

Kelly Cervantes: 00:00 I'm Kelly Cervantes, and this is *Seizing Life*, a weekly podcast produced by Citizens United for Research in Epilepsy, CURE.

Kelly Cervantes: 00:18 Dr. Laura Lubbers has a Ph.D. in neuroscience from the University of Illinois. For the past two years, she has been the Chief Scientific Officer for CURE. During that time, Dr. Lubbers has guided CURE's research strategy, pushing science closer to a cure. Epilepsy also has a meaningful impact on her own family. Her sister Ellyn was born with tuberous sclerosis complex, TSC. After 50 years of countless anti-epileptic drugs and a vagal nerve stimulator, Ellyn is still regularly affected by seizures. That is why Dr. Lubbers leverages her 20 years of experience focusing on research projects that counter the effects of stroke, ALS, Alzheimer's and Parkinson's disease to finding a cure for epilepsy. Today, that conversation focuses on the benefits and drawbacks of CBD and marijuana. Thank you so much for joining us today, Dr. Lubbers.

Laura Lubbers: 01:12 You're so welcome, Kelly. I'm pleased to be here.

Kelly Cervantes: 01:15 I also want to thank you for your dedication and commitment to CURE as our CSO, the work that you do, and knowing your personal connection to this cause. I think it just sort of completes the circle. We're all very appreciative of that.

Laura Lubbers: 01:32 I'm so pleased to be a part of the organization. I really have a passion for the mission, as does the staff. It's really an exciting place to be to make a difference in the lives of those who suffer with epilepsy.

Kelly Cervantes: 01:42 I want to dive right in and start at a definition-level because I think that, in the general conversation about medical marijuana, there's a lot of different types of meds that fall into that larger umbrella. From the very basic and most easily-accessible hemp to the CBD oils to medical marijuana. What is the difference between all of these?

Laura Lubbers: 02:14 There are a lot of differences, frankly. The medical marijuana and the marijuana that's very familiar in our social settings are actually the same thing. It just depends on how it's used.

Kelly Cervantes: 02:26 Cool.

Laura Lubbers: 02:27 But medical marijuana can be administered in a number of ways. It can be inhaled, or it can be delivered orally. But it's very different from CBD, which has become very common in the

press. There's a lot of discussion about cannabidiol, which is referred to as CBD.

- Laura Lubbers: 02:48 Within medical marijuana and marijuana itself, there are many different active substances. The one that people are familiar with that causes that high is called THC. The one that is being explored for use in treating epilepsy is called CBD. Again, these are very different substances. Within a medical marijuana plant, these substances, as well as others, exist. You can see how, if a plant is grown in a different environment, it might differ from plant to plant to plant. So there are lots of differences across the spectrum of what's available out there.
- Kelly Cervantes: 03:31 You hear about some people who have used CBD to treat their seizures, and that helps. But some people need marijuana with the THC to treat their seizures. Is that the same as two different meds, like different prescription drugs, even though they're both coming from the same plant? Do we understand what it is, what the mechanism is, with this particular plant that is helping to control the seizures?
- Laura Lubbers: 04:02 Those are very complex questions. I'm going to try to break it down.
- Kelly Cervantes: 04:05 You're very good at that.
- Laura Lubbers: 04:07 When you think about a marijuana plant, one analogy that I've heard that I thought was very effective for me was thinking about it like grapes that are used for wine. The grapes that are used to make wine differ between France and California. They might be the same grape, but because they're grown in different conditions, they actually might taste differently. They might have different concentrations of substances within them that make them taste differently.
- Laura Lubbers: 04:40 That's the same thing for marijuana, where plants grown in different conditions have different characteristics. Also, plant species differ in terms of the amount of CBD or THC within them. Where somebody may have access to a product that has a high CBD level, it might work well for them. Somebody else might have access to a different type of marijuana plant, or extract from that plant, that might have a different level of CBD in it. This may not be as effective. That's one possible explanation for the differences that people see after taking CBD and its varying effectiveness on epilepsy.

Kelly Cervantes: 05:22 But why does it work? Do we know that answer?

Laura Lubbers: 05:25 That's also a great question. As I mentioned, marijuana itself has many different active compounds within it. THC, that compound that gives you the high, binds certain receptors in the brain called CBD1 and CBD2. These receptors have been long-studied to understand how THC affects them to make people have that sense of feeling high. Interestingly, CBD, which we're using now to treat seizures, doesn't bind either of those receptors. There's been quite an effort in trying to understand how that compound influences activity within the brain. There have been some studies that suggest CBD binds to different kinds of receptors. This will get kind of technical, but there are receptors called G protein-coupled receptors, or GPRs. There's one called GPR55 that researchers think is important. There are other types of receptors in the brain that probably are activated by CBD, but we're still studying that. That's why we need more research in this area.

Kelly Cervantes: 06:35 So, it's a chemical reaction?

Laura Lubbers: 06:37 It is a chemical reaction.

Kelly Cervantes: 06:38 But this is coming from a plant. It is organic in that way, but it is still inducing a chemical reaction just as a pharmaceutical drug would, right?

Laura Lubbers: 06:50 Correct.

Kelly Cervantes: 06:52 I think it is really important for everyone to understand that there will be side effects, just as you would have with a pharmaceutical drug. What are some of the side effects that someone might experience who's using CBD or medical marijuana?

Laura Lubbers: 07:08 Those side effects haven't actually been well-studied at this point because medical marijuana and the various CBD oils have not been well-studied specifically for epilepsy. There is one product called Epidiolex that is now out in the market that has been studied in this way. Epidiolex has been studied in multiple clinical trials in specific populations of people with epilepsy, as well as those who have Lennox-Gastaut syndrome, or LGS, and people who have Dravet syndrome.

Laura Lubbers: 07:39 In these people, in these randomized-controlled trials, the side effects that have been identified include fatigue or sleepiness,

nausea, and vomiting. Those are the most significant side effects that have been identified.

- Kelly Cervantes: 07:56 I guess it is because marijuana is considered a controlled substance that the other research has not been able to be done. Hopefully, we see some of that change in the future because we do see success stories of this actually working to treat seizures. I also think it's incredibly important that people understand the limitations. If you watch an episode of *60 Minutes* or CNN, you see people who are so excited about the results. I think everyone wants it to be a cure.
- Kelly Cervantes: 08:31 But it's not a cure.
- Laura Lubbers: 08:32 Right. Correct.
- Kelly Cervantes: 08:33 What are the realistic success rates? If someone is going on it, what can they expect, specifically for Epidiolex, because that's the only one that we really have true research on at this point? What are the success rates that someone could anticipate?
- Laura Lubbers: 08:50 It's a great question. I'll be frank ... The success rates are lower than we would like. I would love to see a cure, and as you've already said, this is not a cure. It is a treatment. The studies that have been done to date on people with LGS and Dravet demonstrate about 20% efficacy.
- Kelly Cervantes: 09:09 When you say efficacy, does that mean that 20% are seizure-free, or 20% see a reduction in seizures.
- Laura Lubbers: 09:15 20% see a significant reduction in seizures, and some have seen seizure-freedom, which is truly, truly exciting. The thing that's exciting about Epidiolex is that it is well-studied. I think there has been a lot of excitement about medical marijuana and CBD oils, but they haven't been well-studied, and, for some people, they do work well. You do hear those success stories. But for many people, they don't work, and you don't hear about those cases.
- Laura Lubbers: 09:39 With the research and the clinical trials that have been done with Epidiolex, we really understand what the efficacy is in certain populations and what the side effects are. That's why the research in that way is so important.

Kelly Cervantes: 09:51 We want to chat now for a minute specifically about Epidiolex. What it is, for starters, and how is it different from the CBD oil that anyone can order online?

Laura Lubbers: 10:06 Like I already mentioned, marijuana plants are all different. They can be different species, as well as dependent on what the growing conditions are. The thing about the plant that is used to extract Epidiolex is that the company that makes it has a very standardized approach to growing that plant and to extracting that active compound out of it. It's all very standardized and, you can trust that, from batch to batch, it's going to be the same. That's quite different from many of the CBD oils that are available online. That's not to say that there isn't consistency, but you don't really know unless you have it tested, and I would recommend that anybody who is using CBD oil for their child to get testing done on the compound. You can have that done, and, given the importance of treating epilepsy with appropriate levels of the compound, I think it's important to get that testing.

Kelly Cervantes: 11:08 We tried CBD oil for my daughter, Adelaide. We ordered it online. There were all of these different options, with different mixtures of oils, and different strengths and ratios. I had no idea what I should be ordering.

Even if CBD is legally available in your state, the doctors, as a part of these medical institutions, are usually not permitted to help you with it. You are determining dosages using an online guide to try and figure out how much you should be giving and at what ratio. And now you're talking about getting it tested additionally to make sure that you understand the potency. It's complicated ...

Laura Lubbers: 11:51 It is complicated.

Kelly Cervantes: 11:53 ... really complicated. There are drug-to-drug interactions, which we experienced. Our daughter was on another drug, and it interacted with the CBD and affected her liver. We caught it early on, but it could've potentially made her very sick. It is a challenging road to walk down, and it's not as simple as going online and ordering it and trying it. It has been, prior to Epidiolex, much more complicated than that. How does Epidiolex change that?

Laura Lubbers: 12:27 It does give that option to physicians to work closely with the parents, and you are correct that many physicians have struggled. They really want the best for their patients, and they

are willing to try a variety of things to help the patients. However, they don't have the details about what's in that CBD oil that's ordered online either. It's hard to know what your starting dose is. It's hard to know how to monitor it over time, and, because there's such variety in the marketplace, that adds to the complexity.

Laura Lubbers: 12:59 Epidiolex gives parents, as well as physicians, the consistency that they need. They know what the starting dose should be because of the trials that have been done. They know what the dose escalation should be, if they need to do that to find the right dose. They know what the side effects are to watch for. For those other products that aren't as well-tested, everybody's just left shrugging their shoulders and hoping for the best. We know how desperate people are to reduce seizures in their kids.

Laura Lubbers: 13:32 I know that, as a family member of someone with epilepsy, we would try just about anything. But we also wouldn't want to negatively impact my sister, and other families, obviously, feel the same way. Having an FDA-approved product helps the community overall. We need more. We need more options. We need more research to find those options. But this is one new treatment that gives people that option that we understand. We understand it well. That's a benefit.

Kelly Cervantes: 14:01 You talk about multiple strains of marijuana, multiple grapes, if you will, and different varieties. Will there be other forms of Epidiolex from different types of plants that will hit the market? Is that something that we can expect to see in the future? Maybe one strain of Epidiolex didn't work, but another strain could work for someone?

Laura Lubbers: 14:29 I think, when we break it down, research is really focusing around those compounds. CBD is the compound that's been effective in treating epilepsy, but there is another one, CBV ...

Kelly Cervantes: 14:40 Okay.

Laura Lubbers: 14:41 ... that has also been tried. I know that the manufacturers are trying to see where it may be useful. There may be other compounds within that marijuana plant that could be helpful, and that's where more research will provide benefits and, hopefully, more options for people.

Kelly Cervantes: 15:00 I know that there's still so much more research to be done. You mention Lennox-Gastaut and Dravet, two epilepsy disorders

that have been tested. Are there certain seizure types that seem to be better treated by using CBD or marijuana?

- Laura Lubbers: 15:22 That's a good question. The seizure type that's been studied the most, because it's easy to monitor, is called a "drop attack," when people actually do fall. We know when somebody has fallen. It's much harder to measure "absence" types of seizures. Different seizure types have different abilities to be studied. That research hasn't been done yet, but I think, given the efficacy on "drop attacks," it could be useful for other seizure types. There is a clinical trial that is wrapping up soon on tuberous sclerosis complex-related epilepsy, so that may also give us more information.
- Kelly Cervantes: 16:00 Minimal research is being done at this point on CBD, and we've sort of jumped through the legal hurdles there. But where do we stand with THC?
- Laura Lubbers: 16:08 THC does not seem to be effective for treating epilepsy. There may be, again, other compounds within the marijuana plant that are worthy of study, but THC itself doesn't seem to have an effect that we can really identify.
- Kelly Cervantes: 16:24 That's fascinating. I had no idea. I feel like it all gets lumped together and ...
- Laura Lubbers: 16:28 It does, it does. And that's why it's really important to share different information about the different compounds that we're talking about, to get familiar with those things, and to get familiar with the different products that are available.
- Kelly Cervantes: 16:38 How would you love to see the research in this segment moving forward? Where would you like to see that research going?
- Laura Lubbers: 16:48 I would love to see more research on the different populations. We know that there are different syndromes that cause epilepsy. We've already talked about the studies for LGS and Dravet syndrome, and tuberous sclerosis complex that's wrapping up, but certainly studying it more broadly, and different epilepsies I think, would provide benefit to the community. Trying to understand more clearly the pathways that are affected by the CBD may also be a rich area for study. For example, if that compound is hitting say, the GPR receptor I've talked about, or maybe hitting serotonin receptors, or other different pathways. If we can resolve that, then we can focus efforts on these other pathways that may not have been

significantly researched as they relate to epilepsy. That's an exciting avenue.

Kelly Cervantes: 17:43 I want to clarify. Since Epidiolex has gone through the research and the testing that it has, it has been FDA-approved, correct?

Laura Lubbers: 17:54 That is correct.

Kelly Cervantes: 17:55 That is why doctors are permitted to prescribe it?

Laura Lubbers: 17:59 That's correct. They can write a prescription. They can have access. Patients can have access.

Kelly Cervantes: 18:06 What is it in particular about CBD that the medical institutions will not permit their doctors to work with it?

Laura Lubbers: 18:14 It probably varies from hospital to hospital and clinic to clinic to some degree. But if they don't understand that drug, they certainly can't prescribe it. They can suggest. Some doctors will say, "You can try this," but they can't guide the patient in the treatment plan.

Kelly Cervantes: 18:32 I feel like it's less-so today, thanks to so much media coverage, but there still is a stigma around medical marijuana and CBD. To be clear, you cannot get high from CBD by administering CBD to your child or to yourself. There is no high because the THC is not there, right?

Laura Lubbers: 18:56 Correct.

Kelly Cervantes: 18:59 That's super important to note, but there's still stigma there. People still don't understand it. Why is that, do you think?

Laura Lubbers: 19:08 I think because of the cultural association with marijuana. Legally, despite federal regulations still in place against marijuana, certain states have allowed access to marijuana. People are just now trying to understand and digest all this information and figure out where it's appropriate and where it's not. That's why it's so important to talk about it, to help people understand where it can be medically-approved and used to treat devastating disorders like epilepsy.

Kelly Cervantes: 19:41 Does epilepsy help with that, getting that information out into the market?

Laura Lubbers: 19:44 Yes. Yes.

Kelly Cervantes: 19:45 And having a drug like this out there, what does that do for a researcher?

Laura Lubbers: 19:51 For a long time, people have felt that marijuana, or compounds within marijuana, could be useful for epilepsy. However, because marijuana has been illegal and classified as a Schedule 1 narcotic, researchers didn't have access to it and couldn't get federal funding to do the research that was necessary.

Laura Lubbers: 20:13 Now that Epidiolex has been approved by the FDA, the government has had to change the classification to allow researchers to be able to study it a bit more. There's still going to be some access issues for researchers, but it does open the door for more research, again, with a compound that's understood.

Kelly Cervantes: 20:32 Do they see other uses for CBD for other disorders and diseases?

Laura Lubbers: 20:38 Yes. It's certainly being studied for other disease states, syndromes, and conditions. I know they're studying it for a variety of indications like autism. There's interest in studying it for pain. There's a variety of research areas where it will be investigated.

Kelly Cervantes: 21:00 I've also heard from other parents who have used it with their children that, maybe they didn't see seizure control, maybe they didn't even see seizure reduction, but they're seeing improved cognition. Why is that?

Laura Lubbers: 21:18 Good question. That's why we need more research. Because it may be hitting pathways that influence cognition. I've also heard from parents that their children feel less pain. Right now, this is all anecdotal, and it needs to be studied further, but there are potential upsides to the drug in addition to treating the epilepsy. In some cases, even if it's not treating the epilepsy at all.

Kelly Cervantes: 21:41 One thing that you hear so often from different people is the epilepsy affects their memory or ...

Laura Lubbers: 21:50 Absolutely.

Kelly Cervantes: 21:51 ... they feel like it's slowing them down. So even if it's meant to treat a side effect of the seizures, it can still be pretty exciting and beneficial, even if it's not treating the seizures themselves in every case.

Laura Lubbers: 22:04 There may be cases where it's treating subclinical seizures that aren't obvious, but also helping to reduce the overall seizure frequency and improve cognition as well.

Kelly Cervantes: 22:16 It's exciting to have something within the epilepsy community that peaks the interest of those outside the community, something that we can try and get that sort of mainstream coverage for and get the word "epilepsy" out into the world. The excitement around CBD has certainly enabled that to happen. I just always hope that it's tempered with the reality of how much or how little this drug can help. At the end of the day, I think everyone within the epilepsy community is just so excited when another drug hits the market, another drug that is maybe going to be the miracle drug for themselves or for their family member. It just so happens that this one has a little extra excitement around it outside the community as well.

Laura Lubbers: 23:17 It's so exciting that CBD has been approved in the form of Epidiolex. The researchers who have been involved in it are so excited that it is for epilepsy because it does raise awareness for epilepsy. That's something that has been a challenge and continues to be a challenge for the community.

Kelly Cervantes: 23:34 Laura, thank you.

Laura Lubbers: 23:36 Thank you!

Kelly Cervantes: 23:35 It is always so nice to chat with you. You are a wealth of information and always so good at breaking it down for a non-science-minded person like myself. We appreciate everything that you do for CURE and, most importantly, for pushing the research forward.

Laura Lubbers: 23:52 My pleasure, Kelly. It's exciting to have something new and available for our dear population, our people, our loved ones with epilepsy. I'm just excited to share it with you and everyone else.

Kelly Cervantes: 24:02 Yay. Thank you.

Kelly Cervantes: 24:06 Thank you so much, Dr. Lubbers, for your insights into the benefits and drawbacks of CBD and marijuana for epilepsy patients. If you want to learn more, then watch our recent webinar on this topic at CUREepilepsy.org/cbd. Finally, don't forget to visit and follow @seizinglifepodcast on Facebook and Instagram and @SeizingLifePod on Twitter. Thanks so much.

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