

CURE Epilepsy Webinar
Speaking About SUDEP: Arming the Rare Epilepsy Community with the Latest Research
Presenters: Dr. Sam Lhatoo and Abby Tanner
(Transcript)

Dr. Laura Lubbers: [00:01](#)

Welcome everyone to today's webinar. I'm Laura Lubbers, and I'm the Chief Scientific Officer of Cure Epilepsy. I want to thank you for joining us today.

Today's webinar is entitled 'Speaking About SUDEP: Arming the Rare Epilepsy Community With the Latest Research', and it's intended for everyone, including persons with epilepsy, caregivers, and physicians. This webinar is brought to you in partnership with our friends at Partners Against Mortality In Epilepsy or PAME, their friends at Wishes For Elliot, and the collaborative Deep Connections partners.

Sudden unexpected death in epilepsy or SUDEP affects approximately one in a thousand people with epilepsy, regardless of age. While lack of seizure control and seizure severity are the most common concerns for increased risk of SUDEP, there's also a concern that certain genetic mutations may increase SUDEP risk.

This webinar is part of Cure Epilepsy's 2022 Leaders In Research webinar series, where we highlight some of the critical research that's being done on epilepsy. Today's webinar, like all of our webinars, is being recorded for later viewing on the Cure Epilepsy website. You can also download transcripts of all of our webinars for reading.

For over 20 years, Cure Epilepsy has raised millions of dollars to fund epilepsy research that supports our mission, which has defined a cure for epilepsy by promoting and funding patient focused research. Cure Epilepsy provides grants that support novel research projects and that advance the search for cures in more effective treatments. To date, we've raised over 85 million dollars to fund over 270 research projects from investigators around the world.

Today's webinar, we'll discuss what we know about SUDEP, specifically in the rare epilepsy communities, as well as what parents and caregivers of children with rare epilepsies should know about SUDEP prevention and ways to mitigate risk. Presenters will share ideas on how to discuss SUDEP with doctors, both with the perspective of a physician and from a parent of a child diagnosed with a rare genetic epilepsy who has educated herself about SUDEP and taken steps to reduce the risk of SUDEP for her child.

The webinar will also include a discussion about the latest advances in basic and clinical epilepsy research focused on SUDEP risk and prevention. For this webinar, we have engaged two wonderful panelists. First, Dr. Sam Lhatoo as a neurologist and neurophysiologist with expertise in the medical and surgical management of intractable epilepsy. He's been the director of level four epilepsy centers in the UK and the US since 2006. He serves as the head of the International League Against Epilepsy's task force for big data in epilepsy, and he has a particular interest in the epidemiology, phenomenology, and pathogenesis of SUDEP. His published work has described potential biomarkers of SUDEP, including postictal generalized EEG, postictal hypertension, and central apnea.

Today, we also have Abby Tanner with us. Abby is the mom of a child diagnosed with a rare genetic epilepsy caused by a mutation in the KCNT1 gene. Abby and her family are strong advocates for her son Lincoln and those with rare epilepsies. She'll provide her perspective on discussing SUDEP with physicians and other parents in the rare epilepsy community.

So Abby, why don't you come and join us and tell us a bit about your family's epilepsy journey with Lincoln.

Abby Tanner: [03:49](#)

Hi there. Thanks for having me. I'm Abby Tanner. I am married to a wonderful husband. We have four children, and we live in South Carolina.

Our third child, Lincoln, he's five years old, and he has a rare form of epilepsy, like you said, from the KCNT1 gene mutation. His diagnosis is something called malignant migrating partial seizures of infancy. We call that MMPSI for short. It's rare. I think there are 200-300 kids in the world with his condition, and we had no idea that he had it. Then as an infant, he started having seizures, and he was quickly having 200 a day.

Lincoln is an absolute joy. He's one of the best things to happen to our family. He is nonverbal, and he's also not mobile unless he's in a really good stretch or a seizure, but he is absolutely a delight. It's definitely been a long road, and we're only five years into it, but what a privilege to be his mom.

Dr. Laura Lubbers: [05:03](#)

Wonderful. Thank you so much for sharing about Lincoln. Our hearts are with you as you're on this journey together, and hopefully together we can continue to learn and make life better for all.

Abby Tanner: [05:15](#) Absolutely.

Dr. Laura Lubbers: [05:17](#) Before Dr. Lhatoo begins, I'd like to encourage everyone to ask questions. We'll address those questions during the Q&A portion of the webinar. These questions can be directed to both Dr. Lhatoo, as well as Abby, and you can submit your questions anytime during the presentation by typing them into the Q&A tab located on your Zoom panel and click send. We'll do our best to get through as many questions as we can. 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.

With that, I will turn it over to Dr. Lhatoo.

Dr. Lhatoo: [05:17](#) Thank you very much, indeed. Can you hear me okay?

Dr. Laura Lubbers: [05:17](#) Yes.

Dr. Lhatoo: [05:53](#) Okay. Let's get my laser pointer sorted out.

Dr. Laura Lubbers: [06:14](#) We can see it.

Dr. Lhatoo: [06:16](#) Do I have control? Okay. I do have control now. Okay.

Thank you very much to Laura and Brandon for organizing this for us. Thank you all for your attendance and attention. Thank you, of course, to Cure Epilepsy and to Pam for all the great work that they do.

I'm going to speak about SUDEP, in particular as it pertains to the rare epilepsy community. I always start with this particular slide. For those of you who are not too familiar with SUDEP, it's a historical slide which basically tells you that one of the earliest written accounts of SUDEP comes from, actually, George Washington, who wrote about his stepdaughter, Patsy Custis, who suffered from epilepsy and who, by his account, very likely died of SUDEP several hundred years ago.

In the medical community, we've been a little slow, I would say, in catching up. The first large report of SUDEP cases was in 1975. It was another 20 years almost before we agreed on definitions. One of the most influential SUDEP scientific papers was written in 2013, which we refer to as the MORTEMUS study or the Mortality In Epilepsy Monitoring Units Study. In 2015, the NIH funded the SUDEP Center Without Walls, and I will speak about some of the research that came out of that Center

Without Walls. I'm happy to say that we have now entered the phase, and what probably marks that is a small paper that came out in 2021 on anti-SUDEP therapeutics and how specific drugs might lessen SUDEP incidents.

What is SUDEP? SUDEP is sudden unexpected death in epilepsy. It's unexpected, as well as unexplained. It is not caused by trauma or by drowning. It's not due to what we call status epilepticus, which is a very prolonged seizure, which gets patients into trouble.

Postmortems usually don't tell us why a patient has died, so we don't find a toxicological or anatomic cause for death. Depending on the evidence that we have of the circumstances of death, we might classify the death as definite or probable or possible SUDEP. If a patient survives an event that looks like SUDEP, then we refer to it as near SUDEP. Of course, there is another category called SUDEP plus, which is where somebody with epilepsy dies suddenly and in an unexplained manner, but also has a coexisting condition which could have contributed to death. So different variations of the theme of SUDEP.

We come to rare epilepsies now. What are rare epilepsies? The generally accepted definition is that there are less than 200,000 persons worldwide who are affected by that particular condition. Now, some of these epilepsies are extremely rare, so there may be just a couple of families who are involved. There are other epilepsies where there may be a hundred thousand or more individuals worldwide who are affected. Here, I've listed just a few of these, but there are dozens and dozens and dozens of rare epilepsies.

My talk is going to be a little generic in the sense that we don't have a great deal of information on SUDEP in each of these individual rare epilepsies. Seizure types are not usually exclusive to a rare epilepsy. Some may be more common in some rare epilepsies than others, but there isn't an exclusive seizure type as such. There may be multiple seizure types, and some of you may have experience of this.

What complicates matters and increases morbidity and mortality in these rare epilepsies is that there is often coexisting neuropsychiatric or learning difficulty type comorbidities. What is common to the SUDEP theme in the rare epilepsy, though, is that patients usually have generalized tonic-clonic seizures or generalized convulsive seizures; we may even refer to them as grand mal seizures. In whatever epilepsy there is where

generalized convulsive seizures like these are a feature, there is always a SUDEP concern.

The challenges in studying SUDEP in particular rare epilepsies, of course, is that SUDEP itself, thankfully, is a relatively rare occurrence. Studying a relatively rare occurrence in a rare epilepsy is challenging for scientists and for clinicians. Several rare epilepsies, such as Dravet's, for example, and I'll come to that a little more in a bit, are better studied. In others, there is less evidence available on which to make comment.

Some of these rare epilepsies have well defined animal models for study, and so Dravet again is a case in point. There are several ongoing scientific studies, both in the animal and the human domains, where we're able to make comment on SUDEP in that particular condition. Human evidence in rare epilepsies, therefore, is mostly anecdotal and observational because of the challenges we have in studying what are essentially quite rare phenomena.

Most of the rare epilepsies, as you would imagine, have a genetic underpinning, so the question would be, is there a genetic risk for SUDEP? There are several observations that can be made. One is that there is no evidence that SUDEP is a familial phenomenon running from generation to generation. There may or may not be a genetic predisposition, but so far we have not been able to identify a specific SUDEP gene.

There are some studied in animals where the setting for a fatal outcome of the seizures is more common, and I've listed some of those on the left, on the complicated alphabets, but I emphasize that we don't have a specific SUDEP gene as such that we've identified.

Some genetic conditions, like Dravet's, carry a higher risk of SUDEP, and others we don't know as much of. There may be other genetic abnormalities that coexist, and a case in point of course is Long-QT Syndrome where both have a tendency to cardiac arrhythmias and to epilepsy coexist.

How often does SUDEP occur in the rare epilepsy community, per se? I think it'd be fair to say that the risk is probably the same as that of those patients who have uncontrolled epilepsy. That's about one in 250 patients per year. The bar that you see right next to that on the left hand side suggests a risk of approximately one in 300 per year, and that's the box for folks with intellectual disabilities, for example. The true figure probably lies in between those two numbers. As I said before,

it's not a common occurrence, but it does occur, and of course when it occurs, it's a catastrophic outcome which we seek to avoid.

What do we know about SUDEP in specific conditions? Here, for example, is SCN1A or Dravet's Syndrome. Here is SCN8A. You'll see tubular sclerosis there, as well, for example, where we have a rare epilepsy with genetic problems. We have Dup15q, for example. These are all rare epilepsies, and when you ask the question, "What is the SUDEP mechanism in these different rare epilepsies?", almost always the answer boils down to the severity of the epilepsy and to the presence of generalized tonic clonic seizures. That seems to be a common factor in all these rare epilepsies that predispose to SUDEP.

Dravet's Syndrome is a condition that's very often talked about. It's a rare epilepsy, but as I said before, there are existing animal models that make it more easy to study. It's one of the commoner versions of the rare epilepsies. Here, SUDEP rates are about 15 times higher than in the rest of the epilepsy population. The mortality that we see in Dravet's, half of the time happens to be because of a SUDEP.

In many of the other epilepsies, it's longstanding epilepsy that's a risk factor for SUDEP. In the case of Dravet, a lot of the mortality tends to occur in the first 10 years of life. This is somewhat of an exception among the epilepsies.

What predisposes to death? We know that in patients with Dravet's syndrome there is what refer to as autonomic nervous system dysfunction. Control of cardiac rhythm, blood pressure, and so forth tend to be abnormal, and we believe that this predisposes to cardiac arrhythmias and to death. For a long time, we thought that this was the only issue that patients with Dravet's Syndrome faced, but there are more recent studies suggesting that actually patients with Dravet also have breathing difficulties. Here you can see the tracing of a patient who has a seizure. This is a breathing trace, and you can see that after the seizure ends, the breathing trace goes flat. We believe that this sort of thing is not good for the patient and may sometimes lead to death.

One of the interesting developments over the last couple of years is the fact that the FDA has approved medication for Dravet specifically, fenfluramine, and this is a drug, which we know from one study which made an observation on a small number of deaths that it might have an anti-SUDEP kind of

effect. Obviously, this is just one study. We need confirmation, and we do this in a larger scale to see if, indeed, this is true.

What are the risk factors for SUDEP? We've already discussed generalized convulsive seizures. In particular, the frequency of the convulsive seizures is very important. If seizures are frequent and they're convulsive seizures, then that's a setting for a bad outcome. Usually, folks have had epilepsy start in early age, and the epilepsy's been there for a long time. In some situations, males may be at a slightly higher risk than females.

Of course, things that are not good for seizure control also increased risk. That means missed medication, not taking medication in time, poor medication compliance. Of course, alcohol and drugs that make seizures worse are not a good thing. It's also very important to be diagnosed correctly and to have the appropriate treatment for that particular diagnosis. It's very important for patients with uncontrolled epilepsy to see epileptologists and to be assessed in centers that have facilities for epilepsy monitoring units.

You heard me talk about epilepsy severity and what does that mean? It means basically the continued presence of the most dangerous seizure type that we know of, which is basically convulsive seizures or grand mal seizures. Over the last few years, we've become better at identifying breathing and cardiac rhythm problems in our patients. It's very important for patients with uncontrolled epilepsy to have epilepsy monitoring assessments where breathing and cardiac rhythm and cardiac function are also assessed. Seizures that have these complications, breathing complications or cardiac complications, those may be severe seizures and worth taking note of.

Seizure clusters are often associated with SUDEP, so clustering is never a good idea. If patients have clusters, then the physicians need to take note and arm patients and carers with the relevant medication that are bought clusters. Of course, prolonged seizures and status epilepticus often result in hospitalization and brain damage and so forth. These are also a marker of severe epilepsy and severe seizures.

Just to show you what convulsive seizure frequency means, this is a well known study which pool together several case controlled studies of SUDEP. What this essentially tells you is that the odds of a patient dying if they have generalized convulsive seizures, as compared to patients who don't have convulsive seizures, just one or two convulsive seizures per year

increase the odds fivefold. If a patient has three or more convulsive seizures per year, it increases the odds 15 fold. This is a very important risk marker for SUDEP in all epilepsy, rare or not.

How does SUDEP occur? It's usually a grand mal seizure, which is relevant. We believe that during or after a grand mal seizure, something happens to cardiac rhythm and to breathing that puts the patient on a very dangerous path and often results in cardio respiratory arrest. Very rarely, it may happen after a partial seizure, so a non-convulsive seizure. Even more rarely, it sometimes happens without any kind of seizure having occur. It often occurs at night. It often occurs with patients being found prone at night, and it occurs when there is nobody present to observe the seizure and to affect rescue of the patient.

We don't know exactly why some individuals with the same profile are at risk and why some individuals with the same profile are not at risk. This is something that we are actively studying, but we believe that the parts of the brain that modulate or control breathing and heart rhythm are damaged by many years of grand mal seizures because of challenges with oxygenation and things like that. If that's happening on a regular basis, maybe that's not good for the brain.

How do we look for breathing and cardiac rhythm problems? We use all these devices in a modern epilepsy monitoring unit. This looks at carbon dioxide. This looks at breathing rate rhythm. This looks at blood pressure. We use this usually only for research circumstances. With this, we look at oxygen, and this also for carbon dioxide. These are the instruments and gadgets that we use in epilepsy monitoring units to assess cardiac and breathing risk.

What do we find? Here is a brainwave trace or an EEG in somebody who is having a seizure. These last two channels that you see down here are normal breathing during a seizure. This is an individual who has a seizure, but where breathing is occurring normally without any difficulties.

Here is another patient where there is a seizure occurring, and you can see that, before the seizure starts, the patient's breathing fine, but when the patient has a seizure starting, the breathing also stops. This is what we refer to as ictal central apnea. The vast majority of patients, when you look at the duration of the cessation of breathing, they stop breathing just for a few seconds. On this scale here, you see oxygenation, so oxygen levels don't drop very much.

Most patients are in this particular group over here, but in some individuals, the duration of breathing cessation is very long, over a minute, and the drop in oxygen is quite a bit. The oxygenation drops below 75%, and we believe that these are individuals who are at risk of SUDEP.

There is a different type of breathing dysfunction. This is what we refer to as post-convulsive central apnea. This is cessation of breathing after a convulsive seizure. Here is a brainwave trace showing that a patient has just stopped having a seizure. This is the EKG, and you can see with the EKG that the heart is not doing very well. It's kind of stopping and starting. This is the breathing trace down here in blue where you see that there is no regular breathing going on. The breathing is shallow, and it's occurring in fits and starts. Actually, there are long periods where breathing does not take place. This is post-convulsive central apnea, along with a disordered cardiac rhythm, or bradycardia, and we believe that this is dangerous for the patient, too.

What drives this? We believe that there is this molecule called serotonin. It's very important for breathing. It's very important for arousal; all of the things that go wrong after a seizure in patients who die of SUDEP. We know from studies in patients who have this kind of breathing dysfunction after a seizure, that their serotonin levels after a seizure are not very high. This is something that's come to light in recent times with the research that's being done.

All of this stuff; breathing control and cardiac rhythm control; these things in large part are driven by a part of the brain called the brain stem. The brain stem is the part of the brain that senses if a person's not breathing well. If a person doesn't breathe well, their carbon dioxide levels go up. Of course, the normal response is to breathe fast to get rid of that carbon dioxide. If we're not doing that, then there is a problem.

Here, for example, is somebody's carbon dioxide level creeping up, and they're breathing rate creeping up. This is something that is normal. Here is an individual where carbon dioxide levels are going up the scale like this, but their breathing rate is not increasing. The line is flat. This is somebody whose brain stem is not working well.

From animal studies, we know, and we don't know if this transposes to humans or not, but in animals, we know that there's something called spreading depression in the brain stem where, after a seizure, the brain stem slowly shuts down and

prevents normal breathing and normal cardiac rhythm from resuming. The brain stem is a structure that we believe from MRI studies is damaged because of longstanding epilepsy and longstanding compulsive seizures.

How do we know this? This is an MRI study of patients who've died of SUDEP, but in some time in the past have had MRI scans of their brain done. When these scans are analyzed very finely, you find that there are parts of the brain stem that are a bit shrunken. In other words, they're damaged. We believe that this predisposes to SUDEP.

The proof of this comes from the fact that individuals who've died of SUDEP, their brains have actually been examined under the microscope. We've found that neurons in the brain stem, particularly those neurons that have serotonin as the brain molecule for function, those neurons are depleted, so we believe that this predisposes to pap.

Can we identify this kind of dysfunction even before a person dies of SUDEP? The short answer is we have begun to make inroads into that. So I gave you an example of carbon dioxide. We can actually make a patient breathe carbon dioxide and see how their breathing responds. If the breathing doesn't respond very well, then it may be that they're predisposed to SUDEP. We can actually do that identical experiment, so give them carbon dioxide and see how they breathe in the MRI scan.

Here, these are a group of patients with epilepsy, and these are a group of healthy controls. You can see that the pictures look very different. Here, the brain stem absolutely lights up in a patient, and in a healthy control, it doesn't light up very much. Here is a system under stress. This is something that we're actively studying to see if we can use this for premortem risk identification in our patients.

We've become good at figuring out what parts of the brain control breathing and cardiac function and things like that. Here are stimulation experiments to figure out what parts of the brain control breathing. Here in red, you see that these parts of the brain that we can refer to as the amygdala and the hippocampus, these seem to control breathing. This particular part of the brain here that refer to as Brodmann area 25 seems to control blood pressure.

How can we take advantage of this? Here at the University of Texas, we have a talented researcher who actually with cure funding is looking into how we can take advantage of our

knowledge of these brain structures that control breathing. Here, for example, is a patient whose brain structure that we refer to as the anterior singlet is being stimulated electrically. You can see that when the brain is stimulated electrically, patients start breathing faster. Here's the stimulation again, and you can see the patient breathing faster. Here, even more marked with brain stimulation, you can see the patient breathing faster.

I think we have started on the journey where for patients who have disordered breathing during and after seizures, we may be able to do something by stimulating their brain and getting them to breathe.

Something that is tremendously encouraging for people like myself who've been looking at mortality in epilepsy and SUDEP for a long time is this particular study which showed that when we look at two different time periods; 2009 to 2012 and 2013 to 2016; in three different regions of the United States, we find that the mortality from SUDEP has actually declined over time. The rate of incidents of SUDEP in these three areas has gone down, and that's in incredibly encouraging.

The question that you might have is, how come? What's changed, and why is this happening? We believe that there is a relatively simple answer. That is to do with the fact that both patients, carers, doctors, and the community, thanks to the tireless work done by all kinds of folks, organizations like Cure and PAME, and of course, scientists, researchers, and patient advocates have just made knowledge of the problem more widespread. The more we know about it, the more likely we are to pay attention to it, the more likely we are to divert resources to doing something about it.

This is a sobering slide, which woke a lot of us up 10 years ago, which is to say that when neurologists in the United States and Canada were surveyed, we found that a lot of us never really discussed SUDEP with our patients. 12% never discussed it, 30% rarely discussed it, and 33% discussed it sometimes. In my view, this should be almost a 100% discussion in clinic because it's such an important topic.

Studies like this have increased awareness of the problem, and of course, we've listened to the community. This is about acknowledging the problem. When you look at persons with epilepsy who worry about dying of epilepsy, that's the majority of patients, and that's the majority of carers. People want to know about this and want to discuss it and want to know what

can be done about it. I think it's a dynamic where we all come together, talk about the problem, talk about how it pertains to that individual patient; my patient, your loved one; and what we can do to mitigate risk.

This is a slide that I always show. Back when I was a resident in the mid-nineties, this was the sum total of research that was being done in SUDEP. We fast forward to the situation now. There's been exponential increase in research towards SUDEP. I think acknowledging the problem, researching the problem, we've made tremendous progress over the years.

I'll conclude by saying that SUDEP happily is rare overall, but it is a catastrophic outcome when it does occur. It's more frequent in uncontrolled epilepsies. Some rare epilepsies do have higher rates of SUDEP. I talked about Dravet's Syndrome. There are others; Dup15q, for example, where there is a higher rate of SUDEP than other patients who have epilepsy. What seems to underpin risk in all the epilepsies is generalized convulsive seizure occurrence, so frequent convulsive seizures and severe convulsive seizures. We spoke about severity. These are probably responsible.

What underpins this is that there are certain parts of the brain that seem to be damaged by seizures over long periods of time. In particular, the parts of the brain that control breathing and cardiac function; what I refer to as the brain stem. I think we're getting to a point where we may be able to identify specific patients who have brain stem abnormalities before any chance of mortality. We hope to get to a point where we can do this in all patients who are potentially at risk.

Proper assessment of risk in asking questions on risk mitigation with your physician is extremely important. The more it's discussed, the better it is. At the moment, there isn't an anti-SUDEP therapy or an anti-SUDEP drug, but seizure freedom is essentially what is the most effective form of SUDEP prevention, so never stop trying to get your patient free of seizures.

I'll stop here. Thank you.

Dr. Laura Lubbers: [34:03](#)

Thank you so much, Dr. Lhatoo. That was a lot of information. Very helpful to understand the biology and what's happening in the case of seizures in SUDEP.

We'll now begin the Q&A portion of our webinar. Just a reminder that if you have questions, please submit them via the

Q&A tab on your zoom panel and click send. I know there's a lot of questions that have already come in and some great comments in the chat, as well.

I do want to start out in and bring Abby back into the discussion because, Abby, I know that you have a specific story about somebody in your small epilepsy community who was confronted with SUDEP. How did you find out about SUDEP? Tell us more about this family and what's happening in your community.

Abby Tanner:

[34:50](#)

Sure. Yeah. I'll tell you just now is what I've learned about SUDEP was right here on this call with you. I didn't think it applied to us. It wasn't until my son's third birthday when another one of our little buddies in our group, Emma, passed away in her sleep. She had a seizure, and they found her, I think, with her head in the pillow, and it was devastating. It was that point on that my husband and I started monitoring Lincoln, and we had a hospital grade monitor. We hooked him up every night. It used to be that we would only monitor his breathing when he was sick, when we knew that he was compromised, but from that night on, we have put Lincoln on his stat monitor every single night.

I didn't even know that it was because of SUDEP, still. I wasn't associating that with Emma's passing or anything like that. We just knew we needed to monitor him. It's not a conversation that we had with our doctors. Honestly, I thought that Lincoln has lived through so many thousands of seizures that one couldn't possibly be the one to take him out, for lack of better terminology. I think I thought that was a non-issue. Like, "No, he's just had lots of seizures, and he's okay. He comes out of them."

I'm realizing now, thanks to the doctor's presentation, that Lincoln fits all those boxes, and we're not going to have seizure freedom. We're going to keep working for it, but he is very high risk. I'm comforted knowing that we're doing what we can, and I even have questions for the doctor myself. We happened upon a solution. We can't prevent it, but monitoring Lincoln and keeping him in our room is something that we're comfortable with in doing what we can.

Dr. Laura Lubbers:

[37:00](#)

Right, right. Thank you. That's a difficult story, and this is part of the issue in our community is we are not talking about it, and people aren't understanding. It's so important to find ways to have this dialogue, to be aware of it, and then to know how to

bring it up with a physician, because it can be a little intimidating.

Sam, I'm wondering if you can comment on successful ways that parents have brought this issue to your attention. I know you're very attuned to all of this, but what recommendations do you have for parents who want to talk about this and don't know how to bring it up?

Dr. Lhatoo: [37:37](#)

I think the way in which patients have proactively asked me, it's often me discussing SUDEP with patients and their carers, but every once in a while a proactive parent or a proactive carer or a patient himself or herself will bring this up to me. It's a very direct and inoffensive question, which is, "What is the risk of something bad happening to me?" It's a straightforward question that deserves a straightforward answer.

Most of us who have observed a grand mal seizure to occur will know that a lot of the time patients do turn a little blue around the lips and don't breathe very well after a seizure. What does that mean to that individual? I think it's a very important question to be asked and to be addressed. A lot of the time is the answer is reassuring. Sometimes it is okay. These are the specific things that need to look out for, and this is how you can be careful.

Dr. Laura Lubbers: [38:58](#)

Okay. Yes. I think that this pertains, certainly to SUDEP, but seizures in general, because accidents can happen and just putting it out broadly, "How could I be harmed by this, and what can I do to prevent harm?"

In line with that, we have a question from somebody who asks an unlike Abby situation where she's able to have her child sleep in the same room, "What do you recommend for children and teens who want to sleep alone? Is there a specific type of monitoring device, either that they wear or that is connected to the bed, that's helpful?"

Dr. Lhatoo: [39:33](#)

Yeah. That's a very, very important question. I think there was a time when we were very careful about making overbearing recommendations because teenagers in particular have to live their lives. There's a quality of life issue, et cetera, et cetera. But we know from recent scientific studies that one of the most powerful factors that prevents death probably is the presence of somebody else in the room; whether somebody else is in the room sleeping with that particular individual or not. There's something to be said about that kind of observation.

Of course, as you've already alluded to, there's the in between of monitoring devices and a lot of my patients do use them successfully. There are a couple of FDA approved devices that are out there on the market. I personally don't have shares in either, but there is the Empatica, the Embrace device. There's Brain Sentinel. They both use different approaches. What they don't do is prevent SUDEP. What they do, do is let the designated carer or person know that a seizure is occurring or has occurred. I'm an advocate for the use of whatever technology is available for mitigating risk.

Dr. Laura Lubbers: [41:04](#) Okay, great. Thank you.

Here's another device related question, but related to the VNS. "Have there been any studies with SUDEP and VNS patients? If so, are there any differences in the rate of SUDEP?"

Dr. Lhatoo: [41:17](#) Yes. Great question. There is actually a very well-known study where several thousand patients who had had VNS devices implanted were studied over a period of time. It looked as though the rate of SUDEP over a prolonged period of time actually went down in the VNS population. Over a long period of time, it may be protective against SUDEP.

This is obviously one study, but it was sufficiently powered, I think, because there were thousands of patients who were studied to say that there is probably something there. When you couple that with the fact that VNS in some individuals reduces seizure frequency, then there's a case to be made for doing VNS in patients who have not responded to other measures.

Dr. Laura Lubbers: [42:15](#) Okay, but a VNS alone is not completely protective?

Dr. Lhatoo: [42:18](#) I wouldn't say that VNS alone is completely protective. Yeah.

Dr. Laura Lubbers: [42:21](#) Okay. There's another... Lots of devices. "Can a CPAP or other oxygenation aid device help those with SUDEP risk factors at night during sleep?"

Dr. Lhatoo: [42:35](#) That's a pretty nuanced question, I have to say. When it comes to improving sleep quality in patients with epilepsy, yes, absolutely. CPAP and those things might be useful because sleep deprivation, poor sleep quality, et cetera, et cetera. These are all linked to seizure frequency, and of course, seizure frequency is linked to SUDEP.

In somebody who's having a seizure and may be likely to suffer from SUDEP, would CPAP prevent that? Probably not, and I say that for number reasons. Chief among those being that, in a convulsive seizure, you can have all monitoring devices, they become dislodged, there's a lot of movement, shaking, et cetera, et cetera. So I wouldn't rely on CPAP for preventing SUDEP directly like that.

Dr. Laura Lubbers: [43:28](#)

Okay. Here's a slightly more technical question, "Should electrical stimulation of the medulla, and maybe you can explain where the medulla is, be more widely used to study or to prevent SUDEP?"

Dr. Lhatoo: [43:42](#)

Great question. It's obviously somebody who knows neuroanatomy.

The medulla is part of the brain stem, the same structure that I was talking about, and medulla probably is the most important part of the brain stem for a final common pathway to controlling breathing and cardiac rhythm and blood pressure. A very important structure. It's a very challenging part of the brain to study in humans because to stimulate the medulla, you have to put electrode into the brain stem, and that always carries a risk of bleeding hemorrhage and so forth. The outcome of bleeding in that part of the brain stem would be catastrophic, would be death. To my knowledge, nobody has done that in humans yet, but there are researchers who are looking at stimulating other parts of the brain stem; parts of the brain stem that are maybe less risky, but at the same time, likely to impact breathing and cardiac function.

There's more to come. In the next few years, I think we will hear a lot more about brain stem stimulation.

Dr. Laura Lubbers: [45:00](#)

Okay. Thank you. It's interesting to see how the science is evolving, for sure, in tackling these, these difficult areas of the brain to reach.

For uncontrolled seizure patients, how often would you recommend doing an EMU stay? I know that the MORTEMUS study was done using patients in the EMU.

Dr. Lhatoo: [45:22](#)

The EMU has a very specific role. We either send patients there for diagnostic assessment. Here, we're trying to figure out if the patient has epilepsy or a related disorder. Or, we're trying to see what kind of epilepsy it is. That's diagnostic EMU assessment.

Then there's the other kind of EMU assessment, which is the presurgical assessment; studying the seizure in order to do brain surgery. It's the latter type in which we've become more and more practiced at assessing cardiac and breathing function, as well. There isn't much point in repeated EMU assessments for assessing risk. Usually, if intractability or lack of control through medication surgery has been established, then one EMU assessment where cardiac and breathing function are looked at as well is probably enough.

Dr. Laura Lubbers: [46:31](#)

Okay. Yeah, that piece is so important. I think that's not talked about a lot. It's also studying the breathing and the cardiac.

Here's a question related to the rare epilepsy categorization. "Is Lennox-Gastaut a part of this group of rare epilepsies that are impacted more significantly by SUDEP?"

Dr. Lhatoo: [46:55](#)

Yes. I would say that it is. It's one of the commoner varieties of the rare epilepsies, but Lennox-Gastaut really is a syndrome. It's not really one specific genetic condition. Within the Lennox-Gastaut rubric, we actually have dozens of other conditions that make up the syndrome complex that we call Lennox-Gastaut.

Dr. Laura Lubbers: [47:26](#)

Okay.

You've talked a lot about people who may have had longterm epilepsy, lots of seizures, but there are instances where after just a handful of seizures, somebody has passed due to SUDEP. We think of some more public cases like Cameron Boyce who passed away, but there are others. Is it possible to die from SUDEP without either a diagnosis of epilepsy or a first tonic clonic seizure?

Dr. Lhatoo: [47:59](#)

Absolutely, yes. Happily, I would say that that kind of situation where it's not uncontrolled epilepsy is extremely rare, but it does happen. As recently as two months ago, I was contacted by colleagues in another part of the country who had just such a patient who passed after a second tonic clonic seizure. We've come to understand that SUDEP is actually a heterogeneous phenomenon. It's not just one thing, and there isn't just one prototype patient that fits that mold. There's actually a variety of types. There are tragic cases where a first ever or a second ever seizure kills, but I have to say that that is very, very rare.

Dr. Laura Lubbers: [48:57](#)

Okay. That's helpful.

You've talked about the cardiac disturbances, but could you talk a little bit more about that? Does that mean cardiac arrest, or what do you mean by a cardiac disturbance or arrhythmia?

Dr. Lhatoo: [49:10](#)

By cardiac disturbance I mean cardiac rhythm dysfunction. Cardiac rhythm can be disturbed in a variety of ways during seizures. The heart can either be too fast or too slow. When it's too fast, it can happen in a pathological fashion; conditions that we refer to as ventricular tachycardia, ventricular fibrillation, and things like that. Those are very dangerous. In the SUDEP context that seems to happen extremely, extremely rarely. What is more common is the heart beating too slow and maybe even stopping. That's what we refer to as bradycardia and asystole. You can imagine that after a seizure, if a patient is not breathing too well and their heart's not beating too fast either, that their blood pressure's not going to be great. Of course, it sets a vicious spiral that can result in an unfortunate outcome.

Forgive me. I'll just turn my phone off.

Dr. Laura Lubbers: [50:14](#)

Okay.

I'd like to bring Abby back on. Abby, I know that you had some questions. Now that you've heard this discussion, as a parent, what do you think and what sorts of questions would you be coming to your physician with now? Sorry to put you on the spot.

Abby Tanner: [50:31](#)

No, first off, I'm like, "Wow! It's a miracle my son is still here!" We have prolonged QTc. He has intractable epilepsy. He's a boy. He has cluster seizures. I'm thanking God that he's still here.

I feel like quite a few of the questions coming in were kind of along the lines of what I was thinking. My son has a VNS, so I was worried that might be a problem.

Somebody asked about the CPAP, that's something that I have chosen not to put on my son, but I'm wondering if I should? I'm wondering if that makes a difference breathing-wise.

My question would be the sleep studies that my son had done seem like they're separate from EKGs, like these are two different events. I'm wondering, do I need to pursue having them done together? I'm not even quite sure what my question is. It just seems that the breathing patterns that you're looking for are maybe things my neurologist isn't looking at. Is my

neurologist looking at that, or my epileptologist, or are they just looking at seizure activity? Are they focused in on breathing patterns? How do I know if my son's intractable epilepsy is causing breathing issues not related to just, "Oh, his SATs dropped"?

I don't know if that was very clear cut, but that's kind of where I'm going. How do we get everybody together on the same page to talk about this risk?

Dr. Laura Lubbers: [52:19](#) Right. That's an excellent point, and certainly making sure that everyone is educated around the need, it sounds like, to be thinking about these end points.

Abby Tanner: [52:31](#) Absolutely.

Dr. Laura Lubbers: [52:32](#) Parents, physicians...

Abby Tanner: [52:34](#) I'm going to guess that my team hasn't brought this up... All of the specialists that my son has, I'm going to guess they haven't brought this up because they didn't think it applied! I don't know. Maybe they didn't say, "Oh, this is our primary focus right now." I think generally speaking, we're always just trying to get ahead of the next seizure, ahead of the next medical challenge, and that was back seat because it wasn't right here in front of us; the present issue with symptoms.

Dr. Lhatoo: [53:03](#) If I may just make a comment, which is, I shared some of the recent research findings with you folks today, and it is always the case that clinical practice lags a little behind what comes out in research. That's only correct because research findings need to be validated, replicated, reproduced, and so forth before they become standard clinical practice. It is not standard clinical practice in many places to routinely measure breathing. Cardiac rhythm is done. EKG is done in most places, but breathing is not routine. I believe that it should, and there are a group of us who are strong advocates for it.

Over the coming months and years, you'll see more and more folks who will begin to do it in their epilepsy monitor units. But in sleep studies, breathing is very carefully measured, so I would imagine that your child has had that done.

Dr. Laura Lubbers: [54:13](#) Here's a quest-

Abby Tanner: [54:14](#) So then you would say- Oh, sorry.

Dr. Laura Lubbers: [54:14](#) No, please, go ahead. Go ahead, Abby.

Abby Tanner: [54:19](#) I've had a hard time, then, making the choice to put a CPAP on my son because it's a quality of life thing. His SATs aren't dropping, and I don't understand the science quite like his team does.

What would my question be, then? I guess, could you help me with the case for why breathing is so important, that breathing patterns... Obviously, breathing is important, but these breathing patterns, because obviously it is, and I'm not fully awake. I can't see the details of, "Oh, his breathing's this great" or, "It's not this great."

I really appreciate your presentations today, doctor. You've given me a lot of info that I didn't have before.

What would be the case for taking steps like this? The CPAP is such a small thing that would help breathe better, which obviously helps his brain work better. But like you said earlier, too, is it something that's worthwhile if it's a brain stem damage issue? Am I asking something that can't be answered?

Dr. Lhatoo: [55:34](#) No. I think your questions are totally fair. We may be looking at two different things here. One is, of course, a sleep disorder, which is basically what CPAP is for, but a pertinent question, which I think is what you're driving at, is, "Is there breathing dysfunction that specifically relates to your child's seizures?" That's a question that you would want to ask your specialist, and also, make your own observations. What happens after a seizure? Does your child stop breathing? Does he turn blue for a while? That kind of stuff.

Abby Tanner: [56:17](#) That was really helpful just to have that question to be able to take to our sleep doctors.

Dr. Lhatoo: [56:22](#) Of course.

Abby Tanner: [56:23](#) Is it related to a breathing disorder or seizure activity?

Dr. Lhatoo: [56:29](#) Yes, yes.

Abby Tanner: [56:30](#) Thank you for that.

Dr. Laura Lubbers: [56:31](#) Those are great questions and really thinking holistically about what's happening, not just with the seizures, but as a part of the seizures. I think this was an amazing discussion, and I'm sorry to

wrap it up. I know that there's still so many great questions in the chat and in the Q&A. I'm sad we can't get to them all.

I do want to just to encourage people to go to the Partners Against Mortality in Epilepsy, the PAME website. I believe it's pame.org. Gardner, if you're on and you want to put that in the chat, I think that would be awesome because I think we need to continue on as a community to have this discussion and get people thinking about this.

Also, Danny Did is a great resource for devices and more information if you're interested about devices that could help with SUDEP and alerting about seizures. We've got some great partners in this space, but clearly we need to increase the knowledge and our voices in this, including around recording, monitoring, mortality in epilepsy. It's under-reported. We do believe that. We need to change that, as well.

I know we're overtime, but I want to thank Dr. Lhatoo for your great presentation, and Abby for your engagement and your sharing of your family's story, as well. You've given us a lot to think about. I want to thank, again, the folks at PAME, Wishes For Elliot, and Deep Connections for partnering with us on this very important discussion today.

I'd also like to thank this amazing audience. We grow and grow all the time, and we have such good comments and questions that come in. Thank you so much for your participation.

If you have additional questions about this topic, or wish to learn more about Cure Epilepsy's research programs or webinars, please visit our website or email us at research@cureepilepsy.org.

Finally, I'm sure we are all preparing for a busy summer season. Please stay tuned for the announcement of our fall webinars that will be announced later this month. Next month, I'm sorry.

Thank you, again, Dr. Lhatoo and Abby and all of us who are participating in driving this discussion forward. Thank you.