TPWKY	This is Exactly Right.
Anonymous	We were having hat day at school and I am not normally a hat person. I had this numb spot on my head all day long and it just was like a not scratchable itch. It was all day, all day, all day. But I thought, like at first I was like, 'Oh it's just hat day, I'm just not comfortable wearing this ridiculous Christmas tree hat at school.' (laughs) By the weekend, so that started midweek, by that weekend it had started to move down my forehead to like my eyebrow area and that's when it just became this burning, itchy, couldn't really make it go away thing. A few days went by, so this was all at Christmastime, that's when we were driving from where we lived in Buffalo down to my parents on Long Island. And that drive, my forehead felt like someone had a match to it. I think I kind of lucked out with shingles because it was a really small patch that I had but to feel like someone had a lighter on my forehead for as long as it did was just the craziest thing.
	I had no idea what it was though. So I started doing the WebMD thing and I was searching for like 'what's a large red spot', 'red spot with blisters' because it started to get these really small spots over time. And that's kind of when I started to see other pictures of people who had the same thing and people were saying it's shingles, it's shingles, it's shingles. So I finally called my doctor and I said, 'Hey, I have all these symptoms but I don't know what this is.' And they said, 'That sounds like shingles, you need to come to see us right away.' But we're traveling for Christmas. By the time I kind of got all that together we were already en route from Long Island up to Rhode Island for the weekend.
	So that's when I ended up at an out of state urgent care. And I walked in, the receptionist looked at me and she was like, 'Oh look at that, you've got shingles.' And it was just as fast. As soon as they saw that, they were able to prescribe medication and get it under wraps. So by the time I got that they were like it's probably too late because it had been a week since I started showing the first symptom. But the really scary thing that they kept sounding the alarm on was this is really close to your eye. This is really close to your eye. So when I came home I had followups with my eye doctors, I had to go back to my primary care just to continue watching it to make sure that whatever it was wasn't gonna affect the optical nerves and all of those forehead things.
	But like I said, it was just the craziest thing because I didn't know anybody who had ever had it. I didn't know was I gonna pass this onto my mom, was my sister gonna get it? I think everybody hears you get shingles from chickenpox and of my generation like I think I was like the end of the chickenpox party so I was just so afraid that I was gonna pass this on to all of my family members and they were just kind of like, 'No, everything is gonna be fine, just kind of cover it up and go about your day.' So that was my shingles experience, I guess.
TPWKY	(This Podcast Will Kill You intro theme)
Erin Welsh	Thank you so much for taking the time to chat with us and for being willing to share your story.
Erin Allmann Updyke	Thanks.
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	Welcome.

Erin Welsh	Welcome. This is a fun one.
Erin Allmann Updyke	I'm honestly thrilled. I don't know exactly why but I have been looking forward to covering this for a really long time.
Erin Welsh	I have too and I've been kind of like daunted because I didn't know anything about the history and it turns out there's like kind of not that much to it so I hope you don't fall asleep.
Erin Allmann Updyke	I'm sure.
Erin Welsh	(laughs) Or if you're listening to this podcast to fall asleep, I hope you do fall asleep.
Erin Allmann Updyke	(laughs)
Erin Welsh	But yeah I think it's one of... Like we all have experienced it or know someone that's experienced it and I think Erin, you and I are part of the generation, like the last remnants that didn't get the vaccine.
Erin Allmann Updyke	Exactly. We definitely are the last cohort that just got chickenpox which is the subject of today's episode.
Erin Welsh	Here we go. Plus shingles/zoster, whatever you wanna call it.
Erin Allmann Updyke	Exactly.
Erin Welsh	Yeah. Basically the varicella-zoster virus.
Erin Allmann Updyke	Yeah.
Erin Welsh	Erin, when did you get chickenpox?
Erin Allmann Updyke	I don't remember exactly how old I was but it had to have been after 1994 or 1995 and we all four got it in a row. It went boop-boop-boop-boop like down the row of older brother, then me, then my younger brother, then the baby brother. We all got it in age order. And I have a very distinct memory of my first pock.
Erin Welsh	Oh.
Erin Allmann Updyke	I had my very first chickenpock was on my left side, like right on my ribs on my left side and obviously my brother was already sick with it so I knew this is chickenpox. And I showed my mom, I was like, 'Mom, I found this. Is this chickenpox?' And she was like, 'Ugh yes, it's chickenpox.' And I was like, 'Okay but can I still go to gymnastics?'
Erin Welsh	(laughs) Did you go?
Erin Allmann Updyke	I did. As far as I can remember, maybe my memory is off but my mom was like, 'You've already exposed everyone, just keep it covered.'
Erin Welsh	(laughs) That's hilarious.

Erin Allmann Updyke	She might dispute that memory of it, we'll see. Mom, is that what happened? That's how I remember it. I have the scar that I know that that was my first pock.
Erin Welsh	(laughs) I really should've called my mom to ask her my chickenpox story because I don't remember, I think I might've been too young to actually remember but I think it was my older sister and I at the same time got it and then my two younger brothers got it and then I honestly don't know about my younger sister, whether she got it or whether she got the vaccine.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. Anyway. Should we move onto like actual podcast things?
Erin Allmann Updyke	The actual business of our podcast? Maybe.
Erin Welsh	Is it quarantini time?
Erin Allmann Updyke	I think it's definitely quarantini time.
Erin Welsh	What are we drinking this week?
Erin Allmann Updyke	Erin, we're drinking Chicken Scratch.
Erin Welsh	I love this. It works on so many levels, it's like people always complain about how doctors have chicken scratch handwriting.
Erin Allmann Updyke	It's true.
Erin Welsh	And also if you have chickenpox you're definitely gonna be scratching, so yeah.
Erin Allmann Updyke	It's really itchy. And what's in the Chicken Scratch?
Erin Welsh	There is tequila, there is kiwi, there is ginger, and there is mint.
Erin Allmann Updyke	Kind of just a fun, summery bev.
Erin Welsh	Yeah.
Erin Allmann Updyke	We'll post the full recipe for that quarantini as well as our nonalcoholic placeborita on our website thispodcastwillkillyou.com and our social media.
Erin Welsh	And on our website you can find so many different things like transcripts, like alcohol-free episodes, like promo codes for all of the ads that we do, like the links to Bloodmobile who does the music for all of our episodes. We've also got a Patreon. I mean it's endless, just go in there, explore it, and I'm sure you'll come up with something interesting.
Erin Allmann Updyke	Definitely. All right that was a longer intro than we usually do.
Erin Welsh	Yeah it was, it was kinda fun though.

Erin Allmann Updyke	It was, it's fun getting to relive my chickenpox story. Anyways shall we dive into the biology of this thing?
Erin Welsh	Let's do it.
Erin Allmann Updyke	We'll take a quick break first.
TPWKY	(transition theme)
Erin Allmann Updyke	So varicella-zoster or herpes zoster or if you wanna be very official, human alphaherpesvirus 3. So this virus that we're dealing with is a herpesvirus which I think some people might not realize because it's called chickenpox, people might think it's a pox virus. It's a herpes virus and in fact it's very closely related to herpes simplex 1 which is a common cause of oral herpes, can also cause genital herpes, check out our herpesvirus episode for more on that. And so like all of the herpesviruses, this is a DNA virus, it has a double-stranded genome, blah, blah, blah. Like many of the human herpesviruses, this is a very human-specific virus, it doesn't infect any other animals which as we'll see is part of why we don't have a lot of answers about some of the specifics of the diseases that this virus causes because we don't have great animal models in which to study it.
Erin Welsh	That makes sense, yeah.
Erin Allmann Updyke	Yeah. This particular virus doesn't have a lot of variability, there aren't a lot of different strains of varicella, there doesn't seem to be a lot of variation in the virulence across outbreaks or over time, it's a pretty stable virus. And Erin, you asked me something before we started researching this which was why is chickenpox often called varicella-zoster and shingles is called herpes zoster?
Erin Welsh	Yeah.
Erin Allmann Updyke	Did you find an answer to that?
Erin Welsh	Well so the only thing I could think of is the etymology of it. So varicella is another word for chickenpox, like that rash that happens for that initial infection and in a lot of other languages besides English it tends to be not like the equivalent of chickenpox but some sort of variation of varicella.
Erin Allmann Updyke	Right.
Erin Welsh	And the word 'varicella' might come from the diminutive form of 'variola' which is the word for smallpox. And so it might just be like it's analogous where chickenpox is to smallpox as varicella is to variola etymologically. Does that make sense?
Erin Allmann Updyke	Yeah, yeah. It totally makes sense. It genuinely makes sense.
Erin Welsh	And then herpes zoster, 'herpes' is like the old word that was used by Ancient Greeks like Hippocrates and whatnot to describe those rashes.
Erin Allmann Updyke	So it seems to just boil down to the fact that even though we're talking about one single pathogen, we're talking about two completely different clinical diseases.

Erin Welsh	Exactly.
Erin Allmann Updyke	Yeah. So I think that that's something that's interesting, I feel like we've covered a lot of pathogens that just cause one disease where we're like, 'Here's the disease we're talking about and here's the pathogen that causes it.' And then we've talked about some thing like Staph. aureus for example that can cause any number of diseases.
Erin Welsh	Yeah or Strep. pyogenes.
Erin Allmann Updyke	Exactly, right. So yeah, I don't know, I just feel like that's an interesting aspect of this that there's this big distinction between the pathogen and the diseases or the illnesses that they might cause.
Erin Welsh	Yeah.
Erin Allmann Updyke	So let's get into the pathogen and both of these diseases. Shall we?
Erin Welsh	Let's do it.
Erin Allmann Updyke	So I talked about how similar already this human herpesvirus is to other herpesviruses, let's start to talk abut how it's a little different. Unlike many other herpesviruses, varicella is transmitted primarily via the respiratory route.
Erin Welsh	What?
Erin Allmann Updyke	Yeah, isn't that interesting?
Erin Welsh	I wanna know, and I didn't find the evolutionary history, like what about it? How did that happen?
Erin Allmann Updyke	It's a really good question that I still don't fully understand aside from the fact that we've talked on this podcast a number of times about the tropism of different viruses, right. So viruses, because they are dependent on host cells to be able to replicate, oftentimes specific viruses can only infect a limited range of cell types. It seems like varicella can infect a pretty wide range of cell types. So is it just that that's a really easy route of transmission and it happens to be good at invading and replicating within not just our respiratory epithelium but also it's very good at invading and replicating in our white blood cells in lymph nodes. And so a big thing where replicates is in the lymph nodes in our chest and things like that.
Erin Welsh	Oh, that's very interesting because I thought that it also though does have a tropism towards nerves or is that just later?
Erin Allmann Updyke	Oh certainly, certainly.
Erin Welsh	Okay.
Erin Allmann Updyke	Let's get into all of this, shall we?
Erin Welsh	Okay.

Erin Allmann Updyke	Basically I think the bottom line is that it can infect all of those cell types.
Erin Welsh	Interesting, okay. Cool.
Erin Allmann Updyke	Yeah. All right. But primarily the way that people become exposed is via respiratory. So a kid, cause it's usually kids who are infected comes up and is like, 'I don't feel good,' and like breathes right on your face. And you inhale those viral particles.
Erin Welsh	(laughs) You speak from experience, I guess that's it.
Erin Allmann Updyke	I do. And those viral particles travel to those regional lymph nodes and they replicate. And what's really important about the fact that they can infect these white blood cells is from there they can travel anywhere and everywhere, right? So they travel throughout our body and they're able to continue replicating as they invade different cells. In general the incubation period is about 2 weeks, it can be from 10-20 days after exposure to when you first start to show symptoms. But what's important especially for a respiratory virus is that you become infectious and able to infect others at least 2 days before those first symptoms start.
Erin Welsh	Aha.
Erin Allmann Updyke	And this is quite an infectious pathogen, it's pretty contagious. I've seen anywhere from 60-90% of susceptible household contacts are likely to become infected.
Erin Welsh	What is the estimated R0?
Erin Allmann Updyke	According to a lecture from Johns Hopkins School of Public Health, the R0 for chickenpox is 9-10.
Erin Welsh	Oh my goodness.
Erin Allmann Updyke	That's a lot higher than I realized.
Erin Welsh	So when you say respiratory transmission, is it respiratory droplets or is it like aerosol? Airborne?
Erin Allmann Updyke	Good question. I didn't find the specific answer to that, they just say respiratory route so I don't know how long it can hang out in the air. I don't think that it's quite as bad as something like measles that can stay airborne for like hours at a time but with an attack rate that's so high, I would guess that it's probably pretty well airborne, like it's aerosolizing pretty well.
Erin Welsh	Yeah. Okay.
Erin Allmann Updyke	So those chickenpox parties that people used to have, those are probably pretty effective at spreading disease.
Erin Welsh	Oh yes.
Erin Allmann Updyke	Not a good idea, let's talk about why, shall we?
Erin Welsh	Yeah, let's do it.

Erin Allmann Updyke	So once this virus has disseminated throughout our body, one of the main cells that they tend to infect are epidermal cells, our skin cells. Inside of our our skin cells it begins to replicate and this is what causes the typical chickenpox rash that we all know and don't love. So what's really common is that 1-2 days, like 24-48 hours before this rash, kids - I say kids, of course this affect adults too but most often kids - they'll feel kind of cruddy for a day or so beforehand. Maybe a headache, maybe a little tummy ache, maybe like a fever probably. But then comes the rash which si very characteristic and kind of what we call chickenpox. The rash starts, for anyone who hasn't experienced this, starts as very, very itchy red, flat patches and then these patches become raised or get little bumps within them and then those little bumps develop into small, fluid-filled vesicles, tiny little blisters. And these tiny little blisters are chockfull of virus. So this is not only a respiratory pathogen but it can also be transmitted by direct contact.
Erin Welsh	Okay, it's just covering all the bases.
Erin Allmann Updyke	It's covering all the bases, exactly. This rash can also be present on mucus membranes like in the mouth or even the eyes. And the lesions can kind of ulcerate a bit more and be really quite painful not unlike the lesions that we see with herpes simplex, these all cause a very similar-looking lesion. And this rash spread anywhere and everywhere, it's pretty common that they might start on the head or face or like centrally on the trunk but will pretty quickly spread across the entire body. And new lesions, this rash essentially continues to develop over the course of 3-5 days although the range can be anywhere from 1-7 days where you're continually getting more and more little pocks.
Erin Welsh	Oh yeah. I mean I don't remember any of this but sounds obnoxious. (laughs)
Erin Allmann Updyke	It's not great. And of course they're incredibly itchy. If you don't scratch the heck out of them then eventually after a few days these vesicles kind of cloud over, so it's not like a clear fluid anymore. And then they'll encrust. Usually if you don't scratch them off this'll take about a day or two per blister kind of. And once every vesicle is crusted over, that's when someone is no longer infectious. So you're able to spread this disease from about 2 days before you got that fever and headache, so up to 4 days potentially before the rash until every blister is crusted over. Now chickenpox is generally considered a very benign childhood disease, that's why people had things like chickenpox parties because it was generally considered a pretty benign, yes your kid is miserable for a week maybe but they get over it. And most of the time that's true, chickenpox is an annoying but self-limited disease. But-
Erin Welsh	I knew there was a but.
Erin Allmann Updyke	(laughs) There's always a but. There are a number of potential complications associated with varicella and that's before we're even gonna talk about shingles, okay. Let's just focus on this primary infection with varicella virus, aka chickenpox. So first of all these lesions are itchy, itchy, itchy, itchy, itchy and especially for kids it's very difficult to not scratch at an itch. So this inevitably leads to open wounds all over the skin which can lead to a very easy route for a secondary bacterial infection to establish.
Erin Welsh	Yeah.

Erin Allmann Updyke	Our bodies are covered in bacteria, especially all over our skin and bacteria like Strep. pyogenes and Staph. aureus can both invade deeper tissues and cause very serious and potentially fatal infections. So that's one, probably the most common complication. Number two, varicella like we've talked a lot about is this respiratory pathogen, right? Except that for most people who are infected it doesn't actually cause any respiratory symptoms. However it certainly can. And in kids who are immunocompromised especially but also in older teens and adults who are exposed to varicella for the first time, infection tends to be more severe and primary infection, this first time being exposed to varicella virus can cause a viral pneumonia which can be very severe or even fatal.
Erin Welsh	Wow.
Erin Allmann Updyke	Yeah. So the numbers that I saw were that of otherwise healthy-seeming people who were infected with varicella, up to 16% of those people had radiographic evidence. So if you took an X-ray of their chest, you saw that something was going on in their lungs. So even in people who maybe don't have respiratory symptoms, this virus is still doing stuff in their lungs. But only about 1/3 of those would have any respiratory symptoms.
Erin Welsh	Okay.
Erin Allmann Updyke	But before the advent of antivirals, so before we had any kind of antiviral therapy, mortality from varicella pneumonia was as high as 30%.
Erin Welsh	Wow.
Erin Allmann Updyke	And even today with treatment it's still around 10%. So even though this is a very small proportion of people who would go on to develop varicella pneumonia, it's pretty serious when it does occur.
Erin Welsh	Right. I feel like I have heard a lot of people be like, 'Chickenpox vaccine? Why do we need a chickenpox vaccine? Everyone gets it, it's totally fine.' And I mean I was kind of like, I had the chickenpox, should I have gotten a vaccine somehow? But it totally makes sense.
Erin Allmann Updyke	Yeah so I think that's one thing I hope everyone can learn especially in talking about all these complications of varicella as well as shingles which we'll get to in a little bit. Even though all of these complications are very, very rare, because varicella is such or was such a widespread pathogen, literally almost 100% of adults in the U.S. for example and in most temperate regions across the world were exposed and infected by the time they reached adulthood. Almost like 99% of the population. And so when you have that large of a population that's exposed, even these small numbers like proportionally lead to pretty severe morbidity and mortality.
Erin Welsh	Yeah. Right.
Erin Allmann Updyke	Cause again it's not just death, there's other complications. So speaking of other complications, we haven't even really talked about it but we'll talk about it in more detail, this is a virus that is good at infiltrating our nervous system. Right? All herpesviruses are good at kind of getting into our nervous system and lying latent. So it's not surprising then that neurologic complications are another potential serious complications of varicella infection. Overall the incidence of neurologic complications is low, it's estimated at about 1-3 per 10,000 cases have some kind of neurologic involvement whether that's encephalitis or inflammation of the cerebellum which leads to ataxia, that kind of wobbly, not being able to walk and move normally.
Erin Welsh	Okay.

Erin Allmann Updyke	And so it's low incidence, 1-3 per 10,000 but of all those neurologic cases, anywhere from 5-18% of those are fatal.
Erin Welsh	Wow.
Erin Allmann Updyke	Yeah.
Erin Welsh	Fatal how?
Erin Allmann Updyke	Usually from encephalitis.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah. And these complications are most common in very, very young kids like under 5 and then adults over age 20. And then there's a lot of other things. This is a virus that can infect almost any one of our cells, so it can infect the liver or the kidneys, cause liver failure, kidney failure. It can infect your heart muscle and cause myocarditis or pericarditis if it infects the lining of your heart. It can lead to low platelet counts which can lead to hemorrhage. And all of these complications are rare but they happen especially for children who are immunocompromised or adults who get infected for the first time who weren't exposed as children. And if that's not enough, varicella can also cross the placenta and infect a developing fetus. So infection during pregnancy is very bad and can result in congenital varicella syndrome if it happens early in pregnancy which can lead to neurologic development problems, limb development problems, scarring of the skin can be pretty serious. And infection later in pregnancy can result in pneumonia in the newborn that is often fatal.
Erin Welsh	Oh my gosh.
Erin Allmann Updyke	As well as leading to premature delivery. It's not as benign as I think people think it is.
Erin Welsh	Yeah definitely a lot worse than I thought it was.
Erin Allmann Updyke	Yeah. And all of that is just chickenpox. What about shingles?
Erin Welsh	What about shingles?
Erin Allmann Updyke	Okay, shingles. Like other herpesviruses like herpes simplex that we talked about, varicella-zoster is able to invade our nerve cells, hang out there, and chill. Just hang out in our little ganglia, not be detected by all the antibodies that we make against this virus, we make a lot of antibodies.
Erin Welsh	Yeah.

Erin Allmann Updyke	I want to make that clear, it's not like the people who get shingles didn't develop antibodies, they totally did but this virus just hangs out in their nerve cell bodies and eventually when the time is right, this virus can travel back out again along those nerves, back up to the skin surface, and cause a similar but different disease that is shingles. So shingles starts out as pain most often, a pain or like a burning sensation, a tingling sensation. And this nerve pain usually is along one nerve route, this is what we call a dermatome which is the fancy word for the area of skin that your sensory nerve innervates. Like each one of your sensory nerves only innervates one triangle or one section of your skin, right.
Erin Welsh	Yeah.
Erin Allmann Updyke	And so this virus, you can think of it as traveling along that nerve and irritating just the skin just where that nerve is.
Erin Welsh	Gotcha, okay. That makes sense based on the spread, interesting.
Erin Allmann Updyke	And then following this pain or this burning sensation, usually a few days later blisters start to appear. These blisters look a lot like the initial blisters of chickenpox, they have like irregular red borders, these raised fluid-filled vesicles, and they can be itchy but they're often just super painful. And they're often in that same dermatome where that pain is.
Erin Welsh	Yeah, I feel like if there's one word to describe chickenpox it's itchy.
Erin Allmann Updyke	Itchy.
Erin Welsh	And if there's one word to describe shingles it's painful.
Erin Allmann Updyke	Painful. Absolutely, I agree 100%. And it is possible to get lesions away from just this one dermatome or you could even have like multiple dermatomes involved but most of the time it's just like one. So for example T11, so like your 10th and 11th thoracic vertebrae, T10 and 11, that dermatome goes kind of right around your bellybutton.
Erin Welsh	Okay.
Erin Allmann Updyke	All right. And you've got one nerve on the left and one nerve on the right. So it's usually just one of the other. So you'll get pain and a rash on one side wrapping around your belly, wrapping around your back to your belly, and stopping at the midline.
Erin Welsh	Interesting.
Erin Allmann Updyke	Isn't it?
Erin Welsh	I feel like that then, does that make diagnosis fairly straightforward?

Erin Allmann Updyke	Yeah. If it looks like classic shingles, it's a pretty classic shingles presentation. The other very classic area besides the trunk, and of course this can happen anywhere, you have nerves everywhere, but very classically it happens on the trunk or on your head because the other place that they like to hang out is the trigeminal ganglia, so that's the nerve that innervates all of the sensory of your face. And there it'll just be in like one section. So let's say it's V1, that's like just the head, forehead, and nose but not probably like your cheeks and ears and most likely just on the left side or the right side but not both sides. And as uncomfortable as that probably sounds, shingles can be a lot more debilitating than just an uncomfortable, painful rash especially in those who are immunocompromised or the very elderly.
	This rash can become quite widespread, so you can have involvement of a number of different nerves. Or this reactivation can spread beyond just these nerves and cause a disseminated disease just like primary infection, just like the first time you got exposed to varicella. It can leave those nerves and go anywhere. And even in folks who aren't immunocompromised, there is a phenomenon called postherpetic neuralgia. This is when this pain, this numbness, this pain, this tingling can persist long after the rash has come and gone and result in chronic, sometimes lifelong pain.
Erin Welsh	So this is like reason 500 why the vaccine is so crucial.
Erin Allmann Updyke	Right? Yeah. So overall of people who get shingles, I think it's about 10% of people might go on to develop postherpetic neuralgia but in people over 60 the risk can be as high as 40-50%.
Erin Welsh	Now what proportion of people get shingles?
Erin Allmann Updyke	About 30% of people will go on to develop shingles.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah.
Erin Welsh	If you've been naturally infected.
Erin Allmann Updyke	If you've gotten chickenpox.
Erin Welsh	Right.
Erin Allmann Updyke	Yeah.
Erin Welsh	And if there something, like is it sort of like a stress-type thing that triggers it or is it kind of question mark?
Erin Allmann Updyke	Such a good question cause my next thing I have written is like the question is how does this virus do this? And it can't really answer that, Erin.
Erin Welsh	Dang.
Erin Allmann Updyke	Yeah. You know this virus like many other herpesviruses can have these long latent periods but exactly how it gets into our nerves in the first place, how it's so good at evading our immune system, what causes it to come back out and who is going to get shingles and who isn't going to get shingles and when and why we don't fully know.

Erin Welsh	Fascinating.
Erin Allmann Updyke	And like I said earlier, a lot of the reason we don't is because we don't have super great animal models.
Erin Welsh	Right.
Erin Allmann Updyke	So there are a number of different sort of theories and ideas out there but we just don't fully understand these exact mechanisms. Yeah. The good news is there is treatment, it's the same kind of treatment that we use for herpes simplex virus, so it's acyclovir or valacyclovir, it's a specific drug for treating these herpesviruses.
Erin Welsh	Mm-hmm, yeah.
Erin Allmann Updyke	Yeah. It reduces the severity of symptoms and can prevent severe complications like varicella pneumonia but it doesn't rid your body of the virus, just like if you use it to treat herpes simplex.
Erin Welsh	Right, right.
Erin Allmann Updyke	Right. So that's the biology, Erin.
Erin Welsh	Ooh.
Erin Allmann Updyke	There's a vaccine but I'm not gonna talk about it yet cause I've already talked enough. So tell me what's up with this virus, where did it come from and what's going on.
Erin Welsh	I can't wait to try to answer those. We'll take a quick break first.
TPWKY	(transition theme)
Erin Welsh	So you always ask where does this pathogen whatever come from.
Erin Allmann Updyke	I always wanna know!
Erin Welsh	(laughs) Well it turns out that we've actually been down this road before with our herpes simplex 1 and 2 episode that we did last season.
Erin Allmann Updyke	Oh.
Erin Welsh	Erin, that was less than a year ago.
Erin Allmann Updyke	Nuh uh, that was 6 years ago at least.
Erin Welsh	I know, I know. (laughs) It was before we started podcasting.
Erin Allmann Updyke	Yeah. (laughs)

Erin Welsh	But just like with every other episode, I end up forgetting so much of what we talk about. Like as soon as the editing is done and the episode is released it's just like gone from my brain.
Erin Allmann Updyke	Yeah.
Erin Welsh	And so then I come across things that I've read or I've learned before and I'm like oh yeah, that's right. Which was absolutely the case for this episode, I hate to admit but it's the truth. So maybe you remember from the herpes episode but in case you don't, the group herpesviridae which the varicella-zoster virus is part of is very old, like millions and millions of years old group. And this group of viruses in general tends to be like you mentioned super species-specific meaning that a lot of the diversification events where like a new species of herpesvirus emerges, those happen right alongside their host diversifying as well. So that might all be a bit of a review but I did learn one new very fascinating thing.
Erin Allmann Updyke	Ooh.
Erin Welsh	So in the biology section you talked about how varicella-zoster virus, it's a herpesvirus, and like all herpesviruses they tend to infect nervous tissue or nerves. And it turns out that that characteristic, the neurotropism, dates back almost 500 million years.
Erin Allmann Updyke	What?
Erin Welsh	Uh huh. So that's based on how the abalone herpesvirus infects nervous tissue leading to ganglioneuritis and eventual necrosis of the nervous tissue and ultimately death.
Erin Allmann Updyke	I'm sorry, abalone herpes?
Erin Welsh	Uh huh.
Erin Allmann Updyke	Oh my goodness, poor babies.
Erin Welsh	I know, I know. It's amazing and it think that that kind of also goes a little bit towards explaining why this is so good at evading our immune system.
Erin Allmann Updyke	Yeah it's been doing it forever.
Erin Welsh	Forever. Yeah and so that also gives you a sense of just how old these are. And to underline that point, I read that the alphaherpesvirus group which includes herpes simplex 1, HSV-2 and varicella-zoster virus as well as other mammalian and avian viruses, that dates back to around 180-210 million years ago.
Erin Allmann Updyke	Stop.
Erin Welsh	Very old.
Erin Allmann Updyke	Wow.
Erin Welsh	And so like herpes simplex 1 and 2 viruses it seems reasonable then to assume that the chickenpox virus, varicella-zoster virus, I'm gonna use those interchangeably, also evolved with humans, like alongside humans.

Erin Allmann Updyke	Right.
Erin Welsh	And that is what was thought for a while that the varicella-zoster virus originated in Africa where modern humans evolved. This wasn't just like a passing thought though, it wasn't just an assumption. This origin story is backed up by several pieces of evidence. First is that this would follow the trend of like all herpesviruses co-evolving or co-speciating with their hosts. Second, the closest relative of varicella-zoster virus is the simian varicella-zoster virus which infects Old World monkeys. And so the VZV, varicella-zoster virus and the simian varicella virus, they share about 70% identity which is pretty similar. And I turns out that immunization of monkeys with human varicella-zoster virus prevents later infections with simian varicella virus.
Erin Allmann Updyke	All right, all right, all right.
Erin Welsh	So that's like kind of I think suggestive, right? And the third piece of evidence is that some genetic dating analyses put the evolutionary origin of varicella-zoster virus at about 110,000 years ago although I also saw older numbers mentioned a few times like in the millions of years. In either case it was before humans started moving out of Africa which happened around 60,000 years ago. All right, seems pretty straightforward, right?
Erin Allmann Updyke	Yeah.
Erin Welsh	Maybe not so much.
Erin Allmann Updyke	Okay.
Erin Welsh	A recent paper from 2020 seems to question this assumption that the varicella-zoster virus like other herpesviruses evolved with humans in this out of Africa way. Instead the present some evidence that places the emergence of varicella-zoster virus in Europe and also much more recently. But their estimates were a little bit all over the place. So within varicella-zoster virus there are several clades with virus strains in one strain more similar to each other than to strains in other clades, right. And these clades follow some pretty strong geographic distribution patterns. So for instance clade 5 is found pretty much only in Africa, clade 2 is found mostly in Eastern Asia and so on.
	And the authors of this paper then compare these different clades and then the strains within them to try to trace, okay when did they diverge from one another and what is the oldest one? Like what do we think the oldest one was? Which led them to conclude that it was actually the clades found in Europe that seemed to be the oldest. I think there are though - I really wanna point out - a couple important caveats to this. One is that they had very few strains from Africa that they included in the analysis.
Erin Allmann Updyke	Just like not great sampling?
Erin Welsh	No, it was from a very limited geographic range but they had tons of North American and European strains included which of course would have biased those results. And the second thing and the authors noted this one as well is that it's totally possible that of all the clades of varicella-zoster virus that are present today that they did originate in Europe but that even older clades from Africa just went extinct.
Erin Allmann Updyke	Mm-hmm.
Erin Welsh	Which is I think really fascinating to think about. We don't talk a lot about extinction.

Erin Allmann Updyke	Yeah.
Erin Welsh	Accidental extinction. We talk about eradication but we don't really talk about extinction of pathogens just like happenstance.
Erin Allmann Updyke	Yeah, just happening. Which it totally makes sense that it could happen.
Erin Welsh	It totally does. And I remember when I was doing my PhD there are like sloth ticks and there are also ticks that are very specific to certain animals. And one of the things is well if this endangered animal goes extinct then the ticks and everything and the sloth moths and everything will go extinct, too.
Erin Allmann Updyke	That happened with the California condors.
Erin Welsh	Right!
Erin Allmann Updyke	When they rehabilitated California condors from a very small population they lost, I don't know if it was more than one species of bird louse that was specific to the California condor but at least one.
Erin Welsh	Yeah, it's so interesting.
Erin Allmann Updyke	Yeah.
Erin Welsh	But yeah, so going back to varicella-zoster virus, I think this kind of just shows how there's really only so much we can tell about viral or bacterial evolution because so much of it is based on the currently circulating strains and the samples that you collect.
Erin Allmann Updyke	Right.
Erin Welsh	And in the case of varicella-zoster virus things might get trickier as the vaccine strain continues to become more widespread and as recombination events might happen, that's kind of a question mark, I don't know. All right so I don't know if I gave a satisfactory answer for your where did this come from question, it's a lot of murky origins but I think I can at least try to answer how did we get here, right. So regardless of where precisely it came from the varicella-zoster virus is now globally distributed and probably has been so for a long time, like thousands of years. And this type of widespread distribution is something we've seen for a lot of the typical childhood illnesses or what we would think of as childhood illnesses, things like measles, rubella, etc. and in many ways it follows the same epidemic pattern too. Right, you get a critical mass of susceptible individuals in a population and then boom, like one exposure, the virus just races through. Especially with an R0 of 9-10.
Erin Allmann Updyke	Yeah.
Erin Welsh	Oh my gosh.
Erin Allmann Updyke	Oh em gee.

Erin Welsh	Yeah. But there's one key difference between chickenpox and these other childhood diseases and that is that unlike measles for instance which needs a certain population size in order for it not to go extinct, which is why like measles and these other crowd diseases took off after the agricultural revolution, chickenpox doesn't need that because - Erin?
Erin Allmann Updyke	Because shingles!
Erin Welsh	Because shingles, yes. So because this virus, like herpes simplex virus 1 and 2, it hangs out in us forever and it can pop up later in life as shingles/zoster. It has this amazing survival strategy that allows it to persist in even small nomadic populations rather than needing the agricultural revolution to take hold.
Erin Allmann Updyke	Because if we didn't say this already and if listeners, you didn't realize this, shingles rash is absolutely contagious by contact.
Erin Welsh	Yes.
Erin Allmann Updyke	So the virus can persist in a population even decades later.
Erin Welsh	Mm-hmm. But where varicella-zoster virus is like other human herpesviruses in this way, in this sort of latent period and then reactivation, in another sense it's kind of an outlier alongside herpes simplex 2 I guess because of its transmission. So many herpesviruses like HSV-1, cytomegalovirus, human herpesvirus 6, and Epstein-Barr virus, these are often or mostly transmitted vertically within the first few years of life often through saliva transmission like for instance pre-mastication of solid food or through breast milk. But like you said, the varicella-zoster virus doesn't follow this pattern and it's respiratory transmitted which I just thought is so fascinating because instead of being vertically transmitted like so many other herpesviruses, this is still a horizontally transmitted pathogen, so from like an unrelated adult with zoster to some kid to then give them chickenpox.
Erin Allmann Updyke	Right. Yeah and then from that kid to like 10 other kids.
Erin Welsh	Yeah. Yeah literally. So with seemingly no minimum population size and this incredibly high transmissibility, it seems like the varicella-zoster virus would have made itself pretty well known among humans for as long as it's been around.
Erin Allmann Updyke	I mean I could see it going one of two ways here, Erin.
Erin Welsh	(laughs) Okay well what did people say about it? It's kind of like not much to be honest.
Erin Allmann Updyke	Yeah that was gonna be my fear.
Erin Welsh	Yeah, yeah. It was my fear too and then it was realized. I was like oh boy, here's the history. So the link between chickenpox and shingles wasn't really known or at least it wasn't widely suspected until the late 1800s and I'll get to that later. But both diseases had been recognized long before that. So we get the first mention of chickenpox or rather varicella as it was first called in the 1550s when an Italian physician named Giovanni Filippo Ingrassia differentiated it from scarlet fever. The first thorough description though came from English physician William Heberden in 1785 and at the same time he distinguished it from smallpox. And I already went through the etymology, so varicella as this diminutive form of the word variola. But why do we call it chickenpox? I didn't go through that etymology.

Erin Allmann Updyke	Yeah, can you tell me?
Erin Welsh	I mean no one really knows for sure but there are plenty of guesses. One popular guess is that the bumps resembled chickpeas and so it was called chickenpox.
Erin Allmann Updyke	Oh. Okay.
Erin Welsh	That was not very well supported.
Erin Allmann Updyke	Yeah.
Erin Welsh	But another more popular one is that chickenpox kind of resembles smallpox but is way less deadly and horrible and so it was called chickenpox as like the lesser version, the smallfry version of the big bad smallpox.
Erin Allmann Updyke	Like 'you're just a chicken' pox?
Erin Welsh	Yeah, yeah. I mean chickens are cool though, I wonder why the negative connotation of chicken began.
Erin Allmann Updyke	That's a good question.
Erin Welsh	It's a good question. Anyway let us know if you know. (laughs) But shingles goes even further back than chickenpox in terms of its name. So herpes-zoster, the reactivation of the virus was named by Hippocrates from the words for 'to creep' and 'girdle', zoster meaning girdle. And shingles which is the other name for this reactivation is from the Latin word 'singulus' for belt. So where it typically happened.
Erin Allmann Updyke	Yeah, along the girdle. Very common.
Erin Welsh	Yeah, yeah. But I also wanna mention that in Norway they had a bit more colorful or evocative description for the rash.
Erin Allmann Updyke	Ooh.
Erin Welsh	The belt of roses from hell'. Which I love, I love that.
Erin Allmann Updyke	(laughs) That's great.
Erin Welsh	So I'm not sure exactly when the first description of shingles was but by the 1860s its neural qualities were recognized and its focus in the dorsal route ganglion was identified.
Erin Allmann Updyke	Wow! That's impressive!
Erin Welsh	I know, I was very surprised by that too. It was sort of like autopsies were still, if you remember from our puerperal fever episode-
Erin Allmann Updyke	Right, from our puerperal fever. It's just so interesting that they were able to find... I mean they didn't know virus, right?

Erin Welsh	No, they didn't know virus but I think it was actually physical changes.
Erin Allmann Updyke	Right, yeah like the inflammation and things that you always see starting there.
Erin Welsh	Exactly.
Erin Allmann Updyke	So they were like well this is obviously the route.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah, wow.
Erin Welsh	That's pretty cool.
Erin Allmann Updyke	It is.
Erin Welsh	And this period, so from the 1860s on, sort of kicked off a growth in the interest of zoster and chickenpox which probably was just sort of alongside the growth in interest in all diseases that appeared to be infectious, right. And so it makes sense then given this high interest that it was around 1875 that the transmissibility of chickenpox was first demonstrated through inoculation of human quote "volunteers".
Erin Allmann Updyke	Quote. Quote "volunteers", we all know what that means.
Erin Welsh	Quote "volunteers". And then in 1892 the link between chickenpox and zoster was first suggested after the Viennese physician Janos von Bókay noticed that chickenpox tended to pop up in susceptible in a household where there happened to be a zoster case.
Erin Allmann Updyke	Oh, okay. I was wondering how they finally made that connection.
Erin Welsh	Yeah. I mean it makes sense but it was still at that point a hypothesis, right.
Erin Allmann Updyke	Okay, yeah.
Erin Welsh	And it did gain a bit more support when the next year the antigens for the two diseases were shown to be similar but it wasn't until the 1940s that it was finally shown that chickenpox and zoster were caused by the same virus.
Erin Allmann Updyke	Wow.
Erin Welsh	So I talk a lot on this podcast about germ theory and how that reshaped our concept of disease, really altering the way that people saw the world and themselves. But what I haven't really given much time to, unless I'm forgetting that I've talked about it which is entirely possible, is where viruses fit into all of this. Because microscopes and microbiology labs in the 1800s when germ theory first really gained traction, those allowed researchers to grow cultures primarily of bacteria or fungi and visualize them under either the scope or in the dish in colonies. And parasites which are another big contributor to disease were also pretty easily seen. But where does that leave viruses?
Erin Allmann Updyke	Very difficult.

Erin Welsh	Very difficult. And so there's this whole chunk of diseases, measles, smallpox, polio, yellow fever, influenza, chickenpox, diseases that were super prevalent but they still lacked a tangible causative agent. You couldn't see what was causing it.
Erin Allmann Updyke	Right.
Erin Welsh	The infectiousness of these diseases could be demonstrated, again mostly through those human quote "volunteers" but what exactly was being transmitted remained a mystery for decades after the rise of germ theory. In part because human beings and other animals and plants are riddled with bacteria and so it was really easy to culture bacteria from someone's sputum who was sick with influenza and assume that the bacteria you cultured were the responsible ones.
Erin Allmann Updyke	Right, right.
Erin Welsh	And also in part because we lacked the technology that would let researchers actually visualize these causative agents of disease, these viruses. But that didn't stop some people from digging deeper when their proposed bacterial species failed to meet all four of Koch's postulates which is what happened in the late 1800s when a disease was sweeping through tobacco farms in the Netherlands leaving plants withered with patches of dead and living tissue. The farmers were understandably distraught about this and so they enlisted the help of a scientist named Adolf Mayer. And Mayer couldn't find any bacteria or fungi or parasites on the diseased plants that weren't on the healthy ones but he knew there had to be something.
	So he injected sap from diseased plants into healthy ones which then also grew diseased. But the bacteria he isolated from the sap wasn't the culprit and so he grew frustrated and dropped the project which was then picked up a few years later by a couple of other scientists who decided to grind up the plants and pass them through a filter that would block plant cells and bacteria and fungi and parasites. So like what was even left, right?
Erin Allmann Updyke	Yeah.
Erin Welsh	They then injected that fluid into healthy plants and voila, disease. So they called this contagious living fluid a virus or transmissible filterable agent which is what the term was for a lot of these viral diseases later on.
Erin Allmann Updyke	Right. Filtered transmissible agent. I love it.
Erin Welsh	I love it. And then that is when the field of virology was born basically.
Erin Allmann Updyke	What?
Erin Welsh	It just really was the first time doing this episode where I actually though wait a second, we just assume, we lump viruses in with bacteria and parasites and fungi as human pathogens of disease.
Erin Allmann Updyke	Right.
Erin Welsh	But it took a lot longer than these other ones in terms of germ theory.

Erin Allmann Updyke	It's also just so fascinating that they thought to do that.
Erin Welsh	I know.
Erin Allmann Updyke	They though let's use a filter that we know is going to keep back all of the plant tissue, all of the bacteria even and just see what's left.
Erin Welsh	Mm-hmm.
Erin Allmann Updyke	What an idea.
Erin Welsh	I know, I know. It's amazing. It is amazing. And so at this time though when virology was first started as a field, scientist virologists still lacked the tools to actually see what they were working with.
Erin Allmann Updyke	Right.
Erin Welsh	But it didn't stop them from writing papers or books about these viral diseases. But in 1931 the invention of the electron microscope by Ernst Ruska and Max Knoll would change all of that.
Erin Allmann Updyke	Oh.
Erin Welsh	And also I have to shout out X-ray crystallography, one of my favorite things still. Go an listen to our radiation episode. That also helped in terms of somewhat of the structure or viruses or their composition.
Erin Allmann Updyke	Okay.
Erin Welsh	But anyway so Ernst Ruska employed his brother Helmut who was a medical doctor in his lab and had him look at some various samples under this new electron microscope. Among these samples was tobacco mosaic virus and vesicle fluid from chickenpox and zoster rashes.
Erin Allmann Updyke	Okay. Ooh.
Erin Welsh	And so Helmut Ruska became the first person to see the varicella-zoster virus and to definitively link the two diseases together.
Erin Allmann Updyke	That is so cool.
Erin Welsh	It's very cool to think about the first time seeing that.
Erin Allmann Updyke	Yeah, oh my goodness.
Erin Welsh	And the development of the electron microscope would reveal that viruses in general were not just particles of protein, which is what had been thought, but that they had complex and varied structures which was an enormous step forward in virology and molecular biology. And it earned the two inventors the Nobel Prize in 1986. Like a long time after.
Erin Allmann Updyke	Yeah, wow.

Erin Welsh	Yeah. And this Nobel Prize would not be the last one associated with varicella-zoster virus, I was very surprised to learn. The development of the electron microscope was a pretty incredible new tool for this already rapidly growing field of virology and other molecular biology techniques like tissue culture made it just a matter of time already before various viruses were isolated and then characterized. And one of these of course was the varicella-zoster virus in 1952 which was given its name by the virologist Thomas Weller who, Nobel Prize #2, was given a Nobel Prize along with John Enders and Frederick Robbins for their viral discoveries, primarily poliovirus.
Erin Allmann Updyke	Oh, that's why that name is familiar.
Erin Welsh	Yeah from our vaccines episodes way back in the day. And while the varicella-zoster virus may not have been as sexy of a thing to research as something like measles or smallpox, it still did attract a fair bit of attention. A researcher named Edgar Hope-Simpson spent 15 years, so from 1947-1962 studying this virus in a small isolated community and from this amazing data set I imagine made a ton of really important observations about its incidence rate, its pathogenesis, the reactivation of latent virus leading to zoster, and the role of the immune system in infection. And then Nobel Prize #3, our last Nobel Prize. In 1977 Gertrude Elion discovered acycloyvir as an effective treatment for herpesviruses which that Nobel Prize was awarded in 1988.
Erin Allmann Updyke	Wow, okay.
Erin Welsh	Yeah. So that's like three Nobel Prizes linked in some way to this virus which doesn't have much of a big, 'Oh and then it caused this pandemic and this epidemic.'
Erin Allmann Updyke	Right.
Erin Welsh	But still I think it's really cool because it shows just how many different fields of research are involved in understanding, like gaining an understanding about a disease.
Erin Allmann Updyke	Yeah, absolutely.
Erin Welsh	But we still have one more major development in the history of varicella-zoster virus before I turn it back over to you, which is the vaccine.
Erin Allmann Updyke	The vaccine!
Erin Welsh	In the early 1970s a Japanese researcher named Michiaki Takahashi isolated a strain of the varicella-zoster virus from a 3 year old boy and developed a live attenuated vaccine, aka the Oka vaccine which was after the last name of the boy. Within a few years Maurice Hilleman, if you remember that name from our vaccines episode-
Erin Allmann Updyke	Maurice. Let's hear it for Maurice!
Erin Welsh	Let's hear it for Maurice. (laughs) Maurice and colleagues worked on one in the U.S. based off of this Oka strain and in 1984 the first varicella vaccines became commercially available. But this was a pretty controversial vaccine at the start with many scientists in disagreement about the duration of immunity, whether the virus was attenuated enough, and the modeling showing that there might be an increase in shingles which Erin, I know you'll go into.
Erin Allmann Updyke	I'm so excited to talk about it.

Erin Welsh	But ultimately study after study showed that the vaccine was safe and was effective and so the vaccine was introduced to Korea and Japan in 1988 and eventually became available in the U.S. as of 1995.
Erin Allmann Updyke	Yeah.
Erin Welsh	And I think it's really cool that we're doing this episode now 26 years after it became routine in the U.S. because it's probably only now that we're getting a true sense of the impact that it's had. So Erin, tell me about that impact. Where do we stand with chickenpox and shingles today?
Erin Allmann Updyke	I am literally so excited. We'll take a quick break and then talk all about it.
TPWKY	(transition theme)
Erin Allmann Updyke	Okay so let's just talk about vaccines, all right. Because it turns out like you kind of mentioned Erin there's a lot of nuance to this discussion and I'm excited about it.
Erin Welsh	I am too.
Erin Allmann Updyke	So the vaccine that we use against varicella in the U.S. like you mentioned Erin it was licensed in 1995. Since 2005/2006 the recommendations in the U.S. are for two doses, the first at age 12-15 months and the second dose at age 4-6. When they first started giving this, they found it was pretty effective but there were still a good number of breakthrough infections and so that is why about 10 years later they added that second dose and it's much more effective after two doses.
Erin Welsh	Okay.
Erin Allmann Updyke	And like you mentioned Erin, this vaccine is a live attenuated virus vaccine. That means it's a live, whole, real virus but even though wild type varicella is benign this virus is even mire benign. It's doesn't cause disease but it does provide you with the antibodies that protect against wild type varicella. At this point like you said Erin, we have pretty good long term data that shows that in a lot of populations immunity actually is quite good, up to 20 years.
Erin Welsh	That's amazing.
Erin Allmann Updyke	So it's very good immunity and that's awesome. But the biggest question-
Erin Welsh	There's always a but.
Erin Allmann Updyke	(laughs) That's the title. The biggest question that I hear from people is, 'If you get the varicella vaccine instead of getting chickenpox as a kid, are you more susceptible to shingles later on in life because you only got the vaccine?' And I think that idea itself is a little bit off base and I'll talk about why but I think that this idea came about because of these math models that you mentioned, Erin. So when this varicella vaccine was first introduced and even before it was introduced in the U.S. but after it was shown to be quite effective, there were a lot of math models that suggested that by introducing this vaccine what would happen is that we would see a huge increase, a very rapid increase in shingles in adults because the prevailing thought is that part of what protects you against the development of shingles is repeat exposure to varicella in the population.

Erin Welsh	Oh my gosh, that makes sense. Okay.
Erin Allmann Updyke	Right. So it's like a natural booster. You're an adult, you're exposed to kids coming home with chickenpox and your body is like, 'Hey I remember that chickenpox!' Cause the kid just breathed in your face. And then your body's like, 'Well I'm gonna make sure to just re-up my immunity,' and then you're less likely to get shingles.
Erin Welsh	But is that how it works?
Erin Allmann Updyke	So there is data that suggests that people who have frequent or have higher numbers of exposures to varicella are less likely to get shingles. And so that was the data that these math modelers used to predict this increase in shingles. And these math models had such strong data that that's part of the reason that it took quite a long time before this vaccine was introduced into childhood vaccination campaigns well after it had been shown to be safe and effective against preventing varicella disease. So now that this vaccine has been introduced for so long, what has happened with shingles? That's the question, right.
Erin Welsh	Yeah.
Erin Allmann Updyke	Let's talk about it, big picture. Since the introduction - and I'm focusing on the U.S. because first of all I have good data, there was a lot of studies published on the U.S. but also not every country, there's not a ton of countries that have had this as part of their regular childhood vaccine campaign for as long. So anyways that's why a lot of this data's from the U.S. Since the introduction of the vaccine in the U.S. the cases of chickenpox, varicella have declined by like 95-97%. And these declines have even been seen in adults over the age of 20 as well as in infants. And what that tells us is that not only have we prevented illness in the people who have been vaccinated but we have in fact done what these math models predicted which is decrease the potential for community exposure. Because infants under age 1 and anyone over 20 something likely was never vaccinated. So what's going on with shingles? Well shingles rates have been increasing but age specific rates of shingles were increasing before we even started any vaccination campaigns, before nay of these vaccines were used widespread in the U.S.
Erin Welsh	Well that is fascinating.
Erin Allmann Updyke	Isn't it? And we don't know why. Since the introduction of these vaccines there haven't been any additional increases in this already increasing incidence, like there's no acceleration of shingle since the introduction of the vaccines.
Erin Welsh	What kind of increase are we talked about?
Erin Allmann Updyke	Oh gosh. I don't have good numbers on it and the truth is we just don't have good numbers for shingles overall because not everyone who gets shingles is gonna go to the hospital, it's not necessarily a reportable disease, etc etc.
Erin Welsh	Okay. But is it a mild slope or like a cliff?
Erin Allmann Updyke	It's a relatively mild slope. I will link to the paper which was published in 2019 called 'Do varicella vaccination programs change the epidemiology of herpes zoster?' It was a really comprehensive review. It was great.
Erin Welsh	Okay.

Erin Allmann Updyke	So to make things even a little bit more complicated, we don't just have one vaccine, we also have vaccines against shingles.
Erin Welsh	Yeah how does that work?
Erin Allmann Updyke	Yeah. So we have two different vaccines against shingles. The first came out in 2006 and this one like the varicella vaccine was a live attenuated vaccine. But there's been a newer one that has come out in 2017 and this one is a recombinant vaccine. So it's I think just one of the surface proteins of varicella and so it's not a live virus, it doesn't replicate in you.
Erin Welsh	Okay.
Erin Allmann Updyke	And that one came out in 2017 but the rollout in the U.S. especially has been very slow, there's been a lot of like backlog where people just couldn't get vaccines cause there just wasn't enough supply. But in the last like 5 years or so there has actually been a slight decline in the incidence of shingles. But we don't know why that is either and it's probably not just because of these shingles vaccines.
Erin Welsh	Okay but I have a question about these vaccines.
Erin Allmann Updyke	Okay.
Erin Welsh	Because usually when we talk about vaccines we're talking about pathogens.
Erin Allmann Updyke	Yes.
Erin Welsh	And with these two vaccines we're using disease names even though they're both against-
Erin Allmann Updyke	The same virus.
Erin Welsh	Varicella-zoster virus. Yeah and I don't get it.
Erin Allmann Updyke	I quite honestly also don't get it.
Erin Welsh	So for the shingles vaccine, right. If you gave that to someone who has never been exposed to varicella-zoster virus period, what would happen?
Erin Allmann Updyke	You would protect them against varicella and shingles as far as I know.
Erin Welsh	Okay.
Erin Allmann Updyke	I think what you're getting at is what is the real difference between, especially the original shingles vaccine that was developed in 2006 or that was licensed in 2006, that was a live attenuated vaccine. What's the difference between that vaccine and the varicella vaccine that we give to kids?
Erin Welsh	Yeah.

Erin Allmann Updyke	Probably not much, right. It's just who do we give it to? Who was it tested on and who do we give it to? And why?
Erin Welsh	Okay.
Erin Allmann Updyke	All of the data that we have so far, what they tell us about these relatively new varicella vaccines, the ones that we give to kids. Somebody who gets vaccinated with this varicella vaccine is far less likely to develop shingles in their lifetime than someone who gets chickenpox naturally as a kid. So we've seen this in vaccinated cohorts compared to unvaccinated years previous.
Erin Welsh	Right.
Erin Allmann Updyke	That the varicella vaccine strain is less likely to develop this latent infection and reactivate into shingles. So giving someone as a child the varicella vaccine is protective against both chickenpox and shingles, that much we know. And it does not appear in the almost 30 years now, 25+ years that this vaccine has been in use in the U.S. Giving this vaccine to children has not increased the incidence of shingles in the adult population like the math models predicted.
Erin Welsh	Right so what are the recommendations like for shingles vaccination?
Erin Allmann Updyke	Right now in the U.S. the newer shingles vaccine has been shown to be a lot more effective than the older one so the recommendation is that starting at age 50, at age 50 is when you get it, it's a two dose series and I don't know if there's data on whether or not you need boosters after that.
Erin Welsh	Okay.
Erin Allmann Updyke	But right now it's a two dose series starting at age 50. Yeah. But that's just in the U.S. Vaccine uptake for varicella across the world is pretty spotty but there are a number of different papers that really highlight just how big of an impact vaccination campaigns, adding varicella to the childhood vaccination campaigns can really have on a population. And that is chickenpox and shingles.
Erin Welsh	Wow. It was interesting.
Erin Allmann Updyke	Good, right? I think it's a good episode.
Erin Welsh	I think so too. Well should we wrap up the way we usually do?
Erin Allmann Updyke	With our sources, absolutely.
Erin Welsh	(laughs) So I'll shout out just a few papers, I have more but by Gross 2012 'Pangaea and the out-of-Africa model of varicella-zoster virus evolution and phylogeography'. And then also by Oaklander from 1999 'The pathology of shingles: Head and Campbell's 1900 monograph' and another one Pontremoli et al from 2020 'Possible European Origin of Circulating Varicella Zoster Virus Strains'. And I have more and I will post more on our website thispodcastwillkillyou.com.

Erin Allmann Updyke	Yeah I mentioned a couple of my sources already, I have a lot more as well as those two papers I already mentioned, one by Doll and DeCoster in the American Journal of Bioethics and the other by Harpaz that was about the epidemiology of herpes zoster. Check 'em out on our website thispdocastwillkillyou.com.
Erin Welsh	Thank you again so much for sharing your firsthand account with us, we really appreciate it.
Erin Allmann Updyke	Thank you. Thank you also to Bloodmobile for providing the music for this episode and every one of our episodes.
Erin Welsh	And thank you to the Exactly Right network of whom we are a very proud member.
Erin Allmann Updyke	Thank you to all of your listeners and thank you especially to our patrons, we love all of you so very much.
Erin Welsh	Yeah, we do.
Erin Allmann Updyke	Thanks for listening.
Erin Welsh	We hope you liked this episode. Well until next time, wash your hands.
Erin Allmann Updyke	You filthy animals.