

## THE DIAGNOSTIC AND TREATMENT CHALLENGES OF INFANTILE SPASMS (WEBINAR TRANSCRIPT)

- Dr. Laura Lubbers: [00:06](#) Welcome everyone. My name is Laura Lubbers and I am the chief scientific officer of Citizens United for Research in Epilepsy or CURE. I want to thank all of you for joining us today. CURE is pleased to continue our Leaders in Epilepsy Research Webinar Series, which consists of webinars throughout the year that highlight some of the key research that's being done on epilepsy.
- Dr. Laura Lubbers: [00:29](#) Today's webinar, which is being sponsored by our friends at Sunovion, will focus on a relatively rare but catastrophic seizure disorder known as infantile spasms, also referred to as West Syndrome. And it will be presented by Dr. Shaun Hussain.
- Dr. Laura Lubbers: [00:47](#) CURE's mission is to find a cure for epilepsy by promoting and funding patient-focused research. This year we're celebrating 20 years of impact in the field of epilepsy research. CURE has been instrumental in advancing research in many areas including infantile spasms, post-traumatic epilepsy, sudden unexpected death in epilepsy or SUDEP, and genetics, just to name a few.
- Dr. Laura Lubbers: [01:13](#) Today's webinar is entitled Diagnostic and Treatment Challenges of Infantile Spasms, and will discuss the importance of early detection for infantile spasms, as many symptoms can be easily overlooked or mistaken.
- Dr. Laura Lubbers: [01:27](#) In addition, some of the promising advances in both the diagnosis and treatment of infantile spasms will be highlighted. Dr. Shaun Hussain is an assistant professor of Pediatrics at UCLA. He's the director of the UCLA Infantile Spasms Program, and as the inaugural recipient of the Elsie and Isaac Fogelman Endowed Chair in Pediatric Neurology. The focus of his clinical and research endeavors is infantile spasms and other forms of severe pediatric epilepsy, including the syndromes of Lennox-Gastaut and Dravet.
- Dr. Laura Lubbers: [02:04](#) Before Dr. Hussain begins, I'd like to encourage everyone to ask questions. You may submit your questions anytime during the presentation by typing them into the questions tab of the GoToWebinar

control panel and clicking send. My colleagues from CURE, Brandon Laughlin, will read them aloud during the Q&A portion of the webinar.

- Dr. Laura Lubbers: [02:25](#) We do want this webinar to be as interactive and informative as possible. However, to respect everyone's privacy, we ask that you make your questions general and not focused on a specific loved one's epilepsy.
- Dr. Laura Lubbers: [02:39](#) I also want to mention that today's webinar, as well as all previous and future webinars, will be recorded and available on the CURE website. So, with that, I'll turn it over to Dr. Hussain.
- Dr. Shaun Hussain: [02:51](#) Thank you for the kind introduction. So, we're going to be talking about current challenges in diagnosis and treatment, but we will emphasize challenges in treatment.
- Dr. Shaun Hussain: [03:05](#) So, first, some disclosures. I have fortunately or unfortunately received support from multiple pharmaceutical partners who are developing therapies for infantile spasms and epilepsy in general. So, keep those in mind as you consider what I have to say.
- Dr. Shaun Hussain: [03:21](#) So, first, some terminology. Infantile spasms is really the same things as epileptic spasms. Epileptic spasms has been a relatively new term that has been applied. And it's been inspired by the observation that infantile spasms can happen in older children or even adults. But don't worry about this distinction. They really refer to the same thing, this seizure type that we're going to be talking about today.
- Dr. Shaun Hussain: [03:43](#) The second terminology to discuss is West syndrome. So, traditionally, this refers to a triad of infantile spasms, hypsarrhythmia, and developmental delay. And this term is often used interchangeably with West syndrome as well.
- Dr. Shaun Hussain: [04:32](#) So, west syndrome includes infantile spasms, hypsarrhythmia and developmental delay. Now, let's quickly just talk about what hypsarrhythmia is.

Dr. Shaun Hussain: [04:40](#)

So, here we have two panels. The panel on the left is normal looking brainwaves in an infant. You can see that they are discernible. You can follow each line across the screen.

Dr. Shaun Hussain: [04:50](#)

And in contrast, hypsarrhythmia is the typical pattern that's most often accompanying infantile spasms and it's very high voltage and this refers to the very tall and disorganized pattern of these brain waves. You can't really follow an individual line across the screen without getting mixed up. This chaotic pattern has a lot to do with why development is interrupted in infantile spasms. It's just that the brain is not in a calm situation to learn to develop.

Dr. Shaun Hussain: [05:22](#)

When you think about the development of children at the time that infantile spasms begin, about half are normal and about half are abnormal. And our job when we see the onset of infantile spasms is to protect development as best we can, no matter how much damage has already been done. The other big challenge is knowing to what extent development is abnormal because of infantile spasms, or because of the causes of infantile spasms. And that's a really tough judgment to make on an individual patient basis. But we know in general, there's a combination of those two things going on.

Dr. Shaun Hussain: [05:57](#)

We often use the term etiology, and this just means the cause of infantile spasms. And despite a lot of advances in neuroimaging and genetics, still about 33%, one third of cases have no known cause. When we think about categories of the causes of infantile spasms, there's a pretty big variety and the main categories are structural abnormalities, things like stroke or hypoxic ischemic encephalopathy, malformations of the brain like cortical dysplasia.

Dr. Shaun Hussain: [06:26](#)

Now, there are a whole host and a growing list of genetic causes of infantile spasms. There are a few metabolic causes. But again, still, many are unknown. And you can see that if you add up all of these bars, you get to more than 100%. And that's because a lot of these disorders are overlapping. So, disorders like tuberous sclerosis have structural abnormalities and a genetic basis. And you can see that in this rather

complicated Venn diagram showing the overlap of these different categories.

Dr. Shaun Hussain: [06:59](#)

When we look at very specific causes, we see that the number one category is unknown cause. But among those top three known identified causes of infantile spasms, we have FCD or Focal Cortical Dysplasia, Tuberous Sclerosis Complex or TSC. And HIE which is Hypoxic Ischemic Encephalopathy and this refers to a stroke in the newborn period.

Dr. Shaun Hussain: [07:25](#)

So, there have been pretty big advances in genetic testing, and that has really been leveraged to improve the diagnosis of epilepsy. But I would still say we have a long way to go. And when we think about the different testing and modalities available, they range from an easier and cheaper testing and usually what we call first line testing, which is the chromosomal microarray.

Dr. Shaun Hussain: [07:45](#)

And that seems like a complicated name, but it really just refers to a relative easy way to look for extra pieces of DNA or missing pieces of DNA, which can explain the presence of developmental problems or infantile spasms. The yield of this testing though is rather low. It's only about 5 or 10%.

Dr. Shaun Hussain: [08:04](#)

When we do suspect a genetic cause, the next step is usually something we call an epilepsy gene panel. And this varies depending on which company or university is conducting the testing. But it typically involves the sequence of about 100 genes associated with epilepsy. And the yield there is better than a microarray, but it's still modest. It's only about 20%.

Dr. Shaun Hussain: [08:27](#)

Now, in those situations in which a gene panel doesn't give us an answer, we then proceed to a modality called clinical exome sequencing or whole exome sequencing. And this is a relatively broad spectrum testing, meaning that we don't just sequence 100 genes associated with epilepsy, we actually sequence every single gene. And at latest count, that's about 22,000 genes. And you can get a diagnosis yield of about 40% if you sequence all of the genes of a patient and both of their parents. That process where you sequence all three people is called trio exome sequencing. But you'll still see that

the majority of cases even when we suspect a genetic cause still go undiagnosed.

Dr. Shaun Hussain: [09:11](#)

There is also a lot of fanfare surrounding the development and progress in whole genome sequencing. So, not just sequencing the DNA that codes for specific genes and proteins. But all of the DNA in between and that we know that DNA is actually very important, even though a lot of it does not actually code for protein sequences.

Dr. Shaun Hussain: [09:31](#)

But our ability to interpret that data is still very much in the early stages, and the diagnostic yield of genome sequencing is only a shade better than exome sequencing at this point. However, I hope that I give this same lecture in 10 years and that that green bar on the far right is closer to 100%. Well, we'll see how well we can do. But I would also remark that in the last generation, all of these bars were essentially nonexistent, 25 years ago. Our ability to find isolated genetic causes about epilepsy was quite modest.

Dr. Shaun Hussain: [10:04](#)

So, how are kids doing with infantile spasms? If you fast forward to age two, I would say we're just doing okay. And that's probably an overstatement. Only about 20% of kids are normal or near normal at age two. And that reflects the kids who respond well to treatment, who have pre-prompt diagnosis of their epilepsy, and who have causes of infantile spasms that are themselves not terrible.

Dr. Shaun Hussain: [10:30](#)

On the other hand, about 10 to 20% of kids have deceased by age two. And that's usually not because of infantile spasms. It's usually because of complications of the disorders which also cause infantile spasms. So, that may be inspiring a little bit of excessive fear in the viewers.

Dr. Shaun Hussain: [10:47](#)

What is troubling to me is that the great majority of patients are not normal and are often suffering sequelae like intractable epilepsy, other forms of seizures and epilepsy, a lack of normal development, and many of these children are at substantial risk for autism. And we're trying to figure out why that is. And if we can, even in those cases where we can't control seizures, is there a way to still improve development and reduce the risk of autism.

- Dr. Shaun Hussain: [11:17](#) So, here, I want to highlight the urgency of the diagnosis of infantile spasms. So, this is a plot of development. And this is one particular developmental scale called the VABS or Vineland Adaptive Behavior Scales. In general, average is 100. You can see that on the x-axis here. And it ranges from zero to infinity, but the vast majority of patients are in this 70 to 130 range. That's what we call normal development.
- Dr. Shaun Hussain: [11:44](#) Now, in comparison to kids who have diagnosis and the beginning of treatment in less than seven days, in less than one week, that's the goal. If you wait just one week more, those kids will lose about seven points on their development. I'm sorry, about four points on their development just by waiting a week.
- Dr. Shaun Hussain: [12:04](#) And when we compare that to patients who wait even two weeks longer, they lose another four points. And if we go forward even another month, there's another four points of loss. Anything over that, over eight weeks, another four points are lost. This is a tremendous developmental loss that has nothing to do with treatment response. This is just an effect of diagnostic and treatment delay.
- Dr. Shaun Hussain: [12:27](#) So, one of our big struggles is not only to come up with better therapies for infantile spasms, but we need to be on the ball. We need to identify infantile spasms quickly and we need to treat them aggressively. There can't be any delays because that is just adding fuel to the fire.
- Dr. Shaun Hussain: [12:43](#) So, with that said, how are we doing? We don't actually have good data internationally. I'm just sharing UCLA data right here. We surveyed 100 consecutive patients in our center. We saw that about a third had prompt diagnosis and treatment. About a third were poor in this two to eight-week range where they were suffering substantial developmental loss just because of delay. And then about a third had just what I would call abysmal delays in diagnosis. So, clearly, there's room for improvement. And we really need to spread the word about infantile spasms, what these seizures look like.

Dr. Shaun Hussain: [13:18](#) One big question was, well, why is this happening? Before we did the survey, we suspected that there might be effects on as a function of insurance type, like maybe patients with bad insurance are having delayed access to care. Maybe patients with low socioeconomic status, low wealth or income, maybe they are disadvantaged in some way. Maybe specific racial or ethnic groups are suffering disproportionate delays. Maybe patients who live in rural areas, because they don't have close access to the big city. Maybe there's a delay in diagnosis on that basis. We actually saw none of these.

Dr. Shaun Hussain: [13:56](#) Really, all we saw was that the parents of children with infantile spasms who prefer to speak other languages in the home had delayed diagnosis and treatment and in general, at any given time after the onset of infantile spasms, those folks were about half as likely to have a diagnosis and begin effective therapy of infantile spasms.

Dr. Shaun Hussain: [14:16](#) But the real big one is lack of physician awareness of infantile spasms. And this is something that I bet a lot of the viewers of this webcast already know that they had been to multiple pediatricians who didn't know what infantile spasms were, didn't know what to make of a video that was provided to them, or weren't able to coordinate a prompt neurology visit. Or maybe it was an emergency room physician who was falsely reassuring or maybe it was a neurologist, who also didn't know what infantile spasms were.

Dr. Shaun Hussain: [14:47](#) So, top to bottom, we need to increase awareness of infantile spasms. People need to know what infantile spasms look like. And I think that's a big challenge. Infantile spasms simply don't look like what most of us conceptualize as a seizure, certainly not what is presented in the media.

Dr. Shaun Hussain: [15:05](#) Okay, so let's begin and talk about some of the treatments for infantile spasms, what we have what we don't have. So, when we think about the big three, we're usually talking about hormonal therapies and specifically ACTH or adrenocorticotrophic hormone. It's actually a protein that's made in our brains. And it has many functions and it is effective in treating infantile spasms. The second is by vigabatrin.

This is a drug that increases brain levels of an inhibitory neurotransmitter called GABA. So, we know how this one works. And the third we'll talk about is surgery.

Dr. Shaun Hussain: [15:40](#)

Let's take a look at these effectiveness rates. So, for ACTH, it's about 55% effective. And I have to comment that the range of reported effectiveness rates are all over the place. There are studies where in which the effectiveness was as low as 15%. Others were it was 100%. So, there's a big spread.

Dr. Shaun Hussain: [16:00](#)

But these data reflect very contemporary observations from the United States National Infantile Spasms Consortium. There are now about 40 centers who are sharing data. And this reflects a pretty good estimate of nationwide experience in the United States. So, the response rate of ACTH is about 55%. Vigabatrin, it's about 36%. Surgery is upwards of 70%. But we have to remember that the folks who get surgery are those who are good candidates for this.

Dr. Shaun Hussain: [16:32](#)

When we think about the side effects of these therapies, they are impressive, unfortunately. So, when we think about ACTH, there is risk of profound immune suppression which can lead to potentially even lethal infections. Lethal infections, like an ear infection, can become a serious pneumonia or meningitis. There's actually some risk of death that accompanies that.

Dr. Shaun Hussain: [16:53](#)

It's probably on the order of one in several hundred patients or maybe one in 1000 patients. There's also a risk of high blood pressure and blood pressure usually has no symptom. So, in the beginning, you can have actually extraordinarily high blood pressure in an infant and have no symptoms whatsoever. But that poses some risk of congestive heart failure or heart failure. And that is also potentially lethal. So, it is absolutely important for anyone who is beginning hormonal therapy with ACTH or other hormonal therapies that they avoid children or others who are sick. And that blood pressure is monitored closely during that treatment.

Dr. Shaun Hussain: [17:30](#)

With vigabatrin, there is risk of vision loss, we're going to talk about that in more detail and it's certainly a scary side effects for any parent contemplating



therapy for infantile spasms. And in surgery, obviously, you need to remove some brain. So, let's talk about that a little bit.

Dr. Shaun Hussain: [17:44](#)

So, when we evaluate patients for surgery, there are three main tests that go into that equation. The first is the EEG and this is a picture of hypsarrhythmia. The second is the MRI. And here's a picture of a small tumor. And the third is called a PET scan or Positron Emission Tomography. This is a metabolic test that looks at how the brain uses sugar.

Dr. Shaun Hussain: [18:05](#)

And it turns out the areas of the brain that are the source of seizures tend to be very quiet, most of the time that they're not using much sugar. They're very inactive. And then during seizures or during infantile spasms, they are very metabolically active. And this is a picture of an image from a patient who had a source of infantile spasms at the lower right side of that image.

Dr. Shaun Hussain: [18:28](#)

So, if we look at these three studies for a patient, we would say that they're probably not a good candidate, because the EEG looks like it's bad everywhere. The MRI is showing a problem with the left side of the image. The PET scan is showing a problem on the right side of the image. Things aren't matching up.

Dr. Shaun Hussain: [18:42](#)

When they do match up though, those tend to identify good surgical candidates where we can simply remove a piece of likely nonfunctioning brain, which is nevertheless the source of seizures.

Dr. Shaun Hussain: [18:53](#)

So, let's look at a different example. So, in this case, we've got an MRI image that has an abnormality on the left side of the image. Same thing on the PET scan. And this right side of the image is what we call an MRI/PET fusion. So, this is a digital fusion of the MRI image and the PET image. It provides the best way to detect even subtle abnormalities that can cause infantile spasms. So, this was a patient who was a good surgical candidate.

Dr. Shaun Hussain: [19:20](#)

And the next slide will show you what we did. So, this is a picture, I should have told you to avert your eyes if you're queasy. This is actually a picture of this

patient's brain in the operating room. And we're performing a procedure called electrocardiography. It's the last final step to evaluate surgical candidacy and figure out the exact margins of the resection.

Dr. Shaun Hussain: [19:41](#)

And here is a picture of before and after the surgery. You can see that there was a pretty clear abnormality in the left side of that left-sided image and that on the right bigger image, there's a big hole where the brain was taken out. This patient had a functional hemispherectomy and is now essentially normal. So, in good surgical candidates, surgery is a great option, especially when they fail initial therapy with hormonal therapy or by vigabatrin.

Dr. Shaun Hussain: [20:09](#)

But returning back to this table, we have to also consider the costs of therapy. And these are unfortunately astronomical. When you look at ACTH, it is an exceptionally expensive therapy, in the upwards of \$100,000 for a course of therapy. Vigabatrin is similarly quite expensive, about 60,000 for a typical course of therapy. Surgery is no bargain either, typically exceeds more than \$100,000 when you think about all of the costs that are entailed.

Dr. Shaun Hussain: [20:37](#)

But there's some debate and we need to consider different hormonal therapies and their relative effectiveness and cost. So, ACTH and prednisolone are pretty similar. So, ACTH, as we discussed before, is a protein that's made in the brain. It travels down to the kidney and the kidney makes a hormone called cortisol. That cortisol and prednisolone are nearly identical. So, when we give prednisolone, it's as though we're skipping some of the body's natural steps.

Dr. Shaun Hussain: [21:06](#)

What is unclear, though, is that ACTH may have other effects directly in the brain that may be beneficial and which prednisolone can't provide. We actually don't know which of these is most effective. And there's a lot of debate that's much of which is beyond the scope of our brief talk today.

Dr. Shaun Hussain: [21:24](#)

When we think about those response rates, this is debated. In my view, I think these response rates are actually quite similar. And that opinion has been

substantiated by experience with the National Infantile Spasms Consortium.

Dr. Shaun Hussain: [21:36](#) The response rate for both of these therapies is in the 40 to 60% range. Side effects are substantial for both as we described, there is significant risk of infection, significant risk of high blood pressure and other effects, which I believe are identical for these two therapies.

Dr. Shaun Hussain: [21:53](#) There's a big difference in cost. I'm not even sure you can make out this on your image, but the cost of ACTH in general is in this \$125,000 range. A typical course of prednisolone is less than \$100. And that may not even show up in your image. But it's also important to put these costs in perspective. So, here we're plotting the cost of ACTH versus treatment failure. And when you look at the devastation of treatment failure for infantile spasms, you are looking at an incredible price tag.

Dr. Shaun Hussain: [22:27](#) When you think about the cost of lifetime support, of multiple hospitalizations, other diagnostic procedures, it's incredible. And on average, that is in the range of about \$7 million over a lifetime. So, when you think about \$7 million compared to the seemingly high price tag of ACTH, it makes a ACTH look like a bargain. I think it's important that we keep those incredible costs in perspective.

Dr. Shaun Hussain: [22:55](#) So, vigabatrin is the generic name of the drug. Until recently, it was only available the United States as the branded product called Sabril. That market exclusivity just expired. And there are now three manufacturers who are authorized to distribute vigabatrin. So, it goes by many names now. And many people in the audience are probably thinking, well, is it actually okay to use these non-branded forms of vigabatrin?

Dr. Shaun Hussain: [23:21](#) I would say that so far, there's no signal that there's a problem with those other forms of vigabatrin. It's a relatively easy molecule to make. And so far, I have not encountered any problems with the generic product. And I have not heard of any compelling stories of issues with those generic products.

Dr. Shaun Hussain: [23:40](#) Now, when we talk about response rate, it really depends on the cause of infantile spasms. So, vigabatrin, in children with tuberous sclerosis complex is actually exceptionally effective and reported response rates vary all over the place. The figure here is derived from UCLA data and it's almost effective in 60% of cases among the children with TSC. Those without TSC don't seem to respond as well to vigabatrin. The response rates are considerably more modest in the range of about 30 to 40%. So, on the whole, this is less effective than hormonal therapy.

Dr. Shaun Hussain: [24:15](#) Now, what vigabatrin is notorious for is the risk of vision loss. That is certainly a scary side effect. And when we prescribe this therapy, we actually have parents sign a contract acknowledging that they're aware of this risk and that the risk of vision loss approaches 33%. That's really a little bit of a misstatement though.

Dr. Shaun Hussain: [24:35](#) What we have discovered in the year since vigabatrin was approved in the United States is that that vision loss risk is very different depending on the age of a patient. And though while that risk does approach one third of cases among adults and older children who take vigabatrin, the risk in infants seems to be much lower.

Dr. Shaun Hussain: [24:55](#) So, in a series, where we evaluated more than 100 patients at UCLA who took vigabatrin, we actually couldn't find a single patient with clinically meaningful vision loss. So, we've got this big discrepancy where on the one hand, we're saying that well, at our center, no one has vision loss, and yet, we're making you sign a contract that says there's a 33% risk of vision loss.

Dr. Shaun Hussain: [25:18](#) And I would just point out that the risk of vision loss very much depends on age and the dosage regimen. So, lower dose regimens probably have lower risk. Higher dose regimens have higher risk. And certainly in the treatment of infantile spasms with most of those patients being infants, the risk of meaningful vision loss is pretty low.

Dr. Shaun Hussain: [25:36](#) And though while we didn't see substantial rates of vision loss in our series, what we did see were substantial rates of what we call MRI phenomena or

MRI abnormalities. So, when you take an MRI of the brain, you get a picture that is gray and white.

Dr. Shaun Hussain: [25:51](#)

And it turns out that about 20% of kids who are taking vigabatrin will have this color change in those images. And we're actually not sure what that color change presents. But here in panel A, we've got these two egg-shaped things in the middle of that brain. And those are called the thalami, a really important part of the brain. And they are bright white. And those are abnormally white. And this is a picture taken from a patient who was taking vigabatrin and had what we call profound encephalopathy where the kid was just not awake, was not interactive. And it was because of this vigabatrin effect.

Dr. Shaun Hussain: [26:23](#)

When we stopped the drug, we took another picture and saw that that bright white egg-shaped structure in the center turned back to its normal dark gray and the patient improved pretty promptly. So, this is a certainly a noteworthy side effect of vigabatrin. And it is something we should worry about much more than the vision loss in my view. Okay. So, that overall rescue is about 20%. It seems to be related to high dose. It may also be related to the combination of hormonal therapy.

Dr. Shaun Hussain: [26:59](#)

But the big thing, the take home message here and I think the big challenge in getting your head around vigabatrin is realizing that we shouldn't be worried about the risk of vision loss. We shouldn't be worried about the risk of these MRI effects. Really, the biggest problem with vigabatrin and frankly with any therapy for infantile spasms is that they're all inadequately effective. And the risk of lack of response really trumps all of these other concerns.

Dr. Shaun Hussain: [27:26](#)

Okay. So, to summarize it a little bit. It looks like the hormonal therapies are vastly more effective than vigabatrin for most cases. But a contemporary thought as well, even though one seems to be better than the other. Why not combine the two? Is it true that using vigabatrin and a hormonal therapy, whether it be ACTH or prednisolone, maybe that combination is far more effective than hormone therapy alone or more effective than vigabatrin alone? And this seems to be exactly the case.

- Dr. Shaun Hussain: [27:52](#) So, it's only one study, but it was an incredibly large infantile spasm study across multiple countries. It was called the International Collaborative Infantile Spasms study. And they pretty clearly demonstrated that short-term response to the combination therapy was much more effective.
- Dr. Shaun Hussain: [28:12](#) We saw that response rates were substantially better. Seventy two percent for the combination of hormonal therapy and vigabatrin compared to 57% for hormone therapy alone. However, whenever we think about studies that evaluate treatments, it's nice to have multiple studies that show the same thing. And for the moment, we only have one.
- Dr. Shaun Hussain: [28:32](#) The second important point is that we don't have long-term outcomes for these patients. So, we don't actually know that the short-term improvement in response rate when we looked at a few weeks, a few months after therapy. That was certainly better for the combination therapy group, but we don't know that these patients are actually doing better later in life. So, we'll have to stay tuned and see how these patients do.
- Dr. Shaun Hussain: [28:53](#) There's also a confirmatory trial that's going on now in the United States. So, hopefully, within a couple years, we'll have two studies that show the same thing, and it can assure us that this combination therapy approach actually provides better effectiveness.
- Dr. Shaun Hussain: [29:08](#) So, when we weigh these two options, whether to use prednisolone or ACTH and vigabatrin sequentially or alone, compared to the combination therapy on the right, not only think about the response, we have to think about the cost of therapy. So, on the left, if we're using these therapies sequentially, there's lower costs because a lot of patients will respond just to the first therapy and never need that second therapy. There is seems to be lower risk of the MRI phenomena if vigabatrin is taken alone rather than with hormonal therapy.
- Dr. Shaun Hussain: [29:38](#) The other big problem is that we won't know what worked if we treat patients with two therapies at the same time. Yet in general, we like to do one thing at

a time so that we know things are going well or if they're not going well, we'll know why that is.

Dr. Shaun Hussain: [29:52](#)

When we use combination therapies and someone responds well, we won't know whether it was the hormonal therapy or the vigabatrin. But for me, it's really the last one that it is the trump card. And I would just say that the improvement in response appears to be substantial and that really Trumps those other three concerns. We shouldn't be worried about the cost of therapy, the risks of these reversible MRI phenomena.

Dr. Shaun Hussain: [30:17](#)

And if things are going well, it's a good problem to have that you just don't know why they're going well. The chief concern here is just to have the best response possible. And for me and at UCLA, we have embraced that and have adopted combination therapy for first line treatment.

Dr. Shaun Hussain: [30:33](#)

So, this is a complicated slide but the take home message is that at diagnosis right off the bat, we start prednisolone and vigabatrin together. We give that option 14 days to work. We try to verify responses with an overnight EEG to show that hypsarrhythmia has gone and that spasms are definitely gone.

Dr. Shaun Hussain: [30:53](#)

And if it's not working, we exchange prednisolone for ACTH. We continue the vigabatrin. And at that point, if it's not working, then we try other second line therapies. And we'll talk a little bit about those now.

Dr. Shaun Hussain: [31:06](#)

The other point from this image is that we treat with vigabatrin for a long time, with the growing impression that the risk of vision loss is modest and infants and with the observation that those MRI effects are reversible and often asymptomatic, we feel pretty comfortable treating patients for a long time with the hope that continued vigabatrin will reduce the risk of relapse.

Dr. Shaun Hussain: [31:27](#)

And as much as we talk about treatment challenges and trying to get an initial response, what we often gloss over is that the relapse rate is quite substantial for infantile spasms. And that if you follow patients out to about age four, the cumulative risk of a relapse is

about 50%. So, if there are things we can do to reduce that risk, it's definitely worth it.

Dr. Shaun Hussain: [31:47](#)

Okay. It's pretty easy to make a broad statement about the second line treatment and that is that they are just inadequately effective. So, among the popular options, we've got topiramate, which is called got Topamax, zonisamide or Zonegran, clonazepam and clobazam. It appears that these are not highly effective. And compared to vigabatrin and hormonal therapies, they pale in comparison.

Dr. Shaun Hussain: [32:14](#)

Felbamate is an interesting one. It came out in the early 1990s. And when it first came out, it was looking like a very effective drug with broad spectrum action. There was actually a clinical trial for infantile spasms plan, but upon the discovery that several patients had died on therapy, this drug almost fell off the market. And what was discovered was that several patients had died of fatal liver failure and several patients had suffered deaths from a blood disorder called aplastic anemia.

Dr. Shaun Hussain: [32:45](#)

Now, what we've learned since then is that those risks are exceptionally small, but the risk is something like one in 10 to 20,000 exposures. I would tell people well, that is probably not something that you should be worried about if you're dealing with an infantile spasms because the risk posed by continued inadequate treatment of infantile spasms is far, far greater. So, this is a therapy worth thinking about. My sense with limited data so far is just like the others not as effective as vigabatrin and the hormonal therapies.

Dr. Shaun Hussain: [33:16](#)

The next is the vagal nerve stimulator. This has not been rigorously studied in the setting of infantile spasms, but appears to have some effect. Next, there's a lot of debates surrounding the ketogenic diet. And numerous studies have suggested that there's at least modest and perhaps great benefit from the ketogenic diet. My biggest problem with this therapy is that it often takes quite a while to work.

Dr. Shaun Hussain: [33:40](#)

And when we think about most other forms of epilepsy, it takes several months to get the great response. So, although it's a great therapy for



refractory seizures in general, it's not clear that it is a go-to therapy for infantile spasms, at least at UCLA in the treatment of patients who had long delay in treatment and had often failed multiple therapies including the first line therapies, the ketogenic diet has not been highly effective.

Dr. Shaun Hussain: [34:07](#)

But I would say we still have some homework to do. It would be great if there was a great randomized clinical trial showing that the ketogenic diet is actually effective. It could be something that could be used at the same time as vigabatrin or even the hormone therapies. So, there's definitely some potential there.

Dr. Shaun Hussain: [34:23](#)

The topic that most people want to talk about at this point is cannabidiol. So, we'll touch on this briefly. Okay. So, almost everyone in the audience I'm sure has heard of CBD oil or Charlotte's Web and multiple other products that are derived from the cannabis plant or from hemp.

Dr. Shaun Hussain: [34:40](#)

And there are kind of three different products to think about. One is the Charlotte's Web and similar products, which we term artisanal cannabis extracts or cannabidiol enriched cannabis extracts. These are essentially extracts that have been derived from an entire or whole plants that have been bred to have lots of cannabidiol and very little THC, the chemical that is responsible for the high and euphoria of cannabis.

Dr. Shaun Hussain: [35:08](#)

In great contrast, there are several pharmaceutical products and the two being Epidiolex, which is a purified cannabidiol that's marketed and will likely get FDA approval for the treatment of Dravet and Lennox-Gastaut syndromes probably this month. They had been looking at infantile spasms, but appears that that research program has been shut down. And it's not clear whether that's because cannabidiol was simply ineffective in the treatment of those patients with infantile spasms or if the manufacturer is really focusing on those indications which are nearing approval.

Dr. Shaun Hussain: [35:42](#)

The third product is a synthetic cannabidiol. So, this is a product that was never in a plant, but it was made in the laboratory. And we'll talk about the clinical

trials, which I've been involved in, that were sponsored by INSYS.

Dr. Shaun Hussain: [35:58](#)

So, to back up a step, I think if you simply look online and read about cannabidiol, you would get the immediate impression that it is incredible, that it's working for everybody, that it's a miracle. And it's relatively rare to identify a report online that it didn't work. If in contrast, you were a fly on the wall in our pediatric epilepsy clinic, you might get the opposite impression that almost everybody had tried it, and that it wasn't working across the board, except for a few where it did work. And it's actually those few highlighted by this great quote, that I have kind of really inspired that interest in pharmaceutical development.

Dr. Shaun Hussain: [36:35](#)

So, our job was to reconcile these drastically different viewpoints online and in our clinic, figure out what was going on. And to do that, we conducted a relatively crude survey where we recruited parents online who endorsed the use of these products and asked them well, how are things going. And what we found was that patients with infantile spasms or Lennox-Gastaut syndrome were doing pretty darn well that upwards of 90% were seeing benefit and that 13% were seizure free. And that was true as well for those with Dravet syndrome or SMEI, Severe Myoclonic Epilepsy of Infancy and certainly true for parents who were treating their children with other forms of epilepsy.

Dr. Shaun Hussain: [37:17](#)

This observation prompted what we call a phase two trial where we simply took patients who had failed both ACTH and vigabatrin, did an overnight video EEG, confirmed their spasms, looked to see how bad the hypsarrhythmia was, and then treated those patients for 14 days with a relatively high dose of cannabidiol and then repeated that video EEG on day 14.

Dr. Shaun Hussain: [37:39](#)

And then we had a blinded EEG reviewer, look at those EEGs and try to say was there a difference between those EEGs? Was one better than the other? Was their complete response? And what we found that we treated nine patients and there was just one responder. So, that was a little bit of a letdown. But

the thing to keep in mind was that those patients who had failed prednisolone and ACTH or sorry, ACTH and vigabatrin had a relatively low likelihood of responding to an effective therapy in those next two weeks.

Dr. Shaun Hussain: [38:12](#)

So, when you think about the spontaneous resolution of infantile spasms, it's about 1% every two weeks. So, compared to 1%, that one and nine response rate is actually pretty good. And that has actually inspired a much bigger study now so.

Dr. Shaun Hussain: [38:28](#)

Also, that one responder so although the other eight patients had no response whatsoever that there was no benefit in their EEG, so the burden of hypsarrhythmia was unchanged. This one patient seemed to have respond on the first day. The parent in follow-up said that there were no spasms for the first five days, that there was a single cluster of spasms in the sixth day and none up until the follow-up EEG at two weeks.

Dr. Shaun Hussain: [38:51](#)

So, when we look at this patient's EEG, it was also dramatically better. And our blend of reviewer endorsed that there wasn't indeed a difference between these two EEGs. And even though that person didn't know which EEG was which, they identified that the day 14 EEG was substantially better.

Dr. Shaun Hussain: [39:06](#)

Now unfortunately, this patient also relapsed several days after that. So, there was not enduring from infantile spasms, but there was not return of hypsarrhythmia. And this patient's burden at most recent follow-up had not gone anywhere close to baseline. So, there's definitely the hope based on this really severe group of patients with infantile spasms, that cannabidiol may have a role.

Dr. Shaun Hussain: [39:29](#)

So, the next step is what we call a phase three trial and this was just launched with a goal of recruiting 180 patients and randomizing them to two treatment arms. And these are new patients who have not failed any therapies and have not been treated for infantile spasms.

- Dr. Shaun Hussain: [39:43](#) So, right off the bat, they would be randomized to either get vigabatrin plus a placebo, a sugar pill essential, or vigabatrin and cannabidiol together, with the same treatment parameters, being treated for 14 days and have a video EEG after that treatment, and compare those two groups and try to get even more confident that cannabidiol is effective hopefully. We shall see. This study will likely take a couple of years to complete though. So, in the meantime, we have to do what we can with available therapies.
- Dr. Shaun Hussain: [40:13](#) And to summarize that development Epidiolex or pure cannabidiol manufactured by GW Pharma, they have at least paused or discontinued their development of cannabidiol for infantile spasms, but INSYS is plowing ahead and has just launched their phase three trial. So, hopefully the next time we do this presentation, we'll have an FDA-approved product for infantile spasms. And it's awfully clear that we are in need of further therapies.
- Dr. Shaun Hussain: [40:43](#) So, I want to leave you with a few key points. The first is that the hormonal therapies, namely prednisolone, ACTH, are most effective. Combination therapy, meaning hormonal therapy and vigabatrin may be superior, at least in the short term appears that they're clearly superior. We just don't know if those benefits extend into the long term into later childhood and adulthood.
- Dr. Shaun Hussain: [41:04](#) Surgery is an excellent option for those patients who are good candidates for therapy. Unfortunately, all other therapies, the so-called second line therapies have pretty limited effectiveness. But that doesn't mean you shouldn't try them. Our approach is that when patients fail, prednisolone and ACTH, vigabatrin if they are not good surgical candidates, we cycle through those second line therapies. And it's actually not uncommon to get a responder to at least one of those therapies.
- Dr. Shaun Hussain: [41:31](#) The big key message is that you can't hang on to any one therapy too long. In general, if you're not responding to a therapy within a couple weeks or a month, it's time to change that strategy. And last that cannabidiol development is promising. But we still

have a long way to go. Definitive trial is proving that it's effective in the context of infantile spasms, still have at least a year to go.

Dr. Shaun Hussain: [41:56](#)

And lastly, I think my parting words would be don't be afraid of the side effects, costs and other issues that surround these medications. Your biggest concern should be the eradication of infantile spasms and the biggest problem with our first line therapies, our second line therapies and even surgeries that it's not always effective. So, don't focus on these medications. Focus on eradicating infantile spasms. And with that, let's pause and see if we've got any questions.

Dr. Laura Lubbers: [42:28](#)

Thank you, Dr. Hussain. We'll now begin the Q&A session. Again, if you have any questions, please submit them in the questions tab of the GoToWebinar control panel and click send. And Brandon will read them aloud. Brandon, do we have any questions?

Brandon Laughlin: [42:46](#)

We sure do. The first question is more of a clarification for you, Dr. Hussain, and that is, so if you can stop the spasms, if you're lucky enough to actually stop the spasms and normalize the hypsarrhythmia, does that translate into preservation of normal development?

Dr. Shaun Hussain: [43:03](#)

That's a tough question, actually. So, that is certainly the goal of therapy in the short term. And it seems to be pretty clear that if you don't completely abolish spasms and if you don't completely abolish hypsarrhythmia, that development will not be good. I think about the cohort of patients who are followed at UCLA, we follow almost 500 patients, and I can't think of a single one who had a long-term burden of infantile spasms or long-term burden of hypsarrhythmia and did well.

Dr. Shaun Hussain: [43:33](#)

I would say that, in order to get a good developmental outcome, you have to abolish spasms. You have to abolish hypsarrhythmia. And you have to be a little bit lucky. You have to have a cause of infantile spasms that is not itself something that can damage development. But in short, I would say you simply can't tolerate any infantile spasms or hypsarrhythmia. If either of those are present, it means that you need to try different therapy.

- Brandon Laughlin: [43:59](#) Great You actually answered my next question within that answer. Next question comes if a child has no known cause after gene panels but is doing pretty well, seizure and med free for several years, would you still recommend further genetic testing?
- Dr. Shaun Hussain: [44:18](#) It's tough. The answer to that question has to be pretty individualized. I would say for that individual patient, usually the answer is no. The odds of us identifying a meaningful genetic abnormality that impacts our treatment that would tell us to begin or stop a therapy is actually very, very low likelihood at that point.
- Dr. Shaun Hussain: [44:37](#) On the other hand, if the parents are thinking about having another kid, it would be very nice to do that genetic testing and get a sense of whether there is any risk posed to the next child. There is unfortunately, very little data about the risk in general. I would just say in thinking about our cohort here at UCLA of nearly 500 patients, there have been only a couple cases in which a sibling also had infantile spasms after the first child.
- Dr. Shaun Hussain: [45:04](#) Let's say overall, that risk is pretty low. But I would say if it was me, I would want to do that genetic testing and figure it out. But I would also point out that there are risks of genetic testing. That sometimes you might find out that a child or sibling or even the parents are at risk for some other disorder that might be associated with infantile spasms. So, certainly, it's a big discussion, a difficult decision often, and you got to go into that decision-making process knowing all the risks and benefits of genetic testing.
- Brandon Laughlin: [45:35](#) Great, thank you. The next question, if the first course treatment was determined to not be effective or to be a failure, does this equate to a delay in treatment options and poor prognosis for future development?
- Dr. Shaun Hussain: [45:51](#) That's a tough question. We don't actually know the answer. My sense is that there are two things going on, one is the delay in encountering an effective therapy, that probably poses some risk, but we don't know how much.

- Dr. Shaun Hussain: [46:04](#) The other observation is that once you fail that first therapy, it probably identifies that child as somebody who has overall worse infantile spasms and may be at risk for bad outcomes on that basis.
- Dr. Shaun Hussain: [46:17](#) So, the short answer is, I don't know. But the second answer is that it doesn't matter. If you've got ongoing spasms, you just got to change your treatment approach and be aggressive. Don't be afraid of those side effects and focus on eradicating infantile spasms.
- Brandon Laughlin: [46:35](#) Great, thank you. Next question is sort of a two-parter. Is surgery only considered when seizures don't respond to certain medications? Or can it also be an option when the MRI and PET scans indicate a specific portion of the brain that causes abnormal activity on an EEG indicating a risk of seizures, even after hypsarrhythmia has been resolved?
- Dr. Shaun Hussain: [47:01](#) That's an excellent question. There is certainly no consensus in answering that. So, I would point out a couple things. There are patients who have structural abnormalities, things like cortical dysplasia, who will respond to first line therapy and not need that surgery. We have multiple in our cohort who responded to therapy and seemed to be doing just fine.
- Dr. Shaun Hussain: [47:22](#) I will also tell you that there are patients with that exact story where they had infantile spasms. They had a lesion that could have been removed. They responded to therapy and we said, "Well, you don't have hypsarrhythmia, you don't have spasms, you seem to be doing well developmentally."
- Dr. Shaun Hussain: [47:35](#) And then several years later or a decade later, we have either the return of infantile spasms or epileptic spasms or the return of other types of seizures. And then when we start wondering, "Whoa, it would have been nice to have removed that piece of brain back when that patient was an infant and when the risks and costs of surgery would have been less."
- Dr. Shaun Hussain: [47:57](#) So, I would tell you, it's a really tough decision. I think if you asked a neurosurgeon, they would be hard pressed to remove pieces of brain in a patient who

did not have ongoing infantile spasms or ongoing hypsarrhythmia. But I'm not sure that's the right decision.

Dr. Shaun Hussain: [48:14](#)

I would put it this way though, if you have ongoing spasms or hypsarrhythmia and you have identified a lesion that can be removed to potentially cure infantile spasms, that is almost always the right path. We've seen that all the relapse rates are pretty high across the board, they're much lower and those patients who are good surgical candidates and undergo a successful surgery.

Brandon Laughlin: [48:37](#)

Great answer. The next question. You mentioned earlier about this, obviously, the importance of immediate diagnosis. Now, just to clarify that from the first visible spasm or from the onset of hypsarrhythmia, she was wondering if there could have been hypsarrhythmia for weeks or months prior to the first visible spasm?

Dr. Shaun Hussain: [49:01](#)

That's a great question as well. It refers to the interval from the first identified spasm to effective treatment. And it's very possible that hypsarrhythmia is brewing or emerging or growing before that first spasm.

Dr. Shaun Hussain: [49:18](#)

And it's actually a big focus of ongoing research where we're trying to identify patients who are at risk and sequentially check their EEG every few weeks looking for the possibility of hypsarrhythmia or infantile spasms are on the way. And that might be an opportunity to treat infantile spasms when they aren't as bad, where it hasn't blossomed and there's maybe a higher opportunity to prevent them from ever happening at all.

Brandon Laughlin: [49:42](#)

Great. The next question is regarding the ACTH and the combination therapies and what are the chances of stopping spasms with the combination therapy of ACTH and vigabatrin, if they've been going on for say, one, one and a half years?

Dr. Shaun Hussain: [50:01](#)

The odds are not great, but they're not zero. So, when we look at the patients who are relatively fresh, the response rate is in the mid-70s, about 75% is our best estimate. The odds of response after months or years of ongoing spasms or especially with ongoing



hyparrhythmia is considerably lower. But we actually don't have good estimates of what that risk looks like.

Dr. Shaun Hussain: [50:23](#)

But I will tell you, there have been plenty of patients who have had spasms for a year and had failed specific therapies like the first line therapies, but when they were tried a year later, they did work.

Dr. Shaun Hussain: [50:34](#)

So, I think it's worth consideration. Just because a therapy didn't work a year ago doesn't mean that it won't work now. Infantile spasms and hyparrhythmia are dynamic process and they're changing. And just because it didn't work in the past doesn't mean that it won't work now.

Dr. Shaun Hussain: [50:48](#)

Unfortunately, the reverse is also true. You can imagine a patient who was diagnosed quickly, who responded to say ACTH and that spasms returned six months later. Just because they responded the first time doesn't mean that they'll respond the second time.

Brandon Laughlin: [51:06](#)

Great. Interesting question here. If a child is diagnosed with infantile spasms, if the spasms are then brought under control, is this child more likely than the general population to develop epilepsy down the road?

Dr. Shaun Hussain: [51:21](#)

It's absolutely true. We don't quite know the magnitude of that risk. But I would say that it's pretty substantial. It also depends on the cause of epilepsy. So, for example, if a patient has one of the most common structural abnormalities that cause him to infantile spasm, something like a focal cortical dysplasia, the risk of epilepsy down the road in the absence of surgery is pretty substantial. I would say it's probably in the neighborhood of 50 or more percent.

Dr. Shaun Hussain: [51:48](#)

But it really varies. It's hard to predict. I would just say that, yes, you're at elevated risk. You have to be on the lookout for the return of infantile spasms or the emergence of other types of epilepsy.

Brandon Laughlin: [52:01](#)

We have time for a couple more questions here. And you mentioned a few times about the idea of vision loss with infantile spasms. Do you have any advice

where delayed speech is concerned in a child who has suffered from IS?

Dr. Shaun Hussain: [52:11](#)

Can you say that again? When there's delayed speech, you said?

Brandon Laughlin: [52:11](#)

Yeah, any advice on where delayed speech is a concern and a child who has suffered from infantile spasms?

Dr. Shaun Hussain: [52:17](#)

I would say that is actually one of the most common concerns. So, to the extent that infantile spasms and hypsarrhythmia can hurt development, it seems that they disproportionately affect language. And we actually don't know why that is.

Dr. Shaun Hussain: [52:39](#)

When we conceptualized infantile spasms, they are a form of seizure and epilepsy that hijacks the entire brain, but seems like they have a disproportionate impact on the temporal lobes and this is inspired by several lines of data.

Dr. Shaun Hussain: [52:55](#)

But the temporal lobes are very important, especially the left temporal lobe and most patients for processing and understanding language. And that seems to be a pretty big barrier for graduates of infantile spasms, including those who have responded pretty quickly to therapy.

Dr. Shaun Hussain: [53:14](#)

So, we have a very low threshold for referring patients for speech therapy. I would say in many cases, especially those patients who have responded robustly and quickly to therapy, that a lot of them are actually very good responders to speech therapy. So, it is something that is actionable. But it's also not something that should be too alarming. I would say that there are many, many patients who have good outcomes after infantile spasms, and many of them had some degree of speech delay.

Brandon Laughlin: [53:42](#)

Great. I'm going to try to get two more questions in here, right here at the end. This one is regarding the diagnosis of infantile spasms. Can other seizure types early on mask the presence of infantile spasms?

Dr. Shaun Hussain: [54:00](#)

Absolutely. And to the extent that infantile spasms are sometimes subtle and don't really register with most

people. When you think about the general public, if they saw a video of a child having infantile spasms, most people would not say, "Oh, that looks like a seizure." They would say like, "I'm not sure what that is. It's probably nothing. Maybe it's an infant heartburn or gastroesophageal reflux."

Dr. Shaun Hussain: [54:23](#)

They really don't register and they don't really register on that fear meter. But when you think about most other types of seizures, they're rather dramatic, especially if you think about something like a generalized tonic clonic seizure or grand mal seizure, those are much scarier, much more obvious.

Dr. Shaun Hussain: [54:37](#)

And if you imagine a patient who's having both generalized tonic clonic seizures and infantile spasms, it's pretty easy to see how everyone's attention not parents, pediatricians, neurologists, they would likely be focused on those generalized tonic clonic seizures because they're so dramatic. And I would say that is also probably part of the challenge. We have to keep infantile spasms in mind as part of the possibilities of seizures and infancy.

Dr. Shaun Hussain: [55:03](#)

So, when we teach our trainees, our residents and fellows, we're telling them that, "Look, this is an infant. You got to have infantile spasms, at least in the back of your mind, no matter what kind of seizure they're showing you right now."

Brandon Laughlin: [55:17](#)

Great. Last question and a question regarding treatment. One of the questions was, if vigabatrin is known to cause myoclonic jerks and if so, and these are deemed not to be epileptic, can you stop once the child is weaned?

Dr. Shaun Hussain: [55:33](#)

So, this is not exactly clear. I would say that there's a pretty widespread rumor at least, that vigabatrin can cause myoclonic jerks or myoclonic seizures, and they can be classified as epileptic or nonepileptic. And I would say, don't worry about any of that.

Dr. Shaun Hussain: [55:47](#)

I would say I think it's probably true that a minority of patients who are treated with vigabatrin have either worsening or the emergence of myoclonic seizures. And that they are reversible after stopping vigabatrin therapy.

- Dr. Shaun Hussain: [56:04](#) The big question is, well, if vigabatrin is working to stop the spasms, should you stop the vigabatrin to make those myoclonic jerks and myoclonic seizures better. I think that has to be considered on a case by case basis.
- Brandon Laughlin: [56:17](#) Great. Thank you very much. I'll turn it back over to Laura now.
- Dr. Shaun Hussain: [56:20](#) Thank you.
- Dr. Laura Lubbers: [56:21](#) Great. Thank you. This concludes our webinar about infantile spasms. We do want to give a special thank you to Dr. Hussain for a terrific and very informative presentation, and to Sunovion for sponsoring today's webinar.
- Dr. Laura Lubbers: [56:36](#) I do want to just remind everybody to always talk to your doctor about treatment options for your loved one. And I'd also like to thank you for joining us today and engaging in such great questions. If you do have questions about this topic or any of CURE's other research programs, please do visit our website at [www.cureepilepsy.org](http://www.cureepilepsy.org). Or email us at [info@cureepilepsy.org](mailto:info@cureepilepsy.org).
- Dr. Laura Lubbers: [57:04](#) Thank you again and please join us for our next webinar, which is entitled Epilepsy's Impact on Memory and Cognition Over Time, which will be presented by Dr. Bruce Herman from the University of Wisconsin. That webinar is scheduled to take place on Monday, July 9th at 1:00 PM Eastern Time.
- Dr. Laura Lubbers: [57:22](#) Thank you again for a great webinar, very informative. I hope that this information is helpful to you. Thank you.
- Dr. Shaun Hussain: [57:30](#) Thank you.