Childhood Epilepsy Syndromes - Pediatric Grand Rounds-9-12-2025-Meeting Recording

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1h 1m 7s

Calderon, Delia started transcription

Ranch, Daniel 0:05

It's 7:30, so we'll get started. Good morning, everybody, and thank you for attending Pediatric Grand Rounds. As a reminder, as you log in, please mute your devices and the CME code will be placed in the chat periodically. So once again, please do not bug Delia or Doctor Kamat for the code.

Otherwise, it is my great pleasure to introduce our speaker for today, Doctor Natasha Varaguiz, who joined us just this past year. Doctor Varaguiz completed her medical school and child neurology residency at UT Southwestern in Dallas, and then she completed her epilepsy fellowship at Vanderbilt in Nashville.

She is board-certified in neurology with a specialization in child neurology and epilepsy, and her medical interests include complex genetic disorders and syndromes and refractory epilepsy. So everybody, please welcome Doctor Varigis.

Varughese, Natasha A 0:57

Morning. Thank you so much for the kind introduction, Dr. Ranch. It is definitely a privilege to get to to be part of Grand Rounds today. Today I'm going to be talking about childhood epilepsy syndromes.

And I've targeted the information to a depth and level that will hopefully be appropriate and interesting and useful to the pediatrics residents as well as the general pediatricians. I'm focusing just on the childhood epilepsy syndromes as a between age, the ones that present between ages like 3 to 15.

Years or so, because the neonatal and infantile epilepsy syndromes certainly deserve their own hour. So hopefully this will be interesting. And again, the goal is to provide the level of knowledge that would be useful for a general pediatrician.

OK.

Why should we talk about epilepsy? Well, it's certainly, honestly, it is a relatively common condition, certainly not as common as asthma or ADHD. But at a large Children's Hospital, you're certainly seeing epilepsy at least once a week between the

Uh, the the floor or the clinic.
The Epilepsy Foundation, our chapter estimates that there are greater than 160,000 people between adults and children in Central and South Texas. There are at least well over 3000 patient pediatric patients with epilepsy just in the San Antonio metro area and probably an equal or greater number in the Valley region.
And this matters, of course, not to recap common knowledge, but this matters because of the significant morbidity and mortality. Almost all seizures certainly do have a negative impact on development, cognition and memory to some extent, some more than others. And of course, having paroxysmal, unpredictable, you know, lapses of consciousness and control.
Control of your body lead to all kinds of unintended injuries that can go all the way to early mortality from drowning or suffocation and such. So I've organized our talk, this talk as follows, talking first about the self limited epilepsy syndromes.
Then bringing out the focal epilepsies versus the generalized epilepsies, and finally more of the developmental encephalopathies or progressive epilepsies. And again, I'm if you think if it feels like I've left out some important syndromes, it's because I'm focusing on the ones that present between about ages 3 to 15 years of age.
Family vacation that left at 6:00 in the morning. So they get up early, they get their children up at 3:30 in the morning to go catch their flight. And then all of a sudden, as they're going through security at 5:00 in the morning, he has a convulsive seizure for the very first time in his life. Parents freak out and of course by 6:00 AM they're in your emergency department instead of boarding their flight.
As they had previously planned. And when you ask them for details, the parents described that the left side of his face and his mouth first began twitching and they asked him to stop. But he wasn't able to talk to them by the time they by the time they when they tried to interact with him. And then he started drooling profusely and then his whole body developed a convulsion.
Local paramedics were called and they came to the emergency department. And in your Uh, he has a normal head CT, but the EEG shows sleep activated bilateral central temporal spikes with a bifrontal dipole. And for some of you who've been studying for boards, you already know what that answer is that little fray.
Is pathognomonic for a very common childhood syndrome called self-limited epilepsy with central temporal spikes, previously known as benign Rolandic epilepsy. This is highly testable on the pediatrics boards. It's also something you will absolutely see as a general pediatrician.

6 to 7% of all childhood epilepsies. That's the number the International League Against Epilepsy has estimated in their most recent papers. Usually happens in four to 10 year olds approximately, so early elementary school, and it almost universally resolves by puberty.
Status epilepticus is very uncommon. The headed imaging is normal and this is in patients with normal development other than maybe a little learning disability or ADHD. There is possibly there is kind of a thought that poorly controlled selects does worsen learning to some extent. So it's again, it's not completely benign.
But it is self-limited and there is no developmental regression. That's one of the big hallmarks of this case. The patient's development remains normal as these seizures present.
Another common this case illustrates another common childhood epilepsy. This would be and it just is another sort of to start to illustrate how tricky seizures can sometimes be and how often they can mimic other conditions.
This five-year-old boy was seen by his PCP because he had two episodes in the middle of the night over the past few weeks of severe abdominal pain that woke him up. PCP said he was constipated, but the pain occurred again a few weeks later. This time he was vomiting. He was very, very pale. The family swears that he had altered mental status. He was not acting himself and this lasted 10 minutes and then he was sleeping.
Afterwards, PCP is still thinking that it's related to the stomach because of the stomach pain. But finally, after he does a little workup, he reversed to neurology for abdominal migraines. But just couple days before his scheduled neuro appointment, the boy has another episode and this time it evolves into eye deviation. It's a little bit of tonic-clonic activity at the end and so EMS comes, but by the.
Time they come, the event has resolved. This is another very common childhood epilepsy that you will likely see at some point as a general pediatrician self-limited epilepsy with autonomic seizures. Now this one is responsible for about 5% of childhood epilepsy under age 14, according to the International League Guest.
Epilepsy and in fact it's between ages 3:00 to 6:00. Again, according to the IL the official papers, it's responsible for about 13% of epilepsies. This is another one that typically resolves a couple of years after it presents and doesn't tend to have a very high seizure burden.
These seizures, however, do last.

Leary, Linda D 7:17

Can leave this on for just a couple minutes and give some of our meds for now.

Varughese, Natasha A 7:21

Excuse me?

OK, let's see. OK, so um.

These seizures, though, do tend to last a little bit longer and have a very long prodrome that can be a little bit confusing for patients when it first starts in terms of the diagnosis. This one again, the high imaging is normal, but the EEG shows either occipital or multifocal spikes again.

Youth consider this diagnosis in patients who are developmentally normal. The self-limited epilepsy is also called the selfies. It's a very nice little acronym as we've highlighted or current otherwise healthy children with normal development not associated with regression, typically resolved by puberty. This as a group as a larger group.

Bruce is responsible for up to 25% of all the childhood epilepsies. This is good news to share with your patients. OK, 25% of children who present with seizures have one of these syndromes that they will grow out of, maybe even by the time that they're a teenager.

We don't call them benign anymore. That used to be part of the nomenclature that in the most recent sort of iteration of of the International League of Semplepsy. In the most recent set of position papers, the word benign was removed because seizures are not inherently completely harmless. There's still the possibility that you could.

Have one when you're in the bathtub and you know, or you could suffocate on a pillow in the middle of the night, that sort of a thing. They're not completely harmless, but self-limited sort of describes their nature a little bit more accurately.

There was a time again a couple of decades ago that it was recommended not to treat with.

Since the seizures itself resolved, now that medications have a lower side effect profile than they did back then, it is definitely recommended to treat them for the period of time that the seizures are active. Usually they're treated with a sodium channel blocker, Triloptil or Vempap.

Keppra is also perfectly reasonable. Just pick one that has a low side effect profile.

Usually a low dose of a single medication is enough to control the seizures for the couple of years that they are active. And again, there is this. This group of self-limited epilepsies is kind of a class. The most common ones are.
Celeste and Cellius. There are a few other usually arising from the occipital lobe. These also tend to resolve within the first couple of years. They're all part of this group of the self. These are the self-limited epilepsies.
Now those are distinct from the more true focal epilepsies. These might feel those epsilies might feel focal because they because they they do have focality on their EEG, but they should be distinguished from the more true focal epilepsies.
That come from a true lesion in the cortex. You might not see it on MRI, but the focal epilepsy come from some sort of lesion in the cortex that leads to that is the trigger for their seizures. This is another illustrative case of a seizure that could be a little tricky when.
You first when he first presents to you. This nine year old little boy in foster care tells the school nurse that about every couple of days he's having these episodes where his throat feels very, very tight and his whole body feels hot. It'll last a few minutes and go away. So the nurse very understandably and appropriately assumes their panic attacks, which is a very reasonable.
Assumption talks to Foster mom. Foster mom goes home, works on behavioral strategies for anxiety. He's still having them every couple of days. She talks to the PCP. The PCP prescribed Lexapro, which again is a very reasonable course of action for for panic attacks, but these events just continue.
And then he starts to look like he's fidgeting with his hands every time during the episodes. And then finally, during at the end of one of the prolonged episodes, his head starts to deviate to the left sides, and he develops A generalized tonic-clonic seizure. And I include that case as sort of an intro to some of the more.
Some of just to introduce the variety or the the really massive landscape of potential auras and semiologies for focal seizures. This table was taken from the standard textbook on surgical epilepsy. It's certainly not a comprehensive table, but it kind of. Illustrates the variety of symptoms you can have at the onset of a seizure. You can have unprovoked fear that's, and that by itself might be the only symptom of the seizure at the beginning until it sort of progresses and declares itself.
I had one young adult, like a 20 something year old young man patient tell me that the only way he could tell the difference between his emotions and his seizures were like sort of the context. If he felt very, very afraid and he didn't have a reason to feel

afraid, then he knew this must be his seizure coming on. If he felt afraid and there was a clear reason.
In his a clear situational reason, then he wouldn't be as afraid that this is a seizure coming on. And he got pretty accurate at that. But it wasn't that he could tell the difference between the fear. It's because it would start when he was still conscious enough to to assess the context and see what made sense.
Blinking is one of the symptoms of occipital lobe seizures. Focal motor movements, swallowing, hallucinations. There are some seizures that begin with sort of this repetitive auditory hallucination of a song that you have actually like heard before in the past and that you normally would not.
And not be surprised about thinking again. There again, all of these specific subtypes are relatively uncommon. And of course you shouldn't treat every panic attack as if it's a seizure, but it's worth knowing about these just in context if you know treating empirically for stomach pain.
Or, you know, or or anxiety or that sort of a thing is not making any progress. It is worth knowing. It's important to note that seizures can have very tricky, very focal semiology.
And it can be worth. And again, it's kind of it's it's the job of a neurologist to definitively diagnose one way or another, whether something is a psychogenic neurologic symptom or whether this is actually a seizure that we should be worried about. Most of those vocal seizures come in children, at least come from vocal cortical dysplasias that stressed a malformation in the cortex.
Can.
Occur anywhere. A lot of them do run in families. OK, so just because something is due to a brain malformation does not mean that it cannot be hereditary. A lot of those mutations in the mTOR pathway do run in families with incomplete penetrance. These seizures can occur anytime from infancy to late adulthood, but this is just again a common etiology at this age.
They tend to. They're more likely to be resistant to medications. That would be one of your first clues that this is not one of the self-limited epilepsies. And again, it depends entirely on where it's located in the cortex. The M TOR pathway is just worth reviewing very quickly one of the signaling.
Pathways at least to cell growth in many different organ systems. The most common syndrome are the tuberous sclerosis, but quite a number of mutations in various points along this pathway can lead to hereditary.

Focal epilepsies from focal cortical dysplasias.
So these are some of the common genes tested for the genetic panels. The most common focal epilepsy really in both children and adults is temporal lobe epilepsy. Again, much this one is much more common in adults, but it still happens frequently enough in children.
Children usually do have the same auras as adults once they're old enough to articulate their symptoms, and that can be stomach pains, heaviness, fear, deja vu, and then progressed sort of hand automatisms like sort of a picking, rubbing, dystonic posturing. All of those symptoms can help localize where the seizure actually started.
Mouth smacking and then eventually like head version and generalized tonic clonic convulsion. You can absolutely have like short seizures that stop before the convulsion or before the head version as a prodrome to the the for sometimes a long time before they have their first convulsions.
Sometimes, like as I mentioned before, they might run at families from everything. Sometimes there are other lesions in the cortex. One very well described etiology or mechanism for temporal epilepsy are actually prolonged febrile seizures in early childhood. So when you know we counsel patients, children or infants with febrile seizures.
That they have only a 3% risk of epilepsy down the road. This is part of that 3% risk. Some patients, I know we counsel most people that febrile seizures are benign and they usually are most of the time, but it is true that they can actually see the masial temporal lobe leading to epilepsy down the road. The MRI might look normal for many years even if the pathology.
Ology exists.
The temporal lobe, of course, overlaps with both of your language centers of memory, hearing, and that leads not only to those auras that we talked about, but can also over time lead to progressive damage in in things like learning and memory.
OK, so almost all of the medications can be used. You usually, you know, you start with whatever makes sense based on the patient's on the side effect profile of the medication, the patient's other comorbid medical conditions. But this is a good place to bring up the fact that in general for epilepsy, if a patient has failed 2 medications whether from side effects.
Or just because the medication was not effective enough, the standard of care is to start considering pre-surgical evaluations. Start considering whether the patient

would be a good candidate for a surgery to better to reset to better control their epilepsy.
In patients with focal epilepsy, early resection does lead to the best seizure outcomes. It's not necessarily something you should think of as a last resort.
Part of that is because the resection, if it's done early enough, leads to the best seizure outcomes. And if the surgery is delayed for too many years, other parts of the brain, whether it's the contralateral temporal lobe or other foci in the brain, they become entrenched like they sort it seeds the other parts of the brain, they become entrenched in a seizure.
Propagation network. So delayed surgery, if you wait too long, can be significantly less effective. The way I explain it to patients is that your brain becomes really good at anything that you practice. If you practice playing the piano, your brain is good at that. If you practice playing basketball, your brain is good at that. If you practice being grateful, your brain becomes good at that. If you practice having seizures, your brain becomes.
It's good at them and it's harder to stop them. OK, so earlier surgery leads to better seizure outcomes. It also in younger children leads to better rehab potential. Sort of the younger you remove the the not useful piece of the brain, the part that's causing the seizures, the more neuroplasticity you have at your disposal for rehabilitation.
Temporal abetly had the best results in focal cortic dysplasia is depending. Again, it depends on the center and on the mode of selection, but they can have the 50 to 60% seizure freedom in well selected patients. The pre-surgical workup is outside the scope of this talk and would be kind of another hour. It deserves its own hour by itself, but there are a number of imaging modalities.
and other forms of testing that you would do to first of all make sure that the lesion is not overlapping on eloquent cortex, that it's not going, that resection is not going to result in permanent loss of language or memory or certain motor functions or certain visual fields.
And then you also try to localize it well to make sure that you truly understand like exactly where the seizure is coming from and that you're going to have a good epilepsy result at the end again and that specific work up is very individualized to the patient.
And it always should happen in the context of a large epilepsy team. Now there are for patients for whom resection is not medications don't work. Resection is not an option either because it's in too many locations in the brain or it overlaps too heavily

on on.
Eloquent cortex. There are other implants, and I think the most important one to bring up is responsive neurostimulation. This is probably the latest, greatest technology available to us now in epilepsy, but it's been used in adults and children for really.
For quite a few years now, essentially you put a little computer chip in a little what looks like a pacemaker, like right on the surface of your brain. This is a brain implant. And then you have two little electrodes that go that you permanently implant inside the brain, and those electrodes detect when your seizures are happening.
Store it in the little device and then send a signal to try to disrupt the seizure to stop it. OK. And this device is able to gradually over time learn what your seizures look like and learn what kind of stimulus is necessary to break the seizures in your case. And what happens is the all of that data that it's detecting as.
It's sort of continually monitoring the brain gets stored in the device that gets uploaded to a computer about once every couple of weeks, once a month. And then the epileptologist as well as the like the device engineer will will work with the device to train it to change the settings to help it learn your epilepsy, your your patient's epilepsy.
And your patient's best, you know, stimulation settings, it's a big deal to implant people. I don't think anybody's certainly doing it under the age of six or seven years old, but it is a very effective option for patients for whom surgery is not an option. The results for me.
Xial temporal lobe epilepsy are a 70% reduction in seizure frequency and then according to the in the clinical trial, 30% of patients achieved seizure freedom for greater than six months. So with the focal epilepsy, we do have a wide array of options beyond just medications.
Oh, of course, we are just talked about the focal epilepsy. So let's move on to the generalized epilepsy. This is another large fraction of the seizures that we would see on a regular basis in the emergency department. What is this? It's just any seizure who's onset involves all lobes of the brain simultaneously, and they can be generalized tonic convulsions, but absence seizures are also generalized.
Many atonic seizures are also my are generalized. Sometimes myoclonic seizures, you know the different combinations of those various semiologies that all of these can count as a generalized seizure. And just an EEG example to illustrate it just it involves all lobe to the brain right exactly at the same time, the same millisecond.

Hits all of them.
So here's a good typical example that you might see in your general Pediatrics clinic. 13 year old girl comes to the ER for a first time seizure. This time it she presents with a convulsion lasting 3 minutes at school and it just occurred without warning. There was no clear trigger, nothing else was going on.
And you talk to her more and you're asking about what's been going on in the past. Does she have any other medical conditions, any prodrome, anything in the last few months? And she reports that she is a little bit clumsy in the morning for the past year. Often she she's always dropping her toothbrush or dropping like her breakfast, and her siblings have been teasing her about that and they've just been sort of brushing it off as.
That's a joke. Otherwise, though, this is a perfectly healthy child. Honor roll classes traveling for basketball. There is a family history too. Grandmother was on phenobarbital, and then father had this funny history where he was spacey. He didn't do well academically when he was in elementary school, but then he kind of.
Came into his own and as he got older.
Juven. So this is like a very classic case of juvenile myoplonic epilepsy. Again, this is another one that all of you will see at some point as a general pediatrician. It's 9% of all epilepsies. This age of onset's a little bit later than the ones we've talked about before, usually in.
Late elementary school, early adolescence, and it's the combination of myoclonic and generalized tonic-clonic seizures. So that that clumsiness in the morning that she was reporting was from myoclonic seizures. That's usually how it presents. The patient thinks they're clumsy and in retrospect they were just having myoclonus intermittently early in the morning.
This is occurs in patients that are essentially like have normal development. If the patient has cognitive disability, you need to do more work if you can't immediately assume that it's juvenile myoconic epilepsy. This is another one that is normal head imaging. The EE G is characteristic.
But this one, unlike the self-limited epilepsies, is tends to have lifelong disease, at least for the next several decades after after the initial diagnosis. So this is a patient where you have to sit down and counsel them that they.
Need to choose medications that will be safe for them to stay on for the next several stages in life. If it's a girl, please don't put her on and Depakote or Topiramate if you can't help it, because you want her to be stable on some combination of meds so

that during her childbearing years, which are just coming up in about a decade or so. Try to avoid things that have the potential to exacerbate, you know, other comorbid, you know, other common conditions in adulthood. Now the good news is 9060 to 90% of them respond well to medication. So you need to counsel them, counsel most of these patients.
That they are. They probably shouldn't try to be a commercial airline pilot. They probably shouldn't try to go into active combat in the military. But they can do, since most of them are likely to be well controlled, they are probably going to be able to do almost anything else career wise and life wise. They're probably going to be able to learn to drive, go to college, all of those.
Have children, all of those things. And so recognizing this syndrome and like diagnosing it correctly early on is really essential in giving them the correct counseling and management early in the course.
And this is one of a group called the Idiopathic Generalized Epilepsies. OK, this as a group is 10 to 20% of epilepsy in children or adults. It's another thing again, you are going to see this as a general pediatrician. This one is it's heritable. It runs in families, OK, in the sense.
That maybe the dad has juvenile myoclonic epilepsy and the daughter has childhood absence. Or maybe there's a cousin that has just generalized tonic clonic seizures. And then there's a.
You know, and one child that has childhood absence, seizure, childhood absence seizures, but then one cousin, another generation later has juvenile absence. Like that's how it runs in families. They did. There's not necessarily a particular like 1 phenotype doesn't necessarily run in families by itself.
Most of the time these are controlled on medications. Not all the time, but often. This is the subtype of epilepsy that is most likely to activate with either photic stimulation or hyperventilation. So you know how on Eegs we always flash the lights in their face or have them blow on a pinwheel. It's it's mostly for the diagnosis of this little subcategory of epilepsies because they're so common.
And if this, if this is the correct diagnosis, they do not involve evolve to an epileptic encephalopathy.
Just to talk in a little more depth about some of the other subtypes of the IGES, idiopathic generalized epilepsies, child adoptons, epilepsy. Everybody memorizes this one. In Med school, 18% of epilepsy in school age children starts around 4 to 10 years of age. It's the three Hertz spike and my discharges that one. Every medical

student has memorized it.
At some point, the one thing to keep in mind is that I think we memorize this as a universally self-limited epilepsy. This it is true. Most of them resolve around adolescents, but the official number from the position papers of the International League Against Epilepsy is that it's really only 60%.
I would have expected that number to be higher the way that we are taught it, at least in medical school. So that means there are 40% that are going to eventually evolve to a different type of idiopathic epilepsy. So you cannot necessarily counsel these families that their child will grow out of it for sure and never have to think about it again. They have a high chance of.
Growing out of it and never having to think about epilepsy again, but there is a significant minority that eventually developed generalized tonic clonic seizures. OK, so that is an important part of the counseling to include when you talk to these families.
The other piece of it is that at about 110th the incidence of standard childhood Obscence epilepsy, there is also a thing called juvenile Obscence epilepsy. The EEG can look very similar, maybe a little bit faster spike in waves, but I mean it might not be significant enough to pick up on the first diagnosis.
Seizures might last a little bit longer and less frequently. And again, this is in patients where their head imaging is normal and development should be basically normal. But this is it can look fairly similar at the beginning, but these patients almost all develop generalized tonic-clonic seizures down the road.
And these are patients that require lifelong medicine. And again, it would be very easy early in the presentation to confuse it with this more common, more likely to be self-limited epilepsy. And so again when you diagnose patients.
With a generalized epilepsy and abnormal EEG, it is still important to talk to them about seizure precautions. What do you do if your child has a generalized tonic-clonic seizure? What is emergency management of a seizure? And it's still important to talk to them about sort of the range of prognosis so that they're prepared for different possibilities.
Another thing that's worth keeping in mind is that 20% of patients, again, these are numbers from the International League Against Epilepsy, they're position papers. 20% of these patients develop absence status epilepticus, which is an entity that I don't think most of us really ever think about most of the time. But this is a form of status epilepticus. It's very.

Confusing and it's almost a little bit freaky to watch. The patient is going about their activities. They just have slowed response time. They look dazed and they're just not remembering anything. They can't remember that they went to the grocery store, but they did go to the grocery store and sort of go walk around and buy their groceries and they did sort of walk around the host and try to.
To do things, but they're just not acting themselves and it looks a lot like they're intoxicated. And there are patients, especially adults probably, who can where this can last for a couple of days before they're brought to medical attention. Then the EEG shows continuous or semi continuous generalized post speck discharges.
This can be precipitated by basically using the wrong type of seizure medication in a generalized epilepsy or abruptly stopping at a van or a benzodiazepine. The main reason to think about this is not so much because it's common, but because it would be very easy to confuse for intoxication.
So again, these are the idiopathic generalized epilepsies, childhood absence, juvenile absence, and juvenile myoclonic, as well as just generalized tonic-clonic seizures by themselves, and they all overlap a little bit.
But just so you don't get too simplified of a picture of generalized epilepsies, OK, this is its own little box here, but there are quite a number of other types of possible generalized epilepsies, some of which have, you know, genetic etiologies, and most of which start to be less benign in terms of long-term development and cognition.
Is a case that is kind of derived from patients I've seen in clinic. It's an 11 year old little girl. She's been diagnosed with ADHD. She comes to neurology clinic because of these movements. The PCP has diagnosed him as chronic motor tics. She just has rapid eye blinking intermittently.
And of course, at first, PCP consoled, as you normally do for tics. Just ignore it. Let her, you know. You know it should. It should evolve to something else over time. She'll probably grow out of the tic. The more you ignore it, the more likely it's gonna go away. But the episodes just continue happening.
Frequently, especially when she looks up or looks towards the lights again. And that doesn't necessarily make anybody think anything unusual. Of course, you blink more often when you look at the sun or you look at the light in, you know, in your classroom. But at a certain point, the mother is getting frustrated because it's happening too often. The patient's falling behind in school. The mom thinks, OK. Maybe the blinking is distracting the patient. So you tried Guanfacine and there's no improvement. So nothing's getting better. So you get an EEG and there you go. Every

time she has these blinking episodes, you see these sort of high voltage spike discharge, generalized spike discharges that.
Sort of our bifrontal and and they happen every time she has these little like blinking episodes, and they do seem to correlate with a little brief lapse of consciousness every time she has these blinking episodes. This is a classic syndrome that used to be called sunflower syndrome.
Obvious reasons or Javan syndrome after the person who described it, but now it's been updated to a more sort of descriptive term of the seizure semiology. It's epilepsy with eyelid myoclonia. It's a rare epilepsy, but again, it's easy to miss, easy to not pick up.
Onset can be between 3 to 12 years of age, and this the seizure semiology is literally they just have this rhythmic eyelid twitching with a little head extension that's triggered by sunlight or photic stimulation. You can understand how this goes undetected for a long time. Of course you blink when you look at the sun.
Um.
But it is associated with a lapse of consciousness. It's associated with EEG changes with those blinking episodes, and they often, often also have either absence seizures or generalized tonic convulsive seizures eventually usually requires lifelong medication. And this might sound like a benign like etiology, but just imagine if.
If every time, if like you're driving and every time the sunlight hits your eyes, you have a brief lapse of consciousness. Like this is a very disabling disease, even though it doesn't necessarily look disabling on the outside. And so it's important. It's very rare, but it is important to pick up when it presents.
There's another entity called GEPS Plus. It's not so much its own syndrome, and I think it's really easy to get confused when people first teach you about it.
Generalized epilepsy with febrile seizures. Plus, it's just a patient with febrile seizures who again later in childhood develops one other type of generalized seizure. It's this umbrella term.
Family. It's usually runs in families where some patients in the family have simple febrile seizures, other have febrile seizures that just continue beyond the expected age group. Others have idiopathic epilepsies. You might even have driven by 10% of these families with these clusters of various generalized seizures.
Occur with a particular type of mutation called SCN 1A. That is a sodium channel mutation on the interneurons, but there are quite a few other channel of these that have been identified. So it's it doesn't. It's not like this presentation doesn't

necessarily.
Formally diagnose you with this condition, but it is a responsible for high fraction as well as some of the other channelopathies. Just to kind of introduce the this sort of concept, this is another set of epilepsies that just kind of run in families together.
The mechanism of some of these epilepsies is very well described. Onset seizures are thought to be due to thalamic dysregulation. So it and this kind of makes sense. The thalamus is sort of the realized station for everything that is happening like like to the cortex and so if.
The is is a relay station, right? Like some it controls many, many different parts of the cortex. And if you were to, it's involved in like relaying to the basal ganglia, that kind of a thing. And so if you were to have sort of dysregulation of the thalamus or excessive activity of the thalamus, it would you would imagine that it would project to the.
And carotortex at the same time, which is the idea that's the mechanism at this point is pretty well established for seizures by themselves. That's why we use ethesuximide because it specifically targets the calcium channels that are most common in the phallus. Other types of generalized seizures come from channelopathies. Again, that's fairly logical.
If you have a genetic mutation in every sodium channel in the or every potassium channel or every GABA receptor, you would imagine you know the seizure would start in parts of the brain simultaneously. Other generalized seizures, as we talked about with the idiopathic generalized epilepsy, are often polygenic in like they're probably multifactorial just like.
Like your height and weight and things like that. Also a lot of non-specific secondary epilepsies like from chromosomal micro deletions are end up being treated empirically the same as a lot of the generalized epilepsies. The treatment. The most important thing to remember when you're treating epilepsy is to avoid the pure sodium channel blockers.
This is a situation where you should absolutely not use Trileptil or or Vimpak.
Also, pure GABA activity. These are less common medications, but that also can worsen both the epilepsy and the development associated with that epilepsy. Usually Keppira Velparoate are often first line, but Lamotrigine is very reasonable for most of first many of these epilepsies. Clobazam zonisamide is a really.
We go to option when you're more refractory perampanel. We still have a good battery of medications that are very well established as being effective in this in most

of these syndromes. The one thing to remember is that FSX and only helps with true seizures, the only syndrome for which you really should be using.
Using ethasuximide by itself at least is in childhood absence epilepsy because ethasuximide only helps with the sorry ethasuximide only affects the T type calcium channels.
It will not do anything for generalized tonic clonic seizures or myoclonic seizures or any of the others.
As far as childhood absence epilepsy is concerned, of course at the sextamide we everybody memorized in Med school is first line. The other two things that are shown in sort of the standard clinical trial for childhood absence are valproate and Lamotra gene. Usually you pick based on gender juvenile myoclonic epilepsy. You can use almost all of these.
Depending on the patient and so on and so forth.
There is a fraction, maybe 510% depending on the specific syndrome that are going to be refractory. And of course, if that were to happen, the first thing you'd want to make sure is that you have the diagnosis correct, that you're not missing something more progressive or some kind of a subtle focal lesion or something like that.
But in patients who truly have a idiopathic generalized epilepsy and who just aren't responding to any of the medications or who have side effects on all the medications you try, there are a couple other options. Vagal nerve stimulators are a very reasonable thing, can decrease medication burden. I think the generally quoted number is that it can decrease.
Seizures by 50% in about 50% of patients. Certainly not a slam dunk. It's not perfect, but it's a reasonable thing to offer. You can try dietary therapy, which I'll talk about down the road in a couple of slides. In the context of a different syndrome, it has moderate efficacy. It's a perfectly reasonable thing to try if nothing else has worked.
And then currently there is a clinical trial looking at responsive neurostimulation for the idiopathic generalized epilepsies and results of that should be published next year. So for the very, very refractory juvenile myoclonic epilepsy or juvenile absence epilepsy, we might be able to offer RNS.
As a therapeutic option down the road.
But as I said before, if you have a refractory, really, especially a refractory generalized epilepsy, you should start to worry that maybe you need to think about a different diagnosis, especially if the patient's development is now being severely impaired. The developmental epileptic encephalopathies are refractory epilepsies.

Associated with significant developmental delay or regression.
So this is a variation of a couple of patients that I've seen in the last few years. 3 year old boy comes to your clinic with tics. He lives in the valley. Parents just think he moves funny sometimes and they brought him to the pediatrician a few times. And at first the pediatrician said this looks like an exaggerated Morrow, but you don't normally have.
Exaggerated moros and three-year-olds. So he just wanted to rule out other problems, but he called it a tic. He sent it to your clinic for tics and the parents report that this patient is having sudden like arm jerks like multiple times throughout the day. They don't know how many months ago they started. They think the frequency is increasing now and up to this point the patient was developmentally normal like that nobody had any concerns. No, he was thinking too hard about.
About it, he just was kind of he learned to walk and talk at the normal time. But over the last few months he's having daily tantrums. He's getting harder to manage. Grandparents are calling this just a delayed onset of the terrible twos, but he's not sleeping well anymore. He's not consistent in his potty training.
And in clinic, you get to see one of these events that his bilateral arms jerk outward and his head drops momentarily, and then he begins crying.
This would be a very classic presentation of a syndrome called epilepsy with myoclonic atonic seizures, or EMATS. It used to be called DOOSE syndrome DOOSE, but again, the official name is now EMATS.
Because that describes exactly what the syndrome is. It's not terribly common, but it is 2% of childhood epilepsies, and so any neurology clinic will certainly see this at some frequency. This starts between 2:00 to six years of age, usually in patients that are normally have development.
Normal development prior to onset. It doesn't. Most of the time there isn't one specific gene that you can pin this to. Sometimes there are some 5% have GLUT 1 deficiency, but most of the time you can't pin it onto just one single gene.
The EEG shows the generalized polyspike in waves. The head imaging is normal.
And this one has a very characteristic sort of clinical course. There's a stormy phase for several years where you have myoclonic, atonic seizures and generalized tonic, clonic seizures and sometimes some other generalized seizure types and you.
Start Pepper and you start Valpro 8 and and they might slow them down or they'll stop the generalized tonic clonic seizures. But it's very difficult to control these myoclonic atonic jerks.

If you can control it on a couple of seizure medications, that's wonderful. But a large fraction of the time, the only meaningful treatment for this one is the ketogenic diet or one of the modified versions of it. OK, so the people who most of the good studies on this epilepsy syndrome will say very clearly that.
Unlike the ketogenic diet should be considered gold standard for this particular syndrome should be offered early. And part of the reason that this should be offered so early and sort of pushed as a good treatment for this epilepsy is because the seizures themselves often go into remission both three.
Or so years after onset and you're able to lean off the medication, but the subsequent development can either go back to normal or you might retain procedural like deficits. And we do think that some of the cognitive development down the road probably has something to do at least with how well the seizures are. Controlled and so the better you can control the seizures during this stormy phase, hopefully down the road, the better their long-term development is going to be once they get past this stormy phase. So that leads us to just briefly discussing the ketogenic diet. This is probably the best syndrome to discuss it.
And this is probably the best context in which to discuss this as a treatment for epilepsy. This is not quite the same thing as the ketogenic diet for weight loss that family doctors use to help their adults get off their diabetes medications. OK, it has a similar concept.
You're trying to gain your calories more from fat and protein as opposed to carbohydrates, but it's it's a little bit more aggressive. There's a classic ketogenic diet as it was originally developed, and then other versions, including the modified Atkins, are a little bit more tolerable for children who eat by mouth instead of G2.
This is a normal diet.
55% carbohydrate. So that's your apple and your oatmeal. This 30% fat, that's, you know, the olive oil you put on your carrots, that sort of thing. And then 15% protein in the classic ketogenic diet.
Over 90 of your calories are coming from fat, and then in the modified Atkins, like 65 to 70 of your calories, calories are coming from fat. This is not like a easy, standard, natural, healthy diet. Sometimes parents come and try to figure out if there's any way to fix their child's epilepsy.
Just by cleaning up the diet and getting rid of the takis and like eating more vegetables, that sort of thing. That doesn't really work that way, unfortunately. But this like if you're going to use diet to treat epilepsy, this is what you have to do. And

the mechanism is, you know, at the surface level, at least the mechanism is fairly straightforward. Most of us are use.
Carbohydrates is the source of most of our energy. Whatever we don't use gets stored in glycogen and then whatever doesn't get used stored as glycogen. Whenever the glycogen is not used over time, then eventually gets stored into fatty tissue. And when we go into ketosis, when we use one of these dietary strategies, we are bypassing glucose as a mechanism.
Of energy or bypassing the glycogen. We are going straight to fat as a source of energy, which means that the circulating currency for energy in your body is no longer glucose so much as it is the ketones. So all of your cells are being forced to use ketones as their fundamental substrate of energy rather than glucose and for multi-fat.
For factorial reasons, this leads to seizure control being consistently in ketosis. It's not an easy diet to follow, if I haven't said that enough times already, and it's not necessarily a standard healthy diet, but it is an option, and it is sometimes the best option for certain syndromes, most classically hemats.
This is some of the variations of the diet. You know, it's a little bit of lots of fat, a little bit of protein, a little bit of vegetable.
Now, I started with that one because it's a good illustration of the fact that not every refractory epilepsy is Lennox Gastemy. OK, this is its own separate syndrome. I think that this term gets thrown around in medical charts a lot just to mean a child.
Who has seizures that we can't control very well? But as you've seen already, first of all, there are plenty of examples of other epilepsy types that just happen to be difficult to control, and there are other syndromes involving developmental regression and refractory epilepsy that are not exactly the same as.
Lennox Gusto, and that's important because each one of these different syndromes has different prognosis, requires different counselling, and involves different treatment options. OK, Lennox Gusto, this is still the most common developmental epileptic encephalopathy because it's the final common endpoint for many different brain pathologies. So babies who had HIE.
Might eventually develop Lennox gusto. A lot of children and infantile spasms when they're younger eventually become Lennox gusto. It just doesn't declare itself as Lennox gusto usually until they're sort of like toddlers to sometimes like far much later in childhood. This one usually has a very identifiable etiology, either genetic or structural.

Sometimes it might be on a chromosome found on a chromosomal microarray, not just a single gene. You might have abnormal development before it might be normal, but it always worsens cognition and development. Tonic seizures are a mandatory like are mandatory for diagnosis, but you can have all of these other seizure types. EEG is also very, very characteristic. In order to call something Linux gusto, you have to see less than 2.5 Hertz spike in wave and also generalized paroxysol fast activity. So these are two buzzwords that if you see them on a test question or an EEG report, these are cluing you in that now we're talking about Linux gusto and it's important to label this one.

Incorrectly because almost universally these patients have refractory seizures, multiple seizure types and 90% are going to have moderate to severe intellectual disability. OK, it's not a this is a this is not a diagnosis you want to make incorrectly. You would never want to confuse this for example with this one.

Diagnosis is so different and you'd want to make sure that when you're treating the refractory seizures or you're using medications and strategies that are optimal for this particular syndrome.

One other epileptic developmental epileptic encephalopathy that's really important to mention is something called E swaser spike wave activation in sleep. OK, this one used to be called Lendo Kloffner, but as the phenotype was sort of expanded and as the disease was better understood, it has.

Been given also an acronym that just says exactly that tells you exactly what it is. This is very rare. You don't see it very often. It's less than 1% of the epilepsy even at tertiary care centers, but most tertiary care will see this and when it happens, you don't want to miss it. This is developmental regression that correlates with continuous spike wave on the EEG during.

Sleep. OK, so the patient comes in with they're just sort of they've been doing well in school and they are worsening or they were like they were developing fairly normally, but now they're just speech is significantly impaired and nobody knows why they went to.

ENT and things like that and they and nobody can understand why they're not talking as much and then but you finally somebody gets an EEG and you see this. Basically it looks like status epilepticus during sleep, normal during wakefulness or mostly normal during wakefulness, but then it starts to look like continuous spike wave activity during sleep.

And the treatment for this is fairly specific to this syndrome. If it's treated well, you

can certainly rescue some of the developmental outcome in a large fraction of patients. Standard of care is either onfi or diazepam.
Which are both like basically benzodiazepines at night or daily steroids. Onphase that's the lowest side effect profile. Most people start with it next, but sometimes steroids are the only thing that sort of rescues the patient's speech. You never know. So you have to try different things depending on the patient. It does tend to be refractory to medication to some degree. You don't really cure it so much, but the. Significant develop does depend partly on how well you treat the spike wave burden during sleep. And again, rare, but you don't want to miss it when it happens. And as I've highlighted already that in when you're treating the developmental epileptic encephalopathy, the preferred medications are highly dependent on this specific syndrome Lennox gusto.
It's the subject of many clinical trials, so it has a much wider array of medication options than really any of the others, as it should. VNS is often used to decrease medication burner. That's vagal nerve stimulation, the ketogenic diet. This is another even for Lennox gusto or.
Or continuous spike wave and sleep. Ketogenic diet is a very reasonable option, especially in G tube fed patients. And then other implants or neuromodulation devices are being studied. Right now there's a phase two clinical trial going on for RNS for really, really refractory Linux gusto syndrome.
And so that sort of the the syndrome that's covered up till now are sort of the majority of the important syndromes you should recognize like for the epilepsy themselves. I'm just going to now quickly highlight a couple of other more rare genetic or.
Irreversible conditions that you just should be aware of so that you recognize them again if they were to come to the hospital. Rhett syndrome. I'm not going to go into this. This could also this syndrome by itself could be discussed for an entire hour, but this is a rare genetic syndrome caused by a mutation in Mec P2A transcription factor that affects the nervous system as well as.
Other organ systems that result in loss of speech, loss of ability to walk, seizures, movement, surgeon, vital sign abnormality. It starts with normal development and then regression. And the main thing I just bring it up is because you don't want to confuse this with the other epileptic encephalopathies. It's very clearly diagnosed on genetic testing.
There are a couple similar syndromes that are caused by other mutations that have

similar sort of dramatic effects on brain development. This is not curable, but it's a subject of ongoing active research. Progressive myoclonic epilepsies are another subset of epilepsy. They have no cure. They're always on the initially on the.
For myoclonic seizures, very, very rare. But when they do present, they're usually initially misdiagnosed to juvenile myoclonic epilepsy. But then we get genetic testing and we find that never mind, you actually have an incurable disease. The there's these pictures are examples of patients from one of the patient like advocacy web. This girl that the website was named after, you know, completely healthy, normal teenager, beautiful soccer player as a teenager was diagnosed with one of the with this case, it was Lophora disease and within a few years she's wheelchair-bound G tube dependent and then she dies in her early 20s. Same thing happened to this girl, completely healthy, normal.
Active teenager diagnosed with started having myoclonus as a teenager, initially diagnosed with juvenile myoclonic epilepsy, and then within the next 5 to 10 years she's wheelchair dependent, G tube fed, cognitively delayed and dies in her early 20s. This is one I just highlight because again, you don't ever want to miss it.
For the sake of prognosis and it's often this is one of the again one of the things that generally gets misdiagnosed as a more benign syndrome before it gets diagnosed properly. And the treatment for many of these progressive epilepsy syndromes is that you know you try treated aggressively based on the mechanism disease, but they're mostly areas of basic science research.
Just ones you should be aware of. So just kind of to summarize this whole presentation, if you haven't gotten the impression by now, childhood epilepsies are very heterogeneous in their symptoms and their treatment and prognosis, and the correct management is heavily reliant on early diagnostic testing. OK, there are some seizures for which you should.
Prescribe the sodium channel blockers, others for which like they're contraindicated and so the understanding which is should be used in which context depends on understanding the underlying syndrome correctly. Also another good take home point for a general pediatrician. Some seizures can be tricky. Just be very careful with chronic motor tics when they don't respond to an.
Initial treatment, very careful with panic attacks when they happen exactly the same way every single time and just don't respond to other management strategies. I mean, it's never wrong to refer to neurology just to rule things out. Anti-seizure medications, of course, are the mainstay of most treatment, but dietary therapy,

receptive surgery, neuromodulation devices are also important options.
for the appropriately selected patients. And with that, that is all I have for you guys today. It was a pleasure talking to you, and with that, I'll take any questions.

Ranch, Daniel 55:37

Yes, Doctor Vargas, thank you very much for that fantastic overview. I personally definitely heard terms I've not heard before in my career, so thank you for that review. For the audience, if anyone has questions, feel free to place them in the chat box or you can go ahead and unmute yourself to ask your question.
While we're waiting, as a reminder, the CME code is in the chat box as well.
Doctor Fox, I feel like you're trying to ask a question, but your audio is kind of scrambled.
Or not.

Pearson, Rachel M 56:35

Hey, this is Doctor Pearson. Thank you so much. That was a really helpful and thorough. I was wondering if you could talk about your general threshold for genetic testing when you diagnose seizures or epilepsy.

Varughese, Natasha A 56:52

So I honestly once I usually I think the standard at this point is to try to send at least an epilepsy panel for sure really upon diagnosis of of epilepsy, but for sure if they.
If you get the MRI as normal or if you have a lot of it has to do with clinical suspicion, but you really should for sure you should be sending it once a patient is refractory to two medications. You for sure should send it if the MRI is normal. And really it's not wrong to send as soon as you really diagnosed an epilepsy.
Sometimes, you know, sometimes there are like a lot of the more rare diseases on that panel have sort of clinical trials for like experimental diseases. And so it's not wrong to try to just sort of cast a wide net, make sure you're not missing any of them. Also it can be very, very helpful just to.
Rule things out and to be able to reassure families, OK, I think we have a good prognosis based on the syndrome, based on the negative genetic testing and so on and so forth. So honestly, I jumped to it very early, just like I jumped a brain MRI very, very quickly in most of these syndromes.
Now that doesn't mean sending, that doesn't mean sending whole exome

sequencing in every single patient. I think that's the beauty of the epilepsy panels is you can focus on just the relevant epilepsy genes and you don't have to get into counseling on Alzheimer's genes and that sort of a thing.

Ranch, Daniel 58:21

All right. Thank you. There are a couple of questions in the chat box. The first one is, could you please comment on the use of ADHD medications in light of seizure disorders?

Varughese, Natasha A 58:32

OK, so most of the time it's important to just still treat the ADHD just as the same with tics. The same thing with tics. There's kind of this controversy and some parents will choose to avoid like this ADH like the stimulants just based.

On the small chance that it could be worsening epilepsy, and of course in an individual, if you think that their seizures become poorly controlled every time you put them on a stimulant, well, that would be a reason to avoid it. But most of the time, patients on seizure medications are also able to tolerate the stimulants if they need them.

And then based on the primary role of the primary care physician in the care of epilepsy, adjusting meds in more straightforward epilepsy versus subspecialists. So basically, should a PCP be adjusting seizure meds if they think they know the disorder? Most of the time, it's probably better to just leave it to the neurologist. The vast majority of the time. There's nothing wrong with just prescribing Keppra or prescribing ethesuximide when there's a long wait list, or if you're not sure what to do next, that is never a wrong thing to do, but.

It's there's already so much a PCP has to do that management that trying to tease out which epilepsies are following a standard course or which are kind of becoming atypical and which should be pursuing other more nuanced treatment options that really.

It very quickly becomes outside the scope of the pediatrician is something that the neurologist should be doing. And then if you're in a lower resource setting, at least trying to communicate with maybe a neurologist at a bigger center would be probably a good thing to keep in mind. You know there are some PCP's that live so far away from general from a neurologist that you might have to manage it yourself, but then.

At least trying to be in communication at some frequency to your neurology colleagues would be a helpful thing to do.

Ranch, Daniel 1:00:27
Any final questions?

Kamat, Deepak M 1:00:32
There is a question by Doctor Fox in the chat box.

Varughese, Natasha A 1:00:37
Oh, I think I addressed that. Sorry.

Ranch, Daniel 1:00:37
Oh yeah, she answered that. Was that the one you're answering?

Kamat, Deepak M 1:00:39
OK.

Varughese, Natasha A 1:00:42
Yes, I answered both Doctor Fierro and Doctor Fox's in kind of one paragraph.

Ranch, Daniel 1:00:42
Oh, yeah, yeah.

Kamat, Deepak M 1:00:44
OK.

Ranch, Daniel 1:00:45
You can see how efficient Dr. Varughese is. So, all right, well, it is 8:30, so if there are no final questions, thank you everybody for attending. Thank you again, Dr. Varughese, for giving us that wonderful presentation and we'll see you guys at the next Grand Rounds.

Calderon, Delia stopped transcription