Louise

My name is Louise, I live in Johannesburg, South Africa but I'm originally from Cape Town. In roughly early 2004 I started having what seemed like I would blank out basically. So I could be doing anything, I might be in the middle of a sentence and I would just kind of stop. So it would seem like I was conscious, my eyes would be open, but I would essentially be unconscious. I did not know what this was, at first it didn't particularly seem to bother me but it started happening more and more. Sometimes it was accompanied by what I would now describe as an aura, so sort of a strange sensation almost physically inside my brain, it felt like having an electric shock inside my brain. For a while we didn't do much about this, I was about 16 at the time and my mother was of the opinion that this was happening because I was not managing my stress levels sufficiently. I am not entirely sure what that was supposed to mean. And she was not entirely wrong, stress was a factor, but this was not actually me not managing it properly.

So at the end of that year she took me to a psychiatrist to try and see what we could do about this because she said to me if this carried on happening I would not be allowed to get a learner's license. So anyway, my mother takes me to a psychiatrist and I have a session and he says to her take her to a neurologist, she has epilepsy. I get sent for an EEG. Afterwards we go back into the doctor's rooms, he has a look at the EEG, and he says oh yes, this is textbook epilepsy. You had an eight second seizure during the EEG. I have to say my poor mother, that was the first time I've ever seen anyone's jaw literally drop. She was so shocked. I was just really relieved to know that this is not in fact my fault.

So what the doctor explained to me was that I had absence epilepsy which used to be called petit mal. I did not know that there was any kind of epilepsy other than the kind where you fall on the floor and shake, and that was what was epilepsy in my mind. So I was surprised to discover there was something else. So I was put on medication, the brand name here is Epilim or Epilizine is the generic, it's sodium valproate. The doctor told me I should be careful because this can increase my appetite and caused me to gain weight. Now I'm a 16, almost 17 year old girl so this caused me a great deal of anxiety and I remember telling my mother okay, well help me look out for am I eating more. Another side effect is developing acne. Now I had been quite a lucky teenager, I never had serious breakouts, I had the occasional pimple. And suddenly I was developing pretty serious acne. And again, I'm 17, suddenly I have acne, I'm gaining weight. It really did a number on my confidence.

In my early 20s my seizures had been completely controlled for years, since I had initially started on the medication. So 2010 I was 22 and my doctor agreed with me that we could try and lower the dose and if that goes well we can stop the medication and see what happens. So I started having brain zaps again occasionally and I kind of ignored them because I thought no, no, I'm fine. I don't want to be on the medication. And then one day it was after class in the afternoon, I was sitting in the computer lab with some of my classmates, we were busy working on assignments. And the next thing I know I open my eyes and I am flat on my back on the floor and there are several very concerned faces sort of crowding above me.

So what had happened was that I had been in front of my computer and I had all of a sudden had a grand mal seizure, what used to be called grand mal, these days are called tonic-clonic seizures. And this is the classic one where you fall on the floor and your body stiffens and then you shake. I later asked some of my classmates sort of what did it look like. And apparently I had been foaming at the mouth and because I had bitten my tongue there was blood in the saliva which cannot have been easy for them to see. I think I am very lucky that I did not lose bladder or bowel control because that is something that can happen during a tonic-clonic seizure. And obviously it's not something that you can help, it's just a medical thing but I would have been just so embarrassed. I was incredibly confused after the seizure, I was also completely fatigued. I could barely move my body, I couldn't walk.

	So I go back to my previous dose of medication. The year after that, 2011, is when I moved to Joburg. Things seem to be going fine, I of course had to switch to a different doctor. This is also the first time that I find out that you're not supposed to get pregnant while you are on valproate because it has the potential to be teratogenic which none of my previous doctors had told me this. I am a young woman of reproductive age, I'm someone who can get pregnant, and no one bothered to tell me this. So I was quite upset. Fast forward to 2016, November, I am freelancing at an ad agency, I'm doing proofreading for them. I'm sitting in front of the computer and suddenly I opened my eyes and I'm lying flat on my back on the floor and there are several really anxious faces crowded over me and I've just had another grand mal seizure. Again, I'm very confused, I can barely move my limbs. These are people I don't know, I've only been there for a week and on my first day I accidentally got locked in the toilets so I'm already known for that. But now I'm no longer the girl who got stuck in the toilets, I'm the girl who had a seizure in the office. So that's fine.
	So not long after that I go and see my neurologist. This is the first time in several months that he's had a good look at me and he says okay, you have lost a very large amount of weight. Your body is metabolizing your medication too quickly, that is why you had a seizure, on top of all the stress and so on. So we increase, I think actually we doubled my medication. Things have gotten better since then, that was the last seizure of any kind that I've had, my stress levels improved, my acne improved. So things are generally better. Now I have pressed pause on any kind of reproductive decisions for now. I'm turning 35 now so I still have a little bit of time if I want to think about it.
	The epilepsy has been under control for several years now so for the most part it's not giving me grief. But that was quite an unpleasant experience, that realization about just things that I hadn't been told. Maybe it's because I was a teenage girl and my doctor didn't think that it was particularly necessary to tell me about certain side effects apart from gaining weight because obviously that's the only thing that could worry me. For me, my epilepsy experience has been quite a mixed bag. I am technically quite lucky that mine is easily controlled with medication, I can lead a normal life. But it's also been a giant pain in my ass and I would prefer not to have it. I don't have any sort of feelings about oh, it's made me a stronger person or anything like that. And it has also given me some insight into aspects of the medical profession that are disappointing. That's where things stand at this moment. I am hoping for maybe a magical miracle gene therapy or something that will remove this. But we will see where things go.
TPWKY	(This Podcast Will Kill You intro theme)
Erin Welsh	Thank you so much Louise for sharing your story with us.
Erin Allmann Updyke	Yeah, thank you so so much for sharing that.
Erin Welsh	Hi, I'm Erin Welsh.
Erin Allmann Updyke	And I'm Erin Allmann Updyke.
Erin Welsh	And this is This Podcast Will Kill You.
Erin Allmann Updyke	And today it's a very big topic, we're talking about epilepsy.
Erin Welsh	It's the biggest topic that we've covered in a very long time.
Erin Allmann Updyke	Do we say that every single episode? Yes. Is it true this time? Yes.

Erin Welsh	It is absolutely true.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. This is going to be a long but chock full of information and questions episode, I can already tell. And Erin you and I talked about this, it was an interesting and difficult balance to strike between too much detail and not enough detail.
Erin Allmann Updyke	Yeah, it was. It was a difficult episode to kind of piece together for me and I know you said the same. So we'll just see how we did.
Erin Welsh	Yeah.
Erin Allmann Updyke	But first we all know what time it is.
Erin Welsh	Is it quarantini time?
Erin Allmann Updyke	It's quarantini time.
Erin Welsh	What are we drinking this week?
Erin Allmann Updyke	We're drinking The Clonic Tonic.
Erin Welsh	We are. This is one of my favorite names and we were inspired by a listener who sent in a very similar suggestion. So thank you, Robin.
Erin Allmann Updyke	Yep.
Erin Welsh	And The Clonic Tonic is a very simple drink, it is simply Campari and tonic water and a slice of orange. And I love this because I think it's actually surprisingly adaptable to a non alcoholic cocktail because there are bitter non alcoholic liqueurs or whatever, for lack of a better word, that seemed to really take the place of Campari and one of them that I've tried that's delicious is Ghia. But anyway there are options out there. So it's a simple recipe but we will post it for both the quarantini as well as the placeborita on our website thispodcastwillkillyou.com as well as on all of our social media channels.
Erin Allmann Updyke	On our website, since we're still at the beginning of the season, let us tell you about what you can find there. It's fantastic, thispodcastwillkillyou.com. We've got sources from every one of our episodes, we've got transcripts of those episodes as well. We've got links to our merch which is fantastic, we've got a Goodreads list, we've got a link to our bookshop.org affiliate account, we've got Bloodmobile, our music, we've got... There's probably more. Our Patreon, it's there, check it out.
Erin Welsh	It's all there. I'm wearing one of the very cool new crew neck sweatshirts that you can find on our merch page and it's the best, you should get one for yourself everyone.
Erin Allmann Updyke	I was actually wearing one of our new sweatshirts recently when I went out to get a milkshake and somebody was like I love your sweatshirt, I love that podcast! And I got so embarrassed that I just was like thanks, cool! And then I started talking to my dog again.
Erin Welsh	That's amazing! Oh my gosh, I love that.

Erin Allmann Updyke	True story, it's a great sweatshirt. All right, well shall we get into the actual topic of this episode?
Erin Welsh	I think we should right after this break.
TPWKY	(transition theme)
Erin Allmann Updyke	We said it at the top and I do feel like we say almost every episode these days what a huge topic we're dealing with and it's usually true, although we probably also usually exaggerate.
Erin Welsh	For sure.
Erin Allmann Updyke	But when it comes to the topic of epilepsy, this really is something that could probably be split into quite honestly a whole season of episodes depending on how deep you wanted to get in all of the various types of seizures and types of epilepsy and the specific pathophysiology, not to mention history and epidemiology and so on and so forth. It really is an absurdly large topic to try and cover in under two hours hopefully.
Erin Welsh	Overly ambitious of us.
Erin Allmann Updyke	Yeah. So we are not going to cover every detail today, which means that we might not cover any one particular form of epilepsy or type of seizure that some listeners might be hoping for in the amount of detail that you might want. But the good news is we'll have plenty of resources for you who want to dive deeper. And what I'm hoping that we can all get out of this biology section at least is an appreciation of, first of all, what the heck is a seizure anyway?
Erin Welsh	Yeah.
Erin Allmann Updyke	What are some of the various types of seizures? Because spoilers, it's not just what you've seen on TV. How do these seizures differ and what's going on in our brains during this process? And then what is epilepsy in the context of seizures?
Erin Welsh	Yeah.
Erin Allmann Updyke	So that's where we're going to try to get to.
Erin Welsh	Right. I want to know the answers to all of those questions.

Erin Allmann Updyke	I'll do my best. So I'll start out with just some definitions and for these I will quote because love to have a quoted definition. Epilepsy, the definition from the International League Against Epilepsy is defined as quote "a chronic disease of the brain characterized by an enduring predisposition to generate seizures unprovoked by any immediate central nervous system insult." Asterisk Erin's words, that part's really important and we'll get into it. Back to the quote. "And by the neurobiological, cognitive, psychological, and social consequences of seizure recurrence." So let's kind of just reiterate in maybe more easy language, epilepsy is recurrent seizures that happen chronically without a clear provoking cause at least not acutely, like not a single identifiable cause of seizures, and all of the consequences that result from those recurrence of seizures. So clearly to understand what the heck that means, like what the heck epilepsy is in that context, we have to first understand seizures and realize that not all seizures are indicative of or lead to the disease known as epilepsy. So while all people living with epilepsy experience seizures in one form or another, not all people with seizures or who have had seizures have epilepsy by definition.
Erin Welsh	Right.
Erin Allmann Updyke	So what is a seizure then? And again The International League Against Epilepsy has a definition for us. And I quote, "a seizure is a transient occurrence of signs and/or symptoms due to abnormal, excessive, or synchronous neuronal activity in the brain." Episode over, that was so clear, right?
Erin Welsh	I have so many questions already.
Erin Allmann Updyke	I do too, Erin. And while that definition might have been helpful for some people, I actually really struggle with that definition. So I'm going to try and really break this down in the way that my brain makes sense of it, which is on a very basic level. We all know, and I've talked about on this podcast before in other episodes where we've dealt with things like meningitis or other kind of brain-related injuries, that our brain communicates via both electrical and chemical signals. So in general, what happens in our brain is that chemical signals are converted into actual electrical impulses and that is what is transmitting information to allow us to do literally everything like blink, breathe, talk, wave, type, etc. And these electrical signals and the chemical signals as well have to be very tightly regulated, both in their circuits of where they go and how they go and the timing for us to be able to do all of the things.
	So what happens in a seizure is that we see a burst of these electrical impulses, an abnormal amount and/or abnormal networks or pathways of activity. That is what we are seeing in a seizure and that is what is picked up on an EEG when they're hooking up all those electrodes to look at the electrical activity in your brain and they say this looks like a seizure. And this abnormal activity, it can start from just one part of the brain which results in what we call a focal seizure or what used to be called partial seizures. Or sometimes we can see this burst of electrical impulses from both sides, both hemispheres of our brain at the same time. And that results in what we call a generalized seizure. And because our brain is suffice to say very complicated, it's a complex structure with a lot of different layers between which these electrical impulses have to travel. So these abnormal bursts of activity can happen in any given part of our brain which means that those signs or symptoms that we might see or associate with a seizure can actually vary incredibly widely depending on where in the brain they're occurring.
Erin Welsh	I have a question about the word abnormal.
Erin Allmann Updyke	Oh yeah.

Erin Welsh	What is normal and then how far outside of normal is abnormal? What does the range look like? You know what I mean?
Erin Allmann Updyke	Yeah. That is a really, really good question and I'm going to just say I don't have an answer for it. Because I don't know enough about EEG readings and I know that there are sometimes things that can be called by some people, this looks like what we would call an epileptiform or a seizure-like change in an EEG that maybe by other people would be interpreted as not quite that. So it's a really good question and I don't think that there in some cases is a cut and dry answer. But what we see on these electrical readings is basically just impulses that often associate with specific seizure-like activity that we'll talk about in a minute, that also correlate with what we're seeing on an EEG, that is different than a person's baseline brain activity.
Erin Welsh	Okay, two questions. One, when you're comparing to baseline is that that person's baseline or like population baseline? And then number two is who is doing the reading? Is it a person or is it a computer or is it both? Who determines what is an epileptiform pattern?
Erin Allmann Updyke	Excellent questions. For the first one, I don't fully know. There are I think enough EEGs done in the world and being studied for many decades that we have a sense of what typical brain patterns look like across various people. You would still also compare one person's EEG at their baseline when they're not having seizures vs when they are having seizures, so I think it's a little bit of both.
Erin Welsh	Okay.
Erin Allmann Updyke	And it is not me, it's a neurologist who is reading the EEGs.
Erin Welsh	Okay, but it is a human.
Erin Allmann Updyke	It's a human. A lot of times just like with an EKG when we're looking at your heart, there's usually a computer readout component but then an actual human is always going to be the one looking at it and determining... A human with a lot of training, a lot.
Erin Welsh	Okay. Okay, fascinating. Cool.
Erin Allmann Updyke	But it is also true that because of that there is a certain amount of subjectivity, right. That's also true.
Erin Welsh	Right, right, right.

Erin Allmann Updyke	Okay, so what then might some of these different types of seizures look like? I think most people listening likely associate seizures with one very specific type of seizure and that seizure type is called a generalized tonic-clonic seizure. These used to be called grand mal seizures, so that terminology might be familiar to some people. These are the kind that you see on TV where somebody might collapse and is unconscious and then they have a rhythmic jerking of especially the large muscles of their body. They'll be kind of rigid and then have muscle convulsions. They might bite their tongue during this process, they might have loss of bladder or bowel function because of autonomic nervous system involvement. And then usually when they wake up, they have a period of confusion where they're not quite sure what's going on and this might take some time to resolve. That is one type of seizure but it is just one and there are so many more than that. And that makes sense since now we know that any part of the brain can be affected. So let's get into how we can classify seizures. We define seizures first from their point of origin. So like I said before, seizures can be focal which means they start from one part, one hemisphere and one little part of the brain, don't ask me how little, Erin. Just one area of the brain.
Erin Welsh	Okay.
Erin Allmann Updyke	Or they can be generalized meaning that they're starting at onset from both hemispheres of the brain. And a lot of times we actually don't know, we don't know necessarily what that pinpoint origin is and so then these seizures are classified as unknown origin and then we can further classify them by what signs and symptoms we see after that. Then to further break this down, there are also motor and non-motor seizures. So motor seizures have physical skeletal muscle involvement, so moving of usually the extremities or something in some way. This can look like spasms, it can be like a hyperkinetic or a myoclonic stiffening and tightening of muscles. It could be a tightening and relaxing very rapidly which is what results in that tonic-clonic description, that's what tonic-clonic means. It's alternating between tensing and relaxing of muscles with this jerking motion. It could also be much smaller twitches of muscles, just say of the hand or the face. Or it could also be a sudden weakness, so rather than a tension of muscles, it could be a sudden flaccidity of muscles. And that's all just within motor seizures.
	It could also have none of that and be a non-motor seizure which could have a huge variety of symptoms. It could have cognitive symptoms like just a blank stare where people just suddenly have no emotion on their face, it is a blank stare and is unresponsive. It could be sensory symptoms that might even be something that people are feeling or are aware of, sudden sensory changes. Or it could be a complete loss of activity all of a sudden which is called behavioral arrest, where someone just suddenly stops exactly what they're doing. And a whole bunch of other things even within that. And when we especially talk about focal seizures, this is not true for generalized seizures, but then the third step that we have to look at is whether awareness is intact or impaired. So because a focal seizure happens in only one part of the brain, someone may or may not know and be aware that they're having a seizure at the time that they're having it. And so we say that their awareness is either impaired or intact. With generalized seizures, awareness is not intact because it's happening in both hemispheres of your brain at the same time. But a lot of times people do have prodromes or what we call auras prior to a seizure, so they might know that one is coming. And before you ask, because I know you're going to have a million questions-
Erin Welsh	I do. You can already see one on my face.

Erin Allmann Updyke	Yep, I can. All of these different seizure types are not mutually exclusive. Different types of epilepsy or even a single seizure episode can have multiple of these forms within them. So for example, something could start as a focal seizure but could then generalize and become bilateral and then end with something that looks like a generalized tonic-clonic seizure. Or people could have different foci of seizures throughout their brain that result in throughout their lifetime having seizures of multiple types or multiple forms. And my last important note before I let you ask questions that I hope I can answer is that one of the things that's very important to know about seizures is that these are brief episodes. These are brief episodes of this intense neuronal activity. And when I say brief, I mean on the order of seconds to 1-2 minutes.
	Because any seizure lasting more than five minutes or if you have multiple seizures happening within a short time frame where someone does not return to full consciousness inbetween, that results in something known as status epilepticus and is a major medical emergency. We thought I think for a long time in the kind of history of epilepsy that it was 20 or 30 minutes before this became an emergency but it's not. If seizures are happening for five minutes straight, that's a medical emergency because there's so much brain activity that can result in long lasting damage. This is rare, status epilepticus is rare, it most often happens with generalized tonic-clonic seizures, so that seizure that's happening on both sides resulting in that convulsive whole body seizure. But it's also possible to have non-convulsive status epilepticus and that's I think really important where EEGs can be so integral in figuring out what's going on because you might be having more seizures than you even have very obvious signs or symptoms of.
Erin Welsh	Right, that makes sense.
Erin Allmann Updyke	Okay, I know you have a million questions.
Erin Welsh	Yeah, okay. I want to start pretty general.
Erin Allmann Updyke	Okay.
Erin Welsh	We have all of these different seizure classification types, there can be overlap, there can be multiple descriptors for a certain type of seizure. That is important information. What does that information help you decide to do? Does it have an impact on treatment on prognosis? Yeah, like what sort of information do you get from that beyond just what type of seizure it is?
Erin Allmann Updyke	Excellent question. It has implications for kind of so many different things. So for example, especially when it comes to focal seizures, if we can identify that a seizure is coming from one specific focus, then there are potentially treatment options that might be very targeted. Let's say that a seizure is emanating from a particular area of the brain where there is a tumor. That's something that we're going to be more easily able potentially to target and to treat directly. It also does affect what medications might be used. And I don't have a lot of details on that because there are so many different antiepileptic medications and antiseizure medications, but there are different ones that have maybe been shown to be more beneficial in certain types of seizures than other types of seizures. So it's important to note and be able to kind of identify what type of seizure to be able to pick the best medication. And then when you have say focal seizures, whether there's an impairment of awareness or not, that also is going to be important for not only just a person's general life but also determining if it's safe for them to be doing activities like driving, etc.
Erin Welsh	Okay, okay, that makes sense.

Erin Allmann Updyke	Yeah. So there's kind of a lot of layers of why it's important, not just medications but also additional treatments that might be available and just kind of determining what somebody's prognosis might be and things like that as well.
Erin Welsh	Okay. My other question is about something that you mentioned and that is the damage that can result from status epilepticus. But I also wanted to know first of all how does that damage occur? And does that damage happen in people who for instance have epilepsy, not status epilepticus, but repeated seizures throughout their life?
Erin Allmann Updyke	Yeah, absolutely. Excellent question. So the short answer is yes, there are changes in the brain that are going to happen with epilepsy and with recurrent seizures. And one of the things that I always try and touch on in all of our episodes is the pathophysiology of whatever we're covering. And so that usually means trying to get into some of that nitty gritty detail, like what is happening in our brain during this process. When it comes to epilepsy, it's really difficult to get super into the nitty gritty details, not just because I'm not a neurologist but also because the underlying brain changes that can lead to epilepsy, to these recurrence of seizures, are manyfold. There's a lot of different potential changes in the brain that can result in epilepsy. So then it makes the specific details of what's causing seizures also really varied and so it's hard to kind of generalize it. But I'm going to try.
	So the leading hypothesis is that when it comes to epilepsy, when it comes to recurrent unprovoked seizures, what happens is that you end up with an imbalance of excitatory and inhibitory currents at its most basic form. And we've talked on this podcast before about how in our brain we have neurotransmitters and electrical signals that are promoting action, like bend your arm, and we have pathways in our brain that are inhibiting action, like unbend your arm, right, or stop bending. And there's a lot of different neurotransmitters and ions and receptors that are involved in all of this complex signaling and converting these excitatory and inhibitory signals into that electricity, right.
	So epilepsy arises when those signals are malfunctioning. But that can happen through any of those particular pathways, through changes in ion channels, through changes in the concentration of neurotransmitters, from changes in receptors in our brain. And there's some hypothesis that part of the recurrence of seizures in epilepsy is due to inflammation that happens during this seizure process and it might be that inflammation as well plays a really big role in the kind of perpetuation of epilepsy and seizures. I don't know if that fully answers your question but the truth is that it's because seizures can occur from so many different possible sources, it can also result in so many different changes in the brain. Both changes in things like our ion channels or the concentration of neurotransmitters. It can result in changes of the structural cells, the glial cells within our brain. It can also result in changes in the actual connectivity of our neural networks themselves when you have seizures and when you have recurrent seizures. So any and all of the above are possible.
Erin Welsh	Does having one seizure make you more likely to have a second seizure?
Erin Allmann Updyke	That's a good question. I don't think that we can 100% say yes or 100% say no. There are a lot of ways that you can have a seizure that you may never have a seizure again. For example, febrile seizures which happen in kids, usually young kids most commonly like 12-18 months but usually anywhere from six months to five years, can have a seizure in the context of an acute illness where they have a fever that's not from a central nervous system infection because that would be something else entirely. And these most often resolves spontaneously. We don't usually see any permanent or residual damage. And while there may be some association between kids who have febrile seizures and who later do get diagnosed with epilepsy, that doesn't mean that most kids who have febrile seizures are going to develop epilepsy by any means.

Erin Welsh	Okay.
Erin Allmann Updyke	Same thing if you think of someone who's a child or an adult who ends up having a seizure because of metabolic derangements like severe hypoglycemia in the context of something like diabetes.
Erin Welsh	Okay.
Erin Allmann Updyke	That can result in seizures but this would be a reflex or a provoked seizure due to that clear factor, hypoglycemia, causing that seizure. And no matter how many times you might have a hypoglycemic seizure, that doesn't necessarily mean that you have epilepsy.
Erin Welsh	That was my other question which was unprovoked, what is provoked vs unprovoked. Okay, got it.
Erin Allmann Updyke	Exactly, yeah. The same is true for something like alcohol withdrawal which is a very common cause of seizures.
Erin Welsh	Okay.
Erin Allmann Updyke	So if your seizures are only and exclusively in the context of alcohol withdrawal, that doesn't necessarily mean you have epilepsy.
Erin Welsh	Right. And so when you're talking about unprovoked, you're not talking about triggers for epilepsy seizures like flashing lights or which I know is not very-
Erin Allmann Updyke	Correct. Yes. Yeah. Actually that's a really good important point. Yes, I'm not talking about that which can trigger someone who has epilepsy. And one thing I think is really important that I saw in a paper that I never thought of that way is that epileptic seizures, so people who have epilepsy, their seizures are not random, like seizures are not entirely random. We might not know by any means what any provoking factor is for any given particular seizure that someone has but something is going on in a person's brain that ends up leading to a seizure in a person who has epilepsy.
Erin Welsh	Okay.
Erin Allmann Updyke	So they're not entirely random.
Erin Welsh	Gotcha.
Erin Allmann Updyke	Yeah. That's honestly most of what I have for the kind of biology of seizures and of epilepsy.
Erin Welsh	Okay. So then I do have more questions.
Erin Allmann Updyke	Great. I was going to talk about treatment but I want to know if you have any more questions first.
Erin Welsh	So you went through a bunch of different types of seizures. Epilepsy also comes in many different forms.

Erin Allmann Updyke	It does.
Erin Welsh	What are some of those forms?
Erin Allmann Updyke	Yeah. And I will say that the terminology surrounding epilepsy, much like the terminology surrounding seizures themselves, has changed a lot in recent years. I'm going to talk about the most current terminology that we have. So in general today, epilepsy is classified as either genetic, meaning predominantly arising from an identifiable genetic cause, be that a single mutation or multiples, or structural or metabolic, which means it's caused initially at least by something like say a stroke or a trauma, like a traumatic brain injury, or a tumor in the case of structural, or even a malformation of the brain itself which might be congenital, or various metabolic syndromes that might lead to seizures which can also be genetic so it gets a little confusing, or instigated by something like a meningitis or an encephalitis that later leads to recurrent seizures. And then if we can't pinpoint any of those then an epilepsy would be classified as unknown and a really big proportion of epilepsy, and I don't have an exact number on this, is actually unknown origin. So we don't always know what the instigating factor was.
Erin Welsh	Okay. And then what about different types of epilepsy?
Erin Allmann Updyke	Yeah, I know. I mean this one is hard I think because I think it was more common in the past to separate out very specific forms of epilepsy. And now I think we have started lumping a lot more of them together based on those classifications that I mentioned, like what type of seizures do you have with your epilepsy?
Erin Welsh	Okay.
Erin Allmann Updyke	So I know when I was in med school I had to memorize a whole bunch of different seizure types and a whole bunch of different types of epilepsy. And it seems like the trend now is more to focus on what seizure types does a person with epilepsy experience and classify it based on that. So as an example of that, a lot of people might have heard of temporal lobe epilepsy. Temporal lobe epilepsy means seizures that are arising from the temporal lobe which is one lobe of our brain, we have one temporal lobe on each side. So now it would be more common to classify that as a person who has epilepsy whose seizure type is a focal onset impaired awareness seizure originating from the temporal lobe with motor symptoms of various forms.
Erin Welsh	Okay.
Erin Allmann Updyke	Does that makes sense?
Erin Welsh	Yeah.
Erin Allmann Updyke	So it's like more cumbersome but a lot more specific.
Erin Welsh	Right. And it makes sense in terms of treatment too, I would imagine.
Erin Allmann Updyke	Exactly. And then within that you'll still be able to classify the type of epilepsy based on whether it's genetic or whether it was from a structural change or a metabolic disorder, etc.
Erin Welsh	Right. Important also that genetic does not mean hereditary necessarily.
Erin Allmann Updyke	Yes, absolutely.

Erin Welsh	Speaking of treatment-
Erin Allmann Updyke	Yeah, let's.
Erin Welsh	What treatments are there? How do they work?
Erin Allmann Updyke	Great question. There are a whole host of antiepileptic or antiseizure medications. And the good news that I have is that most data that I saw suggests that up to 70% or some places say 80% of people living with epilepsy will achieve remission. And often this happens with the first drug tried, the first antiseizure medication that somebody tries regardless of what one they end up trying. There are too many different antiseizure medications for me to list. Some of them act, for example, on sodium channels and so they're modulating some of those chemical signals. Some of them might act on certain neuroreceptors or other neurotransmitters like GABA or glutamate. So I'm not going to get into the nitty gritty of how each of these different medications work but you can imagine that if we can pinpoint any specifics about a seizure, we might be able to pick one antiseizure medication over another, right. And 70% remission sounds pretty good. But it also means that right now 30% of people do not or will not necessarily achieve remission.
Erin Welsh	What proportion of that is lack of access vs not finding the right drug?
Erin Allmann Updyke	That's a good question. That's not counting lack of access.
Erin Welsh	Oh wow.
Erin Allmann Updyke	That's people who are tried on antiseizure medication.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah. Which is really important because we'll get into lack of access later.
Erin Welsh	Yeah.
Erin Allmann Updyke	This is where it becomes really important to be able to identify as much as we can about seizures because for some people who can't achieve remission with medication so far, there may be surgical options depending on the focality of their epilepsy. So surgery might mean resection or destruction of an area of epileptic focus or it might be nerve stimulation, usually peripheral nerve stimulation rather than deep brain stimulation. Various forms of this have been shown in some cases to lead to a reduction in seizure burden, maybe not complete remission. Another treatment that a lot of people have probably heard of because it's all over everything is a dietary control known as the ketogenic diet. The ketogenic diet is very interesting and probably could be its whole own episode. In general, the quality of evidence that we have is not all that great but likely because of small sample sizes. But it has been shown for treatment-resistant childhood epilepsy to improve the chances of seizure reduction or remission.

	There's a lot less evidence for less restrictive diets, like there's a modified Atkins, there's a low glycemic index version. But for someone who is living with very frequent seizures, even a small reduction in seizure burden might be a pretty big deal and pretty life changing. But the data that we have is just not all that strong. And a true ketogenic diet like is used in these studies to look at epilepsy is incredibly difficult to achieve. It is very, very restrictive. So it's not the keto diet that's on the news. Just throwing that out there. I also am really just personally very interested in the potential mechanisms of the ketogenic diet, so I do have a couple papers if people want to read more about it. Spoilers, we don't know but there's a lot of different hypotheses with various levels of potential theoretical and actual support on how this change in forcing our brain to use ketones rather than glucose might shift basically metabolism or mitochondrial function to then change the way that electrical impulses are generated. It's pretty cool but it's all kind of theoretical at this point. So yeah.
Erin Welsh	Yeah. Okay, interesting.
Erin Allmann Updyke	It's interesting and there's more if you want to read about it. But that essentially is what I have at least about epilepsy and seizures.
Erin Welsh	I have two questions.
Erin Allmann Updyke	Okay.
Erin Welsh	My first question is how many recurrent seizures does it take to be diagnosed as epilepsy?
Erin Allmann Updyke	Great question. Two.
Erin Welsh	Oh really? Okay.
Erin Allmann Updyke	Two or more. I can give you like a full, even more formal definitions. Two or more unprovoked seizures greater than 24 hours apart, so not within the same day. Or, and this part is very interesting and has really huge implications for the treatment of people with epilepsy going forward, it can also be a single unprovoked seizure in a person who has a greater than 60% risk of having another seizure over the next 10 years. And the way that they determine that is by looking at an EEG to see if the findings on there look like there are changes in the brain already that have the potential to result in seizures, or any epileptiform activity that you can see on an EEG even if you're not having seizures at the time. And so those two things with a 60% probability would then even with a single seizure mean that you have epilepsy.
Erin Welsh	Okay.
Erin Allmann Updyke	And then the third thing would be also if you have an epilepsy syndrome, so like a genetic or other disorder that is known to be associated with epilepsy.
Erin Welsh	Gotcha.
Erin Allmann Updyke	Yeah.
Erin Welsh	My second question is you talked about how epilepsy a lot of the time, we don't know what causes someone's epilepsy.
Erin Allmann Updyke	Yeah.

Erin Welsh	A lot of the time also epilepsy can just stop.
Erin Allmann Updyke	Yeah.
Erin Welsh	Why? How? When does that happen? Under what circumstances? How often?
Erin Allmann Updyke	Yeah. If I had those answers, Erin... It is more common I believe with childhood epilepsies that they may resolve over time. Why? I don't know. And beyond that it's just a really good and interesting question. Some people... And maybe it could also be related to if there is an instigating factor, let's say a meningitis infection or a traumatic brain injury, something that changes the brain enough that you have this chance of recurrent seizures or you've had two seizures greater than 24 hours apart, so you meet this definition for epilepsy but over time maybe your brain remodels itself enough to then no longer have this epileptiform activity. Then you can, yes, resolve your epilepsy.
Erin Welsh	That's fascinating.
Erin Allmann Updyke	Yeah. And that's also part of the change in the definition of epilepsy that happened relatively recently is that it can be a disease that is also resolved.
Erin Welsh	Okay, okay. Temporary chronic disease.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah.
Erin Allmann Updyke	Well and also something that is classified as a disease and not a disorder. And that was a very intentional change when they kind of updated these definitions which I think is very interesting. So Erin, that was a lot.
Erin Welsh	It was.
Erin Allmann Updyke	And also probably not enough.
Erin Welsh	Yup.
Erin Allmann Updyke	So tell me, where did all of this come from? How did we get here? Have we always had epilepsy? What?
Erin Welsh	I will start the deep deep dive into the history section right after this break.
TPWKY	(transition theme)
Erin Welsh	Quote: "A history of epilepsy seems a premature, perhaps even a doubtful enterprise. There is no unanimity about the range of the concept of epilepsy and the nature of the disease is as yet obscure." Endquote.
Erin Allmann Updyke	Wow. So the end, huh?

Erin Welsh	The end. I borrowed this quote from a book called 'The Falling Sickness' by Owsei Temkin, considered to be the authority on the history of epilepsy in the western world. These words mark the very beginning of the first edition of this book, published back in 1945, and when 26 years later the author revised and published a second edition, there they stayed right at the beginning. And I think they were even in the fourth edition published in the mid 90s.
Erin Allmann Updyke	Oh no.
Erin Welsh	Yeah. Because when that fourth edition came out in 1994, they remained just as true as they were in 1945.
Erin Allmann Updyke	Wow.
Erin Welsh	And now in 2023, I feel like they're still an accurate description of the mystery that surrounds epilepsy. So that's why I thought it was the perfect way to start the history section.
Erin Allmann Updyke	Great.
Erin Welsh	Even though we've come a tremendously long way in our understanding and treatment of epilepsy since those words were first written, as the biology section just demonstrated there are still so very many unanswered questions. But having unanswered questions isn't a bad thing necessarily. Look at the nature of those questions and how specific they are. That alone I think shows incredible progress in our knowledge of epilepsy. And that progress, along with the historical social perceptions of epilepsy, is what I want to talk about today, particularly in the western world since that's where most of the sources that I found concentrated on. When did humans first recognize epilepsy? How did the meaning of this condition shift over time? What did people think caused epilepsy? And how did they treat it? This is a massive topic like we keep saying and I'm going to try my best but there are parts that I simply won't get to or won't go into in great depth. And like we keep saying, the good news is that we will give you plenty of material to read on if you are still curious.
Erin Allmann Updyke	Always.
Erin Welsh	Always. The other challenge, or maybe not necessarily challenge but something that I want to note, is that the definition of epilepsy has changed substantially throughout history and even at any one given point in time you would probably get a dozen different answers if you asked a dozen different people what epilepsy was. In ancient times and into the Middle Ages and the Renaissance, epilepsy, seizure, attack, convulsion, many different words or terms were all used interchangeably. So while today we think of epilepsy as a chronic condition, in the past it could have meant that or it could have meant an isolated seizure. So keep that in mind. I usually try in these history sections to talk a bit about the evolutionary origins of whatever topic we're covering. But I decided not to attempt that for epilepsy for several reasons. There is still so much unknown about its pathophysiology, you can't even really say its pathophysiology since there are so many different types of seizures-
Erin Allmann Updyke	Right.

Erin Welsh	Each with different histories and causes and triggers. And so I felt that a discussion of each of those evolutionary histories would probably have been more confusing than enlightening. I will go so far as to say that it's likely that humans have experienced epilepsy for as long as we've been human and probably long before that. And instead I'll start with the very first observations of epilepsy which come from the ancient world. Some researchers have speculated that trepanation, which is a practice that's been performed for thousands of years where you make a small hole in the skull and remove the bone, that was done to treat epilepsy and that ancient trepanned skulls indicate their knowledge of the disease. But this remains controversial and it's something that we're never going to know for sure.
Erin Allmann Updyke	Yeah.
Erin Welsh	Why people used trepanation in ancient times. The earliest written description of epilepsy comes from Mesopotamia around 2500 BCE in an Ancient Sumerian text describing, quote, "a person whose neck turns left, whose hands and feet are tense and eyes wide open, froth flowing from the mouth, and consciousness being lost." Which pretty well describes a focal unaware tonic seizure. This condition was called antasubbu and was thought to be related to the hand of sin, the god of the moon. And already we have our first theme in the history of epilepsy, a theme that kind of I think overshadows most any other theme that I would call attention to, the belief that the condition had links to the supernatural, to religion, to magic of some sort, that it was more than a physical condition.
Erin Allmann Updyke	Yep.
Erin Welsh	As we'll see, this gave epilepsy a whole host of different meanings. Some positive like oh, you are prophetic or you're a chosen genius, and some most negative like it being a sign that you're possessed by an evil demon or spirit.
Erin Allmann Updyke	I feel like that is the one that I think of the most when you think of like historical associations with epilepsy or seizures.
Erin Welsh	Yep, for sure.
Erin Allmann Updyke	Yeah.
Erin Welsh	And we'll get into all of it. But a big part of this theme is that these beliefs about the supernatural cause of epilepsy were in continuous conflict for much of history with scientists or physicians who believed that there was a physical biological explanation for what was happening. Sometimes superstition dominated popular thought and other times science. This dichotomy is an oversimplification, it's much more nuanced than how I'm presenting it but I wanted to point it out because it shapes the prevailing perception and treatment of epilepsy over the next several 1000 years give or take. For instance, in one of the Hippocratic texts written around 400 BCE, it is said that the seat of the disease is in the brain, it's a hereditary condition, and that an excess of phlegm in the blood is what leads to seizures.
Erin Allmann Updyke	It's always the phlegm.

Erin Welsh	It's always the phlegm. And that's part of the humoral theory of disease. In this text called 'On The Sacred Disease', the author also argues against the labeling of epilepsy as a divine disease. Quote, "I am about to discuss the disease called sacred. It is not, in my opinion, any more divine or sacred than any other diseases but has a natural cause and its supposed divine origins is due to men's inexperience and to their wonder at its peculiar character. But if it is to be considered divine just because it is wonderful, there would be not one sacred disease but many." Which is kind of amazing considering that was like thousands of years ago.
Erin Allmann Updyke	Yeah.
Erin Welsh	And so much happened inbetween then and now.
Erin Allmann Updyke	Yeah.
Erin Welsh	And this isn't to say that the science behind what these Ancient Greek physicians believed caused epilepsy was sound by today's standards, for instance it was caused by the weather, hot wind, dry wind, whatever. But it was a clear and important distinction to them, to many physicians at that time. And I think that's really interesting.
Erin Allmann Updyke	Yeah.
Erin Welsh	However that was certainly not the case as we move on to Ancient Rome and then especially the Middle Ages. In Ancient Rome, the scientific lens through which many Hippocratic era physicians viewed epilepsy shifted to one that was a bit more supernatural, or at least one where a supernatural explanation was more willingly considered. An epileptic seizure could be a bad omen and it was often thought to be brought on by an unwelcomed god or demon. A person who had epilepsy was considered unclean and their condition contagious by touch or by sharing food or drink. While occasionally it was viewed as a blessing or a sign of prophecy, by and large it was a negative stigmatizing disease. The meaning that epilepsy held or the importance with which people viewed it can be seen in part by looking at the names that it has had over time. Let's start with the word epilepsy which has roots in the Greek verb 'epilambanein', I probably completely destroyed that, but that word means to seize or to attack.
Erin Allmann Updyke	Okay.
Erin Welsh	So epilepsy seems to have been used in these ancient texts simply to mean seizure, a single medical event without any connotations of supernatural or magic elements. The chronic condition was often referred to in Ancient Greece and Rome as the sacred disease or the great disease, which eventually turned into the Latin 'morbus maior' and then into the French 'grand mal' which is also a term that we used to use for a certain type of seizure. In the Middle Ages the name most commonly used to describe the condition was something involving falling, the falling sickness, the falling evil, 'caducus' meaning falling, something that falls. And I will also note that the falling sickness was what the disease was called in the first descriptions in Ancient Chinese medical texts dating back to 770 BCE. But also in the Middle Ages the disease began to be associated with more loaded words such as 'daemonicus' and 'lunaticus' referring to the belief that epilepsy was a type of madness or that it was a sign of possession.

	Speaking of lunaticus, I don't know if I'm saying that right, probably not, which is where the word lunatic comes from, it originates from the Latin 'luna' meaning moon since it was believed that the moon could cause bouts of insanity or epilepsy. During this time period, people with epilepsy were often described as being seized by quote "the disease of the moon". Why the moon? Well perhaps it was the vengeance of the goddess of the moon or you could go with a scientific explanation that quote "the waxing moon heated the atmosphere surrounding the earth and consequently melted the brain, thus provoking an attack". But I mean this is something that kept occurring to me is that we look back at that now and we laugh but that was science.
Erin Allmann Updyke	Right.
Erin Welsh	The goddess was the superstition part.
Erin Allmann Updyke	Right.
Erin Welsh	The science part was the moon melting your brain.
Erin Allmann Updyke	Yeah.
Erin Welsh	There are many different ways to distinguish between superstition and science, or wishful thinking or magical thinking and science, and some was done at the time of the writings and some is done from our perspective today.
Erin Allmann Updyke	Right.
Erin Welsh	So we could look at that and go oh well both of those are definitely superstitious beliefs, how could you ever think that the moon would melt your brain? But back then that was science.
Erin Allmann Updyke	Ugh yeah.
Erin Welsh	Something I kept thinking about. Epilepsy was also thought to be from demonic possession or caused by the devil and its reputation as an evil disease gets a mention even in Dante's Inferno. Many people with epilepsy were forbidden to go to church or if they were allowed they could not take the Eucharist or touch anything in the church because again, people thought it was contagious. Epilepsy was linked to witchcraft and in the handbook on witch hunting, Malleus Maleficarum, written by two Dominican friars and published in 1494, it was said that seizures were characteristic of witches and also that witches could cause epilepsy to develop. Yeah.
Erin Allmann Updyke	A lot of feelings there.
Erin Welsh	But again, I will say that there was no overall consensus on epilepsy as an evil disease at any point in time. There were also mentions of it as a saintly disease, Saint Valentine is the patron saint of epilepsy, and one that marked you as chosen in a good way or a genius. Continuing into the Renaissance, epilepsy was still a disease fraught with meaning and it was still the doctor or the priest or society that got to choose what that meaning was. Priests were sometimes called in to determine whether someone was possessed or simply had epilepsy. And people with epilepsy were believed to have the power of prophecy but that their prophecies should be taken with a grain of salt. I suspect it was something along the lines of we should believe them if it's a favorable prophecy and we should shun them otherwise.

Erin Allmann Updyke	I'm so curious if there was any correlation between different seizure types and whether someone was considered to be demonic vs saintly or possessed vs a fortune teller. It's so interesting to try and... We can't know I guess.
Erin Welsh	We can't know. And as I'll talk about, people did recognize many different seizure types.
Erin Allmann Updyke	Yeah.
Erin Welsh	But I think it was so difficult to spread this information, but also to look back now and go oh, that was this type of seizure or oh, they were seeing this.
Erin Allmann Updyke	Right, right, right.
Erin Welsh	Was what they were writing about even a seizure?
Erin Allmann Updyke	Right?
Erin Welsh	I don't know.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah.
Erin Allmann Updyke	Ugh yeah.
Erin Welsh	But it is around this time during the Renaissance that scientific thought and the medical writings of ancient physicians like Hippocrates and Avicenna began to experience a resurgence as people became more and more skeptical of supernatural or magical explanations. And this led to epilepsy being viewed and researched with more of a medical lens rather than solely with a moral one. Which isn't to say that epilepsy became a neutral disease, not at all. As one author put it, superstitions were exchanged, not discarded. But before I continue on to that, I want to go back and ask not what epilepsy meant to people from ancient times to the Renaissance, but what people actually knew about what epilepsy was. As I'm sure you'll talk more about Erin, epilepsy in its many forms is incredibly prevalent and this likely isn't a new phenomenon given the extent to which epilepsy was written about historically.
	Even some of the oldest descriptions of epilepsy that we have talk about different forms of the condition, variations in seizure appearance and duration, and they do a pretty good job of recognizing patterns in its epidemiology. For instance although descriptions of seizures vary, the common features among them include fall to the ground, unconsciousness, insensibility to pain, and no recollection of the attack upon regaining consciousness. They observed that epilepsy most often occurred early in life, especially during teething and that it was uncommon for it to first show up after 20 years of age. Some writers suggested it was hereditary, while others said it was congenital. One of the more popular and persistent superstitions from the Renaissance was that if a pregnant person saw someone having a seizure, that baby would develop epilepsy eventually.
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	Yeah.

Erin Allmann Updyke	Okay.
Erin Welsh	Yeah. Not what happens.
Erin Allmann Updyke	No.
Erin Welsh	Writers early on recognized that a seizure was often preceded by what they called and what we still call an aura, meaning breeze, which got its name when a young boy described a sensation like a cold breeze entering his head right before he had a seizure. A range of pre seizure signs or symptoms was recognized, slow speech, headache, dizziness, stiff hands, ringing in the ears, just to name a few. And beginning in the Middle Ages, major divisions in epilepsy began to be made, often associated with where it was thought to originate in the body. Which I think is interesting knowing that that's how we characterize a lot of seizures types as well as like where it originates in the brain.
Erin Allmann Updyke	In the brain. Yeah.
Erin Welsh	Yeah. This was in the body. So for instance, there was epilepsy which was the condition that originated in the head and then analepsy, the form arising from the stomach, and then catalepsy was from any other part of the body. Epilepsy was also linked to hysteria when the seizures were thought to originate in the uterus and eclampsia was also thought to be a special form of epilepsy arising from a pregnant uterus.
Erin Allmann Updyke	Yeah, I mean that's interesting because it's not epilepsy, but yeah.
Erin Welsh	Yeah.
Erin Allmann Updyke	But it's a seizure. Yeah, that's really interesting.
Erin Welsh	Yeah. And then divisions were made more along the lines of major vs minor. Platearius in the 12th century wrote quote, "major epilepsy is a complete obstruction of the principal ventricles of the brain. People suffering from it fall down quickly, the mouth and face are distorted, and there's also a trembling movement of the neck and of the whole body and clenching of the teeth. Sometimes they pass urine, feces, and seed involuntarily. They snore and froth and when the froth has been wiped off, they froth again. Minor epilepsy is an incomplete obstruction of the ventricles of the brain. People suffering from it sometimes fall down, sometimes they do not fall down but faint. The froth once having been wiped off does not reappear and they are quickly relieved."
Erin Allmann Updyke	Interesting.
Erin Welsh	Yeah. Although physicians from the Renaissance largely echoed with the preceding generations had written about epilepsy, particularly Ancient Greek physicians, they did make one important observation that broadened the concept of the condition, that epilepsy or seizures could result as a complication from another illness such as smallpox or scurvy or measles or the newly emerging syphilis. Essentially the idea that epilepsy could be a symptom or a complication and wasn't just a disease unto itself.
Erin Allmann Updyke	That is super interesting.

Erin Welsh	Isn't that? And as this definition of epilepsy expanded, the classification came to be more about perfect or simple epilepsy, the most common form, the form that you see the most. And then there was imperfect epilepsy, anything that was out of the ordinary. And while these physician writers certainly weren't right about everything, the extensive writings with largely accurate representations of prognosis, range of seizure types, timing of onset, and association with certain traumatic events such as the head injury, shows that these physicians were thinking about the disease and writing about it in a systematic way.
Erin Allmann Updyke	Yeah.
Erin Welsh	What they did struggle with was the ultimate cause of epilepsy which I think we can empathize with given just how many things can cause epilepsy, how much of the time we don't know what causes it, how many different types of seizures there are, and how we are still struggling to understand the pathophysiology of this condition.
Erin Allmann Updyke	Right.
Erin Welsh	Scientific explanations were varied. Hot weather or dry weather or too temperate weather, drinking too much alcohol or not enough, exercising or lack of exercise, too much sleep or not enough, anger, fright, bad smells. Anything could be blamed for epilepsy. And we've already gone through some of the moral explanations. Nothing seemed to fit, nothing seemed to be a satisfyingly consistent answer. And so is it any wonder really that we have a million and one explanations for epilepsy from these times? And for every one of those explanations we have at least 10 cures.
Erin Allmann Updyke	Our favorite.
Erin Welsh	And that also makes complete sense given that epilepsy can sometimes resolve on its own, like we talked about, medications can work differently from person to person and from type to type, and it can take a long time even today to see whether a medication for epilepsy is actually effective. I don't know though if I have ever seen as extensive a list of cures and treatments for any illness as I have for epilepsy.
Erin Allmann Updyke	Ooh!
Erin Welsh	I loved this quote from neurologist Edward Sieveking in 1861. Quote: "There is scarcely a substance in the world capable of passing through the gullet of man that has not at one time or another enjoyed the reputation of being an antiepileptic." Endquote.
Erin Allmann Updyke	That's really funny. I feel like that's honestly still true sometimes.
Erin Welsh	Right? And I won't go through this absolutely massive list because I eventually just stopped writing them down, I was like I can't, this is all of my notes now and it would be an entire episode. But I did want to go through a variety of them. Mistletoe is commonly featured, especially mistletoe collected at the new moon; an amulet containing coral, peony, and the root of strychnos, peony also shows up frequently. An iron nail or weapon; avoidance of iron; the first vertebra of a human; drinking human blood, especially gladiator blood.
Erin Allmann Updyke	Okay.
Erin Welsh	Lichens of horses or mules, I don't know exactly what that is. Genitals of seals.

Erin Allmann Updyke	Nope.
Erin Welsh	Testicles of the hippopotamus.
Erin Allmann Updyke	No, also no.
Erin Welsh	Also no. Blood of the tortoise or of the flatfish.
Erin Allmann Updyke	What?
Erin Welsh	The skin of a lizard. This lovely combination, feces of the land crocodile, the heart and genitals of the hare, and blood of the sea tortoise.
Erin Allmann Updyke	I...
Erin Welsh	A frog's liver; burned human bones in a cocktail; avoidance of goats; menstrual blood rubbed over the soles of your feet.
Erin Allmann Updyke	Just stop it.
Erin Welsh	I have two more. Kill a dog and let the patient have its bile. And my absolute favorite is quote "to let the person who first saw him fall urinate into his own shoe, stir the urine, and give it as a drink to the patient."
Erin Allmann Updyke	Erin. I know we talk about not judging people back then but like come on.
Erin Welsh	I know, it's really... I mean there are lots of things like burned human bones and pee shoe.
Erin Allmann Updyke	Pee shoe. Like that's not ever going to be a thing.
Erin Welsh	I mean I think it does demonstrate how desperate people were for a cure.
Erin Allmann Updyke	It seems even beyond.
Erin Welsh	Yeah. I also wonder sometimes like were any of these ever written as a joke?
Erin Allmann Updyke	Right.
Erin Welsh	They're like ha ha, look at these ridiculous things that people have tried and no one actually has ever done any of these.
Erin Allmann Updyke	That's what that one feels like quite honestly.
Erin Welsh	It does.
Erin Allmann Updyke	It feels like what you tell like your little brother to do, you know?
Erin Welsh	Yes.

Erin Allmann Updyke	And then you're like I didn't mean for you to actually do it.
Erin Welsh	Mom!
Erin Allmann Updyke	Yeah, yeah. 100%.
Erin Welsh	Well fortunately as we move on to the Age of Enlightenment and beyond, so like the 17th/18th century onwards, epilepsy becomes less about drinking someone's pee from a shoe and more about systematic study.
Erin Allmann Updyke	Okay, love it.
Erin Welsh	One thing that helped tremendously with this was the rise in anatomical dissections, which I think we've talked about before for hundreds of years prior had been viewed as sacrilegious. And so for the first time anatomists were able to link certain diseases with observable changes in the structure or function of body parts and that included epilepsy and changes in the brain, such as an abscess or a tumor or a hemorrhage in someone with the condition. And the rise of statistics had its own role to play, something that we've talked about in several other episodes of the podcast. In the case of epilepsy, institutions were created to house and care for people with the disease since it was believed that they could or should not live independently. And these institutions were viewed as opportunities to collect medical data for statistical purposes, which did lead to advancements in understanding the hereditary nature of some forms, characterizing the age of onset, patterns and seizure triggers, incidents of certain forms, and also rejecting some of the long held beliefs like the phase of the moon affected the likelihood of a seizure.
	But they were 18th and 19th century institutions nonetheless and likely pretty miserable places to be forced to live. Demonic possession or association with quote unquote "insanity" continued to be used as a justification for locking someone with epilepsy away. And it was only in the early to mid 1800s that separate buildings were established for people with epilepsy and people deemed quote unquote "insane", with one major distinction between the groups being that the epilepsy group could attend mass while the quote unquote "insane" group could not. Clearly the stigmatization of epilepsy didn't lessen over time, it just changed in flavor, despite the many medical advancements made throughout the 1800s. Sure, some completely unsupported ideas about the underlying cause of epilepsy gained traction, specifically that masturbation lead to epilepsy, with some doctors recommending circumcision or even castration or clitoridectomy to literally no effect.
Erin Allmann Updyke	Oh dear.
Erin Welsh	Yep.
Erin Allmann Updyke	Oh gosh.

Erin Welsh	But overall, the rise of experimental observational science and the specialization of medical branches like neurology led to tremendous progress in our understanding of seizures and epilepsy. What had been previously divided into two main groups, idiopathic epilepsy originating in the brain and sympathetic epilepsy originating anywhere else, soon became more and more complex with terminology developed to describe different types of seizures, like grand mal, petit mal, and absence. The physiology of nerves and reflexes began to be uncovered and that helped to better understand why seizures looked like they did and experiments altering blood flow to and from the brain showed how unconsciousness or convulsions could result from the duration or intensity of blockage. Slowly but surely scientists were chipping away at the mystery that was epilepsy and finding that with every question answered 10 more sprung up in its place.
Erin Allmann Updyke	Inevitably.
Erin Welsh	Inevitably. But the questions were becoming more targeted, more detailed, revealing just how quickly progress is being made due in large part to the rejection of superstitious thinking, the need for scientific claims to be supported by observational or experimental data, and a tendency to look at everything with a healthy dose of skepticism, including the teachings of the Ancient Greek physicians which previously had been taken more or less as gospel. Perhaps the biggest turning point in the history of epilepsy during this time came with the invention of the human EEG, electroencephalogram, by Hans Berger in 1929. This could be its own episode really. It could be, maybe someday. But what it did for epilepsy was allow physicians to diagnose a type of seizure or epilepsy without actually having to observe the person having a seizure.
	Researchers, especially Frederic Andrews Gibbs, Erna Leonhardt Gibbs, and William Lennox, described three major types of clinical seizures using EEG patterns, petit mal, grand mal, and psychomotor seizures. We all call these different things today. And this last one, psychomotor seizures or in today's terms focal seizures arising from the temporal lobe, prior to this most of the people experiencing one of these seizures were labeled as hysterical. And the application of EEG to animal models also really opened up the world of epilepsy, making it very clear that we desperately needed to revamp our classification system. And so in 1964, the International League Against Epilepsy proposed a new classification system which has since been continually revised and refined, with big changes occurring every few decades. And I kind of love that it's constantly changing.
Erin Allmann Updyke	Yeah.
Erin Welsh	Because it's like hey, let's reconsider, maybe we should change this word or that word. That's how progress is made, I love it.
Erin Allmann Updyke	Right.
Erin Welsh	Cellular and molecular advancements have also vastly improved our understanding of the underlying pathophysiology of seizures and have shown some promise for novel therapies. The late 1800s and into the 1900s also saw innovation in effective treatments for epilepsy beginning with potassium bromide in the late 1800s, phenobarbital in the early 1900s, phenytoin or Dilantin in the 1930s, trimethadione, carbamazepine, primidone, sodium valproate.
Erin Allmann Updyke	The list goes on.

Erin Welsh	The list goes on and on and on. And it's still growing constantly all the time, and I'm sure you'll talk about some more that are on the horizon. And then there was non pharmaceutical treatments that were also successfully applied, including vagus nerve stimulation and some surgical procedures. I hope that I've shown by now that the 1800s and 1900s were a time of incredible progress in terms of understanding and treating epilepsy. But the rise in quote unquote "scientific" or rational thinking didn't mean that the stigma of epilepsy disappeared. In the previous centuries, epilepsy had been feared or looked upon negatively likely because it was a mystery. You fear what you don't know. No one knew what caused it, no one knew why it happened when it happened. And so science couldn't answer it, it must be a devil, it must be a god, it must be whatever, the moon. But when we finally gained enough concrete knowledge about epilepsy to conclude that it wasn't demonic possession, that knowledge wasn't used to dispel the harmful stigma surrounding epilepsy but rather to perpetuate it. Beginning in the late 1800s and early 1900s, the United Kingdom and many states in the US created laws for the sterilization of people with epilepsy and laws forbidding marriage if you had epilepsy. I know, I know. At the same time, I will point out that marriage was often prescribed for women to cure their epilepsy.
Erin Allmann Updyke	Stop it.
Erin Welsh	Not pregnancy necessarily but just marriage.
Erin Allmann Updyke	Stop it.
Erin Welsh	Will calm you down and lead you to not have seizures.
Erin Allmann Updyke	No, no.
Erin Welsh	These sterilization and marriage laws were bolstered by some of the earliest research into the genetics of epilepsy which was done in the early 1900s. And if all of this screams eugenics to you, that's because it is.
Erin Allmann Updyke	It is.
Erin Welsh	This is straight from the eugenics handbook. A horrifyingly prevalent opinion, the 20th century's demonic possession, held by so many people who were making the policy and healthcare decisions for these people. It's horrific. These laws forbidding marriage and permitting sterilization of people with epilepsy weren't repealed in some states until the 1960s.
Erin Allmann Updyke	I somehow knew that you were going to say the 1960s even. Ugh.
Erin Welsh	By 1966, three states, West Virginia, North Carolina, and Virginia still had eugenic marriage laws and 13 states still had eugenic sterilization laws against people with epilepsy.
Erin Allmann Updyke	Oh dear.
Erin Welsh	13 states. The last law was repealed only in 1980.
Erin Allmann Updyke	Oh no.

Erin Welsh	Only in 1970 in the UK was a law prohibiting people with epilepsy from marrying repealed. And in the US up until the 1970s it was legal to deny people who had seizures into public spaces like restaurants, theaters, recreational centers, and so on. And even though we now have laws in much of the world prohibiting such discrimination, that doesn't mean that it's not done, nor does it mean that stigma disappeared overnight. In fact people with epilepsy today often report feelings of stigma and the negative impact it has on overall quality of life, which I'm guessing you might talk more about. The story of epilepsy is huge and it's so much more than how we learned this or that, how the EED came to be, how we decided that this seizure was different than this seizure. It's a story about the meaning that diseases can hold, how science can be manipulated to perpetuate discrimination, and how there's never an end to the questions we ask. Speaking of questions Erin, where do we stand with epilepsy today?
Erin Allmann Updyke	Oh, I can't wait to tell you right after this short break.
TPWKY	(transition theme)
Erin Allmann Updyke	Epilepsy is so much more prevalent than I realized before researching this episode. Globally more than 50 million people worldwide have epilepsy.
Erin Welsh	What?
Erin Allmann Updyke	50 million people worldwide. And overall lifetime prevalence is thought to be about 1% on average.
Erin Welsh	Wow.
Erin Allmann Updyke	I know, right?
Erin Welsh	Whoa.
Erin Allmann Updyke	Disproportionately epilepsy affects people living in low and middle income countries and there's probably a whole myriad of reasons for that and we'll get into a lot of issues associated with that as well. And another statistic that I think is important is that worldwide there's an estimated 125,000 deaths each year related to epilepsy. And I think we often don't think of epilepsy as a disease causing death.
Erin Welsh	Yeah.
Erin Allmann Updyke	Because most of the time it doesn't. But the risk of premature death for people with epilepsy is estimated to be 3x higher than that of the general population and in low resource settings, this risk may be up to 7x higher.
Erin Welsh	Can you talk about why?
Erin Allmann Updyke	It's a whole lot of different reasons. It could be things like drownings or car accidents, like traumatic incidences that happen in the context of a seizure.
Erin Welsh	Okay.

Erin Allmann Updyke	It could also be due to infections that result perhaps like following a seizure that isn't adequately treated or as a result of status epilepticus resulting in certain brain changes that might make you more susceptible to infection later on, things like that. Which is why I think we see such higher burden in low and middle income countries where you're maybe not having as much diagnosis or access to treatment, especially in the cases of things that get more severe. We can look at the statistics for epilepsy both in terms of adults vs children as well as by different seizure type or different epilepsy type. And so we can just kind of briefly go over that because I think it's always an interesting part. Prevalence overall, unsurprisingly for a chronic disease, is highest in adults, right. Far more adults are living with epilepsy than children just because of the numbers of adults that exist. But when we look at incidence, so new diagnosis of epilepsy, it's highest in the youngest and the oldest age groups which is really interesting. So it has kind of a bimodal incidence.
Erin Welsh	Yeah.
Erin Allmann Updyke	Where you'll see an increase, especially in the first year of life, although in low and middle income countries it's maybe the first few years of life, and then a decline in the incidence, so new rates of new infection throughout adulthood and then a subsequent increase again in people who are over age 85. Now the types of epilepsy are going to be very different in those two age groups.
Erin Welsh	Okay.
Erin Allmann Updyke	Where older adults, it's more likely to be as a consequence of something that happened, say a stroke or a trauma or etc. If we look at epilepsy by seizure type, one thing that I think is really interesting is that it's actually focal seizures that are the predominant seizure type in both children and adults. Despite the fact that popular media would make you think that it's these generalized tonic-clonic very extreme seizures that are the only thing that represents a seizure. But the most common type overall is focal seizures, usually focal impaired awareness seizures which account for about 36% of people with seizures. So this would be a seizure that starts from only one place in the brain, may or may not have motor involvement, but does result in the person being unaware of having the seizure at the time of the seizure.
Erin Welsh	Okay.
Erin Allmann Updyke	So again it can look a lot of different ways but focal seizures are more common overall. So interesting. And overall, unknown etiology of epilepsy is the most common. So even though we know that epilepsy can be genetic, it can be from structural or metabolic changes, it can be the result of a trauma, most of the time we don't know what the actual underlying cause is which makes it really difficult. So then that brings us to where we go from here.
Erin Welsh	Yeah.
Erin Allmann Updyke	And I honestly didn't even know where to start when thinking about this, like current future directions because there's so much ground to cover. In terms of therapeutics there has been a huge amount of advancements in recent decades, there are dozens of new medications that are safer, that we have better monitoring for. But I don't have any like here's the newest most exciting thing to tell you about! Because we don't have one single mindblowing new drug. One thing that I thought was interesting was the idea of seizure prediction which is something that people have been working on for a very long time and I think in the 80s and 90s there was a lot of hype around it.
Erin Welsh	Okay.

Erin Allmann Updyke	But then in the early 2000s a review came out that was like all that data was actually really flawed and we are nowhere closer to a model to be able to predict seizure onset than we were 30 years ago. But since then people are still working on it which I just think is very interesting. There's a lot of kind of flaws with the data that exists and the ways that people are trying to do it thus far. But with advances in EEG technology, it's more likely I think than it ever has been which is really, really fascinating because so much of the burden of epilepsy is this recurrence of seizures that you may or may not know are coming, right. And so being able to predict seizure onset could have huge implications for quality of life.
Erin Welsh	Right.
Erin Allmann Updyke	And speaking of quality of life, I think one big takeaway from all of this is just how far we have to go especially in low and middle income countries when it comes to not only the treatment but also the identification of epilepsy.
Erin Welsh	Yeah.
Erin Allmann Updyke	So just last year in December 2022, the World Health Organization published a brief that was titled 'Improving the lives of people with epilepsy'. And most of their biggest points were all focused on addressing the treatment gap and integrating the treatment of epilepsy into a primary care setting since so much of the world doesn't have access to these specialized neurologists and epileptologists. So I think that is kind of one of the things that I'm most excited for going forward is just getting this knowledge to a place where it's more applicable to people who are already living with this. So that's epilepsy, Erin.
Erin Welsh	I mean we covered so much ground, Erin, but...
Erin Allmann Updyke	But I know nothing.
Erin Welsh	I know nothing. Oh my gosh.
Erin Allmann Updyke	I know.
Erin Welsh	I mean I know a lot more.
Erin Allmann Updyke	Same, same.
Erin Welsh	But not everything. And I feel like that's how we could sum up epilepsy and seizures in general.
Erin Allmann Updyke	It's so true.
Erin Welsh	Wow.
Erin Allmann Updyke	Wow.
Erin Welsh	Well speaking of learning more.
Erin Allmann Updyke	Let's all do it. With sources.

Erin Welsh	Let's talk about sources. So I had several, I'm going to shout out just one and that is the book that I already mentioned called 'The Falling Sickness' by Owsei Temkin. And I also want to shout out a book that I have not read but is on my list, has been for a really long time and is supposed to be an incredible work of nonfiction called 'The Spirit Catches You And You Fall Down' by Anne Fadiman. And these will both be on our website, both be on our list as well as a bunch of papers that I also drew from.
Erin Allmann Updyke	I also had quite a number of papers with so much more detail for those of you who want that nitty gritty, I promise you I have it. Some of the papers that I really loved were one that was kind of pretty basic but it was titled 'The Epidemiology of Epilepsy', it was published in Neuroepidemiology in 2020. You can't get more effective than that.
Erin Welsh	Perfect.
Erin Allmann Updyke	There was also a really interesting one that has a lot more detail on how we think epilepsy develops over time, that was published in Nature Reviews Neuroscience in 2019. And then I've got details on ketogenic diet if you want more of that, more on where we stand with the pharmacology of epilepsy, and then of course a link as well to the World Health Organization brief that I mentioned. All of these are on our website thispodcastwillkillyou.com under the EPISODES tab along with the sources from every other one of our episodes.
Erin Welsh	Thank you again to Louise for being willing to share your story with us and with everyone.
Erin Allmann Updyke	Thank you also to Lianna Squillace for help with our audio mixing for this episode.
Erin Welsh	And thank you to Bloodmobile for providing the music for this episode and all of our episodes.
Erin Allmann Updyke	And thank you to Exactly Right network.
Erin Welsh	And thank you to you, listeners.
Erin Allmann Updyke	There's so many thank yous!
Erin Welsh	So many thank yous. But we don't want to forget about you, you allow us to make this podcast happen.
Erin Allmann Updyke	Seriously. We love it. Thanks for listening. A special shout out to our patrons, it means so much to have your support.
Erin Welsh	It really does. Big topic over.
Erin Allmann Updyke	We're done for the season.
Erin Welsh	We're done for the season!
Erin Allmann Updyke	Just kidding.
Erin Welsh	Just kidding. Okay everyone, well we'll be back in a couple weeks with a new episode. Until then, wash your hands.

Erin Allmann Updyke	You filthy animals!