

TPWKY

This is Exactly Right.

Erin Welsh

"She began to feel feverish and achy and believed she had the flu. When the aches and pains grew more severe, she sought medical attention and was hospitalized before the respiratory symptoms appeared. She speaks of drowning, of perceiving a great weight on her chest and a great exhaustion. She speaks of wanting to see her children one last time and then of her mixed emotions about being sedated. 'I wanted to live,' she said. 'Of course I did, I didn't want to leave my family. They needed me. But I was just so tired, I was just so tired.' She did survive and sometimes she says she still grows so weary that she realized she'll never fully recover from her encounter with the virus. She says, 'It's the most horrible feeling. The tubes, the liquid in your lungs, the choking. You don't wanna die that way but you know you can't live that way either.'"

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

Shoot.

Erin Welsh

Yeah.

Erin Allmann Updyke

Dang. Heavy.

Erin Welsh

This is a bad one.

Erin Allmann Updyke

(singing) Every episode!

Erin Welsh

(laughs) Hello.

Erin Allmann Updyke

Hello.

Erin Welsh

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

Yeah, it is.

Erin Welsh

And this week we're talking all about hantaviruses.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so what you just heard was an excerpt from the book 'Of Mice, Men, and Microbes' which goes into the history of hantaviruses with particular focus on the Sin Nombre outbreak which you'll hear a lot more about in a bit.

Erin Allmann Updyke

Yeah. Cool.

Erin Welsh

Okay. Cool.

Erin Allmann Updyke

So let's get into our business.

Erin Welsh	And our business is?
Erin Allmann Updyke	Quarantini time.
Erin Welsh	Quarantinis. What are we drinking this week?
Erin Allmann Updyke	This week we're drinking The Mouse Trap.
Erin Welsh	It is so cool.
Erin Allmann Updyke	It's unbelievably delicious.
Erin Welsh	It has tequila-
Erin Allmann Updyke	Which is arguably the best liquor.
Erin Welsh	I'm not even gonna, that's... I'm immediately cutting that.
Erin Allmann Updyke	(laughs)
Erin Welsh	It could be argued but I think I have a different one in mind.
Erin Allmann Updyke	All right, anyways.
Erin Welsh	It's also got rosemary simple syrup, blood orange juice, lime juice, and a splash of soda water. So we will post the recipe for this quarantini, The Mouse Trap, as well as the placeborita on all of our social media channels.
Erin Allmann Updyke	Which is our nonalcoholic version of our quarantini. You'll be able to find the full recipes on our website as well as @thispodcastwillkillyou on Facebook and Instagram and @TPWKY on Twitter.
Erin Welsh	Okay. So I'm very excited for this episode and I know that I say that every episode and I genuinely mean it every episode.
Erin Allmann Updyke	That's because every episode is exciting, it's something new and we learn stuff while we're researching it and then we get to learn more stuff as we listen to each other teach us the things that we didn't know.
Erin Welsh	Let's get started! Tell me about the biology, Erin.
Erin Allmann Updyke	Okay, I'd love to.
TPWKY	(transition theme)
Erin Allmann Updyke	Hantavirus is aka orthohantaviruses. This is a group of viruses, they are single-stranded, they are in an envelope, and they're an RNA virus. You just learned so much.

Erin Welsh	Okay. And what is the 'ortho' part of all that?
Erin Allmann Updyke	I don't know why they changed the name from hantaviruses to orthohantaviruses at some point recently.
Erin Welsh	What?
Erin Allmann Updyke	The phylogeny of this is confusing to me, sometimes they call it the order Bunyvirales, sometimes they call that the family Bunyviridae. Who knows? If you see the word 'bunyavirus' that is a larger group of viruses that includes the hantaviruses. It also includes a lot of other viruses which cause horrible diseases, including Crimean Congo hemorrhagic fever, Rift Valley Fever, several different encephalitis viruses, and so many more.
Erin Welsh	So this is a pretty gnarly family, group, order of viruses.
Erin Allmann Updyke	Yes. It's a gnarly group. It's a gnarly group of viruses that love to infect humans, which not all virus groups love to do that. These ones do. What's interesting about hantaviruses specifically in this family or order or whatever is that they're the only ones for the most part that aren't transmitted by ticks and mosquitoes. So most of the other viruses in this Bunyviridae or Bunyvirales group are transmitted by ticks or mosquitoes, not hantaviruses.
Erin Welsh	Right.
Erin Allmann Updyke	So hantaviruses, in contrast, are transmitted through rodent excrement.
Erin Welsh	Yummy.
Erin Allmann Updyke	It's so fun. What I love is that, so arthropod-borne viruses that are transmitted by ticks and mosquitoes are often called arboviruses, you could call these 'roboviruses'.
Erin Welsh	(laughs)
Erin Allmann Updyke	Rodent-borne. I love it. Anyways.
Erin Welsh	Very sci-fi.
Erin Allmann Updyke	It's very sci-fi. So hantaviruses are transmitted by rodent excrement. What does that mean? It means that these viruses live their life cycle inside of rodents and they're naturally found in rodent populations honestly across the globe. Various different hantaviruses are found in almost every continent in different rodent species. And they circulate in these rodent populations really without causing a lot of damage. They don't harm the rodent populations really.
Erin Welsh	They kind of do.
Erin Allmann Updyke	Okay.
Erin Welsh	Overwintering survival.

Erin Allmann Updyke

Okay, so that counts. But they don't cause the kind of damage that they cause in humans in general in the rodent populations.

Erin Welsh

No, no.

Erin Allmann Updyke

Which suggests that they have sort of a history, like these are the groups of animals that they are sort of evolved to infect, if that makes sense. So in humans, hantaviruses - of which there are a number, and I'll tell you the names of a bunch of them - they cause two major diseases, sort of two distinct groups of illnesses. The first that you might have heard of is called hantavirus pulmonary syndrome. You've heard of that, Erin.

Erin Welsh

Of course.

Erin Allmann Updyke

And the other is called hemorrhagic fever with renal syndrome.

Erin Welsh

That sounds quite bad.

Erin Allmann Updyke

Right? If you had to guess which one of that sounds the worst?

Erin Welsh

I mean hemorrhagic fever I would automatically say, oh my gosh.

Erin Allmann Updyke

That sounds terrible.

Erin Welsh

Right but knowing hantaviruses and knowing this leading question.

Erin Allmann Updyke

Knowing hantaviruses. So yes, it's actually hantavirus pulmonary syndrome that is the more severe of the two disorders. So what I'm gonna do is I'm gonna go through each of these two disorders, hantavirus pulmonary syndrome and hemorrhagic fever with renal syndrome, talk about what's different about them and then talk about what's similar about them.

Erin Welsh

Cool.

Erin Allmann Updyke

Sounds good? Cool.

Erin Welsh

Sounds great.

Erin Allmann Updyke

So hantavirus pulmonary syndrome, we'll start with that cause it's my personal favorite, and it's the one that-

Erin Welsh

(laughs)

Erin Allmann Updyke

It's the one that people are probably more familiar with if you live in the United States because this is caused primarily by Sin Nombre virus. And this is the hantavirus that exists in the United States in the southwest. It's hosted or its reservoir host I the deer mouse.

Erin Welsh

I like the term 'hosted' actually.

Erin Allmann Updyke

(laughs) It's hosted by the lovely deer mouse. And it causes a disease that has a death rate of 38-50%.

Erin Welsh

That's enormous.

Erin Allmann Updyke

It's enormous, it's a very, very scary illness. So here's how it happens. There's four different phases of HPS, hantavirus pulmonary syndrome.

Erin Welsh

Okay.

Erin Allmann Updyke

It starts after an incubation period of between 9-24 days, usually about 1-5 weeks which is a pretty wide incubation period, and that's again the time from when you're infected to the time when you first show symptoms. And so after that incubation period, the first phase is the febrile phase. Febrile means fever, so as you can guess this starts with a fever. You'll also have muscle aches and malaise, you'll probably have a headache, some dizziness, kind of like you have the flu, you might even have some nausea or abdominal pain. But what's important is that you don't have upper respiratory symptoms like you would with a cold the flu. So no stuffy nose, no sore throat, things like that. You could end up with a cough at the end of this phase. Now this phase, the febrile phase, lasts between 3-5 days but it could last as long as 12. So again-

Erin Welsh

Is it because... Are these wide-ranging incubation times in certain phases because there are just a relatively low number of cases for comparison or is it just that the virus really is host like individual dependent?

Erin Allmann Updyke

Probably. I think it's probably a combination of both. So hantavirus pulmonary syndrome, there haven't been a ton of cases of this so you're definitely not gonna have wider variation because of that when you have a small sample size, but it's also very likely that your exposure will determine how much virus you're exposed to and then that can have a really huge impact on incubation period.

Erin Welsh

Right.

Erin Allmann Updyke

Yeah.

Erin Welsh

Also I really like, this is just a total side note but 'it started with a fever' would have also been a great name for this podcast.

Erin Allmann Updyke

(laughs) Oh! It would have been! Oh shoot! Oh god, that's a good name. Future podcast.

Erin Welsh

Future podcast.

Erin Allmann Updyke

And the bummer about this first phase is that it's super hard to diagnose because your symptoms are very nondescript and you're about to see that after this phase it gets bad really quick. So phase two is the cardiopulmonary phase. This is the beefy part of the disease and it happens really fast. Within 24-48 hours after these symptoms start, up to 50% of infected people will die.

Erin Welsh

Ooh.

Erin Allmann Updyke

Yeah. So basically you present with shock and pulmonary edema. So let's talk about these. We've talked about shock before. Shock is what happens when for some reason your blood pressure is going to drop and you're not going to get blood perfusion to your tissues, so your organs are gonna start to die because they don't have adequate blood flow. In this case the symptoms that happen are in large part due to what's called vascular permeability which means your blood vessels become leaky, especially the blood vessels in your lungs. So the fluid that's supposed to be in your blood vessels, aka your blood, starts leaking out into the space between your cells in your lungs and that results in what's called pulmonary edema which means fluid on your lungs.

Erin Welsh

Oh so I knew that that's what that meant but I didn't know how that happened. That's very interesting.

Erin Allmann Updyke

Yeah, that's how it happens in this case. Pulmonary edema can happen other ways as well.

Erin Welsh

Ooh I wanna know all the ways.

Erin Allmann Updyke

(laughs) I'm sure we'll have so many diseases to talk about various forms of pulmonary edema. But it's often from fluid leaking out from your blood vessels, it's not always straight-up blood. Like in this case it's often whole blood that's able to get through, sometimes it's just plasma or just the fluid and not like your entire red blood cells and stuff, it just depends on how big the holes that are allowing the leakage are, if that kind of makes sense.

Erin Welsh

That's so interesting.

Erin Allmann Updyke

It's very cool. You can imagine that all of this edema makes it really hard to breathe. It also, because your heart is sort of right inbetween your lungs, makes it hard for your heart to beat and so that's why you end up going into cardiogenic shock which means your heart... The reason that you go into shock is because your heart is not pumping enough blood out.

Erin Welsh

And that's only because it's restricted in space by your lungs filling up with your own fluid/blood?

Erin Allmann Updyke

Yeah and because you're bleeding out into your own body so there's not enough blood getting to your heart, so it's a double-

Erin Welsh

So your blood pressure is just like totally down.

Erin Allmann Updyke

Exactly. Yeah. Yeah, cool right?

Erin Welsh

Mm-hmm.

Erin Allmann Updyke

So this results-

Erin Welsh

This is horrifying.

Erin Allmann Updyke

It's very horrifying. Because of this, cause of all the blood that your leaking out, your blood is then not making it to your other organs, so your kidneys will likely start to fail so you might end up with what's called oliguria which means low urine, few urine. It's not good. And yeah so basically 50% of people are going to die. However the other 50% or sometimes more could be as low as 30% of people who die. So 50-70% of people will then somehow progress to the diuretic phase which is phase 3 of this disease which is when your pulmonary edema clears up, your urine output increases, and the fever and shock resolve.

Erin Welsh

Okay.

Erin Allmann Updyke

Don't ask me exactly how that happens.

Erin Welsh

How?

Erin Allmann Updyke

(laughs) I would love to have a great answer on that, it is unclear to me. If your urine output goes low, that's a very bad sign. If you then all of a sudden start peeing out a lot, that's actually a good sign because it means that somehow your body is try to re-equilibrate and then you're entering the diuretic phase. After that, during what's called the convalescent phase which can last for several months, so this is a very long recovery period, and often people recover fully but it is also possible to have long-term pulmonary symptoms like decreases blood flow in your lungs because of just how much damage has been caused.

Erin Welsh

Okay. Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

And the damage in your lungs is caused by... Like in the blood vessels themselves or what?

Erin Allmann Updyke

Yeah, we'll talk about exactly what causes that, what allows for that blood to leak out in just a second, cause it's a really important part of this disease. So that's HPS, hantavirus pulmonary syndrome. Let's talk about hemorrhagic fever with renal syndrome. So this is the other form of hantavirus which many people, I guess if you live in Europe or Asia this might be what's more familiar to you, if you live in the U.S. you might never have heard of this. This is caused by a number of different hantaviruses including Seoul virus, which was first discovered in Seoul, Korea and is hosted by the Norway rat and the black rat, Hantaan virus, also discovered in Korea which is hosted by the striped field mouse, Puumala - is that how you say that?

Erin Welsh

Mm-hmm, Puumala.

Erin Allmann Updyke

Puumala virus, which is from Finland and hosted by the bank vole, and Dobrava virus, Dobrava? Dobrava. Dobrava virus, whatever.

Erin Welsh

One of those.

Erin Allmann Updyke

Which was discovered in Slovenia and is hosted by the yellow-necked field mouse. That's a lot of viruses. So all of these viruses, which are different hantaviruses, cause various forms of HFRS, hemorrhagic fever with renal syndrome.

Erin Welsh

So one of the things, just to pause, that I noticed: too many acronyms.

Erin Allmann Updyke

Mm-hmm. Tell me about it, it's ridiculous.

Erin Welsh

It's ridiculous. Okay so then the hemorrhagic one.

Erin Allmann Updyke

So the hemorrhagic one, we've got at least 4 different viruses that we're talking about here and they cause the same disease but with varying degrees of severity. So for example, Puumala virus in Finland has a very low estimated mortality rate between 1-3% whereas Hantaan virus has a mortality rate of between 5-15%, so it's a much more severe illness. What's interesting is that because these viruses cause diseases of varying severity, in different countries they have different names for them. So for a while the disease that Hantaan virus causes was called KHF or Korean hemorrhagic fever, Puumala virus, the disease it causes is often called nephropathia epidemica. It's absurd, they're all the same disease. I'm gonna argue - and hopefully you'll agree with me by the end of this episode - that all of the diseases caused by hantaviruses should be called the same thing. I'm not alone, I have an article to cite for it.

Erin Welsh

(laughs)

Erin Allmann Updyke

So let's get into it. HFRS. It has five stages, not just four like we saw with HPS.

Erin Welsh

Ooh.

Erin Allmann Updyke

And it starts similarly. First phase: febrile. Fever, muscle aches, headache, nausea. You also might get flushing of your face and that's because again we know there's gonna be vascular involvement and so anytime your blood vessels are dilating you might get flushing of your face cause you've got blood flow there. That make sense?

Erin Welsh

Yeah.

Erin Allmann Updyke

And you'll move more quickly into the second phase which is the hypotensive phase.

Erin Welsh

Okay.

Erin Allmann Updyke

So this is again where your blood pressure drops. You'll also likely have what's called thrombocytopenia which you also do see in HPS and it just means that you have a low platelet count. A low platelet count is bad because it means you're likely to bleed out. So platelets are what's responsible for clotting. So without platelets, you are at a higher risk of bleeding. So then because of the thrombocytopenia you might have certain skin bleeding manifestations, little red/purple dots which basically are small hemorrhages happening under your skin. And then you'll move into the oliguric phase which, though we didn't have a phase called oliguria in HPS, we did see that you also have a drop in urine output. The biggest difference here is that the effects of HFRS tend to happen mostly in kidneys instead of in the lungs. So we see your kidneys starting to fail first rather than your lungs filling up with fluid. So you're not gonna have a cough, you're not gonna have the pulmonary edema. Does that make sense?

Erin Welsh

Why are they different? Or am I jumping the gun?

Erin Allmann Updyke

You're jumping the gun a little bit, let's finish out this HFRS. Once you see that decrease in urine output, it's bad news but again HFRS overall has a much lower mortality rate so most people are going to start to recover and then they'll enter the polyuric phase which means a lot of pee, they'll start to diurese and pee a whole bunch out and then convalesce. Cool?

Erin Welsh

Cool.

Erin Allmann Updyke

So the question is-

Erin Welsh

Not cool, it's terrible.

Erin Allmann Updyke

It's not cool. (laughs) But here's the thing, what I think is really important and what makes these diseases really, really cool and also why pathophysiology is my favorite subject right now, is that even though these sound like, okay, HPS you're going to have fluid all over your heart and lungs and you're gonna die because you can't breathe and your heart can't beat. HFRS, your kidneys are going to shut down and maybe you'll be able to recover and maybe you won't. These two seem like very different diseases but they're not. They're so closely related and if you understand what's happening inside of your cells, it's the exact same thing.

So here's what happens. Hantaviruses infect your endothelial cells. These are the cells that line your blood vessels. Okay? They get into those endothelial cells, they replicate, and they cause damage. They don't necessarily kill the cells themselves but they cause enough damage that other cells come in and things like histamine are released which causes vasodilation and increased vascular permeability. This means that your blood vessels are now leaky, so you have fluid loss and blood loss and hypotension. This is the exact same mechanism that happens in HPS and in HFRS. The only difference is what tissue is the hantavirus primarily infecting. The endothelial cells of your lungs or the endothelial cells of your kidneys?

Erin Welsh

And why is there a difference? Like why is there a differential preference?

Erin Allmann Updyke

Right, that, no idea.

Erin Welsh

Huh.

Erin Allmann Updyke

Yeah.

Erin Welsh

Interesting.

Erin Allmann Updyke

Right?

Erin Welsh

Is it really sort of this Old World/New World situation in terms of pulmonary vs renal?

Erin Allmann Updyke

Yeah so the ones in South America do tend to cause more HPS-like symptoms, at least from what I read.

Erin Welsh

Okay.

Erin Allmann Updyke

So yeah. It's so interesting. But yeah they are transmitted in exactly the same way, so they're transmitted in the excrement of rodents. So basically you have to aerosolize pee or poop from a rat or a mouse or a vole that's infected and inhale it. But what I think is so cool is that you have these two diseases which on their face seem so different and yet the underlying mechanism that causes the disease is exactly the same.

Erin Welsh

Yeah. That's super interesting.

Erin Allmann Updyke

Oh, I should say very importantly for the most part this disease cannot be transmitted person to person. There's like one case where a hantavirus Andes virus in South America was possibly transmitted person to person but every other hantavirus in as many studies as they've tried has never been shown to be able to be transmitted from person to person, it's exclusively from aerosolized rodent excrement. So Erin, tell me about this. How did we get here? How did this all start?

Erin Welsh

Okay. I think I can answer that.

TPWKY

(transition theme)

Erin Welsh

When we picked hantaviruses to cover this season I don't think either of us realized just how large the world of hantaviruses is and also how much this story is still developing.

Erin Allmann Updyke

Mm-hmm.

Erin Welsh

Okay but before we get to where we are today, let's as always go back to where we started or at least where the virus started. Hantaviruses have been around for millions of years. They can be found in rodents on every continent except for Antarctica and their diversity is astounding. But when did humans start to get involved?

Erin Allmann Updyke

Yeah.

Erin Welsh

As early humans began to farm and form stationary settlements and store food, which is a key factor, many rodent species settled with them and the easy access to food and shelter promoted this close relationship. Because of this, humans have probably been exposed to or infected with hantaviruses for millennia. But it's not until really like a long time ago, 960 AD... I'm like, 'Oh but it's not until...'

Erin Allmann Updyke

That's a long time.

Erin Welsh

(laughs) Right. So 960 AD, a thousand years ago, that we get our first bit of evidence for this. A Chinese medical account of a disease that sounds a whole lot like hemorrhagic fever with renal syndrome. But then it more or less disappears from medical textbooks for almost a thousand years. Although sidenote, some people believe that the mysterious sweating sickness that plagued England and continental Europe during the 15th and 16th centuries might have been caused by a hantavirus.

Erin Allmann Updyke

(gasps) Really?

Erin Welsh

Yeah. So apparently the symptoms were fairly similar, there was this seasonal pattern, and then these regular intervals.

Erin Allmann Updyke

Ooh!

Erin Welsh

But it's still far from conclusive.

Erin Allmann Updyke

Yeah.

Erin Welsh: So for one thing, the sweating sickness seemed to be transmitted person to person which is rarely or never seen in hantavirus outbreaks. And for another, outbreaks appeared suddenly and disappeared suddenly without any mention of previous cases or reports of rodent population increases. But just in case, we should probably do a full episode on sweating sickness just to, you know, cover the basics.

Erin Allmann Updyke: It's on our list. (laughs)

Erin Welsh: (laughs) Yeah, it is. It is. In any case it's not really until the 1860s that we get a clearer sense of hantavirus outbreaks in humans. In the U.S. in the 1860s, the S's were not very U.

Erin Allmann Updyke: What?

Erin Welsh: In the U.S.-

Erin Allmann Updyke: (laughs) That was so dorky, Erin!

Erin Welsh: (laughs)

Erin Allmann Updyke: I liked it.

Erin Welsh: It's pretty dorky.

Erin Allmann Updyke: It's good.

Erin Welsh: Okay, well.

Erin Allmann Updyke: So the S's aren't so U.

Erin Welsh: The American Civil War was raging as were cases of what was being called war nephritis or trench nephritis. The outbreak reached its peak between 1862 and 1863 and an estimated 14,000 soldiers came down with this disease whose symptoms strongly resembled that of the field nephritis experienced by troops in Flanders during WWI. Hantavirus infections make another appearance again in wars, this time a little more global, when the Japanese military invaded Manchuria and also during WWII in Finnish and German soldiers. These outbreaks prompted modern descriptions of the disease though the link between the European and Asian infections was yet to be discovered. Scientists investigating these diseases had plenty to keep them occupied and maybe a bit too much license.

At this point you may have noticed the link between these infections and war conditions. The disease was seen most commonly in soldiers and not just any soldiers but ones who were huddled in trenches for long bouts of time. Researchers in the 1930s and 40s also picked up on this and they started looking for the route of transmission. Rodents were immediately implicated as were arthropods such as mites and ticks, which were also common in crowded conditions like that.

Erin Allmann Updyke: Right.

Erin Welsh: But how to test, how to test? How about human experimentation?

Erin Allmann Updyke: Of course!

Erin Welsh: Great choice. Not really. But it is the choice that some Japanese scientists opted for during WWII, the most notorious of these programs being Unit 731 whose official innocuous title was the Epidemic Prevention and Water Purification Department.

Erin Allmann Updyke: Ooh.

Erin Welsh: Throughout the 8 year existence of this program, over 3000 men, women, and children, both prisoners of war as well as civilians were experimented on with death being the most common outcome. There was frostbite testing, vivisection with no anesthetic, injections with various infectious diseases including hantavirus material even though they didn't know exactly what that was yet, weapons testing-

Erin Allmann Updyke: This was WWII?

Erin Welsh: Yes.

Erin Allmann Updyke: Oh my god.

Erin Welsh: Oh just wait, it gets so much worse.

Erin Allmann Updyke: I know, it's just humans, man.

Erin Welsh: Weapons testing, starvation and dehydration, really the list goes on and on and on. The results of many of these experiments were published in peer reviewed journals with any mention of human subjects changed to a nonhuman primate species.

Erin Allmann Updyke: Whoa! Are you serious?

Erin Welsh: Mm-hmm.

Erin Allmann Updyke: So they fully, it's not like they were just like, 'Oh it's fine.' They were like, 'We know this is not fine, we're just gonna do it anyway and pretend like we did it on a monkey.'

Erin Welsh: Yeah.

Erin Allmann Updyke: Cool, cool, cool, cool. Cool. Cool. Cool.

Erin Welsh: Right. Okay. But I haven't even gotten to one of the most outrageous parts of this.

Erin Allmann Updyke: Okay.

Erin Welsh: Which is that when the U.S. found out about this human experimentation, instead of prosecuting any of the researchers or leaders involved in Unit 731, the U.S. granted them complete immunity as long as they provided all of their results to the U.S. and none of the other Allies, namely the Soviet Union.

Erin Allmann Updyke: That is 0% surprising, quite honestly.

Erin Welsh: I know, which is also very sad.

Erin Allmann Updyke

It's very sad but not surprising. (laughs)

Erin Welsh

But yeah. But you should really like, if you have time, just check out the Wikipedia page, even with just a skim it is shocking and something that deserves a lot more attention than what I'm giving it right now.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

So maybe another episode. Anyway. But yeah, Unit 731 was unsuccessful in determining the causative agent of the war-associated hemorrhagic fever and they still didn't have a conclusive answer for how it was transmitted. And they weren't alone, both in their human experimentation and in their failure. The Soviet Union had their own experiments running around the same time in which they injected human quote "volunteers" with various materials to try to bring about infection. By 1950 various European and Asian countries were familiar with hantavirus-caused infections and their association with rodents, even if they still didn't know what a hantavirus was. It's gonna take another war to get the interest and funding to solve that problem. In this case, the Korean War. Tensions had been running high between North and South Korea for a long time and it came to a head in June of 1950 when North Korean troops invaded South Korea seeking complete control of the divided country. U.N. forces largely comprised of U.S. military were sent to South Korea to stop this offensive.

The war lasted three years and resulted in casualties ranging in the tens of thousands to over a million dead. As in all wars, combat is just one of the leading causes of death, often going hand in hand with things like starvation and disease. And with so much of this war fought in the trenches and the frontline barely moving from the 38th parallel. Trench nephritis or hemorrhagic fever with renal syndrome was one of those diseases. In general, case estimates of hemorrhagic fever aren't very good for this conflict but we do know that approximately 3200 U.N. soldiers came down with the illness and 121 died. Obviously this got people searching for the source of the infection. Ticks and fleas and mites were once again investigated and ruled out and rodents were found to be the likely culprit. And not just any rodent: *Apodemus agrarius*. The Asian striped field mouse.

Similar disease ecology research was being done in Fennoscandia to narrow down which rodent might be responsible for disease outbreaks there. In that case, a totally different species was implicated as you mentioned, *Myodes glareolus*, the bank vole. But if there was any hope of lessening the suffering caused by this disease, the causative agent still had to be identified. And that's where Dr. Ho Wang Lee comes in. A physician, epidemiologist, and virologist from South Korea, Dr. Lee had set his sights on discovering what was hiding in these rodents that caused illness in humans. And in 1976, he achieved his goal when he found evidence of viral antigen predominantly in lung tissue of an Asian striped field mouse. So it's in the lungs of these guys.

Erin Allmann Updyke

Yeah! Fascinating.

Erin Welsh

He would go on to develop a diagnostic test for hemorrhagic fever with renal syndrome and a vaccine for a strain of hantavirus as well as a lot of other really important ecological and medical research on hantaviruses. And sidenote, actually according to Wikipedia he is the first person in the history of medicine to identify a virus that causes human disease, develop a diagnostic tool for the disease, and develop a vaccine for it as well.

Erin Allmann Updyke

To do all three? That's cool.

Erin Welsh

Yeah, isn't that amazing?

Erin Allmann Updyke

That's really cool.

Erin Welsh

Okay. We're at the point in the story where I tell you the etymology of our pathogen or disease. While in general the trend has been going away from using things like the name of a country or city in naming, often other geographical markers are still used. Dr. Lee chose to name the virus after the Hantan River. This river flows near the 38th parallel which divides North from South Korea. This area was a hotspot for hemorrhagic fever with renal syndrome during the Korean War and continued to be an endemic region for the disease after the war had ended. But in his book, Dr. Lee explains that he didn't just name the virus for the river's association with the disease but also because to him it represented the tragic history of the country in hopes for reunification. The name, as you know, stuck. The virus plagued that part of the world would be known as the Hantaan virus and it would soon gain many relatives. So earlier when you mentioned that hantaviruses are transmitted through rodent excrement whereas all the other Bunyaviridae are transmitted through arthropods.

Erin Allmann Updyke

Yeah.

Erin Welsh

So some researchers believe that it could indicate that hantaviruses are actually older, they're a more basal subgroup within Bunyaviridae.

Erin Allmann Updyke

Cool. Ah, cool.

Erin Welsh

Yeah. Okay anyway. With this diagnostic test that Dr. Lee had developed, it was now possible to test patients from all over the world, particularly in those regions where a similar hemorrhagic fever or renal syndrome of unknown origin was known to pop up. This led to the discovery of Puumala virus, Seoul virus, Prospect Hill virus, etc. you know, all these other viruses. And these viruses were all similar but not identical and their discovery hinted at the enormous diversity that this group of viruses would later be found to have.

Erin Allmann Updyke

So cool.

Erin Welsh

On that note, let's travel to the American Southwest, May 1993.

Erin Allmann Updyke

Yes! I've been waiting for this.

Erin Welsh

Bill Clinton is president, Beanie Babies have just hit the shelves for the first time.

Erin Allmann Updyke

Oh my god.

Erin Welsh

The Sandlot is in theaters. Two Princes by The Spin Doctors is on the radio. And the Four Corners region of the U.S., which is where Colorado, Utah, Arizona, and New Mexico meet, is in the early stages of a terrifying and tragic outbreak of unknown origin. A 21 year old Navajo woman named Florena Woody, mother to a 5 month old son, started feeling achy and feverish. Within a couple of days her symptoms progressed into pneumonia and she began to have difficulty breathing. At the hospital where she was admitted, the doctors tried in vain to keep her oxygen levels high and her lung fluid levels low. 11 days after the first symptoms appeared, Florena died on Mother's Day 1993.

Erin Allmann Updyke

Ugh.

Erin Welsh

Her fiance, a 19 year old Navajo man named Merrill Bahe, a terrific athlete, felt too sick to attend her funeral and some of his relatives decided to drive him to the hospital as his condition rapidly deteriorated. On the drive to the hospital, Merrill began gasping for air and collapsed. He was pronounced dead on arrival five days after the death of Florena.

Erin Allmann Updyke

Aw they have a 5 month old baby.

Erin Welsh

It's so heartbreaking. Yeah. It's horrible.

Erin Allmann Updyke

It's horrible.

Erin Welsh

And the deaths of these two otherwise healthy young individuals threw up red flags for the attending physician who alerted the state medical examiner's office and the Indian Health Service, IHS, epidemiologist. Autopsies revealed that Florena and Merrill had essentially drowned as their lungs filled up with fluid and the medical examiner realized she had seen a similar case just a month prior. More calls followed and as different branches of the IHS learned of the mysterious deaths, a couple other similar cases came to light. In total, five severe illnesses with respiratory symptoms were put in a report which was distributed to hospitals all over the Four Corners area asking physicians to look for similar cases. Within a few weeks, 24 suspected cases had been identified, mostly adults or young adults, mostly otherwise healthy. The hunt for the cause had begun and it was all hands on deck. The CDC showed up in full force with EIS agents decked out in their space suits and every lead was followed. Could it be pneumonic plague? This region is endemic for plague and pneumonic plague carries a high mortality rate.

Erin Allmann Updyke

Yeah.

Erin Welsh

But that form was rare there and screening quickly ruled it out. What about a 1918-like influenza? There were some striking similarities. The health and youth of most of the victims, the drowning in the lungs, it seemed plausible. Another influenza outbreak like the 1918 one would be, well-

Erin Allmann Updyke

Horrible?

Erin Welsh

Yeah.

Erin Allmann Updyke

The worst.

Erin Welsh

Yeah, you'd know, especially if you listened to our first episode.

Erin Allmann Updyke

Yeah.

Erin Welsh

But again tests came back negative. Maybe it wasn't an infectious disease at all. Maybe it was a poison which is another common cause of acute respiratory distress. But testing of homes revealed no potential poisons. The usual suspects were out, it was time to widen the search. Tissue samples from those killed by the infection were sent to the CDC in Atlanta, Georgia to screen against their enormous database of pathogens. Several different types of viruses were selected for the first run due to the way they caused disease. Among these were hantaviruses, fortunately.

Erin Allmann Updyke

Yes.

Erin Welsh: Which matched the tissue samples. There it was, the first piece of this puzzle. But in some ways this clue raised a lot more questions like is this a virus we've seen before or is this a brand new species of hantavirus? And if it's brand new, where did it come from and why are we only seeing it now?

Erin Allmann Updyke: Yeah, 1993. Like where did this just pop up out of nowhere from?

Erin Welsh: Yeah.

Erin Allmann Updyke: Tell me.

Erin Welsh: By this time, the press had picked up on this apparent outbreak and as per usual began wild speculations as to the cause of the disease. They also gave it a name initially: Navajo Flu.

Erin Allmann Updyke: Terrible.

Erin Welsh: Yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: And they gave it this name because the first several people who were infected with the virus were Navajo but this name was both stigmatizing and inaccurate. Since this was a hantavirus, close association with rodents was undoubtedly implicated as a risk for infection and in popular media it was implied that living in poverty or unsanitary conditions greatly increased that risk, which simply wasn't true.

Erin Allmann Updyke: Yeah.

Erin Welsh: Both rodents and the infection were not limited to any particular ethnicity or income level.

Erin Allmann Updyke: Yeah.

Erin Welsh: But the damage was done. Associating a diagnosis with shame often makes people less willing to come forward to either seek treatment or discuss any aspect of their disease and with a case fatality rate of 75%, this was not in the best interest of anyone. When it came time to name the virus, which had been confirmed to be a new species of hantavirus, there was an effort to be more judicious with the naming. The names of nearby geographical features were put forth and ultimately Sin Nombre, meaning 'without name', was chosen, supposedly after a canyon named Sin Nombre but apparently no one has been able to find it on a map.

Erin Allmann Updyke: (laughs) I did not know that about the canyon. But I love the name Sin Nombre virus.

Erin Welsh: I know.

Erin Allmann Updyke: I think it is the most BA, it's so fitting for a virus that is this scary.

Erin Welsh: Yeah. Well it was so contentious, the naming was so contentious because the CDC wanted to name it one thing and someone else wanted to name it something else and it was just like, you know what? It is the perfect name.

Erin Allmann Updyke: It's the perfect name.

Erin Welsh: It's a shame that it could only be used once. (laughs)

Erin Allmann Updyke: (laughs) Once.

Erin Welsh: But still, even though this name existed, the question 'why now?' Remained.

Erin Allmann Updyke: Yeah.

Erin Welsh: The first step to answering that was to determine which animal was responsible for the outbreak. Since it was a hantavirus it had to be a rodent, so individuals of 12 different rodent species were rounded up and tested. The culprit? *Peromyscus maniculatus*, the deer mouse.

Erin Allmann Updyke: A little babe!

Erin Welsh: So cute.

Erin Allmann Updyke: They're so cute.

Erin Welsh: But it wasn't like deer mouse had suddenly moved to the Four Corners region, the species actually had an enormous distribution covering most of North America. So why was this the first time we were seeing a disease associated with it? The short answer is that deer mouse population levels in 1993 were high.

Erin Allmann Updyke: Yeah.

Erin Welsh: In other parts of the world, peaks of hantavirus cases were known to follow peaks in rodent populations and this pattern has been well established in Fennoscandia for instance, where the carrier of Puumala virus, the bank vole, has about this three year population cycle.

Erin Allmann Updyke: You guys, if you don't know, Erin Welsh is studying voles and disease in Finland right now during her postdoc.

Erin Welsh: You blew my cover!

Erin Allmann Updyke: So she has an extra smile on her face describing the life cycle of a vole to you right now. (laughs)

Erin Welsh: I'm very thrilled about this.

Erin Allmann Updyke: I love it.

Erin Welsh: I'm very thrilled. (laughs) But trying to figure out what is driving those cycles is pretty dang complicated because it often ends up being a mixture of many things including resource availability, predator abundance, competition within species and among different species, I mean the list goes on.

Erin Allmann Updyke: Yeah, ecology, man.

Erin Welsh

Ecology. And ecology also means long-term monitoring of these rodent populations is necessary if you wanna understand the cycle, especially if you wanna understand the cycle enough to predict it. Unfortunately there wasn't really extensive long-term monitoring so while anecdotal reports of why high rodent populations in 1993 were plentiful, any empirical evidence of population increase was hard to come by. But there were a few clues. An El Nino year in 1992 meant increased rainfall to the Four Corners region. This increase in rainfall meant a huge harvest year for pinion pines which produce nuts that act as a favorite food source for our little deer mouse friends. These plentiful food resources and a relatively mild winter allowed the rodents to A) survive, and B) throw in an extra breeding cycle which increased their population quite a bit.

So researchers turned their focus to the past. This may be a newly described virus but it wasn't new to the deer mice that carried it. In fact it had probably been around for millions of years, adapting alongside its host. And further scrutiny of past medical records and examination of preserved tissue showed that Sin Nombre virus had actually struck in the U.S. decades before. Not as extremely as it did in 1993 but it has been around. Why it was only recognized in 1993 was probably a combination of a lot of things, like the observant eye of healthcare practitioners, rodent population dynamics, El Nino, blame it on El Nino, and other factors. Since the 1993 outbreak of Sin Nombre virus, there has been an explosion of other hantaviruses coming to light all over the world. Some with worrying traits like is that one in South America, possibly the Andes virus, is that transmitted person to person? Who knows?

Erin Allmann Updyke

Right. Terrifying if it is.

Erin Welsh

But yeah and if that's the case, how would we even begin to control that? It is an alarming thing.

Erin Allmann Updyke

Yeah cause by the way, there is no treatment for this.

Erin Welsh

Spoilers!

Erin Allmann Updyke

Sorry. I should've said it in the biology. (laughs)

Erin Welsh

I should've asked it in the biology. But yeah, like I said, the history of hantaviruses is still ongoing and I'm super curious to hear where we stand in terms of treatments which apparently is nil, vaccines, etc. Erin, tell me about hantaviruses today, please.

Erin Allmann Updyke

Okay.

TPWKY

(transition theme)

Erin Allmann Updyke

So what part of hantaviruses do you wanna talk about the most?

Erin Welsh

I wanna know two things in particular.

Erin Allmann Updyke

Okay.

Erin Welsh

One is how many people get sick every year all over the world with these different pulmonary or hemorrhagic syndromes? And then I also wanna know how are we actually preventing it?

Erin Allmann Updyke

Yeah, good questions. So in the U.S., we'll start there cause that's where we ended with the history. In the U.S. there have been a few outbreaks recently, probably the most famous one that you might have heard about was in 2012, there was a relatively large outbreak of HPS in Yosemite, there were 10 confirmed cases and 3 fatalities.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. So that happened. There was also in 2017 an outbreak of Seoul virus, so not HPS but HFRS caused by Seoul virus in the U.S. in 11 different states, there were 16 people infected. And they also found 31 infected ratteries. Tell me what's a rattery? Where they breed rats.

Erin Welsh

Wait. Is that real?

Erin Allmann Updyke

Yeah, that's real! (laughs)

Erin Welsh

A rattery is something where you breed rats?

Erin Allmann Updyke

I mean I'm assuming that's what... I have 'What is a rattery?' in my notes but I'm assuming that's what a rattery is.

Erin Welsh

It is also a village and civil parish in Devon, England.

Erin Allmann Updyke

Well, there you go. (laughs) But as of January 2017, in the U.S. there have been 728 cases of hantavirus that have been definitively identified across 36 states, mostly New Mexico, Colorado, Arizona, and California.

Erin Welsh

Okay.

Erin Allmann Updyke

That's in the U.S. But obviously the U.S. for whatever reason has very, very low case numbers. In China there are thousands of cases annually, likely between 12-20,000 cases every year. In Finland there have been some years where up to 3000 cases have been reported. And then elsewhere in Europe in Germany, in Slovenia, there can be up to 1000 or so cases a year. In some areas they've done testing to try and just figure out what seroprevalence is and it's as high as 2% which means that up to 2% of the total population has been exposed at some point. And then there's also been clusters of cases throughout South America as well, in Paraguay, Argentina, Panama, Brazil, Uruguay, and most of these are due to Andes virus.

Erin Welsh

That's a lot of hanta.

Erin Allmann Updyke

It's a lot of hanta, it's way more than I expected. In terms of current research, it's really interesting. So there was a vaccine that was developed in the early 90s actually, so I think as far as I know it was actually before Sin Nombre virus was discovered, this virus was in development.

Erin Welsh

Okay.

Erin Allmann Updyke

In China it's called HantaVax. It is licensed I believe in both China and Korea and it's a vaccine, they have it, you can get it there. It's only effective for Hantaan and Seoul viruses and it hasn't been approved for use in Europe or the U.S. but it's thought that it wouldn't be effective against the viruses that circulate in the U.S. and Europe anyways.

Erin Welsh: Okay.

Erin Allmann Updyke: But by using this vaccine they have pretty substantially decreased the number of cases of HFRS in China.

Erin Welsh: That was like 25 years ago.

Erin Allmann Updyke: Yeah.

Erin Welsh: Basically. So are there other vaccines? Because it seems like it would be, if there's already a vaccine for one hanta it wouldn't be that difficult to make vaccines for other ones.

Erin Allmann Updyke: Yeah, it's very interesting. It's interesting to me that there's definitely a lot of research going on about vaccines. So there are various different vaccines that are in development, there aren't any other that are licensed and from what I can tell it seems like most of them are still in rather early phases of development. And I think that in part, in the U.S. at least, it's likely because this causes so few cases every year that there's not a lot of incentive, right. There's not a lot of financial incentive to protect against a disease that's only caused "only" quote unquote 700 cases over the last 25 years.

Erin Welsh: Right.

Erin Allmann Updyke: Unfortunately (laughs)

Erin Welsh: Right, yeah.

Erin Allmann Updyke: Right. But in other parts of Europe, it causes a significant amount of disease but it's not that lethal of a disease. But there are vaccines that are being developed, what's very cool is that a lot of the research that's being done right now is on DNA vaccines and I will admit i don't know that much about DNA vaccines.

Erin Welsh: Yeah what does that mean?

Erin Allmann Updyke: So, okay. Most vaccines, what you're injecting is either a whole virus or parts of the outside of the virus, like the proteins of the virus or the toxin of the bacteria, like inactivated toxoid from bacteria.

Erin Welsh: Right.

Erin Allmann Updyke: Bc that's what your body is gonna generate an immune response against are those outer proteins. DNA vaccines are vaccines that include DNA that codes for those viral proteins rather than the viral proteins themselves.

Erin Welsh: Why is that an advantage over the proteins?

Erin Allmann Updyke: So one thing is that it's easier to make multivalent vaccines, so you can make one plasmid that has proteins for a whole bunch of different hantaviruses.

Erin Welsh: Oh. Em. Gee!

Erin Allmann Updyke

(laughs) I'm so glad, that worked really well the way that you asked that because that's really good flow.

Erin Welsh

(laughs)

Erin Allmann Updyke

Cause I had it all right there, that's good. Yeah. So it's pretty cool.

Erin Welsh

That's so cool!

Erin Allmann Updyke

It's very cool. I don't know a ton about them, I know they're kind of one of these hot things in vaccines right now and I'm sure I'll do a lot more research on them for our vaccine episode in the future. But it's very cool and it's definitely something that's in the works. In animal models they do seem to be effective, they've started to test them on humans but from what I understand, one of the biggest issues is the mode of delivery, so trying to make sure that the way that you deliver this DNA vaccine is going to be the most effective. So.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

That is fascinating though.

Erin Allmann Updyke

It's very fascinating. So there's very cool research being done right now with hantaviruses and with vaccine development. It's a cool area.

Erin Welsh

Wow.

Erin Allmann Updyke

Yeah!

Erin Welsh

Oh man, my mind is blown open at this DNA vaccine situation, I'm gonna have to go on a little dive.

Erin Allmann Updyke

It's pretty cool, it's pretty cool stuff.

Erin Welsh

Does infection with one of the hantaviruses make you immune to subsequent infections or make you immune to other infection, to other hantavirus infections?

Erin Allmann Updyke

As far as I know it definitely does not make you immune to infection with other hantaviruses which is part of why the Hantavax vaccine doesn't work for...yeah.

Erin Welsh

Okay. Yeah.

Erin Allmann Updyke

I don't know, I would assume that once you've been infected with say Sin Nombre virus, if you survive you probably won't be infected with Sin Nombre virus again.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. So probably what everyone wants to know is how to not get hantavirus.

Erin Welsh

Yeah.

Erin Allmann Updyke

Since we don't have a vaccine in the U.S. and-

Erin Welsh

And we have friends who work on mice and voles and...

Erin Allmann Updyke

Yep, including you. So Erin, here's how you can not get hantavirus in the future.

Erin Welsh

Thanks.

Erin Allmann Updyke

Basically if you are in a place, like you're cleaning out your grandma's cabin or something, assume that it's infested with rats or mice because it probably is and first you air things out before you clean anything out, you try and get rid of any rodent infestation if you can, and don't vacuum up dry mouse poop and stuff.

Erin Welsh

Or like with a broom or anything.

Erin Allmann Updyke

Or with a broom, yeah. So CDC recommends that you wet everything down with 10% bleach or some other disinfectant and let it sit for a while and then you make sure that everything is wet essentially when you clean it up instead of cleaning everything up when it's dry. So.

Erin Welsh

I mean if you're inhaling the particles, so just think about how to prevent yourself from inhaling these, you know, poop particles and pee particles.

Erin Allmann Updyke

Poop particles. Pee particles. (laughs) Yeah. It's like a lot of bleach in spray bottles is what the CDC recommends. They say wear protective gear and do this in a well ventilated area, don't just sit in an attic full of rat pee.

Erin Welsh

I do have a question.

Erin Allmann Updyke

Mm-hmm.

Erin Welsh

How scared should we be of hantaviruses?

Erin Allmann Updyke

You living in Finland or me living in Illinois? Or everyone who's listening?

Erin Welsh

Everyone who's listening.

Erin Allmann Updyke

Everyone who's listening, meh. Not so scared.

Erin Welsh

Okay.

Erin Allmann Updyke

It's a scary illness but it's not super common and you can protect yourself from it. But yeah, I would say not super scared, don't let this one keep you up at night.

Erin Welsh

Okay well there's plenty else to keep us up at night.

Erin Allmann Updyke

Exactly. (laughs) There's plenty of things to have anxiety about.

Erin Welsh

MRSA and prions and...

Erin Allmann Updyke

(laughs) Yeah.

So we recorded this episode a few weeks ago and since then there have actually been some updates on the status of hantavirus worldwide. Specifically there have been a couple of outbreaks that have been reported since we last recorded, so I wanted to give you guys an update so that you're as up to date as possible. Number one, there have been at least 103 confirmed cases that happened in Panama over the course of 2018, including 51 of those which were classified as hantavirus without pulmonary syndrome and 48 that were classified as HPS, including 4 deaths. In Argentina there's actually an outbreak happening currently. As of January 15, 2019, the most recent numbers that I've found are at least 28 people in the hospital currently under observation for hantavirus infection and 11 people that have died so far. So this is an ongoing outbreak, so we'll try and keep you guys updated on Twitter and our social media as to what's going on. Update over.

Sources?

Erin Welsh

Sources. I used a couple of sources. One is a book called 'Of Mice, Men, and Microbes' by Andrea S. Meyer and David R. Harper. Another is called 'Hantavirus Hunting' by Ho Wang Lee, and so that is the man who discovered the virus, did the diagnostic test, vaccine, etc.

Erin Allmann Updyke

Cool.

Erin Welsh

And then finally some excerpts from a book titled 'Hantaviruses' which is edited by C. Schmaljohn and S. T. Nichol. And then also apparently in the X-Files movie it's mentioned that hantaviruses were brought by aliens.

Erin Allmann Updyke

(laughs)

Erin Welsh

(laughs) I didn't manage to watch it to verify but yeah.

Erin Allmann Updyke

Amazing. I have a number of articles, we as always will post all of our sources, books and articles on our website thispodcastwillkillyou.com so you can find them all there.

Erin Welsh

I really enjoyed learning about hantaviruses.

Erin Allmann Updyke

Me too. It was a fun one to research.

Erin Welsh

Yeah. It really was.

Erin Allmann Updyke

Thank you to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Welsh

And thank you to you, listeners. And to everyone who has ever written a message to us, we really appreciate it and if we haven't responded, we're really sorry, we want to and we're going to try to.

Erin Allmann Updyke

Yeah.

Erin Welsh

We're just two people and we're doing this, we each have full-time jobs in addition to doing this and-

Erin Allmann Updyke

Yeah. This is all for funs and it's super fun to get to hear from you guys and we really love it so we apologize if we haven't written you back, we've read your message and loved it. And we're trying to reply to you all.

Erin Welsh

So keep sending 'em.

Erin Allmann Updyke

Yes. Okay.

Erin Welsh

Okay well, wash your hands.

Erin Allmann Updyke

You filthy animals. (laughs)