Managing Lennox-Gastaut Syndrome really represents a challenge. The number one challenge is to individualize treatment. Each one of the kids with Lennox-Gastaut Syndrome and the adults, will have a very unique set of problems, different etiology, multiple seizure types, maybe one is more frequent than others. The challenges are really many.

The polymorphism of different seizure types, and the type of etiology for what is the cause of the Lennox-Gastaut Syndrome, really needs to be taken into consideration when choosing any treatment modalities. As I look at the patient with Lennox-Gastaut Syndrome, I will never be able to treat unless I take care of the cognitive aspect, the behavior aspect, and of course, the seizure syndrome.

The principles that guide us to treat patients with Lennox-Gastaut Syndrome are many. Number one, the seizures are very difficult to treat so sometimes, you have to make a choice. Do I give them extra medicine and make them tired, dizzy, not able to get out of bed, or do we settle for having clusters of smaller seizures that are not going to interfere with their daily activities? This is a negotiation that has to occur with the family, the caregivers, and making a decision as to what is too much and what is an acceptable side effect, which is really unique for each individual patient.

Often, we need to combine medication. Taken into consideration is this medicine going to increase the level of the other one or the same, taking away one induce medication may increase the level of the other drug and indeed cause a major problem. We end up with a very complex polypharmacy. You really have to understand the pharmacokinetic interactions of these drugs when you start to engage in this complex polypharmacy.

Rescue medicines, when can we use rescue medicine? What is an appropriate timeline? What do we accept as the regular cluster versus something that we have to intervene? I’m going to try to parade you though my way of thinking when I manage a patient with Lennox-Gastaut Syndrome. Over treatment is always a problem because we are trained and we’re always pursuing that goal of no seizures. With Lennox-Gastaut Syndrome, you have to understand what you are treating is that polymorphism of different seizure types, cognitive problems, and you really have to make a good balance there.
Tonic seizures are often the predominant seizure type and they tend to be very difficult to treat. You may always see a cluster in the mornings, which is the most common time for these clusters of seizures. You may not need to give very extensive or large amounts of medications. There is always the transient effect of medication when you start. Be mindful of those medicines that you have to readjust either because they have tolerance or because they need an adjustment or autoinduction later on.

This is it. The treatment goal for Lennox-Gastaut Syndrome is good quality of life, reduction of seizures, and of course, prevention of all kinds of injuries. When I looked at the first drug, second drug, and when do I start looking at what else can we do, different pharmacokinetic, the pharmacological treatment of the seizures, then I start engaging in family meetings and deciding where do we look at next.

The number one selection criteria for the first drug is what is the seizure type now. The kids may present, as we discussed earlier, with West Syndrome, the infantile spasm, and there are certain drugs that are more unique for that seizure type. If the onset of seizures is really with generalized tonic-clonic seizures, you may not need to use ACTH or vigabatrin, which are drugs that are very unique for specific seizure types at presentation.

Looking at the second choice, what is the best drug that we can combine with the first drug or are we looking at another monotherapy trial. As we go to the third combination trial or monotherapy trial, we like to start looking at other types of treatments, ketogenic diet, vagal nerve stimulator, surgery, and that’s what is on the other side of the screen, looking again to get to that good quality of life in treating epilepsy in the Lennox-Gastaut Syndrome.

Drug development for Lennox-Gastaut Syndrome is very unique because there is no one single animal model that will help us develop drug specific for this syndrome. It is a syndrome, which means it’s a constellation of symptoms that will include multiple etiologies, multiple seizure types, and all the behavior aspects of it. That’s always a challenge when we develop drugs for Lennox-Gastaut Syndrome. It is very difficult to do a monotherapy trial for Lennox-Gastaut Syndrome because of the multiple seizure types and the severity of the seizures, the frequent and non-convulsive status. It is mostly developing drugs with combination therapy, and very often, drugs that are there for a long time or are very high doses and you add a third drug or a second drug that may not truly tell us what is going to be the behavior because it’s such a complex polypharmacy.

This is what I call the dimensions or the aspects of treating and managing patients with Lennox-Gastaut Syndrome. Quality of life at the center and then it’s the comorbidities. You’re looking at comorbidities of what are the primary pathologies. Is this a child with TS? Is this a child with developmental problems? Is this a person that had a severe anoxic encephalopathy? All the etiologies may represent a different challenge. We’re looking here at the cognitive decline. We’re watching someone deteriorate and we want to stop that progression. But by doing so, we want to be very careful that it’s not going to be caused by the side effects of the medicines that we’re giving these patients. The psychosocial aspect, aggression, the ability to stay in the classroom, the ability to stay with a babysitter, all those things do represent a major aspect of managing patients with Lennox-Gastaut Syndrome.

I’m going to review some of the drugs that we use often in Lennox-Gastaut Syndrome. Valproic acid has been a favorite, but we don’t have a single trial that has looked at Lennox-Gastaut Syndrome patients using valproic acid. It was never done in monotherapy. It’s very often in the mix when we do clinical trials for newer drugs now. There are many concerns with the younger patient when they start using the valproic acid, managing the liver function test, and it’s
something that we all see in the pediatric population. Very often, these patients continue on to the adult life using valproic acid.

New generations of drugs like lamotrigine, Topomax, clobazam, and felbamate have been studied in clinical trials, add-on trials, for seizures associated with Lennox-Gastaut Syndrome. When I say that, there are many different seizure types that will be measured during that clinical trial and we have at least more data, more information to guide us through that.

Benzodiazepines, from early on in the treatment of Lennox-Gastaut Syndrome, we’ve been using benzodiazepines. They tend to be very effective for the tonic seizures. They are also being used quite often for rescue medication, and most recently, we’ve had a clinical trial where the clobazam, which is one of the benzodiazepines that is very effective in the treatment of the atonic seizures, and it’s been a great addition to the armamentarium. When we look at the benzodiazepine, we also want to look at side effects like sedation. Clobazam seems to be one of the benzodiazepines that is not going to be as sedating. It’s also available in multiple strengths so we can titrate it slowly and for younger patients, we can have a very unique dose schedule.

Felbamate, we really have to talk about felbamate when we talk about the Lennox-Gastaut Syndrome. This was a significant development in the treatment of Lennox-Gastaut Syndrome. It’s an effective drug, but with side effects of aplastic anemia and liver toxicity. The family has to consent and be very aware that the only way we can use felbamate is by choosing the right patient that can be monitored with liver function tests and complete blood cell count to prevent any aplastic anemia and liver toxicity.

The treatment algorithm goes like this: first drug, second drug, start looking at the third drug for other things. I’m going to parade you through the next session of management, which includes surgery, ketogenic diet, and vagal nerve stimulator.

When we look at the vagal nerve stimulator and the immunotherapy, those are great additions, but it’s not for everyone. You have to look at the selection of what patient is going to be good for this type of treatment.

The epilepsy surgery evaluation includes the video monitoring, a good imaging study, many ways to look at imaging in epilepsy, but there are very big challenges is resective surgery for Lennox-Gastaut Syndrome.

The number one challenge is that they are often multifocal. It’s not one spot. We said it’s part of a very complex etiology umbrella, and very often, it’s not just focal epilepsy. It’s is very common to see Lennox-Gastaut Syndrome originating from frontal origins, regional origins, and epilepsy resective surgery is not an option.

Corpus callosum may present a good surgical option to prevent drops, to prevent injuries, and often, it’s helpful in helping to prevent status epilepticus. It is not always for long term. It may reoccur. The interior two-thirds of the corpus callosum surgery is often the initial way to do it.

Vagal nerve stimulator is a therapy that we use to prevent seizures. It’s a generator. It has a coil with a vagal nerve impulse that will help to prevent seizures. It is very similar to any other pacemaker. This one is set all the time. It is not on the demand. There are three component and they are the generator, the coil that is to the vagal nerve, and the
device that we use from outside to regulate or titrate the dosing of the different parameters that we can use to help with the seizure control and also to prevent side effects.

The number one way to do it is to start very slow with the titration of the covering, and then to increase according to the way the patient is tolerating. You can do that in the office and wait until the patient is able to tolerate the side effects well. The parameters are many. The length of the stimulation, the amount of current delivered, the amount of current delivered by the magnet, all that can be modified and titrated according to tolerability.

Ketogenic diet is really a unique way of looking at treatment of seizures and a lot of my patients would like to see if there is anything I could do with the diet that can help control the seizures without giving more chemicals. This is sort of the reverse of what we consider our Mediterranealian diet. The idea is that by doing the ketogenic diet, we are shifting the carbohydrate metabolism to a more fat-based metabolism. There are different theories of how it works by creating ketones and that becomes the source or energy for the brain. It is used in different modalities in my algorithm. I looked at the diet as a supplement to the medications. It is often used in addition to medicine. It can be used with a stimulator. It can be used early on or for some families, it becomes a last resource because it is a big commitment from the family. The result of the diet varies according to how well the family is able to follow.

I have a very important way of looking at this low-carb ketogenic diet can also be a modified Atkins diet. Some of my adult patients benefit from this modification of low-carb going for to the high fat, and they can help the control of the seizures for Lennox-Gastaut Syndrome by adding a diet control to the whole armamentarium.

Non-convulsive status is very common in the treatment of Lennox-Gastaut Syndrome, so a big challenge is when we change medicines, we have to be very careful because it’s often subclinical or subacute, but you have to be very suspicious about non-convulsive status when someone is having a major change in mental status, they’re not able to engage in their normal activities. It is indeed a medical emergency.

When we look at the tips, always simplify the regiment. It’s very important to not keep adding different medicines. The medication selection targets the seizure types that are more frequent or more dangerous. That's a real important clue because otherwise, you’ll be dealing with a very complex polypharmacy. The medication changes often require hospitalization. Do it slowly because the incidents of non-convulsive status. Always keep in mind the cognitive impairment. It’s really key here.

Looking at the comprehensive care, you must include the behavioral aspect. Treat the aggression. Treat the behavior problems. Very often, that translates more to quality of life for the parent and also for the child and the adult whereas the patient cared for is as important as the treatment of a different seizure type. Treatment options that are newer may have better side effects, less sedation, and may represent a better alternative to older drugs.

Look at the management of Lennox-Gastaut Syndrome as a comprehensive care, seizure type, comorbidity, drug selection, and please keep in mind that the family is very much a part of this.