there's actually five different causes of rare epilepsies. So genetics we just talked about, and then we've got metabolic disorders, we've got structural disorders. So the structure of the brain. Immune related disorders and then infectious. And then some of these really overlap. So you can be in two different boxes at once. For instance, tubular sclerosis complex. That's both has a genetic component to it, but it's also a structural problem. So just because you're in one box, doesn't mean you might not be in another one.

Kelly Cervantes: 05:45 Got it. Now, what is your personal connection to all of this? I know you are the founder of Ring14 USA, which is a member of the rare epilepsy network. Talk to us about both of those organizations and why you're involved.

Yssa DeWoody: 06:03 So like a lot of leaders in this field, there's a very personal connection, and I'm no different. I have a daughter, really, I have three daughters actually. But my youngest daughter, Marie, who is about to turn 17 on Friday, she has ring chromosome 14 disorder. So she started having seizures when she was three months old. And at the time, this was a long time ago, right? And so the standard genetic test at the time was a

Karyotype type, where you blow up the chromosomes and you look at them.

Yssa DeWoody: 06:37 And it's really easy to see a ring chromosome because it looks like a circle, if you look at that display of the chromosomes. And so our life was profoundly affected by this beautiful child. And that's kind of what drove me to kind of co-found Ring14 USA. I had the opportunity to go to Italy and see and go to an international meeting, and meet other families. And thought, we need this for the United States. We need to get on board and we need to do our part. And so that's kind of the origin. Got together with a couple of other moms and we started Ring14 USA.

Yssa DeWoody: 07:17 Now, as far as the rare epilepsy network. The origin of rare epilepsy network, it came out of creating a registry for rare epilepsies. With the idea being that we could look across the rare epilepsies, and then also the individual rare epilepsies, on this patient reported outcome. And so Ring14 USA got in on kind of the second movement of that registry. And then we decided that, wow, we could do more than this registry. And it really helps to build partnerships, and to collaborate, because a lot of us are answering the same questions for our families that we support. And we have common goals towards getting to clinical trials and everything.

Yssa DeWoody: 08:09 And so we came up with a structure of the rare epilepsy network. Where we knew that what we really wanted to be is, we wanted to really work with urgency, to collaboratively improve the outcomes of the rare epilepsy patients and their families. With really a focus on research and advocacy and things like that. And so instead of working on just a really little syndrome, now to be able to expand my scope, if you will, to all of these others. And to really just raise the awareness of all of these. Because, as you've said before, individually we're quite aware. But collectively we're not. And so that's a huge voice that we can speak with.

Kelly Cervantes: 08:57 Leveraging all of those rare voices into one powerful voice has done an immense amount of good. I'm always impressed with what is coming out of REN, the Rare Epilepsy Network.

Brandon: 09:13 Hi, this is Brandon from Cure Epilepsy. Since 1998, Cure Epilepsy has raised over 85 million dollars to fund more than 270 epilepsy research projects in 17 countries. Learn what you can do to support epilepsy research by going to cureepilepsy.org. Now back to Seizing Life.

Kelly Cervantes: 09:34 Now, Yssa, we've spoken on this podcast before about how difficult and challenging it can be to receive a diagnosis for one of these rare epilepsy syndromes. Can you sort of walk us through what that diagnostic process looks like?

Yssa DeWoody: 09:49 Yeah, I can try. I guess the main thing that I would say is that you have to go into this with the idea that it's not just one test and done. So often these journeys will start off in the ER when your child is having a seizure, or perhaps a severe event, like status. And so kind of the common tools that come into play first are things like an MRI, even a lumbar puncture, or a spinal tap to look for infections. So these are things that happen typically right off the bat. Also an MRI is very useful to find structural type anomalies. And I'm going to say a little bit about the EEG. It's such a powerful diagnostic tool. But it's confusing because you can have an abnormal EEG and still not have epilepsy, and vice versa.

Yssa DeWoody: 10:50 You can have a normal EEG and have epilepsy. But if you catch a seizure, then that certainly gives some diagnostic tools. It's focal seizure, or this and that. And certain syndromes have different EEG signatures. So it can be very useful. But once those kind of tests go through, then you're often left with some kind of genetic testing. And there are many different types of genetic testing these days. So you can do a micro array analysis, and that's where you're looking for missing pieces of chromosomes. So deletions, duplications, and things like that. And I have to make a plug for my syndrome. If you have deletion on the end of a chromosome, it might be useful to do a Karyotype, because that's actually the most useful diagnostic tool for finding ring chromosomes.

Kelly Cervantes: 11:46 And a Karyotype, but correct me if I'm wrong, that is when someone is pregnant and has an amniocentesis done, is that sort of the same type of thing?

Yssa DeWoody: 11:56 Sure. They often do a Karyotype. Because it'll also find things like down syndrome and common things like that. But these are what are called structural anomalies. So you're kind of, now you're looking at each individual tree, if you will. So yes, if you do an amniocentesis, they often do a Karyotype. But then you can also do DNA sequencing. And this comes in many forms. So you can either do a gene panel test where they're looking for mutations on particular genes that are known to be associated with epilepsy. Or you can do whole exome sequencing. And this is where they're looking at, they're sequencing out exomes for exomes sequence for protein. So they're looking for any kind of mutations that occur on these. And then you can actually do

whole genome sequencing where it's actually really sequencing out your whole DNA, every letter along the way. And they can look at it that way.

Yssa DeWoody: 13:04 So there's different levels of, if you're peering in really close, or you're looking out far. And all of these tests are actually, they're useful for diagnosing certain syndromes. But not every, not one test is going to catch every syndrome. So if you do one and it comes up blank, then you have to push for another one, and you have to push for another one. And sometimes it may take longer. You know what I mean? As new genes are being discovered, you may have to retest that stuff. This is a lot of information. So you don't do this without a genetic counselor. They're at your side to kind of talk you through the diagnosis and the implications of that. And also the implications for your whole family. So that role, I want to put a plug in, it's very helpful to help you walk along this journey.

Kelly Cervantes: 14:01 That's really great advice. And so a two part question for you here. What advice do you give to parents who, or caregivers who, find that diagnosis through that process? And conversely, what do you tell the parents who are still searching?

Yssa DeWoody: 14:21 Well, if you're lucky enough to find a diagnosis, then my big advice to you is to find those people. Find those people with the same shared experience with you. Because if any child needs a village, then a rare child needs something more than a village. You know what I mean? They need an extended family, is what they need. And so when you get a diagnosis like that, it can lead you to support groups and advocacy groups where, depending upon where you're led, maybe all you want is support. And that's great. But also being connected with your people might speeden if there's clinical trials, or there's new advances. Then being connected to that community gets you to those answers a little bit quicker. And so that's great. And it also presents an opportunity to participate in research. Because we're never going to know more about these syndromes until more people raise their hand and say, I want to share my experience. I want to do what I can. I want to raise funds.

Yssa DeWoody: 15:37 All of these things are necessary if we want to get to a cure. For those who aren't lucky, who don't have a diagnosis yet, I would say, one, keep trying. And two, there are some wonderful general support groups, even if you don't know the underlying etiology of your syndrome. But keep trying. And I just want to say, not all of this is easy. You know what I mean?

Yssa DeWoody: 16:11 I just don't want to put forth the idea that everybody's going to always get a diagnosis. I hope that most people get a diagnosis. But I just want to acknowledge the fact that we're still a ways from doing a hundred percent diagnosis on these. And that we as a community need to lift up and feel a kinship with all those with epilepsies. I like to see myself in concentric circles. There's Ring 14, there's the rare epilepsy. There's the whole epilepsy world, and hopefully you find a spot in that circle that you can make your home.

Kelly Cervantes: 16:46 Yeah, that's a really incredible sentiment. We've talked about some of the various physical, emotional, and psychological conditions of epilepsy. Are there any specific comorbidities that come along with the rare epilepsies in particular?

Yssa DeWoody: 17:06 Well, that's a great question. And I just want to say, first of all, the very definition that it's rare means that you have a really small population size to deal with. So on some of the really rare of the rare, they don't have natural history studies. You know what I mean? It's parents coming together and it's this, "My kid has this. My kid has that." And hopefully you're going about this in a scientific way. But sometimes it's not often clear what's associated with the rare epilepsy, and what's associated with just all the other 2,000 genes that are out there, on there.

Yssa DeWoody: 17:47 So really nailing down what are the comorbidities of a rare epilepsy? First of all, I want to say that it's not as simple as it sounds sometimes. But what we can't say is that a lot of the rare epilepsies, the common comorbidities, they seem to be GI issues, language impairment, hypotonia, you've got movement disorders, sleep disorders, behaviors that come along that may stem just from a lack of communication being on the autistic spectrum.

Yssa DeWoody: 18:27 And then developmental delays are often also associated with this. But I also want to mention that almost all of these rare epilepsy have a spectrum of outcomes. So some of the kids will do really well, and some of the kids don't do so well. And this can depend on the particular mutation. If it's a gain of function, loss of function, all kinds of stuff. So when I list out all of these, I always want to put an asterisk that says, "This may be your child, but it may not be your child." Because everything has a range of a spectrum associated, even within the rear epilepsy.

Kelly Cervantes: 19:22 Can you explain also, what is multidisciplinary care? And why that's so important, in particular for these rare epilepsy patients?

- Yssa DeWoody: 19:31 Okay. So we've already spent a little bit of time talking about all the comorbidities. And so something that you hear a lot is epilepsy, it's not just the seizures. Meaning it's just giving color to all these different comorbidities that often are almost just as confounding as the epilepsy, really, sometimes and everything interacts. So for instance, if my daughter's having GI problems, then you know, that can lead to constipation, that can lead to more seizures. But if she has a bunch of seizures and I give meds to control the seizures, that slows down the GI tract, and you see how you can go in this circle. And it's the same with respiratory issues and movement disorders. So we have to understand that when we're given anti-seizure medications, this affects the brain. It has lots of different effects. And all of these drugs interact.
- Yssa DeWoody: 20:34 And so what's nice is to have inter... Multidisciplinary care where they're aware of all the different problems that your child is having. They're not just focused on the seizures and the epilepsy. But they're looking at the whole child here. And then they can come together and they can develop a more holistic plan for your child that really includes, okay, if I tweak this over here, is this going to be affected? And you know what, which one of these does the parent value most? How does this affect the child's quality of life? Which a team that's all talking together, they can implement a plan that really takes into account the values that the parents have, and the wishes that they have, for their life. But if you're seeing doctors in isolation, it's really hard to coordinate that. And what happens is you end up being the quarterback.
- Yssa DeWoody: 21:38 Well, I'm no quarterback. You know what I mean? That's a lot to keep track of. And it's a lot to put on our parents' plates. And so right now at the Rare Epilepsy Network, this is really one of our initiatives is how to come up with flexible recipes, if you will, to develop these multidisciplinary clinics. How patient advocacy organizations to work together. Because you can imagine if you have just 20 to 30 families in the United States, where does it make sense to place that clinic? And how are you going to fund that with that? So there's ways that we can work together to create this, to create better, more holistic care for our patients.
- Kelly Cervantes: 22:33 Yeah, I think it was something that surprised me when entering this epilepsy world, and the medically complex world, was that our doctors didn't naturally communicate with each other. That that really was something that we had to facilitate. And sometimes even when they're in the same hospital, that doesn't mean the same medical network. That doesn't necessarily mean that they're still going to communicate. That is something that

you have to advocate for, and push for, unless you are at one of the few institutions that do this on their own. And it is, it was a big learning curve.

- Yssa DeWoody: 23:13 Sure. And so you can see that this has such benefit to the families, but it also has benefit to the patient advocacy organizations for collecting information. So if you're going to really nail down on what are all the comorbidities, and really standardize that information so that it's research ready for other people to look at, then these clinics really facilitate that. And also, it has value to drug industries who are to put on clinical trials and things like that.
- Yssa DeWoody: 23:47 So I think that it just has benefit to all the different stakeholders. We've just got to find a way to harness that, and really create a network that's across the United States. So some of our rare organizations, some of these advocacy organizations, man, they're doing a great job. And they've got them all over. But some of us don't have any of this care. So we're just either going to a general epilepsy clinic. That's great. That's a good start. You know what I mean? But we've got to do a better way of making sure that there's a network across the United States that all of our families can take advantage of.
- Kelly Cervantes: 24:24 Absolutely. Can you tell us about some of the research clinical trials that are on the horizon, or currently being conducted for rare epilepsy?
- Yssa DeWoody: 24:34 I am certainly not an expert on all the different things that are going on, especially in the research realm. But I will say I'm going to start with the idea that there are really two different types of therapies going on here. We have got now this distinction between anti seizure drugs, so drugs that are targeted to stop seizures. And there have been a lot of, a couple of different clinical trials that have gone through. There's a new drug for a CDK-L5, that's just come out. That's really what we call kind of a targeted therapy. So there's something about the mechanism under which that rare disease operates on that they're targeting with that anti-seizure medication. And then on the horizon, we also really have anti epilepsy medications that are really trying to cure the underlying cause of the epilepsy. So it's the first time that we're kind of distinguishing between these two mechanisms.
- Yssa DeWoody: 25:43 So that's interesting. I know that Angelman syndrome has got a clinical trial going on. I know that [Jerday 00:25:51] syndrome's got a couple of different clinical trials. TSC, the tubular sclerosis has got to prevent trial, so if we treat early enough in a child's

life, can we stop the progression you know of these drugs? So exciting stuff is on the horizon, no doubt. But there's still a lot of work to be done. And we've got to create methods so that we can start to not just attack these rare epilepsies one epilepsy at a time, but how can we be able to affect more than one at a time? And that's where these collaborations are so important.

Kelly Cervantes: 26:35

Now I know that Cure and REN recently announced a collaboration, a collaborative research grant mechanism. Can you tell me about that?

Yssa DeWoody: 26:47

Yeah, this is actually one of the things that I'm really excited about. That's come out of the Rare Epilepsy Network. And of course, Cure is a member of the Rare Epilepsy Network with their mission to cure epilepsies. It fits right in there. But research is really expensive to do. And there's a certain amount of basic science that has to be done before you can get to targeted therapies and things like that. So we have developed a partnership where Cure is going to help promote this research RFA, this proposal. So one of the things that's really hard as a new organization is to find researchers who are willing to take on looking at your syndrome. So Cure has developed such a rich and broad number of researchers that follow them. That it's really an important thing that they're publicizing this grant proposal, and then it's a match one for one.

Yssa DeWoody: 27:55

And so what's going to come out of this is a hundred thousand dollars grant to a researcher, that's really directed at one of the rare epilepsies in partnership with that particular [inaudible 00:28:07] that supports that rare epilepsy to fund this one year grant. And so it's a wonderful example of how a big older brother is helping out one of the little baby sibs come up through the ranks. And really kind of defines this, that we want to work together. Because we all just really want to help these kids. We want to help these families, these kids, these adults, too. All these kiddos are growing up into adults, right? And so anyway, real happy with that collaboration.

Kelly Cervantes: 28:42

I love hearing about the collaboration, the collaborative work, and knowing that these rare epilepsy organizations aren't siloed in the way that they once were. That these organizations, these families, are working together and lifting each other up and hoping to come up with treatments, and ideally cures, that can one day help the community and can be shared amongst many patients. Yssa, thank you so, so much for sharing your insight and knowledge with us today. This was absolutely enlightening for me. And wishing you and your family all the best.

Yssa DeWoody:	29:24	Thank you very much, Kelly. Thank you for having me on. I appreciate it.
Kelly Cervantes:	29:30	Thank you, Yssa, for educating us about rare epilepsies, and for the work that you do with Ring14 USA and the rare epilepsy network to raise awareness and funding for research into rare epilepsies. Your work really helps improve the quality of life for those families living with a rare epilepsy syndrome. As you heard during our conversation, Cure Epilepsy is partnering with several rare epilepsy groups to fund research into rare epilepsy syndromes. Since 1998, Cure Epilepsy has raised more than 85 million dollars for epilepsy research. If you would like to help us continue advancing science towards a cure, please visit cureepilepsy.org/donate . Through research, there is hope. Thank you.
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