Eliza

So it was a Monday in November. I woke up just feeling like ordinarily unwell. I thought it was a strange sort of cold or flu. I felt a bit feverish, had some aches and pains but I didn't think too much of it. What I did notice at the time though was I had a bit of a strange rash on my lower legs that looked like petechiae. So I went down to see my GP and just said hey look, I'm feeling unwell, I've taken the day off work. I've also got these like strange little red dots on my legs. Can we just get some bloods and see what's happening? And so that was it. I went and did a blood test. I went home, woke up the next day on the Tuesday. I was still feeling quite unwell. Took another day off work, didn't think too much of it. The little red dots, the petechiae were still there on my lower legs. They'd spread a little bit more, they were getting quite numerous. But I'd already done the bloods with my doctor so I wasn't too concerned. So I just spent the rest of the day in bed.

I then woke up on the Wednesday, thought I was feeling slightly better but still really, really off, the fevers were coming and going. But I'd already taken two days off work. I was a nurse, I didn't want to leave my workplace short staffed. So I thought all right, I'm just gonna crack on with it. I'm gonna head into work and I'll see what happens. Within 10 minutes of driving to work I was like I cannot possibly do this, I am so unwell, I'm feverish, I'm sweating, I'm covered in this rash. I ended up turning up to work and going I'm just having, like I have to go home. And they said someone else has already called in sick, like you've got to stay for a bit until we can get someone to cover for you. So I just sat around in my job, just sort of waiting for another nurse to turn up which was about 5pm at that stage, it was an afternoon shift.

So eventually this nurse turned up and I was able to go home. And I was really itchy at that stage so I took an antihistamine. And I was laying in bed and I realized I was really, really thirsty. So I went up to go get some water, I made it to the fridge and I just hit the ground and that was that, I just completely passed out. I sort of came to and started calling out for help from my family and they came downstairs and grabbed me. And my mom at the time had just been diagnosed with high blood pressure so there was an automatic blood pressure machine just on the kitchen bench. And I just sort of remember kind of vaguely gesturing towards this blood pressure machine going put it on, put it on. So my mum took my blood pressure. And at the time I wasn't really able to vocalize or say anything but my blood pressure was 70/40 and I just remember trying to explain to my family you need to call an ambulance, this will kill me. And they didn't.

I remember being carried into bed and I woke up in the morning and I just remember thinking oh my gosh, I've made it, I'm awake, I'm alive. I honestly didn't expect I was going to wake up. And of course my family aren't health practitioners, they weren't aware that that was an incredibly dangerous blood pressure to have and that I might not have made it that night. But thankfully that blood pressure was hopefully only postural and I ended up being okay and I woke up. So I went back to my doctor that day because I was starting to get a really stiff pain in my neck and I was a bit light sensitive and my doctor had warned me to be a bit careful about meningitis, I was in that sort of age range where it was possible. And I went oh yeah, okay, this is a bit of a concern. So I went back to my GP and I said look, this rash is getting worse, I'm now covered in these petechiae all over my legs, my arms, I've got this strange little red sort of rashes all over my torso as well. I was really flushed, the fever kept coming, my aches and pains were getting much worse.

And he looked at my bloods and he goes oh Eliza, your platelets are in your boots. You need to go to the hospital. And I said oh okay. Like now? Do I have to go right now? He said look, you need to go pretty much today. You have to go get some things when you go home, I expect you to be admitted as an inpatient. This isn't looking fantastic. So make sure you get there as soon as you can. And at the time the closest hospital to me was also the one that I worked at, which is a lot of fun. So they were able to rule out meningitis in the ED but they were obviously really concerned about the platelets that I had and they wanted to admit me because they were concerned that if the platelets dropped any further, there would be potential for needing a blood transfusion, which was a lot of fun.

So I got admitted into a general medical unit. It was one of the units that was used uh mostly for managing older people and palliative care. And this particular unit I was admitted into overlooked the ward that I worked at. So I could see the comings and goings of my fellow coworkers, which was quite amusing. So what happened on that first night was obviously I was quite distressed, I'd never spent a night in a hospital before I was a young and healthy woman. I was only 22, just graduated basically from nursing. So I was a bit startled and concerned that I'd gotten myself into this predicament so quickly where it suddenly declined so far down. And I was the one now needing care and having nurses look after me. It was a really startling experience. So that was a Thursday I got admitted.

On the Friday the fevers kept going, the aches and pains were still there, the petechiae just kept spreading. Every time they wanted to take my blood pressure, I would end up with these welts under the blood pressure cuff where the petechiae would just bloom from all the bruising they were causing. Eventually the fever started to drop and on the Saturday they were like look, your platelets aren't great but we can see they're starting to improve. We can look at maybe letting you go home. So my mom came to pick me up and then I spiked another fever. And they did my bloods again and the platelets had dropped yet again. And the joint aches and pains kept getting worse. So I was then in the hospital for another night. What kept happening was every time the fever would pick up, the joint aches and pains would get worse and worse. And eventually what had happened was my fingers became quite gnarled. I was unable to use my hands. I developed quite severe pain in my knees, my hips, my shoulders, and I lost my ability to walk very well. So I was needing strong pain medications just to get me up and moving.

But what ended up happening was I wasn't even able to attend to my own sort of personal needs in a safe manner. It was a very humbling experience, I would say, to have that happen to you at such a young age when you'd been like the week prior the person providing that care, to be the one having to receive it so quickly and rapidly was quite a challenging experience. It took a long time for the diagnosis of parvovirus to occur, I think it was probably on the Tuesday. So by that time I'd been sick for over a week, I'd been in hospital for four days when they were finally able to say oh we think we found the cause of what's happening for you. You have parvovirus. I did say to them isn't that what dogs have? I get my dog vaccinated for parvovirus, have I gotten this from an animal? And they said no, that's not what's happened, like there's humans that get parvovirus, it's normally seen in kids in daycare. You've just somehow ended up with it.

	The fevers kept coming and going but I was slowly getting better and eventually I was able to reduce down on the pain medication. And by the Friday, so I'd been in hospital for just over a week, they were able to discharge me home. Finally that all started to clear but what did happen was they did warn me I could still get the joint aches and pains for a couple of weeks but it could last a bit longer. I was unlucky and they did last a bit longer. I would have days where I would be absolutely well, I could move about just fine and then suddenly everything would just stop working. I remember going to a Christmas party and I was feeling absolutely fine that day. I had a couple of drinks, I was dancing for about an hour in a club. And I sat down because I was like needing to get a breath, I just wanted some water. I sat down and I could not stand back up.
	My friends had to carry me out of this club and explain to the bouncers and the security that no, she's not inebriated, she has this virus and her joints aren't working, she can't move. And I had to be carried into this Uber and this poor Uber driver had to basically carry me into my house and get my mom to meet me at the door and put me into bed because my legs just stopped working. But for about two months, I was in and out of my physio having to relearn basically how to lift my arm over my head, how to take a normal stride because my pace would suddenly start getting shuffling, how to open and close my hand well enough because every now and then my hands would just seize and my fingers wouldn't co-operate. It took about two months all up. But in the end, I was completely fine. The petechiae all resolved, the rash resolved. The joint aches and pains finally left.
	It did leave a bit of a lasting impact that now every time I seem to get a virus, I do respond with that sort of viral arthralgia. It's just part of it now. So I know whenever I get a cold or a flu or even COVID, the first time I had COVID it did kick in, but it's never that intense anymore. It's always pretty mild and it's something that can easily be managed with Nurofen. But yeah, it was quite a fun experience.
TPWKY	(This Podcast Will Kill You intro theme)
Erin Welsh	Oh my gosh. First of all, I just had no idea about parvoviruses but also what a wild story. What a wild ride.
Erin Allmann Updyke	Terrifying.
Erin Welsh	Terrifying.
Erin Allmann Updyke	Honestly.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	Thank you so much for sharing your story with us, truly.
Erin Allmann Updyke	Yeah. My goodness. Thank you.
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	Today we're talking about parvo.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	And all the different kinds. Well a couple of the many different kinds.
Erin Allmann Updyke	We will mention the many different kinds and focus on a few.
Erin Welsh	Yep, yep, yep. But there are so many more than I expected.
Erin Allmann Updyke	Yeah.
Erin Welsh	I mean, yeah.
Erin Allmann Updyke	It's par for the course This Podcast Will Kill You, come on.
Erin Welsh	I know, I know. Why are we surprised by anything at this point?
Erin Allmann Updyke	No, we can't be.
Erin Welsh	We can't be.
Erin Allmann Updyke	But it's going to be an interesting episode. I am excited to learn about the history of this virus that I know nothing about.
Erin Welsh	I'm excited to learn about the biology of this virus that I know nothing about.
Erin Allmann Updyke	It's really interesting. So I'm excited to tell you about it.
Erin Welsh	And I'm also really excited that we get to talk with another expert.
Erin Allmann Updyke	Yeah.
Erin Welsh	We are bringing on later in the episode a very special guest, Dr. Steph Horgan Smith, who is a veterinarian, to answer some of your burning questions about parvoviruses in dogs.
Erin Allmann Updyke	Yeah, I'm really excited about that because I am not a vet.
Erin Welsh	Nor am I. But I have a dog and so I'm interested.
Erin Allmann Updyke	Same.
Erin Welsh	Even if I didn't have a dog, I'd still be interested. This is a mess. Let's just get to the quarantini.
Erin Allmann Updyke	It's quarantini time. Shall we?

Erin Welsh	Yes. Yes we shall. What are we drinking this week?
Erin Allmann Updyke	We're drinking Sick As A Dog.
Erin Welsh	Yeah. I mean-
Erin Allmann Updyke	So named.
Erin Welsh	So named because yeah, parvo infects a bunch of different animals but it is terrifying and deadly in dogs, as we'll learn more about. But before we do that, what is in Sick As A Dog?
Erin Allmann Updyke	It is tequila and lime juice and ginger syrup. And it's quite refreshing.
Erin Welsh	Yeah. Simple and delicious.
Erin Allmann Updyke	Can't go wrong.
Erin Welsh	What could be better? Yeah.
Erin Allmann Updyke	We'll post the full recipe for that quarantini as well as the non alcoholic placeborita on our website thispodcastwillkillyou.com and on our social media.
Erin Welsh	On our website, you can find all sorts of cool things. Let me just pull it up to confirm.
Erin Allmann Updyke	Okay. To confirm it's still there.
Erin Welsh	It's still functional. You can find the sources for each and every one of our episodes, you can find transcripts, you can find a submit your firsthand account form, which to all the people that have done that, thank you. It's been amazing. You can find things like our bookshop.org affiliate account, our Goodreads list, merch. There's amazing merch. We have excellent merch. You can find links to music by Bloodmobile, Patreon. There's a lot of stuff.
Erin Allmann Updyke	Just so much there.
Erin Welsh	Yeah. Can we get to the actual content now?
Erin Allmann Updyke	Can we?
Erin Welsh	Okay.
Erin Allmann Updyke	Was this a long enough intro?
Erin Welsh	Yeah, I think it is.
Erin Allmann Updyke	Okay. Let's take a quick break and then talk about the biology of parvoviruses.
TPWKY	(transition theme)

Erin Allmann Updyke	I want to talk very briefly about parvoviruses as a general group of viruses because I think that understanding some of their common characteristics will be informative to understand how variable the presentation can be when we talk about parvoviruses in different animals with our vet later on. But we'll focus for this biology section on human parvovirus, AKA parvovirus B19. And then I'll briefly mention some of the other parvoviruses, like canine parvovirus and things like that. But to understand parvoviruses in general at first, parvoviruses are DNA viruses. They happen to be really tiny DNA viruses, which I just find cute. And as always, we're not talking about one virus. The family Parvoviridae includes a number of different genera of viruses that infect a huge range of animals and insects and all kinds of things. And as a very broad general rule, one thing to know about parvoviruses is that they tend to infect preferentially rapidly dividing cells. That is a key characteristic of parvoviruses. And it makes sense then why they infect the cells that they do and therefore cause the diseases that they cause.
Erin Welsh	Very interesting.
Erin Allmann Updyke	Yeah. They can infect a wide variety of cells when you look across all the parvoviruses and different parvoviruses are more specific, they have a more specific tropism for individual types of cells. But across the board, it's rapidly dividing cells.
Erin Welsh	I find that so interesting to think about, like the pros and cons of infecting rapidly dividing cells vs not rapidly dividing cells.
Erin Allmann Updyke	Yeah.
Erin Welsh	I know it's not like the viruses are not all sat there in a boardroom being like all right, put that one on the pros list. But something like rabies that infects-
Erin Allmann Updyke	Nerve cells.
Erin Welsh	Nerve cells.
Erin Allmann Updyke	Yeah.
Erin Welsh	Like what? Yeah, yeah. I don't have anything more to go with that thought.
Erin Allmann Updyke	It's interesting. It is really interesting. Especially because parvovirus is killing and destroying cells. That's what they do, these parvovirused. So they're infecting cells and then they're absolutely killing and destroying them. So it makes sense then that for them to be able to have a fresh supply of cells to invade, that they are invading rapidly dividing cells. Again, they didn't make that as a decision.
Erin Welsh	Right but-
Erin Allmann Updyke	But they kind of go together well with the cell types that infect.
Erin Welsh	I wonder too if it has anything to do with like the host immune system and how rapidly they're detected, like how do you outrun the immune system? Do you do the sneak and hide approach?
Erin Allmann Updyke	Right.

Erin Welsh	Or do you just go in-
Erin Allmann Updyke	And go ham.
Erin Welsh	Yeah, go ham.
Erin Allmann Updyke	Yeah. So that is what they do in general, Canine parvovirus and feline panleukopenia virus and a number of others are in the genus protoparvovirus, as is porcine parvovirus, a lot of kind of the famous parvovirused. One that kept coming up in research that I don't know if most people have heard of but it literally kept coming up was the Aleutian mink virus, disease, virus?
Erin Welsh	Yeah, of course.
Erin Allmann Updyke	Of course, the Aleutian minks. This is in a whole different genera of parvovirus called the Amdoparvovirus. There's a few other genera of parvoviruses, one of which I will mention because I'll talk about it at the very end, is called the Dependoparvovirus genus.
Erin Welsh	I'm so excited that you're talking about these later.
Erin Allmann Updyke	Yeah. These are viruses that depend on other viruses. I didn't do that pun but somebody did.
Erin Welsh	Yep.
Erin Allmann Updyke	These viruses depend on the presence of other viruses to be able to infect cells. We'll get to it, I promise. And then there's human parvovirus, AKA parvovirus B19. And this is a member of the genera called Erythrovirus genus. The reason that it got the name Erythrovirus is because this virus, parvovirus B19 and a few other related viruses that infect primates, have very strong tropism, AKA they preferentially infect erythroid precursor cells. What does that mean? Our erythrocytes are our red blood cells. So parvovirus B19 is infecting and replicating in, preferentially and close to exclusively, though not entirely exclusively, in the cells in our bone marrow that become red blood cells. Like our baby red blood cells. These are cells that are very rapidly dividing, right, because we make new red blood cells all the time. So the way I'm going to structure this is let's go over the nitty gritty pathophysiology of what is happening in our human bodies when we're exposed to parvo B19. And then how that effect can manifest in what turns out to be a really wide spectrum of illness. And then I'll briefly touch at the end on some of the other animal parvoviruses. Cool? So B19, can we just call it that?
Erin Welsh	Yeah, sure, why not?
Erin Allmann Updyke	Okay, great. It's our podcast, we can do whatever we want.
Erin Welsh	So why we do this?
Erin Allmann Updyke	So B19 is a human specific virus. That's the first off. It's transmitted in respiratory droplets primarily, though since this is a virus that's in red blood cells and their precursors, it can also be transmitted in blood products. And it can cross the placenta during pregnancy and infect a developing fetus, which is an important part of the parvovirus story. But once this virus makes it into our body, it hones in really quickly and specifically on our bone marrow, since it's really specific to these precursor red blood cells. And the reason why this is the cell that it infects is because the receptor that it binds to, to be able to enter our cells, happens to be found on our erythroid precursor cells. It's called blood antigen P.

	Anyways, so once it's in our cells, over the course of a few days to a few weeks, this virus is just replicating, replicating, replicating. And as it does this, it induces a complex series of changes within the cell, within these erythroblast precursor cells, that leads to DNA damage, a rest of the cell cycle, so they stop dividing, and death of these cells. And during this time, while this virus is replicating in our blood cells, if you were to check what's called a reticulocyte count, this is some really nerdy fun stuff. Reticulocytes are what we call immature red blood cells when we look at them on a blood smear.
Erin Welsh	Okay.
Erin Allmann Updyke	And their measurement is something that we check in the case of things like anemia, right. If a person doesn't have enough red blood cells, then they should have an increase in this reticulocyte count because that means their body is going into overdrive to make more red blood cells. They're like making more babies to eventually make more adults.
Erin Welsh	Okay, what is the timeline between a reticulocyte and red blood cell?
Erin Allmann Updyke	That's a great question. The total lifespan of a red blood cell is usually about 120 days but I don't actually remember how many days it takes to become a mature red blood cell.
Erin Welsh	Okay.
Erin Allmann Updyke	It's probably something I should have googled because it's googleable.
Erin Welsh	And what happens if you have a low reticulocyte count? Like what does that mean?
Erin Allmann Updyke	Well great question because that's what we see in parvovirus. The reticulocyte count-
Erin Welsh	Oh, that wasn't planned.
Erin Allmann Updyke	It really wasn't. But that's what we see. Because parvovirus is infecting these reticulocytes and our erythroblasts, the reticulocyte count, if you were to check it in someone in an early part of their parvovirus disease course, it drops to almost zero. This virus is attacking and killing off all of these reticulocytes very specifically. So because of that, you also would then see very often a drop in our hemoglobin. And the hemoglobin is the way that we measure how many red blood cells we have. It's not a direct measurement but it's the way that we see so you have enough red blood cells? Usually this is a pretty small drop by say about one point which is not a lot for most people. And most of the time for most people with this infection, this is transient. This virus is killing off a whole bunch of our reticulocytes all at once but then our body responds by very quickly making neutralizing antibodies that are highly effective. We neutralize this infection, kick this virus out, and then our reticulocyte count will bounce back and then eventually so will our hemoglobin.
Erin Welsh	Okay but if you say... I know that you're poised to say 'but'.
Erin Allmann Updyke	I am, you can see the 'B' on my lips.
Erin Welsh	Yeah, I can see it. And I'm going to preempt it by asking a question, which is so you said that the lifespan of a red blood cell is like 120 days. And so what is the lag time then between when this parvovirus, when B19 starts killing off those reticulocytes and then when symptoms are being felt?

Erin Allmann Updyke	Ooh, Erin. I just can't wait to tell you. It's so much more detailed than that.
Erin Welsh	Okay, okay. Now I'll let you continue with your 'but'.
Erin Allmann Updyke	Yes. By the way, I just googled it just so that we have a little bit more information.
Erin Welsh	Okay.
Erin Allmann Updyke	According to the Google, it's like two days from when reticulocytes are first sent out of the bone marrow into our bloodstream to then become red blood cells. But there is also a maturation process within our bone marrow itself.
Erin Welsh	Okay. Because this is all happening within the bone marrow and not in our circulatory system.
Erin Allmann Updyke	Right. Exactly, exactly.
Erin Welsh	Okay.
Erin Allmann Updyke	So these are... This virus is infecting the cells that are precursors in our bone marrow and causing them to not be able to release any more of those reticulocytes. So then the red blood cells that are mature already in our body are just doing their normal death process. They die in waves. And then that's why the reticulocytes aren't there for a time period to be able to make up for the natural course of our red blood cells, so that hemoglobin drops. And then once we can bounce back because we've fought off this infection, then no problem.
Erin Welsh	Okay, okay.
Erin Allmann Updyke	But.
Erin Welsh	But.
Erin Allmann Updyke	Sometimes it doesn't happen that way. So that is kind of what is happening in our body. And now that we understand that, we can talk about what it looks like when we have symptoms of this disease and how wide of a range these symptoms can present to us.
Erin Welsh	Yeah.
Erin Allmann Updyke	There are so many different ways that this can present that there are a lot of different names for the syndromes that are caused by B19. The first is erythema infectiosum, I think is how you say that, or fifth disease. Which are you going to get into this in the history, Erin?
Erin Welsh	I sure am.
Erin Allmann Updyke	Okay good.
Erin Welsh	Briefly.
Erin Allmann Updyke	Because I have a sentence but I was like maybe I won't say it out loud.
Erin Welsh	I mean I have like two sentences so...

Erin Allmann Updyke	More than me. So erythema infectiosum or fifth disease is the classic little kid disease that's caused by parvovirus B19. The way that it tends to look is this: early on, like in that early phase of viral infection and replication which takes maybe a few days to a week after exposure, now we're talking timeline, most kids that get infected with parvo will have a mild, very non-specific illness. You may or may not even notice that they're sick. They'll have some fevers, maybe a runny nose, maybe not, headaches, maybe some nausea, and that's it. This is the time frame in which people are viremic. So this is the time frame when they're just feeling kind of cruddy that they are getting their friends and family sick. And by the way, if you'd like to ask how infectious is this, how contagious is this disease?
Erin Welsh	Yeah. I'd love to ask that.
Erin Allmann Updyke	I couldn't find an R0 reliably but the attack rates, especially among household contacts, are very high. So up to 50% of kids among exposed household contacts who haven't had parvo B19 will get parvo B19, and 20%-30% of adults in a household or a classroom setting if they haven't yet been exposed.
Erin Welsh	Okay.
Erin Allmann Updyke	So pretty infectious.
Erin Welsh	And so if they haven't yet been exposed, so they is pretty good... Like how durable is the immunity?
Erin Allmann Updyke	Yeah. Great question. As far as I can tell, quite durable.
Erin Welsh	Okay.
Erin Allmann Updyke	And most of the studies of like the epidemiology really just looks at like seroconversion where like by old age, 85% of people have been exposed and have antibodies to parvo B19.
Erin Welsh	So what's the rate of asymptomatic vs symptomatic then?
Erin Allmann Updyke	Excellent question. I didn't see this exact, I saw one paper that said about 20% of people won't have any symptoms whatsoever. But I think that it's probably even more variable than that because of especially how different the disease can present in children vs adults.
Erin Welsh	Okay.
Erin Allmann Updyke	If that makes sense.
Erin Welsh	Yeah.
Erin Allmann Updyke	And we'll get into it. But at least 20% and possibly more percent of the time people might be entirely asymptomatic.
Erin Welsh	Okay.

Erin Allmann Updyke	At least from my reading. Great question. But that's just the initial, like I am feeling a little bit cruddy from a non-specific illness and I'm exposing all of my friends. Then kids get better. And then about two weeks after exposure at least, after this initial infection will come a rash. And the rash is on the face. It's this red splotchiness on the cheeks that usually doesn't extend down to the mouth. So what it looks like is like you got slapped on the cheek and your cheek turned red. It's literally called a slapped cheek rash. And it really does look like that because it's so isolated to the cheeks and just this kind of red sploosh on the cheeks.
	And then over the course of 1-4 days thereafter, it can extend down the body, down the arms and the trunk and things. And this rash, as it moves, looks like a lot of viral rashes. It's like these pink little splotches, they're not usually raised, sometimes they can be kind of lacy looking. And this rash, especially the one that kind of extends down the body, it can kind of come and go. So it can be there for a day or so and then go away for a few days and then come back maybe under a time of stress and then eventually over a few weeks or so you might not see the rash anymore at all.
Erin Welsh	All right. Why? Why does it come and go and why does it start on your cheeks?
Erin Allmann Updyke	Great question. I don't know, as always. But what's interesting is that all of these symptoms that we associate with this specific syndrome, erythema infectiosum or fifth disease, these are immunologically mediated. This is our body's response post viral. Like if you were to check a viral load at this point, most of the time you can't find one in kids with this. So this is all from our bodies, antibodies, and immune response causing this rash and these rashes that kind of come and go.
Erin Welsh	Wow. So it's coming in and just like letting somebody spread everything with these very gene mild symptoms?
Erin Allmann Updyke	Exactly.
Erin Welsh	Okay.
Erin Allmann Updyke	Exactly. Isn't that fascinating? Now I think we've talked about doing a whole thing on rashes because I do think it's very interesting. There's a lot of rashes that we see associated with viral syndromes and they usually are this immune-mediated kind of rash. And I don't understand why some viruses tend to cause a more specific rash than other viruses. But still in general, there's a look to these viral rashes and this is one of those viruses that causes one of these viral rashes with the addition of the specific slapped cheekness of it.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah, right?
Erin Welsh	Yeah.
Erin Allmann Updyke	So that's in kids. And in adults, as per usual when adults get a quote "childhood illness", it tends to be a bit more severe. And in the case of parvovirus, this comes with joint pain. So adults may still have that initial non-specific illness or they may not. But the part of parvovirus that's more severe in adults tends to be joint pains and inflammation. You can see this in kids as well but almost always if an adult gets parvo B19, you're going to have some degree of arthritis and arthralgia as the common presenting feature.

Erin Welsh	Why? Why is there a difference?
Erin Allmann Updyke	It's immune-mediated again. So is it just the difference between a child's immune system and an adult's immune system, which are totally different?
Erin Welsh	Yeah but what are those differences?
Erin Allmann Updyke	That we could do a whole episode on.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah. But in adults, it's this bilateral arthralgia. It can be the hands, it could be the knees, the ankles, the wrists, really anywhere. And sometimes this can really mimic rheumatoid arthritis. And there was some thought back when that parvo B19 might be one of the kind of triggers for something like rheumatoid arthritis. There's not really a lot of data for that from what I can tell.
Erin Welsh	Okay.
Erin Allmann Updyke	But the symptoms can be really similar. And what's really tough is that for many people these joint pains resolve over time but time could mean weeks or months or even years. So the mechanism here is still immunologic. It's our bodies making these antibodies and then these antibodies getting deposited in our joints and causing joint pain and inflammation. Very similar to a lot of autoimmune disorders that cause arthritis and arthralgias.
Erin Welsh	Okay.
Erin Allmann Updyke	Isn't that interesting?
Erin Welsh	That is fascinating.
Erin Allmann Updyke	So that is all the mild cases of parvo B19.
Erin Welsh	Right.
Erin Allmann Updyke	But as we heard in our firsthand account, parvo is not always a mild illness. It can also cause very severe disease, both acutely and chronically. So let's get into it. Because this is a virus infecting and destroying, remember, our red blood cell precursors, in most people it results in a transient reduction in hemoglobin. Most of the time you probably would never even see that because people aren't getting sick enough to have their hemoglobin measured multiple times over the course of this illness. However in some people, especially in people who have any kind of baseline either decrease in their red blood cell production capacity or a baseline of a higher than typical red blood cell destruction, this transient small hemoglobin drop can actually result in profound anemia in what's called a transient aplastic crisis or aplastic anemia.

	And by profound, I mean that this can cause a hemoglobin drop that is so low that it can be lethal. And if this happens, the symptoms of this disease are vastly different. People are incredibly weak, they're lethargic, they have very significant pallor, so their skin is incredibly pale. Even if they have dark skin, their mucus membranes, the palms of their hands, these things are just like without color because they have no hemoglobin. And if you checked their hemoglobin, they would be incredibly low. And I don't know exactly how low but I do know that I have seen people present with very, very low hemoglobins in other contexts and the hematology specialists are always thinking could this be from parvovirus B19? So a normal hemoglobin can range from 12-16 depending on the situation. And so we're talking about hemoglobins less than 7, 6, 5, incredibly low.
Erin Welsh	Whoa.
Erin Allmann Updyke	Yep.
Erin Welsh	Okay.
Erin Allmann Updyke	So a big question is what are the conditions that put you at highest risk of this?
Erin Welsh	Yeah.
Erin Allmann Updyke	And the list can be really long. Things that result in a decrease in red blood cell production are things as simple as iron deficiency anemia, which many people who menstruate have some degree of iron deficiency anemia.
Erin Welsh	Right.
Erin Allmann Updyke	It can be genetic things like thalassemias. And then we also can see things that cause an increase in red blood cell destruction like hereditary spherocytosis, which is when your red blood cells have a slightly different shape and so as they pass through the spleen, they're more likely to get destroyed and sheared.
Erin Welsh	Okay.
Erin Allmann Updyke	Or not having a spleen altogether or sickle cell disease or chronic hemolytic anemia, there's a whole lot of different things that cause an increase in the turnover of red blood cells. So instead of existing for 120 days, their lifespan is shorter and therefore this drop in hemoglobin is more significant even if it's short. Does that makes sense?
Erin Welsh	Yeah, it does. There are so many different ways for this to have an impact.
Erin Allmann Updyke	Right.
Erin Welsh	Okay.
Erin Allmann Updyke	The good news is that even in this case, this tends to be a transient phenomenon. So if it is identified, it can be treated with supportive care. Red blood cell transfusions, fluids, supportive care in general. However even though it's self limited and eventually most of the time in this aplastic crisis case, people's immune system will mount an antibody response and will fight off this infection and their red blood cell count will be able to come back, it can be so severe that it can be fatal. Because this significant anemia can result in heart failure, it can result in strokes, it can really be significant. So it's quite scary.

Erin Welsh	What would some of the signs and symptoms be that somebody would experience when like things are getting really bad that would prompt them to go to the hospital for instance?
Erin Allmann Updyke	Yeah, it's a great question. Really it would be things like fatigue, weakness, lethargy, there's nothing that looks particularly infectious per se. So it's not necessarily like fevers, chills, that kind of a thing. It's more about the signs of anemia, so pallor, fatigue, lethargy, those kinds of things.
Erin Welsh	But by this time, again the virus is no longer there or is it could be?
Erin Allmann Updyke	It's a good question. I saw mixed answers to that in some of the literature. But I think that given that this is the timeframe in which the virus is still replicating and destroying your red blood cells, you would likely still see some degree of viremia.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah. Just depends on when in that course of time you get super sick. Yeah. So that's one of the severe manifestations. There's more, a few more. Parvovirus B19 is also one of the TORCH infections. And these are infections that are considered incredibly severe in pregnancy, that lead to severe fetal infection and potentially pregnancy loss or significant congenital manifestations in the fetus. So during pregnancy, especially in the second trimester-ish, so like 11-23 weeks, a primary infection, so a first time infection with parvovirus B19, can cross the placenta and infect the fetus. And in a fetus, it does a very similar thing that it does in a grown person or a child. And that is that it can cause severe anemia. It can cause this transient aplastic crisis.
	In the case of the fetus, it's by this virus infecting the fetal liver because that is the site of red blood cell production for a lot of development in the fetus. But as you can imagine, severe anemia in a fetus can be incredibly dangerous. The anemia can lead to a form of high output heart failure. Because our red blood cells are carrying oxygen with less oxygen delivery capacity in the fetus, that fetus's heart has to start pumping over time in an effort to increase blood flow enough to make up the difference, right. Like your capacity is down, there's not as many trains running, so they're running the trains faster. But eventually the conductors, the heart, just can't keep up with running trains at this pace. And so it burns out and it can't pump and that leads to heart failure. Heart failure leads to blood backing up in the vessels because it's not getting pumped out and this leads to an increase in pressure in the blood vessels, which leads to leaky blood vessels, which causes edema.
	An edema in a fetus that gets severe like this is called hydrops fetalis. It's incredibly serious and it is very often fatal. It's a sign of really severe disease. Parvovirus is by no means the only thing that can cause hydrops fetalis but it is one of them and that is kind of the mechanism by which it happens in this case. Parvovirus B19 in a fetus also seems to sometimes infect their myocytes, the heart cells themselves, which is especially fascinating since normally this is only infecting rapidly dividing cells. But apparently the viral receptors in the red blood cells are also on fetal heart cells, which is just interesting. And this can cause a myositis or an inflammation in the fetal heart and contribute to that development of heart failure.
Erin Welsh	Okay. That's awful.

Erin Allmann Updyke	It's awful. It's really scary. And so a parvovirus B19 infection is one of those that is kind of scary in pregnancy. I will say that it is still very rare. And it's rare not only because it's estimated that about 50% of people by the time that they get pregnant are still able to get infected essentially, like 50% of people are already immune to parvo. But even in those 50% of people, if an infection occurs during pregnancy, most sources that I read estimated that it's only about 5% of the time that there's any abnormality as a result, even though it can be up to 30% of the time that the fetus does end up getting infected. So kind of just like with parvovirus in kids or adults, most of the time it doesn't cause this severe outcome but some of the times it can.
Erin Welsh	Okay. I have a few questions.
Erin Allmann Updyke	Okay.
Erin Welsh	You said TORCH. What does that stand for?
Erin Allmann Updyke	TORCH. So TORCH stands for toxoplasma, the O is other, which includes syphilis, parvovirus, varicella, and listeria.
Erin Welsh	Okay.
Erin Allmann Updyke	And then rubella is the R, cytomegalovirus, CMV, is the C, and then the H is herpes simplex virus.
Erin Welsh	Okay.
Erin Allmann Updyke	TORCH. So these are all viruses that can the placenta and then result in pretty severe disease in the fetus. We've covered quite a lot of these on the podcast already.
Erin Welsh	We have. Okay, another question was sort of the timeline of infection in these severe cases where heart failure does happen. What is the timeline of that? And follow up question, is there any treatment?
Erin Allmann Updyke	Excellent question. So the timeline of it I actually don't fully know in terms of like once the fetus is infected, what's the timeline to development of severe disease? I don't know.
Erin Welsh	Okay.
Erin Allmann Updyke	It is infection in the second trimester of pregnancy that we know is highest risk because that's when the fetus is like making a lot of these red blood cells and things like that. Whereas later on, they have enough of a reserve that they might be less affected by an infection and earlier than that, they don't have as much of a circular student system yet kind of a thing.
Erin Welsh	Right.
Erin Allmann Updyke	But there is treatment that can be done, which is great.
Erin Welsh	Okay.

Erin Allmann Updyke	It's definitely not something that is available everywhere but things like intrauterine transfusions are things that can be done, especially if you identify an infection and then what you do is you serially monitor with ultrasound to see how the fetus is doing and if there's any evidence of infection and then you would be able to treat it with things like transfusions.
Erin Welsh	Wow.
Erin Allmann Updyke	And it can significantly reduce mortality in the case of the development of hydrops.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah.
Erin Welsh	Is there a vaccine for humans?
Erin Allmann Updyke	No.
Erin Welsh	Okay.
Erin Allmann Updyke	No. That was an easy answer unfortunately.
Erin Welsh	Yeah.
Erin Allmann Updyke	There's one more thing that I want to mention and that is what's called chronic red cell aplasia. And this is very similar to transient aplastic crisis, except that like the name implies, it's chronic. And so in individuals that already have a severe bone marrow deficiency for one reason or another, like they already have leukemia or they've had an organ transplant so they're on immunosuppressives or they're undergoing cancer treatment. In these cases, infection with parvo B19 can cause not a transient but a chronic anemia that can be pretty profound but can improve if like for example the chemotherapy is stopped, then things can kind of bounce back. But that's just kind of one last thing. And in this case, what's interesting is that it does tend to result in a chronic viremia.
Erin Welsh	Oh.
Erin Allmann Updyke	Where this virus is still present, you can still detect it, and it's still causing this damage.
Erin Welsh	Okay. Fascinating.
Erin Allmann Updyke	Fascinating is right. So that is kind of most of all of the manifestations of parvo B19 in humans.
Erin Welsh	There's a lot.
Erin Allmann Updyke	There's a lot. And that's just the human parvovirus.
Erin Welsh	That's just one virus.
Erin Allmann Updyke	It's one virus.
Erin Welsh	One host.

Erin Allmann Updyke	There's a few subgroups of it nowadays.
Erin Welsh	Yeah.
Erin Allmann Updyke	But that's parvo B19. But this is a huge group of viruses that infect a huge variety of mammals and a lot of pet owners are probably even more familiar with canine parvovirus or with feline panleukopenia virus than they are or were with human parvo B19. Now just like with human parvovirus, these animal parvoviruses are infecting rapidly dividing cells. But in most cases, they happen to have tropisms that are more specific for the lymphoid tissue in the intestinal crypt cells. So this is rapidly dividing lymph tissue in the intestines of these animals. And because of that, there's some pretty notable differences in the disease course and the mode of transmission when it comes to these animal viruses compared to human parvoviruses.
	So animal parvoviruses tend to be transmitted fecal-oral because these viruses are infecting the intestinal cells rather than bone marrow cells and then being transmitted in our respiratory secretions. And as our lovely vet will talk more about later, the symptoms of the disease tend to be more gastrointestinal but there's a lot more to it than just that. And we'll talk about that later on. But Erin, now can you tell me where the heck this virus came from and how we got to this point?
Erin Welsh	Yeah, I mean kinda.
Erin Allmann Updyke	Or these viruses, I guess.
Erin Welsh	Right.
Erin Allmann Updyke	All of them.
Erin Welsh	We'll see what exactly I can tell you right after this break.
TPWKY	(transition theme)
Erin Welsh	I want to start off the history section with possibly the cringiest opener yet but I couldn't help myself.
Erin Allmann Updyke	I can't wait.
Erin Welsh	The history of parvoviruses begins not with a bang, not even with a whimper, but rather a squeak.
Erin Allmann Updyke	That's hilarious.
Erin Welsh	Erin, I just, I don't know.
Erin Allmann Updyke	I love it.
Erin Welsh	I had to. I wrote it down and I was like should I? Should I not? And then...
Erin Allmann Updyke	Wait, wait. Here's my question.

Erin Welsh	Yeah.
Erin Allmann Updyke	Did you write that quote or did you find that quote?
Erin Welsh	I mean like the whole not with a bang wimp but with a whimper or whatever.
Erin Allmann Updyke	Yeah.
Erin Welsh	That's old. But like I added the squeak part.
Erin Allmann Updyke	Oh I love it.
Erin Welsh	Okay.
Erin Allmann Updyke	I really loved it.
Erin Welsh	But I said squeak, I say squeak because the first parvovirus described, which was isolated in 1959, came from a rat.
Erin Allmann Updyke	It's nerdier than you would think.
Erin Welsh	Right, right? I mean I don't know how to do it any other way.
Erin Allmann Updyke	I wouldn't want it any other way.
Erin Welsh	It's discoverers, Kilham and Olivier, named it, fittingly, rat virus.
Erin Allmann Updyke	Okay. Can you imagine anything else?
Erin Welsh	But like why imagine?
Erin Allmann Updyke	Right.
Erin Welsh	Can you imagine being a virologist during this time and being able to name something rat virus?
Erin Allmann Updyke	Rat virus.
Erin Welsh	What a time, what a time.
Erin Allmann Updyke	Wow.
Erin Welsh	Later, presumably because people quickly realized that there wasn't just one rat virus, it became known as Kilham rat virus.
Erin Allmann Updyke	Okay.

Erin Welsh	Kilham and Olivier found the virus while looking for a tumor-inducing virus in rats. And what they found was rat virus, which did not appear to make the rats sick or cause tumors or seem to be able to infect other species. But the researchers still did find the virus interesting enough to write up. And over the next 10 or so years, their paper describing this rat virus would be referenced in more papers describing similar viruses also newly discovered, first primarily detected in like immunosuppressed lab rodents or in cell culture lines with a very wide range of pathogenesis from asymptomatic infections to neonatal death and rodents for instance.
Erin Allmann Updyke	Okay.
Erin Welsh	And later they began to find these viruses from non lab settings and non lab mammals like the greater wax moth and subsequently a whole bunch more arthropod species and at least one crustacean. For the most part, these small seemingly related viruses didn't make too much of a stir in the virology community until the mid 1960s. Epidemics of enteritis, panleukopenia, and congenital cerebellar ataxia had been popping up in domestic cats for decades. And around 1965-1966, researchers identified the causative virus as being similar to these small rodent and arthropod viruses that they had found. And they named it feline panleukopenia virus, which I think was also the first real indication that this group of viruses might have a substantial effect on their hosts in like natural settings. But what was this group? It still needed a name. I mean we know that what it is now but I'll tell you how we got there. So Carlos Brailovsky proposed the name parvovirus rati for a Latin naming system for rat virus, parvo from the Latin 'parvis' for small. And he suggested that this group of small DNA viruses be designated the parvoviruses. Very small, seems reasonable.
Erin Allmann Updyke	Yeah.
Erin Welsh	But somehow this seemingly innocuous, reasonable suggestion got a whole lot of people upset. Like I saw the phrase, quote, "somewhat rancorous debate" used to describe it.
Erin Allmann Updyke	Interesting.
Erin Welsh	Yeah. And so on one side was the pro parvovirus and the other side was pro picodnavirus, kind of like in parallel with picornaviruses, small RNA viruses. But then like you have picornaviruses and picodnaviruses, like all you have to do is have one typo.
Erin Allmann Updyke	Mess up the D for the R. Also picodna sounds silly.
Erin Welsh	Well I mean I know. But I mean if it had been that, we wouldn't think it sounded silly today.
Erin Allmann Updyke	I would still think it sounds silly. I'm going to stand by that. I'm going to die on that hill.
Erin Welsh	Well in any case, to quote from a paper: "reason and clarity prevailed and the name parvovirus was adopted."
Erin Allmann Updyke	I like that.
Erin Welsh	Throughout the rest of the 1960s and into the 1970s, the Parvovirus family continued to grow one by one with the first human parvoviruses, adenovirus-associated viruses or adeno-associated viruses, AKA AAVs, so-called because they upon adenoviruses for their own replication-
Erin Allmann Updyke	The dependoviruses.

Erin Welsh	The dependoviruses. These were discovered in the mid 1960s.
Erin Allmann Updyke	Oh okay.
Erin Welsh	But, and I know you'll talk more about these later and I'm really excited for that, these were considered, are considered non pathogenic, question mark? We'll see if that stands I guess. But a human pathogenic parvovirus was just around the corner waiting to be identified. In 1975, researchers were evaluating a newly developed test that was used to detect hepatitis B virus in donor serum and they found a different antigen that had like precipitated with this test. And this was definitely not the hepatitis B antigen. And it more closely resembled a parvovirus than a hepatitis virus. So they wrote it up, a new human parvovirus that seemed to infect a not small proportion of samples that they tested but whose pathogenicity was totally unknown. And I feel like, okay, this does happen from time to time and I know we've talked about it on the podcast before but it does seem uncommon for a pathogen to be discovered before... Not discovered, but like the pathogen was discovered not in association with a particular disease.
Erin Allmann Updyke	Right, like completely independently of.
Erin Welsh	Yeah.
Erin Allmann Updyke	I don't think that that happens very often, at least from what we've talked about on the podcast. But it is really interesting and I feel like in this case kind of makes sense.
Erin Welsh	Yes.
Erin Allmann Updyke	Yeah.
Erin Welsh	For sure.
Erin Allmann Updyke	Yeah.
Erin Welsh	So this virus would become known as B19, which the name allegedly comes from the fact that the virus was found in specimen 19 of panel B.
Erin Allmann Updyke	That's so boring. But logical.
Erin Welsh	Yeah. Now that parvovirus B19 was identified, all that was left to do is find out like did it make people sick? What did it make people sick with?
Erin Allmann Updyke	Yeah.
Erin Welsh	So Erin, you mentioned aplastic crisis in people with sickle cell anemia and many other types of blood disorders. Instances of aplastic crisis often happen in families concurrently and are often preceded by symptoms of viral infection. And so for decades, physicians have thought okay, maybe it's triggered by some sort of infectious agent but we just don't know what it is. Then in the early 1980s, researchers found parvovirus B19 or antibodies to parvovirus B19 in the serum of people with sickle cell anemia who were experiencing aplastic crises. And the evidence that this virus was the principal cause of aplastic crisis as well as hemolytic anemia began to mount. But I love that still it's like we're finding the most severe manifestations first for this.

Erin Allmann Updyke	Yeah.
Erin Welsh	And not like literally the most common cause.
Erin Allmann Updyke	Right.
Erin Welsh	Or the most common manifestation. But making the link between B19 and the most common and often mild manifestation did happen like shortly after. So researchers were finding B19 in simultaneous outbreaks of aplastic crises and erythema infectiosum. And then they were like okay, let's look for just in erythema infectiosum some in children. And of course they found the virus again. As you mentioned, erythema infectiosum is also called fifth disease.
Erin Allmann Updyke	I love this.
Erin Welsh	A brief history.
Erin Allmann Updyke	I love this, I love it so much. I don't know why because it's silly.
Erin Welsh	It is silly.
Erin Allmann Updyke	But I really like it.
Erin Welsh	So silly. It never would have occurred to me that this was the reason why it was called this.
Erin Allmann Updyke	Yeah.
Erin Welsh	Like it's just, what? Okay, so the earliest possible mention of this common infection of childhood comes from the late 1700s, early 1800s with the description of a disease called rubeola sine catarrho. So it wasn't called fifth disease then.
Erin Allmann Updyke	Right.
Erin Welsh	And that seems to be debated whether it was actually fifth disease. But whatever, the first real reference to fifth disease or erythema infectiosum comes from 1899 when Tschamer described a childhood rash characterized by the slapped cheek appearance. The disease came to be known in western Europe as erythema infectiosum and then in 1905, fifth disease, to distinguish it from the other four rashy illnesses common in childhood: measles, scarlet fever, rubella, and epidemic pseudo-scarlatina, Dukes' disease, which is a variant of scarlet fever related to staphylococcal exotoxin.
Erin Allmann Updyke	Yeah. Apparently people are now like Dukes' disease doesn't exist, fourths is not real. And now there's also a sixth disease, roseola.
Erin Welsh	Okay. But are people still using one, two, like first, second, third, fourth?
Erin Allmann Updyke	So first, second, third, no.
Erin Welsh	Okay.
Erin Allmann Updyke	Fourths, no, I have never heard anybody use. But fifth, sixth, yes.

Erin Welsh	I can't get over it. So yeah, erythema infectiosum B19, whatever, that was fifth. It seems like the most confusing naming system because not only do you have to remember the order... Like it's just why? Yeah.
Erin Allmann Updyke	Well it's also in part because we now have vaccines against measles, we don't get scarlet fever because we can treat bacterial infections, rubella we also have a vaccine against. So really it's just fifth that's left and then yeah, roseola as well.
Erin Welsh	But still like even pre vaccines, a kid would come in and you would go oh that's measles. Oh wait, no, that's first or is that second? I don't know. Like you know what I mean?
Erin Allmann Updyke	Well wasn't it more just like oh yeah, this rash is first, this rash is second, this rash is third?
Erin Welsh	I mean maybe there is a method to the order of these. But I feel strongly opposed.
Erin Allmann Updyke	Anyways.
Erin Welsh	Well anyway, over the first half of the 20th century people would have plenty of reason at least to remember the name fifth disease because it grew more and more common. So one paper said, quote: "Fifth disease is now annoyingly familiar to pediatricians, school administrators, and public health officials throughout the United States." End quote.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah. It was clear that it was an infectious disease of some sort, contagious just given the nature of outbreaks. But the route of transmission and the causative agent, parvovirus B19, wasn't linked to it until like 1983-1984 which is kind of amazing.
Erin Allmann Updyke	Wow. Yeah.
Erin Welsh	Yeah. And it took another 20 or so years after that 30 years since the discovery of B19 that another human parvovirus was discovered. So we're still very much in an active area of research and discovery with human parvoviruses. But these are only one branch of this big Parvovirus family, arguably not even the most famous branch. So should we get into the famous one?
Erin Allmann Updyke	Let's.
Erin Welsh	Okay. Throughout the 1960s and into the 1970s, additional parvoviruses were isolated from new animal species and the known host ranges of parvoviruses were expanding, like feline panleukopenia virus which was also found in mink and raccoons. But despite the creeping realization that parvoviruses were A) globally distributed, and B) that the name of a specific virus, like raccoon parvovirus for example, might not capture the full host range of that virus. The public I think for the most part was unfamiliar with this new group of pathogens. Maybe, maybe feline panleukopenia virus but that's it. Until 1978.
Erin Allmann Updyke	Uh oh.

Erin Welsh	When blurbs about a deadly new disease in dogs began popping up in newspapers. First small little paragraphs on like page 12 or whatever but later, as the extensive spread of this disease became apparent, these articles began showing up in countries around the world simultaneously, making headline news. From an article in the Schenectady Gazette on May 27th, 1978, quote: "A serious viral disease affecting dogs has been reported to have reached this area. A representative of the capital district Veterinary Medical Society said the virus has been identified as belonging to the Coronavirus group."
Erin Allmann Updyke	Ooh.
Erin Welsh	Yeah. "It causes acute gastroenteritis, exhibiting vomiting, and several hemorrhagic diarrhea, resulting in severe dehydration and an imbalance of the dog's electrolytes which leads to death. The Veterinary Society recommends that any dog exhibiting symptoms be immediately taken to a veterinarian for treatment, especially dogs who have been to dog shows or among other groups of dogs such as at classes, etc. The progress of the disease and its serious effect on the dogs is extremely rapid after the first sign of symptoms. Dogs have died within 12 hours. According to a report in the American Kennel Gazette Purebred Dogs magazine's April 1978 issue, the problem with this virus became widely known in February following a specialty show sponsored by a national parent club and it has rapidly spread throughout the country since then." End quote. Long quote. Yeah. I found it very like jarring to see Coronaviruses suggested. Obviously it wasn't a Coronavirus, it was a Parvovirus but I saw that and my heart went (gasp).
Erin Allmann Updyke	I know, same. Another one, no! Please!
Erin Welsh	Yeah, it gave me this little jolt of anxiety. But yeah, so his is one of the first descriptions of parvovirus. And so I want to read some snippets from later news articles to kind of trace the spread of parvo and awareness of it. That's kind of fun, like history through the headlines.
Erin Allmann Updyke	Yeah.
Erin Welsh	I don't know. This is from a Canadian press article from October 25th, 1978.
Erin Allmann Updyke	Okay.
Erin Welsh	Titled 'Virus Kills Dog in Five Days'. Quote: "Dog owners are being warned to watch for signs of a new virus which can kill a healthy animal in five days. Veterinarians say they don't know much yet about the virus called enteritis, except that it is an intestinal infection and appears to dehydrate a dog, mainly through vomiting and diarrhea. Enteritis has been found from the Maritimes to Saskatchewan and is reported to be widespread in the United States. It does not pose a threat to other animals or to humans. Gary Thompson, a pathologist at the University of Guelph, said the problem first appeared among show and kennel dogs but now has shown up among dogs who get no further than their own neighborhood." End quote.
Erin Allmann Updyke	No further than their own neighborhood.
Erin Welsh	I know.
Erin Allmann Updyke	Yeah.
Erin Welsh	It's really scary to like read about the spread.
Erin Allmann Updyke	Yeah.

Erin Welsh	A few months later in January 1979, there's an article from the Associated Press titled, quote, 'New Virus Infects Dogs, Cats May Be to Blame'. End quote.
Erin Allmann Updyke	Oh my gosh, so rude.
Erin Welsh	Right? And this article mentions that scientists are calling the virus canine parvovirus and that it is similar to quote unquote "feline distemper", AKA feline panleukopenia, which is also confusingly called cat plague. It's just like what?
Erin Allmann Updyke	Why do you have to have so many names?
Erin Welsh	I know. Also distemper is like a different thing entirely.
Erin Allmann Updyke	It's a completely different thing. We'll do it someday, I swear.
Erin Welsh	We will, yeah. It's been on our list, yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	But this was clearly not the same exact virus as feline panleukopenia virus since A) this is like the first time that people were seeing it in dogs, and also there were studies from the 1960s showing that experimental infection of dogs with feline panleukopenia virus were unsuccessful, like the dogs didn't get infected. Nor was it the minute virus of canines, I'm assuming it's my-noot, not min-it.
Erin Allmann Updyke	Yeah. I think it's my-noot because they're little viruses.
Erin Welsh	They're little viruses. Dude, I was like reading it and I was like oh wait, I guess I never considered.
Erin Allmann Updyke	Dude, English is rough.
Erin Welsh	Right?
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. But the minute virus of canines is now called canine parvovirus type 1 and that was discovered in 1967 and not really considered to be of great concern. Like it did seem to possibly cause infertility and pregnancy loss in dogs but not enteritis or this super high mortality. From its first identification and description as quote unquote "show dog disease" which was what it was called in its early days to canine parvovirus, that took less than a year. And another big development was not far behind, a vaccine. Once researchers made the link between this new deadly canine parvovirus and feline panleukopenia virus, the next natural step was to wonder whether the vaccine for feline panleukopenia virus, which had been developed in the late 1960s, would work on this new virus. Seemed like they're related, was worth a shot. The answer can be found in another news article title from March 1980, again by the Canadian press. Quote: 'Cat Vaccine Helps Quell Dog Disease'. End quote.
Erin Allmann Updyke	A full 180, I love it.

Erin Welsh	I know. I do have more from that article. Quote: "Some Canadian veterinarians, in an effort to quell a disease that killed an estimated 1000 dogs in Canada last year, have turned to an unlikely source for help. They're using a cat vaccine which although not yet licensed for use in Canada has met with success and is licensed for use in the United States." End quote.
Erin Allmann Updyke	An unlikely source, a cat vaccine.
Erin Welsh	Actually it's like fairly likely.
Erin Allmann Updyke	Very likely. I love it though.
Erin Welsh	But that's okay. So this was excellent news, right? Especially since the this new canine parvo virus was starting to show signs of being able to infect cats. But where did it come from? Were cats to blame?
Erin Allmann Updyke	No.
Erin Welsh	And so, okay, we have this vaccine, control is possible, but we have a lot of unanswered questions about the origins of canine parvovirus. And so now I want to get into a bit of the history of canine parvovirus type 2, I should say, not as the general public was reading about it like over coffee and cereal but as the virologist and evolutionary biologists pieced together using molecular clues.
Erin Allmann Updyke	Love it.
Erin Welsh	The canine parvovirus that began making headlines around the world in 1978 was, like I mentioned, the second canine parvovirus to be identified. Hence the type 2 attached to its name. Most people call it canine parvovirus because it is like the one.
Erin Allmann Updyke	The one.
Erin Welsh	But anyway.
Erin Allmann Updyke	It's number two.
Erin Welsh	It's number two. And canine parvovirus type 2 did not evolve from the minute virus of canines, AKA canine parvovirus type 1. And it probably comes as no surprise that 1978 was certainly not the first year that it began circulating in dogs. Researchers tested sera from dogs from 1974 and 1976 and found antibodies to the virus. And it's pretty amazing, maybe not surprising for this COVID world, that within a few years this virus had become global. A true pandemic virus. Like yes, it had been circulating but I think that the earliest signs were 1974-1976.
Erin Allmann Updyke	Wow.
Erin Welsh	And then it was global.
Erin Allmann Updyke	It's just, I feel like I don't know why I feel this way but it feels especially impressive that it's dogs and then it spread. But I guess like wild animals. Yeah, I don't know.
Erin Welsh	Yeah. No, and I think actually that aspect of it was really concerning to a lot of people.

Erin Allmann Updyke	Yeah.
Erin Welsh	Because all these countries have specific quarantine restrictions.
Erin Allmann Updyke	Right.
Erin Welsh	And like legal limits on can you bring a dog in here? Can you bring this animal? How many animals can you bring in? Like the contact, signs of disease, steps. Like how did this happen?
Erin Allmann Updyke	Yeah.
Erin Welsh	And I'm not going to talk about it from like a disease control perspective but that is something that I think still people are making sure, like where were the cracks in the system?
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. But anyway, so once this virus had become pandemic, it underwent some genetic tweaking to reach its full potential, as pandemic viruses do. A few amino acid changes here and there led to a new genetic variant called parvovirus type 2a which emerged in 1979, so just like a year after sort of the first rumblings in newspapers and so on. And in a short time, just a couple of years really, parvovirus type 2a completely replaced parvovirus type 2.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah. Since then there have been a few more variants like B and C and so on and I'm not going to get into those. Type 2a was definitely, from a pandemic virus perspective, a level up from type 2. Not only was it better adapted to its canine hosts, it also had an expanded host range, able to infect cats and wild carnivores. And it seemed deadlier. After a decline in cases of canine parvovirus in like 1980-1981, as herd immunity kind of slowed transmission a bit, things exploded again in 1981-1982. But this time the disease seemed more severe. Quote: "Pups collapsed suddenly in a shock-like state and died with or without enteric signs. Many pups also developed an acute rapidly progressing illness with exceptionally severe hemorrhagic enteritis that was not commonly seen in the initial outbreaks." End quote.
Erin Allmann Updyke	Goodness.
Erin Welsh	Yeah. Fortunately though another improved vaccine was developed pretty quickly. But the sudden shift with a new deadly variant was obviously really concerning.
Erin Allmann Updyke	Yeah.
Erin Welsh	Because it kind of begged the question like okay, what next?
Erin Allmann Updyke	Yeah.

Erin Welsh	Would this virus keep evolving until it could escape a vaccine? Until it can infect other animals outside of its existing host range? Could that eventually include humans? And as always with this podcast, to understand where we might be going, we have to look back at where we came from. Perhaps untangling the origins of canine parvovirus type 2 would help researchers to predict whether or not this virus was likely to expand its host range beyond what currently existed. Initially when canine parvovirus type 2 first appeared, most scientists thought it had jumped hosts from cats, the feline panleukopenia virus evolving to infect dogs. And maybe even it was like the vaccine strain of that virus that had sort of turned into a virus capable of infecting dogs. But it doesn't have a whole lot of support and it seems actually unlikely. So first, canine parvovirus type 2 was unrelated to those vaccine strains.
Erin Allmann Updyke	Well that's a big fat no then.
Erin Welsh	That's a big fat no. Second, despite the long history of cats and dogs being in proximity, this was the first detected instance of this virus or another kind of similar virus hopping from one species to the other. At least that we know of. Of course, there's always that hedge. But the third reason I think is the strongest, which is that intermediate viruses between feline panleukopenia virus and canine parvovirus type 2 have not been detected in domestic cat or dog populations. And that's what we would expect to see if the virus evolved from cats to infect dogs. We would see those in between strains. So canine parvovirus type 2 is seen as a host range variant of feline parvovirus. So if it didn't come from cats, like where did it come from? How is that possible?
Erin Allmann Updyke	Yeah.
Erin Welsh	Well the answer is a different host range variant of feline panleukopenia virus. So feline panleukopenia virus is actually comprised of a bunch of strains of virus which can infect other hosts besides cats, including mink, raccoons, and foxes. And so maybe this taxonomy is, like I read a paper about like the history of the taxonomy of parvoviruses but it was from 2008, so maybe this is a little bit out of date. But in any case, that was my understanding of the organization of these viruses.
Erin Allmann Updyke	Got it.
Erin Welsh	Yeah. So researchers think that canine parvovirus type 2 may have evolved from one of those feline panleukopenia virus variants. So like dogs somehow got into contact with raccoons, mink, foxes, whatever.
Erin Allmann Updyke	Foxes, raccoons.
Erin Welsh	And then that virus infected dogs and then yeah.
Erin Allmann Updyke	I feel like this just shows the problems with the way that we name things and the way that we name viruses.
Erin Welsh	For sure.
Erin Allmann Updyke	Because the parvoviruses especially seem like what a mess.
Erin Welsh	What a mess. And it's clearly named after the first animal that it was detected in.

Erin Allmann Updyke	Right. Which is just what? And also why? This one is called panleukopenia virus and then this one is called parvovirus and then this one is called something else. And I'm just like stop it.
Erin Welsh	I know.
Erin Allmann Updyke	Stop.
Erin Welsh	Well.
Erin Allmann Updyke	Anyways.
Erin Welsh	Anyways.
Erin Allmann Updyke	It's just me.
Erin Welsh	No, it's not.
Erin Allmann Updyke	Complaining.
Erin Welsh	It's definitely not just you. And so I don't think that, at least I couldn't get a clear answer on what they think that animal was that was the source of sort of like the initial spillover I guess.
Erin Allmann Updyke	But like don't blame the cats.
Erin Welsh	Don't blame the cats.
Erin Allmann Updyke	Okay.
Erin Welsh	We can blame the raccoons though because it does seem, there is some research to suggest that once canine parvovirus type 2 emerged from whatever feline panleukopenia virus variant, it then further evolved possibly in raccoons. So like spilled over from dogs into raccoons and then kind of evolved, tweaked things a little bit more, to become canine parvovirus type 2a.
Erin Allmann Updyke	Ah.
Erin Welsh	Yeah. So the parvovirus that infects raccoons seems to fall between canine parvovirus type 2 and type 2a.
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	Okay. This is like a lot of nitty gritty and I'm done. So you're welcome. But the bottom line is that we don't know exactly which animal feline panleukopenia virus jumped from into dogs, probably not cats. And the other bottom line is that canine parvovirus type 2 evolved into type 2a possibly with the help of raccoons.
Erin Allmann Updyke	Okay.
Erin Welsh	But why is all this nitty gritty important? Why am I like stumbling over the taxonomy of all of this? Because any time a pandemic virus emerges, we want to know how it happened.

Erin Allmann Updyke	Yeah.
Erin Welsh	We want to be able to trace that road map to understand how a virus mutated, how it was able to come into contact with another host, AKA spillover, how it continued to evolve to infect that host, and how it was able to rapidly spread around the world, looking at both the biological properties of a virus as well as the societal or political or infrastructural properties that allowed the pandemic to happen. I also think that the canine parvovirus pandemic is especially interesting given that it's a single stranded DNA virus, where we tend to think of RNA viruses as the ones of pandemic potential because of their high rate of mutation. But hey, don't forget about the single strand of DNA viruses.
Erin Allmann Updyke	Let's not.
Erin Welsh	Yeah. So clearly the story of parvoviruses is very much ongoing. We're finding new parvoviruses or variants of existing parvoviruses in new species and canine parvovirus very much remains a threat to domestic dogs and cats and wild animal populations around the world. But before we get into where we are with the human side of parvoviruses today, we wanted to bring on a very special guest who can share some insight from the veterinary side of things.
Erin Allmann Updyke	Yes.
Erin Welsh	We'll take a short break here and then jump in.
TPWKY	(transition theme)
Erin Welsh	So far in this episode we've covered a lot of ground but what we haven't gotten into, and this is probably especially obvious to those dog and cat owners out there, is the animal side of things. Like we've mentioned, parvoviruses are quite a diverse group and if we went into each and every one of them, we'd be here all day and probably tomorrow too. So instead what we're going to do is spend a bit more time on two parvoviruses in particular, canine parvovirus and feline panleukopenia virus. And to help us do that, we've enlisted the help of the amazing Dr. Steph Horgan Smith. Dr. Steph graduated from Ontario Veterinary College in 2011 and now owns and runs a veterinary hospital in York region in Ontario, Canada. And we are so excited to chat with her today. And just to note, this interview was recorded on November 20th, 2023. Dr. Steph, thank you so much for joining me today. I can't wait to talk about parvoviruses from the veterinary side of things.
Steph Horgan Smith	Thank you for having me, I'm very excited.
Erin Welsh	So let's just jump right into it. We talked a little bit about canine parvovirus throughout the biology and the history but we didn't really get into like what it looks like in dogs. So what are some of the signs and symptoms of infection?
Steph Horgan Smith	So the classic what we see in clinic is with puppies really, it's mostly in puppies. Adult dogs can get it but their immune system is definitely better at fighting it off. So the classic is a puppy that comes in and by the time we see them that they're sick, they're vomiting, they're having some diarrhea, and most of the time that diarrhea is bloody. They're sometimes eating by that point or not, they're pretty sick and flat. So as soon as we get a puppy that's vomiting, diarrhea, we're all testing for parvo. A lot of them are actually pretty painful in their stomach and their intestinal tract just from the virus kind of getting through that area.

Erin Welsh	When we talked about parvo B19, which is one of the viruses that infect humans, we talked about it being spread through respiratory droplets. But that's not the same for dogs. So how is parvo spread between dogs?
Steph Horgan Smith	So in dogs it's actually more fecal-oral. The virus is shed way more in feces and so the virus itself is pretty stable in the environment and will last on surfaces or toys or shoes that have walked through with virus attached and can be spread to other dogs that way. It can be passed in utero sometimes from mum to puppies. But that's I would say not as common, we see it mostly in puppies that are out in the environment and they're catching it that way.
Erin Welsh	Durability. It's pretty dang durable, right?
Steph Horgan Smith	Yes.
Erin Welsh	Like months, even longer?
Steph Horgan Smith	Up to a year in the right conditions.
Erin Welsh	Wow. Okay.
Steph Horgan Smith	So if there's organic material that's still left over, it's going to survive in that organic material. So actually scrubbing cleaning is a big one and making sure that all the organic material is gone. UV rays will actually kill the virus eventually. So indoors, it can stay a long time.
Erin Welsh	We talked a little bit about how one of the newer variants that emerged, well, several decades ago, could also be spread to cats. But what about other animals?
Steph Horgan Smith	So yeah, there are reports, they're not sure if it's a canine parvovirus or feline panleukopenia, which type. But there have been reports in like coyotes, wolves, pumas, bobcats even, and then raccoons and skunks. So all of those animals seem to get some type of parvo. And then separate to the canine and feline parvovirus, porcine parvovirus is a really important virus in pigs and pig production because mostly it actually just causes fetal death. So it changes your litter size. So yeah, there's a vaccine for that also. So at least we can help try and prevent that.
Erin Welsh	Prognosis. So canine parvovirus, obviously a very severe disease. But like what is the prognosis? And how does that vary based on the age of the dog or puppy and other factors like overall health status or breeds or anything like that?
Steph Horgan Smith	Yeah, the younger the puppy, the more susceptible they're going to be to the virus. Because it's infecting those rapidly dividing cells, it runs through the immune system and the bone marrow and infects all their immune cells and then to the GI tract and it just wipes out the villi, all the little intestinal villi that are absorbing all of the puppy's food. So then we basically supportive care, have to just keep that puppy alive until the cells regenerate in that kind of 10-14 day mark where they the new cells grow up from the crypts. That's where survival kind of depends on how young they are, how prone to other complications like hypovolemic shock or low blood sugar because they can't keep up their sugar and stuff.

	And then unfortunately with veterinary medicine, cost comes into it. So what level of care an owner can do, if they can do intensive management in a hospital setting for two weeks, that's pretty pricey. But generally survival is about 90%. It kind of goes down from there, again depending on age of the puppy. But if we have to do outpatient treatment, it can work. But survival is a little bit lower than kind of the ideal gold standard. But obviously not everybody has that much money to keep a puppy in intensive care for two weeks. It's a lot.
Erin Welsh	Right. And treatment is sort of like you said, just supportive. Does that just mean like fluids and monitoring?
Steph Horgan Smith	Yep.
Erin Welsh	Yeah, okay.
Steph Horgan Smith	So that puppy is hooked up to IV fluids, nutritional support, so either a feeding tube or down right into their belly, we do that. They're getting their electrolytes checked all the time to make sure that those are staying normal and supplementing whatever they need. And then keeping them in the hospital, keeping them monitored. That's always been our classic main treatment. There is actually a new monoclonal antibody that has been licensed, that sounds quite exciting. It's showing some really promising quick turnarounds that maybe those puppies won't be as sick for as long, which is amazing in so many ways. So that's really exciting that we might actually have a specific treatment where it's blocking the virus from being able to get into the cells.
Erin Welsh	Whoa.
Steph Horgan Smith	So that's really exciting potentially on the future horizon.
Erin Welsh	That's amazing. Oh that's really cool.
Steph Horgan Smith	Yeah, it's really cool.
Erin Welsh	Oh I love that. In the history section I talked about how canine parvovirus likely evolved from a related parvovirus, one of the host variants of the feline panleukopenia virus. Can you tell me a little bit about that virus and what are some of the signs and symptoms in cats?
Steph Horgan Smith	Yeah. So that one actually is maybe a little bit more similar to the human one because it can be infectious through any body secretion. So saliva or potentially respiratory droplets as well, also can be fecal oral. So it kind of just ranges the whole thing.
Erin Welsh	Anything.
Steph Horgan Smith	Anything. But yeah, that one, again it's going to infect those rapidly dividing cells. We see not as severe gastrointestinal symptoms with cats. What a lot of the time we see is sometimes the queen gets infected, so then vertical transmission to the kittens or very, very young kittens while they're still nursing. One of the like classic symptoms that we learn about and we see sometimes is the virus actually goes and starts affecting their cerebellar development. So that specific part of the brain, kittens are still developing that for like about two weeks after they're born.

	So even if they get infected really young, they can get this cerebellar hyperplasia where it just doesn't develop completely normally. And they'll have these tremors because that's movements and fine movements is part of what the cerebellum helps with. So these kittens will grow up and they'll have these intention tremors probably for life. But if they recover from the virus, then they can survive, they can kind of be normal. But yeah, they get this very specific symptom that you can kind of look at them later and say oh that cat probably had panleukopenia when it was a kitten because it has this very specific intention tremor.
Erin Welsh	Is panleukopenia in kittens as severe as canine parvo is in puppies? Is the prognosis pretty similar?
Steph Horgan Smith	No, I'll say for whatever reason we see it more in extra young kittens, so when they're still nursing. And so unfortunately some of those kittens when they're that young, they kind of just get this fading kitten and some of them will just not survive. And then again with the cerebellar hyperplasia. But we just don't see it as often as we would like a parvo puppy, I think partly because of how we keep cats in general, they're not out in the environment meeting other cats, right. So if they're picking it up, it's because someone in their household has it and hasn't been vaccinated for it. So it's not as widespread as puppies who are seeing other dogs all the time or being introduced to other environments.
Erin Welsh	Okay. So when do puppies and kittens get vaccinated for parvovirus or panleukopenia? And how many rounds of vaccination are there?
Steph Horgan Smith	So luckily it's the same for cats and dogs, so we can talk about it at the same time.
Erin Welsh	Excellent.
Steph Horgan Smith	We start at anywhere between 6-8 weeks to get that vaccine into them. That's where it's a bit tricky depending on the whole situation with mum because if mum is well vaccinated, she's giving those puppies or kittens her maternal antibodies in the milk and they are still active at definitely 6-8 weeks for most of those babies. We start then just in case mum doesn't have great immunity, we want to catch those ones that are not getting immunity from mum. But then we have to re-vaccinate every four weeks up until they're about 16 weeks old.
	At 16 weeks old, mum's maternal antibodies won't be there anymore and we'll be stimulating that puppy or kittens own immune system to fight the virus. It's generally a series of 3-4 vaccinations starting at 6-8 weeks. Parvo is the main reason that most vets will recommend being really careful with where you take your new puppy until they get at least a couple of vaccines into them because parvoviruses can be anywhere, it can be shed and then just left in the environment. So that's the main reason why we have to be careful with where puppies are going and who they're meeting right when they're really young.
Erin Welsh	During COVID, the last 10, 20, 30 years even, we've seen a big upward trend, especially here in the US but I think globally as well, in vaccine hesitancy and anti-vaccine sentiment for like human vaccines. But have you seen something like this as well for people and their pets?

Steph Horgan Smith	Yes, we definitely have clients that are vaccine hesitant and just not 100% sure what the science is and what's going on. But the one thing I will say about parvo vaccination, and especially in dogs but in cats as well, it's really effective, getting those puppies in when they're young and bringing them back every month for that booster vaccine. I couldn't find an actual number when I looked at it but there's very rare breakthrough actual parvovirus infections in dogs that have been fully vaccinated. They do need re-vaccination though, the immunity, we don't know exactly how long it lasts in every dog, their own immune system is going to be different. So we generally do a booster at a year later and then re-vaccinations every 1-3 years after that.
Erin Welsh	So I have one last question for you and it's not about parvovirus but it's instead about this new canine respiratory illness that seems to be popping up throughout the United States, at least all over it's here in the front range in Colorado. What do we know about this infection? And why has it gotten people so concerned?
Steph Horgan Smith	I hate to say but we're not sure yet.
Erin Welsh	It's all right, we say it all the time on the podcast.
Steph Horgan Smith	Yeah. We don't know.
Erin Welsh	We don't know.
Steph Horgan Smith	Yeah, it's been around. There's been reports of some kind of respiratory infection since I would say late spring in different parts of the US. We've been tracking it. I personally haven't seen any reports, I'm up in Ontario, haven't seen too many things here. But it started with is it kennel cough or some type of kennel cough kind of organism that is just not responding to normal treatment? Most of the labs that we use have a pretty extensive respiratory panel. So if we get samples, we can send that out to our labs and try to see all the common stuff is on there, including influenza, Bordetella, parainfluenza, things that cause kennel cough and other common respiratory infections. And it's testing negative for all of those.
	And then it just seems to be unfortunately the dog's own immune system, whether they get this cough and it just lingers but they're okay otherwise. I've heard reports of it lasting for like 6-8 weeks in some dogs and then some unlucky ones it does seem to turn into more of a pneumonia and those dogs are needing, some of them, hospitalization, pretty intensive management to help get them through it. So they haven't really even found what the difference is between those cases, why some dogs are just getting a cough and then some of them are getting quite sick with pneumonia. It's a bit scary that we don't know still what it is.
Erin Welsh	Yeah, for sure. It's very scary. It definitely has echoes of like the early parvovirus news articles. Like there's this mysterious thing that's spreading and we don't know what it is.
Steph Horgan Smith	Yeah. But anyway, well thank you so, so much for taking the time to chat and answer all of our questions about canine parvovirus and panleukopenia virus. I mean I feel like we definitely could have talked for hours and I really, really appreciate it.
Erin Welsh	You're very welcome. I'm glad that I could help and hopefully shed some light on the canine and feline pet side of parvovirus.
TPWKY	(transition theme)

Erin Allmann Updyke	Thank you so much, Dr. Steph, for walking us through that. I love getting to hear about animal diseases from someone who actually knows.
Erin Welsh	Yes. Yeah, totally.
Erin Allmann Updyke	Yeah. I really appreciate it.
Erin Welsh	That was great, thank you.
Erin Allmann Updyke	So let's talk a little bit about where we stand with parvoviruses today.
Erin Welsh	Let's do it.
Erin Allmann Updyke	Again here I'm going to focus on human parvovirus B19, in part because I couldn't find data on the prevalence of feline panleukopenia virus or canine parvovirus 2, except studies that were like this country in these years, you know what I mean? That was like very specific. Like the point is those viruses are everywhere all the time.
Erin Welsh	Yeah.
Erin Allmann Updyke	The end. So for humans, the story is almost exactly the same. I couldn't get a handle on breaking things down much more than letting you know that when we look at serology studies by age, by the time someone is about six years old, anywhere from 2%-15% of kids will have antibodies. But by the time you get to adulthood, over 60% of adults have antibodies to parvo B19. And by the time you get to be geriatric, over 85% of people have antibodies.
Erin Welsh	Okay.
Erin Allmann Updyke	So everyone gets parvo at some point. And there is, at least in temperate regions, seasonal variation in parvovirus infection. So peak incidence tends to be late winter, early spring, which makes sense, that's when a lot of viruses circulate. And like we have seen with other childhood infections, there can be these outbreak years where every 3-4 years or so we'll see an increase in infections overall and they call these epidemic years.
Erin Welsh	Okay.
Erin Allmann Updyke	Now during these outbreaks and these epidemic years, we see that about 10% of all the cases will occur among children that are about five years old and 70% of them will be in kids between age 5-15 and then 20% of cases are in people older than 15. So that's like the age breakdown, where the youngest of kids might be a little bit more protected and it's that middle school age kids that are the highest risk for infection.
Erin Welsh	Okay.
Erin Allmann Updyke	Now what I wanted to be able to get a handle on is like what percentage of kids or people who get infected will have more severe manifestations like aplastic crisis.
Erin Welsh	Yeah.
Erin Allmann Updyke	I don't know.

Erin Welsh	Okay.
Erin Allmann Updyke	I don't know.
Erin Welsh	I mean cool.
Erin Allmann Updyke	But that is parvo B19 epidemiology. When I tried to get a handle on where we stand in terms of vaccines or treatments, I also didn't find very much. It was kind of disappointing. I found one paper that was talking about a few different vaccines that are kind of in trials which are made from these what are called virus-like particles. It's kind of weird and interesting. Basically like parvo proteins, parvovirus proteins do weird stuff essentially and form these little nuggets that look like viruses. And so people are taking these and trying to use them to make vaccines. I don't know, I don't know a lot of details about it. But apparently they haven't worked great so far in clinical trials. And so a paper that I found which is old now, like 2013, was trying to make different virus-like particles that would cause less illness in people and still be able to induce a good immunity. But they were still in animal model stages and I really couldn't find anything more recent. So if someone knows of more actual parvo B19 vaccine research going on, hit me up. I'd like to know.
Erin Welsh	Okay.
Erin Allmann Updyke	But I have more to talk about, I'm not done.
Erin Welsh	I know, I'm excited.
Erin Allmann Updyke	Because I want to give a shout out to some very important parvo viruses that we haven't talked in detail about. And that is the adeno-associated viruses, the dependoviruses, or AAVs. And these are parvoviruses that can't infect cells without a concomitant co-infection with either an adenovirus or a herpes virus. What?
Erin Welsh	Yeah. I love it.
Erin Allmann Updyke	I love it. We mentioned this concept even like very briefly in our hepatitis B episode.
Erin Welsh	Yep.
Erin Allmann Updyke	Because hepatitis D is a similar virus that requires the presence of hepatitis B persistently to be able to cause infection because it needs hepatitis B to leave the cells or whatever. So okay, these AAVs are super tiny parvoviruses and their genomes essentially, they're very simple. They encode for a capsid protein and a couple of other proteins and that's it. They're really basic. And they generally are considered to everyone's knowledge, asterisk, to not cause any disease in humans. But they infect humans quite readily in the presence of a helper virus. They're really efficient at getting into our cells and replicating and specifically integrating into our genome and laying latent, particularly in this one specific place on chromosome 19. At least when we're talking about wild type AAV. And this characteristic, being able to infect our cells and get into our DNA and hang out there, makes them an ideal candidate for gene therapy. Phenomenal.
Erin Welsh	Amazing.

Erin Allmann Updyke	So AAVs have actually been the kind of leading platform for gene therapy thus far. And I think I've probably said the words adeno-associated virus on this podcast in the past because additionally one of the COVID virus vaccines, it is an adeno-associated virus vector vaccine. But I didn't even really know what that meant before researching this episode. So essentially you can make recombinant AAVs that use this same capsid protein but you can replace the rest of their tiny little genome with genes that code for whatever proteins you want. And now you have this really efficient little machine that, yeah, needs some help from an adenovirus to get into our cells but then can be in our cells churning out whatever proteins we asked it to make and not causing any disease. That's pretty cool.
Erin Welsh	It's like a whole new world. I just, I love it.
Erin Allmann Updyke	Yeah. There are already gene therapy platforms that are out there that are being used for things like spinal muscular atrophy, some forms of congenital blindness, and there are more in the pipeline for so many genetic conditions. It's phenomenal. You can read a lot more about it. I have a few papers but there's even more out there. But one last thing, there was an asterisk.
Erin Welsh	Yeah, I saw that.
Erin Allmann Updyke	Historically this adeno-associated virus or adeno-associated viruses in general have never been shown to cause disease. But just these past years, in 2022, the end of 2021, 2022, and 2023, it has recently been shown that AAV2 has been associated with some pretty severe outbreaks of hepatitis among kids. So in like 35 different countries, several hundred kids got very super sick and in some cases died. And after some really intense investigation and these extensive case control studies in a few different countries, what they have found so far is that AAV2 is at least associated in some ways with these outbreaks. But what's really interesting is that we don't know still if there's a causative link as to why kids got so sick or whether AAV2 existing was a marker of a primary adenovirus infection. But we don't often see as severe disease with primary adenovirus infections.
	One really interesting part of this story, and I know this is such an abbreviated story, but one part of it is that some thought was that this all happened kind of just post pandemic, right. Like obviously COVID still exists y'all. But once all of the restrictions from COVID were lifted, one hypothesis is that susceptible kids may have had a higher chance at all of a sudden at the same time being exposed to both an adenovirus and AAV2 at the same time that caused this synchronized wave of severe disease, where previously kids might have been exposed to one virus and then another and then another on a larger time scale, if that makes sense.
Erin Welsh	Right. Interesting.
Erin Allmann Updyke	So this is very early, these papers were just published a few months ago.
Erin Welsh	Yeah.
Erin Allmann Updyke	But it's really interesting because it shows just how much we still don't know about so many viruses that exist.
Erin Welsh	Yeah. And like down the line repercussions.
Erin Allmann Updyke	Yeah, yeah.
Erin Welsh	Yeah.

Erin Allmann Updyke	It's fascinating.
Erin Welsh	Yeah.
Erin Allmann Updyke	But again, you can read so much more. I've got papers. We've got sources for you.
Erin Welsh	Let us go through some of those sources. Erin, I have so many for this.
Erin Allmann Updyke	Really?
Erin Welsh	I kept finding little snippets here and there and just trying to piece through it all, whatever. I'll just name a few of them right now and then the rest I'll post. So there's one by Carmichael from 2005 called 'An annotated historical account of canine parvovirus'. By Parrish and Kawaoka from 2005, 'The origins of new pandemic viruses, the acquisition of new host ranges'. And by Thurn from 1988, 'Human parvovirus B19: Historical and clinical review'.
Erin Allmann Updyke	Love it. Actually most of my papers were kind of old for this but they were solid. So there was a paper called 'Human parvovirus B19' in Clinical Microbiology Reviews from all the way back in 2002.
Erin Welsh	Wow.
Erin Allmann Updyke	And another one on parvo B19 from the New England Journal of Medicine from 2004. A few others on more specific aspects like parvo in pregnancy, etc. And then a bunch on the AAVs, both as platforms for gene therapy and this association with hepatitis, etc. Plus I threw in a few on canine and feline parvoviruses as well. You can find all of the sources from this episode and all of our episodes on our website thispodcastwillkillyou.com and all of our social media channels.
Erin Welsh	Thank you again so much to Eliza for sharing your story with us.
Erin Allmann Updyke	Thank you again, Dr. Steph, for providing our veterinary expertise for this episode.
Erin Welsh	Thank you to Bloodmobile for providing the music for this episode and all of our episodes.
Erin Allmann Updyke	Thank you to Tom Breyfogle for the incredible audio mixing.
Erin Welsh	Thank you to Exactly Right.
Erin Allmann Updyke	And we have so many people to thank, especially thank you, listeners. Thanks for listening to all these thank yous.
Erin Welsh	Yes. I hope you learn more about parvoviruses. Yeah.
Erin Allmann Updyke	Yeah, yeah.
Erin Welsh	And a special thank you as always to our wonderful, generous, amazing patrons. Your support really means the world to us.

Erin Allmann Updyke	It does. We love it. Thank you.
Erin Welsh	Well until next time, wash your hands.
Erin Allmann Updyke	You filthy animals!