

Erin Allmann Updyke

"A pathologist, R. S., aged 30 years, had been working with Rift Valley fever virus for several weeks before the onset of his illness. On the evening of December 22, 1932, he felt chilly while walking home and complained that his eyes and the calves of his legs ached. During the night, his rest was disturbed by general malaise and pains especially around the knees and hips. On awakening, the second day of illness, his temperature was 101°F. He attempted to continue his work but had several chills during the day and felt so miserable that he took to bed. He complained at this time of a vague soreness over his abdomen, constant dull headache, and pain behind the eyes associated with slight photophobia. There was no sore throat, rhinitis, nausea, or vomiting. He was admitted to the hospital of the Rockefeller Institute 24 hours after the onset of symptoms.

On admission, the temperature was 102.6°F, pulse 140, respirations 24. The patient was definitely prostrated by his illness but rational and cooperative. The throat culture was negative for hemolytic streptococci and influenza bacilli and blood cultures in infusion broth remained sterile. A tentative diagnosis of Rift Valley fever or influenza was made. In an attempt to confirm the tentative diagnosis of Rift Valley fever, 6 CCs of the patient's blood was injected into six mice. All of the mice died within 48 hours. Almost immediately after admission, the patient began to improve. The temperature, which reached a peak of 103.8°F on the night of admission, fell promptly to normal within 24 hours. The symptoms however abated somewhat less rapidly. By the 12th day of illness the patient had improved to such an extent that he was allowed to sit in a chair for a short time and on the following day was permitted to walk a short distance.

On the evening of the 16th day however he complained of pain in the left leg. The patient was returned to bed and the leg was immobilized in an elevated position. Four days later, 20th day of illness, the patient awakened with pain in the right chest which was more pronounced during deep inspiration or exhalation. In the X-ray photograph made at this time there was a distinct shadow at the base of the right lung. On several occasions blood was expectorated in small amounts. On the 38th day of illness, recovery seemed to be proceeding uneventfully. On the morning of the 45th day of illness however the patient suddenly collapsed and died within a few minutes. Death was apparently due to a large embolus in the pulmonary vessels."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

Oof.

Erin Allmann Updyke

That's a tough, tough story, Erin.

Erin Welsh

Yeah. And what a roller coaster too.

Erin Allmann Updyke

It really is. Like you have no idea where it's gonna go until you're there.

Erin Welsh

Yeah. I don't know anything about the pathophysiology of Rift Valley fever so I'm very curious to know how well this fits in with like the clinical picture that has been seen.

Erin Allmann Updyke

Not super well but...

Erin Welsh

Interesting.

Erin Allmann Updyke

But I can see how these things ended up happening. So when we talk about the pathology, we can kind of tie back into it.

Erin Welsh: Okay. So that firsthand account was from a paper by Schwenker and Rivers from 1934 titled 'Rift Valley Fever in Man: Report of a Fatal Laboratory Infection Complicated by Thrombophlebitis'. And this actually is the first recorded death due to Rift Valley fever.

Erin Allmann Updyke: Oh interesting.

Erin Welsh: I mean likely not the first death in humans.

Erin Allmann Updyke: Right.

Erin Welsh: But the first recorded human death.

Erin Allmann Updyke: First detailed, recorded.

Erin Welsh: Yeah. Hi, I'm Erin Welsh.

Erin Allmann Updyke: And I'm Erin Allmann Updyke.

Erin Welsh: And this is This Podcast Will Kill You.

Erin Allmann Updyke: And today we're talking about Rift Valley fever. We've had a lot of requests for this one which I feel like is surprising because I knew almost nothing about it except I had heard there is Rift Valley fever. Like I knew that it existed, I knew it was mosquito-borne. That's all I knew.

Erin Welsh: Yeah, same. I was like oh, this is a dangerous virus but I didn't really know much more than that. And I was kind of shocked when I got into the history of outbreaks.

Erin Allmann Updyke: I am shocked at how little I knew considering that we were deep in disease ecology for so long.

Erin Welsh: Oh yeah. I mean I would like to flip through parasite books for fun.

Erin Allmann Updyke: Yeah, yeah.

Erin Welsh: But somehow... Just goes to show that there is no limit to the number of diseases and viruses and pathogens and parasites and fungi out there.

Erin Allmann Updyke: Yeah, it's true. So Rift Valley fever is the one we're talking about today. But before we can tell you all about it and all the things that we learned, it's quarantini time.

Erin Welsh: It is. Erin, what are we drinking this week?

Erin Allmann Updyke: We're drinking Wolf In Sheep's Clothing. It'll make sense.

Erin Welsh: It'll make sense. Sheep are involved.

Erin Allmann Updyke: Very involved.

Erin Welsh: The wolf is the virus. Love to over explain a joke. It's how I do it.

Erin Allmann Updyke We went back and forth by text on the wolf is the virus, the virus is the wolf. Yes, okay. It's a great name. Oh, what's in a Wolf In Sheep's Clothing?

Erin Welsh A Wolf In Sheep's Clothing is your basic concoction of mezcal, grapefruit juice, a lemon-lime soda of your choice, and maybe a squirt of lime or something.

Erin Allmann Updyke And some jalapenos, right? A little spicy mezcal paloma situation.

Erin Welsh Yes. The crucial muddled jalapenos.

Erin Allmann Updyke And we'll post the full recipe for that quarantini as well as the non-alcoholic, equally delicious placeborita on our website thispodcastwillkillyou.com and all of our socials. So if you're not already following us, you should because the pics are delicious.

Erin Welsh On our website thispodcastwillkillyou.com you can find all manner of things. There's transcripts for all of our episodes, you can find links to our bookshop.org affiliate account, our Goodreads list, music by Bloodmobile, cool merch. We've got great merch.

Erin Allmann Updyke We do.

Erin Welsh Links to Patreon, links to a submit your firsthand account form, links to a contact us form. There's more there too.

Erin Allmann Updyke There's so much. Thispodcastwillkillyou.com, check it out.

Erin Welsh Yeah.

Erin Allmann Updyke If you haven't already, please check your podcatcher, make sure you're subscribed. If you haven't left us a review or a rating and you'd like to, now's your opportunity. You can do that right now and we would so appreciate it. We would really love it, it really helps the show. So thank you.

Erin Welsh She's not lying, she's totally right.

Erin Allmann Updyke We appreciate it and it helps us. Well then, shall we get into this virus?

Erin Welsh Let's do it. Let's take a quick break and begin.

TPWKY (transition theme)

Erin Allmann Updyke I think part of what surprised me about how little I knew about Rift Valley fever is how much of a classic TPWKY story it really is.

Erin Welsh Yeah.

Erin Allmann Updyke

I know that we are getting back to the roots of this podcast when I can go on the World Health Organization's website and find so much of the information that I'm looking for and even more so when there's a page on the World Organization for Animal Health website. So buckle up, this is a really classic piece of TPWKY content. So Rift Valley fever is a disease that's caused by a virus called Rift Valley fever virus. It's not very creative. And this is an RNA virus in the genus Phlebovirus, I think that's how you say it. And I think that the phylogeny of this group of viruses has changed relatively recently.

Erin Welsh

Okay.

Erin Allmann Updyke

But in any case, it's in the order Bunyvirales which is the same group that includes hantaviruses and Lassa fever virus and some others that we haven't yet covered.

Erin Welsh

Have we done Lassa fever, Erin?

Erin Allmann Updyke

No, we haven't done Lassa fever but maybe people have heard of Lassa fever. I know we haven't done it.

Erin Welsh

Wow, okay.

Erin Allmann Updyke

Erin, there's so many that we haven't done yet.

Erin Welsh

Yeah.

Erin Allmann Updyke

But hantaviruses we have. And with the exception really of the hantaviruses and Lassa fever and other arenaviruses, most all of the other viruses in this order, Bunyvirales, are transmitted primarily by arthropod vectors like ticks and mosquitoes. And Rift Valley fever virus is no exception, asterisk, but let's talk about it. So Rift Valley fever in humans is really considered a zoonotic disease which means that primarily it's not affecting humans, it's infecting animals. And it's generally considered to be only these spillover events that end up causing disease in humans. So there has to generally be some kind of animal outbreak, which we call an epizootic, before there is then a human outbreak. And this virus infects a pretty wide variety of animals. And the ones that end up being most important for us as humans are our livestock.

So this virus infects cattle, sheep, goats and other small ruminants, and camels. And sheep and goats tend to be the most severely affected. And it's transmitted to these livestock primarily by mosquitoes. But not just any one mosquito, no, no, no. Whole bunches of mosquitoes in multiple different genera, mostly transmitted by Aedes mosquitoes of dengue fever, yellow fever, chikungunya, like all the viruses, Aedes mosquitoes. As well as Culex mosquitoes of like West Nile virus and Japanese encephalitis virus fame.

Erin Welsh

It's so strange because usually viruses are so hyper adapted to their mosquito vector hosts, like that specific species. But this isn't. So what? How?

Erin Allmann Updyke

I have so many questions, Erin, about the pathophysiology or the life cycle of this virus in mosquitoes. Because we don't have as much information as I expect. Okay? And it's really interesting. So there's at least like 50 different species of mosquito that have been found to harbor this virus. And the transmission is like usually when we picture like a transmission cycle among let's say vector, host, maybe there's a secondary host, it's like a circle, right. The transmission of this virus, when you look at this, it's not a circle, it's like a circle with a line and another line and like two other branches. It's a mess.

Erin Welsh: Creative geometry.

Erin Allmann Updyke: It's a web. Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: So how does it go really? Usually when we're covering a vector-borne disease on this podcast, I can start like this and I'll start like this for this episode. Ready? A female mosquito, it's always a female mosquito, takes a blood meal from a host. Let's call it a sheep for accuracy.

Erin Welsh: Sure.

Erin Allmann Updyke: It drinks up some of the virus in that blood meal because the sheep is infected. And after some amount of time in the mosquito and varying amounts of this virus moving through the mosquito, it maybe makes it to the salivary glands or something like that. And then that mosquito takes another blood meal, spits the virus into the host, and boom, now you've completed the transmission cycle. And that cycle can happen in Rift Valley fever. But how long does it have to exist in the mosquito? How long does this virus have to be there?

Erin Welsh: Yeah.

Erin Allmann Updyke: I don't know. What does it do inside this mosquito? I don't know. Where does it go? Does it travel to the salivary glands or does it not? I don't know. I don't know, Erin.

Erin Welsh: Okay. And I anticipate that the answer to this question is I don't know but are different mosquito species differently capable of harboring, transmitting the virus?

Erin Allmann Updyke: Almost certainly, yes. Which one's more likely than less? I don't know. Here's where we can add another layer of complication. In addition to that transmission cycle, this virus can also be and is known to be transmitted from female mosquitoes into their eggs. This is called vertical transmission. And we know this happens at least in some species of Aedes mosquitoes but maybe not in all species, we're not sure.

Erin Welsh: Which has huge implications for the distribution of this virus in the landscape and the potential for outbreaks to happen in subsequent years, even outside of like big outbreaks like the intra-epidemic years or whatever.

Erin Allmann Updyke: It sure does, Erin. You're 100% right.

Erin Welsh: Wow.

Erin Allmann Updyke: Because it means that mosquito babies are essentially born infected, so they can inject virus into their host with the very first blood meal that they take. So not only can this virus potentially persist like among different seasons without necessarily needing to have reservoir hosts that are infected, you also can then have viral transmission even if mosquitoes aren't living long enough to transmit from animal to animal to animal because the very first blood meal that they take, they can potentially transmit this virus.

Erin Welsh: Okay. So here's another question though. It's not just the mosquito.

Erin Allmann Updyke: It's not just the mosquitoes.

Erin Welsh

It's not a question but you know where I'm going with that.

Erin Allmann Updyke

Let's keep going, shall we? I said that this was a web, so we shall continue along this transmission web.

Erin Welsh

Okay.

Erin Allmann Updyke

Once an animal host is infected, and again mostly in this case we're talking about livestock, ruminants, sheep, cattle, goats, camels, all of these animals also have vertical transmission themselves. So if a pregnant animal gets infected from a mosquito, it will almost inevitably pass that virus through the placenta to their offspring and this almost always causes spontaneous abortion or pregnancy loss. This virus can also be transmitted from mosquitoes to other wildlife and we don't fully understand the whole wildlife cycle. That's just like a black box. We know that it happens but we don't know what hosts are important, are they amplifying hosts or are they not, etc.

Erin Welsh

Are they maintenance hosts? Yeah.

Erin Allmann Updyke

But then we get to humans. How do we get infected in this tangled web? Well it could be the same way that our animal friends are getting infected via these mosquitoes. But what's far more common is that humans are infected from our infected animal friends themselves, either from direct contact with something like their blood, their raw milk, or other bodily fluids directly getting into our eyes, mouth, or other mucous membranes, or through breaks in our skin in the process of caring for or slaughtering these animals, or from inhaling aerosolized bodily fluids. So it's usually a kind of more direct transmission from animal to humans that ends up causing disease in humans. And then we as humans can also pass this virus through the placenta and potentially cause infection in a fetus. The only good thing thus far is that horizontal, meaning human to human transmission, has yet to be documented.

Erin Welsh

Okay.

Erin Allmann Updyke

And the same is true for direct transmission from animals to animals, like among a herd. So then why is it that humans can get infected from animals? We don't know. Is it just because of the ways that we happen to be interacting with and handling their tissues and bodily fluids? I don't know. But that is the like good news that I can say about the transmission of this virus.

Erin Welsh

Okay. I mean that makes sense because it's not like the animals are doing the slaughtering and inhaling the blood.

Erin Allmann Updyke

Right.

Erin Welsh

Yeah, humans are doing that. Okay. How many viral particles?

Erin Allmann Updyke

Ooh, no idea. Great question though.

Erin Welsh

Okay, okay. And it is through the aerosolization. Is it also contaminated surfaces? What's the durability of this virus in the environment?

Erin Allmann Updyke

There's so many other questions I could have tried to go down rabbit holes to answer that I don't have the answers for Erin. Yes, so there's differential virulence and that's likely due to, like you asked, how many viral particles does it take and things like that. People get more or less sick depending on what route they were more likely exposed to. And aerosol transmission seems to be the most virulent, so most likely to cause really severe disease is when you're inhaling it and it's going into your mucous membranes that way. The other common way that people get infected, and this could be from contaminated surfaces, but it's through contact with like broken skin. So you have an injury and blood or something like that gets into your bloodstream from that. So those are kind of the two most common ways. There have been some cases of things like raw milk which means that that could be potentially an oral or a GI exposure but we have just less data on that overall.

Erin Welsh

Interesting, okay.

Erin Allmann Updyke

Yes.

TPWKY

(transition theme)

Erin Welsh

This is maybe jumping ahead a little bit.

Erin Allmann Updyke

Okay, jump ahead.

Erin Welsh

But in an outbreak where it's not just livestock impacted but also humans, is there any known breakdown between how people have gotten exposed, like what proportion is mosquito vs direct contact, that kind of thing?

Erin Allmann Updyke

Of all the outbreaks that we have good data on primarily are happening from direct contact with animal fluids. It is very likely that mosquito-borne transmission absolutely plays a role in some outbreaks but it seems that overall across the board it is animal to human transmission that causes the vast majority of human cases.

Erin Welsh

Okay.

Erin Allmann Updyke

Which means that the people at highest risk are people who work in industries where they are coming into contact with animals.

Erin Welsh

Okay.

Erin Allmann Updyke

But as I'm sure you know and will probably talk about, some of the historic outbreaks have been very large.

Erin Welsh

Yeah.

Erin Allmann Updyke

Which means that certainly there's other things that are going on. And why in those cases did the outbreaks get so big? There presumably must have been also mosquito-borne transmission happening. So yes, it definitely can happen. But does it also just depend on like are mosquitoes more likely to bite humans or to bite animals and what mosquito species are circulating in those regions? Because again, this is so many different mosquito species. So yeah, there's a lot of layers. And we don't have great data on a lot of details on a lot of these outbreaks.

Erin Welsh

Yeah.

Erin Allmann Updyke

I wish we had more data. I wish that we had more data.

Erin Welsh

I mean don't we all?

Erin Allmann Updyke

Don't we? Yes. We do know some more about like what does this disease do, like what does it look like if an animal or if a person gets Rift Valley fever. Unsurprisingly given that this is a virus that infects so many different species, it presents very differently across different animals but even within humans it can present very differently. Across the board though we know that there's two main cell types in mammalian bodies that this virus is predominantly infecting. And everyone who listens to this show is well aware at this point that a virus has to infect a host cell in order to use our machinery to replicate. So which cells it's infecting tend to be really important in what kind of symptoms and what kind of disease we see.

So in the case of Rift Valley fever, the two main cell types that this virus is infecting are liver cells. So we'll talk about what that ends up doing. And then monocytes which are a type of white blood cell. And so especially in severe cases, the liver is one of the main sites of damage. So what does that end up actually looking like? If we look at animals, again the symptoms will vary depending on the type of animal that's infected as well as how old that animal is because universally young animals, so fetuses as well as newborn animals, are much more severely affected than older animals.

But in general, in almost all animals that are infected, all of these livestock animals, we see things like fever, we'll see the animal stop eating, they stop moving about, they don't really like walk around or get up and go around, they become really listless and lethargic. Especially in sheep you might start to see like evidence of GI inflammation, abdominal pain, bloody diarrhea. And these animals are like visibly in pain and uncomfortable. But the way that this virus ends up wiping out entire populations of livestock is because it passes through the placenta and then causes spontaneous abortions in pregnant animals and then has massive mortality rates in newborn and young animals. So in these livestock herds, especially in lambs and kids, which are baby goats, the mortality rate can be as high as 70%-100%.

Erin Welsh

It's devastating.

Erin Allmann Updyke

It's devastating. And even in adult sheep and things like baby cows or calves and adult cattle, the mortality rates can be as high as 20%-70%. So this is a very lethal infection for livestock animals. When it comes to humans, there is a really wide range of how this disease can present. Most papers across the board estimate that about 50% of people who are infected are essentially asymptomatic, like don't really show any symptoms whatsoever. And most people who do have symptoms will have a relatively mild disease and only a small percentage, and most papers say maybe 1%-2%, develop severe symptoms. And we'll talk about what those severe symptoms look like. But I want to caveat early on those numbers because A) it seems like maybe that 1%-2% is an underestimate for recent outbreaks or more modern outbreaks. And some papers cite this number, instead of saying 1%-2% of all cases, they'll say it's like 8% -10% of symptomatic cases.

Erin Welsh

Okay.

Erin Allmann Updyke

And I feel like looking at it that way really changes your perspective on this disease. Because as we'll go through some of these symptoms, this can be incredibly terrifying and really severe and so I think trying to understand like how big are these outbreaks that we're talking about and how many people are affected are really, really important. So let's talk about what it ends up looking like. If somebody is going to show symptoms of Rift Valley fever, symptoms usually start between 2-6 days after exposure. And it usually starts, as the name suggests, with a fever. Along with a headache, you'll have muscle or joint pains. Very often we see some like neurologic symptoms like vertigo or like in the firsthand account that photophobia, like it hurts to look at light.

Erin Welsh

Yeah.

Erin Allmann Updyke

You might have nausea or vomiting. And then if it remains a mild case, then this might last anywhere from like a few days, like 4 days to a week or so, and then often that person will get better. Sometimes it's not uncommon that people will have like a biphasic illness which means they'll get better and then a couple of days later their fever will spike again and they'll get sick for another few days before they improve for good. But there are several ways, three different ways really, that this can cause a much more severe illness. Here's the three ways. It can infect your eye, it can infect your brain and spinal cord, or it can destroy your liver and then you have a hemorrhagic illness. So let's go through those.

Erin Welsh

And these are not mutually exclusive.

Erin Allmann Updyke

They're not mutually exclusive but they're very different and so I don't know how often they happen all together.

Erin Welsh

Okay.

Erin Allmann Updyke

So in some people this virus seems to infect the eye, the back of the eye. And it can infect like a whole variety of parts of that. It could be the retina itself, it could be your nerve in your eye, it could be the macula, a whole bunch of different parts. And in those cases, that person might have had the same mild illness that I already described, get better, and then a week or several weeks later they'll start to have blurry vision or decreased vision. And then this can last a few months or it can end up causing permanent damage depending on which part of the eye ends up being infected with this virus.

Erin Welsh

Why the eye?

Erin Allmann Updyke

Why the eye? I don't know.

Erin Welsh

Okay.

Erin Allmann Updyke

Is it just an easy target? There's good blood supply there. Is it just that that's where the virus was close to? I have no idea. Also why is it so long after the initial infection? I don't know the like specific pathophysiology of what's going on. But that's not the only way that you can see this delayed response. Another way that it could go is that again a few weeks or even months after an initial infection, somebody might come down with a severe headache and signs of brain inflammation. That might look like confusion, disorientation, vertigo, even things like hallucinations or loss of memory. And this can progress to seizures, coma, and potentially death. And this is all a meningoencephalitis, so inflammation that's happening in the brain and the spinal cord as a result of Rift Valley fever.

Erin Welsh: Okay. And so this is like a consequence. This isn't the virus attacking those things necessarily, it's like a consequence of our immune response's reaction to the virus?

Erin Allmann Updyke: I don't know, Erin.

Erin Welsh: Okay.

Erin Allmann Updyke: Because we know a lot, and I'll link to a bunch of specific papers that look at like the gross anatomic pathology that's happening in these cases. We know that it's a lot of inflammation. Is it that virus is laying latent and then reactivating and causing this or is it that you're having delayed immune reaction to the virus? I am not 100% sure from all of my reading.

Erin Welsh: Okay.

Erin Allmann Updyke: And it could be that I'm not interpreting the reading correctly. Given the delay, it seems more likely that it's an inflammatory reaction, like an immune response.

Erin Welsh: Right.

Erin Allmann Updyke: But it's a little bit unclear to me from all of the reading that I did.

Erin Welsh: Well and I will say too, in that firsthand account, they talked about how as this person seemed to get better and then got worse and worse and then got better again and then worse. Later on they retested, they retook blood and re-injected it into mice to see is this still Rift Valley fever and the mice were fine.

Erin Allmann Updyke: Yeah. Okay, interesting.

Erin Welsh: So that's, I mean...

Erin Allmann Updyke: So then it suggests that it's more immune-mediated.

Erin Welsh: I mean the paper is from 1934.

Erin Allmann Updyke: Yeah.

Erin Welsh: Like who knows? But still, but still.

Erin Allmann Updyke: And just timing-wise that's sort of what it seems like, right?

Erin Welsh: Right.

Erin Allmann Updyke: This kind of neurologic disease when it happens can cause like long term neurologic complications and some sources suggest that it doesn't tend to cause death. But there was an outbreak in Saudi Arabia in the early 2000s which like 50% of people that ended up having neurologic complications died from that. So I don't think it's entirely accurate to say that you would never have death as a result of this type of neurologic manifestation of Rift Valley fever.

Erin Welsh: Yeah.

Erin Allmann Updyke

But it's less common than the final manifestation which is the most severe and that is when this virus causes a hemorrhagic disease. And it does this because of damage to the liver. So the way that this might present is that during that acute illness, so during that time when someone is sick with a fever, etc, someone might then start to appear jaundiced, so their skin or their nails or their eyes are starting to turn yellow. And that's a sign of liver damage because that yellowness is caused by something called bilirubin building up in your skin or your eyes because your liver can't break it down into the form that you can excrete.

And as your liver gets damaged, because your liver is also in charge of making most all of our clotting factors, now all of a sudden your blood can't clot the way that it should. So you start to have signs of bleeding and this could be things like large bruises or purpura, which are these like big dark purple splotches on the skin that are essentially just signs of bleeding underneath the skin. You might see bleeding from mucous membranes like your nose or your gums, you'll see bloody vomiting or diarrhea, really heavy menstrual bleeding. If this person is already hospitalized and getting poked for things like blood draws or IVs, they'll start to have bleeding from these sites of venipuncture. And this form of hemorrhagic disease is the most severe form. About 50% of people who develop hemorrhagic disease from Rift Valley fever will usually die within 3-6 days of the first sign of these hemorrhagic symptoms.

Erin Welsh

Do we know what factors make someone more likely to develop the hemorrhagic form or the ocular form or the neurological form or be completely asymptomatic?

Erin Allmann Updyke

Yeah, it's such a good question. It's probably similar to different species of animals that we see, it likely depends on host factors, right. So like who you are and what your immune system does in response to this virus. But also things like the route of transmission. So overall, like I said, the intranasal or airborne transmission seems to be more likely to cause severe disease than in animal models where we've like injected this virus into animals. But beyond that, there's like a lot that we don't know and don't understand. And again, I have several papers that go really deep into detail on what we do know which is a lot about like viral receptors and the histopathology of what's happening in your liver and what's happening where in your brain is there inflammation. But like how does this actually happen? Why are some people so severely affected and others are not? I don't have a good answer to that question.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

And you mentioned that the virus can also be transmitted from pregnant person to fetus. What does the infection look like in that situation?

Erin Allmann Updyke

Yeah, it depends. And we don't have a lot of data on this because there haven't been that many well documented cases. There's been enough to show that it is very likely that this virus can cross the placenta and infect a fetus. It can cause potentially, like it does in animals, spontaneous abortion. But again we haven't seen significant increased rates of spontaneous abortion in areas where there have been outbreaks, which is good news. But certainly it can also then cause infection in a newborn and because newborns have very little immune system, that infection is likely more likely to be severe. So there have been cases of neonatal deaths from this virus.

Erin Welsh

And where do we stand on treatment?

Erin Allmann Updyke

Yeah. We don't stand.

Erin Welsh

Yeah, okay.

Erin Allmann Updyke

There are no treatments that are specific for this virus which means that there's a lot of things that we have to do to try and prevent it. So mosquito control is an important part of that. Vaccines, and there are a couple of different vaccines for livestock, no vaccines for humans. But there are both like live attenuated vaccines and there are inactivated or killed virus vaccines. Pros and cons to both of those but they both exist and they both can be used both like on a regular basis in endemic areas in livestock as well as in the case of outbreaks, at least the inactivated form. But yeah, that's Rift Valley fever. It can be a really severe infection. And we'll talk more in detail about recent outbreaks that have happened, like why is it so severe sometimes or is it getting more severe? I don't know, Erin.

Erin Welsh

That is a great question.

Erin Allmann Updyke

It is. I still have the question. So Erin, when did we first find out about this virus? When did it spillover from animals to humans? What do we know about it?

Erin Welsh

Let me see what I can answer right after this break.

TPWKY

(transition theme)

Erin Welsh

On the surface, history and disease ecology seem like two entirely different fields. History of course deals with past events, especially from a human perspective, while disease ecology examines the relationship between a pathogen or pathogens, its host or hosts, and the environment. Like what would you learn in a history class that would be repeated in a class on disease ecology, besides the discovery of one disease or another?

Erin Allmann Updyke

Not a lot, Erin. That's why I love our podcast.

Erin Welsh

Me too, Erin. But as I was reading about Rift Valley fever, the first described outbreaks, the potential impact of climate change and land use change on future outbreaks, I realized how similar the approach that these two fields take really is. Because it all comes down to understanding the context. Why did this happen when it did and what can the past tell us about the future?

Erin Allmann Updyke

Ooh, love that.

Erin Welsh

Yeah, I know. This is my like hyper nerd... I was like whoa, disease ecology and history are the same thing. I finally get why I love this.

Erin Allmann Updyke

It finally all makes sense.

Erin Welsh

It all makes sense. But let's start with the first part of that, the why did this happen when it did, getting at the earliest known emergence of Rift Valley fever. In August of 1913, the Department of Agriculture of quote unquote "British East Africa" published its annual report. On the whole, it's some pretty dry reading. Crop counts, detailed descriptions of personnel vacations, the number of ingoing and outgoing letters for each subdepartment. Like do you want to know how many letters the veterinary department received and wrote in 1913?

Erin Allmann Updyke

I actually do.

Erin Welsh

It's 6800.

Erin Allmann Updyke: Wow.

Erin Welsh: It's more than I thought.

Erin Allmann Updyke: Yeah, that seems like a lot.

Erin Welsh: I know.

Erin Allmann Updyke: I mean they didn't have email. Think about how many emails they probably send now.

Erin Welsh: I know. It's kind of... I was like wow, that's a lot.

Erin Allmann Updyke: It's a lot. That's a lot of letters.

Erin Welsh: And these reports also included casual mentions of land theft and forceful removal under the guise of manifest destiny.

Erin Allmann Updyke: Yeah.

Erin Welsh: Right?

Erin Allmann Updyke: Okay.

Erin Welsh: So quote, "In June 1912 the removal of the Maasai and their stock from Laikipia was commenced and was brought to a successful conclusion on the 27th of March 1913." End quote.

Erin Allmann Updyke: Wow. Imagine just talking about like decimating human populations-

Erin Welsh: Right.

Erin Allmann Updyke: And forcibly removing human beings from their home that way.

Erin Welsh: Yeah.

Erin Allmann Updyke: Cool.

Erin Welsh: Yeah. I mean success definitely in the eye of the beholder in that successful conclusion.

Erin Allmann Updyke: Yeah.

Erin Welsh: Because just for a little bit of extra context, this removal broke the 1904 promise that the British had made to the Maasai to stop taking their land, which they ultimately stole about 70% of to make space for the incoming settlers. And they were like oh, the Laikipia plateau being at higher elevation, it's going to be more hospitable to the Europeans that are coming.

Erin Allmann Updyke: Wow.

Erin Welsh

Like it's just all part of it. Yeah. Yeah. But if you keep scrolling past this detached reporting of land theft and so on, you'll eventually come to a mention of a devastating disease impacting sheep. Quote: "A mortality of 90% was recorded among the lambs at government farm Naivasha. Other farms in the Rift Valley also suffered considerable loss. In some cases the symptoms were very acute and death occurred within a few hours. In others the disease ran a more subacute or chronic course. In the acute form the only symptoms shown were dullness, rapid respirations, collapse, and death within 4 hours. In postmortem the liver was found to be soft and friable and the kidneys congested. In the subacute or chronic form the umbilicus was incompletely closed and swelling of the joints occurred. Investigation pointed to the disease resulting from infection gaining entrance through the umbilicus." End quote.

Yeah. The sheep that were primarily impacted by this disease were Merino which were introduced for their wool. But there didn't seem to be much follow up or concern about this particular disease, perhaps because, quote, "the setback was only a temporary one." End quote. So this brief mention from 1912, buried in pages upon pages of bureaucratic minutia, stands out as the first description of what was likely Rift Valley fever.

Erin Allmann Updyke

Yeah.

Erin Welsh

Why then? Why in 1912, right?

Erin Allmann Updyke

Just because you brought all them sheeps there?

Erin Welsh

I mean that's part of it but it also does seem to impact the native species there as well. So maybe it's just visibility, like these Merino sheep are more susceptible, that's part of it. But I think there are some other things going on too. So later genetic analyses would place the origin of the Rift Valley fever virus as recently as the 1880s-1890s.

Erin Allmann Updyke

What?

Erin Welsh

Yeah. So it could have just been that this was one of the earliest outbreaks that this virus caused.

Erin Allmann Updyke

Interesting. So where did this virus come from?

Erin Welsh

Great question. I don't know. Because also viruses do this thing where one strain tends to dominate in an outbreak and it replaces all the other strains and kind of makes it look like it's the only one. And so this could underestimate how old the virus truly is. So maybe it is a lot older but it's just sort of doing this whole strain replacement type of thing. But regardless of when the virus evolved, it likely had caused infections prior to 1912. And the reason though that it was first described then is probably because of colonization, right. Importing Merino sheep which might be more susceptible to the virus as we talked about. But also there's the looking for it.

Erin Allmann Updyke

Right.

Erin Welsh

In these agricultural reports, the British were monitoring their investments, seeing how well the introduced crops and livestock like Merino sheep did on the lands that they stole and noting what diseases posed a threat to their income, like Rift Valley fever. This is the reason that tropical medicine was founded as a field of study.

Erin Allmann Updyke

Right. Yep, yep, yep.

Erin Welsh

To better understand, prevent, and treat the diseases that were prevalent in an area undergoing colonization. The chief veterinary officer who made the initial report, R. J. Stordy, wasn't noting this sheep disease out of academic curiosity but out of a 'oh, this might be something we have to look out for as settlers set up their farms here' type of a thing.

Erin Allmann Updyke

Right.

Erin Welsh

R. E. Montgomery, the veterinary pathologist at the time, even signed off his report with quote: "In conclusion, I may add that only such diseases as appeared to me to possess considerable interest to the stock owner have been dealt with in this report. There have been a considerable number of others which are as yet fortunately of minor importance. I consider it our duty so far as possible to undertake the preliminary investigation of all diseases which come within our knowledge and by doing so to be in some measure prepared for eventualities." End quote. Science and the questions that we ask in science have always been guided by certain values or principles or interests.

Erin Allmann Updyke

Oh yeah. Yeah.

Erin Welsh

And I just feel like that part doesn't really get highlighted a whole lot in this type of research, yeah.

Erin Allmann Updyke

Oh no. Because it's stories of like discovery for discovery's sake.

Erin Welsh

Yes.

Erin Allmann Updyke

Or like this is so cool and interesting and then was used. But yeah, no, I mean...

Erin Welsh

Right.

Erin Allmann Updyke

Much of the time specific things were being studied at the bottom line for money.

Erin Welsh

Yeah. I mean then the chief veterinary officer for the Department of Agriculture wasn't just like screening sheep left and right. They're more interested in diseases affecting sheep than the diseases affecting wildlife.

Erin Allmann Updyke

Right.

Erin Welsh

Because sheep was where the money was, not wildlife.

Erin Allmann Updyke

100%.

Erin Welsh

Okay. But what happens next, right? Like what happens after 1912? Well nearly 20 years would pass before the disease appeared in another scientific publication, one that would give it its name and identify the causative agent. In 1931, Daubney and Hudson from the Division of Veterinary Research Kenya Colony described a devastating outbreak of unknown cause in sheep, Merino sheep, on a farm in the Rift Valley. The disease primarily impacted newborn lambs or pregnant sheep. At the start of the outbreak, 60 of the 80 lambs born died within a matter of weeks. The authors noted that the farm manager chose July and August as the lambing season that year which was somewhat unusual. Normally it was May or October to November, right. So you choose like when the lambs are born.

Erin Allmann Updyke

You... Sorry, how do you choose that?

Erin Welsh

You put the sheep together at a certain time.

Erin Allmann Updyke

Oh wow.

Erin Welsh

Yeah.

Erin Allmann Updyke

I didn't know you could...

Erin Welsh

Well you do this so that you can time it with like when-

Erin Allmann Updyke

Rainfall.

Erin Welsh

Rainfall, when grass is available.

Erin Allmann Updyke

Grass.

Erin Welsh

Grazing lands, etc.

Erin Allmann Updyke

Interesting. Okay.

Erin Welsh

So why July and August of that year? Well it turns out that in that same year the area had received an unusually large amount of rainfall, over 45 inches compared to the annual average of 25, which is a ton. So this meant more grazing habitat during the dry season and so the manager figured it would be safe to lamb in July and August, especially if the heavy rains in the beginning of the year were repeated in November which would make it harder on the lambs that were born then. So kind of just like hedging your bets. Like well things are looking good right now, let's lamb right now. Or like however many months from now.

Erin Allmann Updyke

And the rainfall and mosquitoes.

Erin Welsh

The excess rainfall, yep, also meant more habitat for other critters like midges which can transmit a virus that causes the livestock disease bluetongue, which I also saw peak in that year, and mosquitoes which of course carry the Rift Valley fever virus. Those 60 lamb deaths in early July turned out to be only the tip of the iceberg as the disease tore through the flock, killing lambs and ewes within hours of the first symptoms appearing. By August 10, 1930, about a month after the outbreak began, quote, "the total mortality in lambs had reached approximately 3500 and upwards of 1200 youths had died." End quote.

Erin Allmann Updyke

Wow.

Erin Welsh

I think it was a mortality of 95%.

Erin Allmann Updyke

Oh my god.

Erin Welsh

Yeah. The farm manager was desperate to save the surviving sheep and so he transported them to another farm higher up, around 7000-8500 ft in altitude which is 2100-2600 m.

Erin Allmann Updyke

Okay.

Erin Welsh

The other farm, the original farm was about 5500-6000 ft, 1700-1800 m. After arriving there at higher up, the deaths continued for a few days but eventually stopped.

Erin Allmann Updyke

Okay.

Erin Welsh

But the disease continued on the original farm for months after. And so this could be because there aren't as many mosquitoes at higher elevations, maybe like the temperatures keep it down or the humidity or whatever it is. Or the mosquitoes that carry the virus don't live at higher elevations even if there are other mosquitoes there or the mosquitoes at those higher altitudes just weren't infected. And so to try to answer this, I did a little bit of digging and found a 2016 paper that noted that the risk of Rift Valley fever tended to go down as altitude went up. But it doesn't seem like there's been extensive research about the altitudinal range of the vector mosquitoes. Or like all of these questions that are like are mosquitoes capable of transmitting the virus existing or living at higher altitudes?

Erin Allmann Updyke

Right. Well and it's hard because there's so many species, Erin. Like which one do you pick?

Erin Welsh

So many species, right?

Erin Allmann Updyke

Yeah.

Erin Welsh

And then like if higher altitude means less likely infection, will that change as the climate changes? Probably. But I'm getting ahead of myself. Daubney and Hudson, the authors of this 1931 paper, got to the farm and began their susceptibility tests, their postmortems, their analyses. And they isolated a virus that they named the Rift Valley fever virus, found that it caused the highest mortality in sheep but that goats and cattle could also be infected, as could humans.

Quote: "During the course of the investigation, all the four Europeans engaged developed a dengue-like fever which we now know to have been due to infection with the virus. The first person to be attacked was Mr. F. Lyons, the laboratory assistant in charge of the exposure experiment on the farm where the disease first appeared. Mr. E. J. Hall, who assisted in the laboratory investigation, was next attacked. A few days later both writers developed symptoms within a few hours of each other. In every case the onset of the attack was characterized by a very brief period of general malaise, followed rapidly by sharp rigors and headache. The temperature rose to about 103°F and the face was brightly flushed. And from 3-6 hours after the rigors had passed off, pains developed in or near the joints extending from the base of the skull to the extremities. Fever persisted for a period of from 12-36 hours and the pains gradually disappeared within about four days."

And then they would go on to say that every quote unquote "native" that was herding sheep during the attack also got sick with fever and aches and pains and that the manager just chalked it up to eating, quote, "the somewhat decomposed carcasses of dead sheep." End quote.

Erin Allmann Updyke

Great, great.

Erin Welsh

Yeah.

Erin Allmann Updyke

Okay.

Erin Welsh: Yeah, just some casual racism thrown into that paper.

Erin Allmann Updyke: Not surprising at all.

Erin Welsh: Nope, nope. This 1931 paper clearly described this newly recognized disease, the responsible virus, the symptoms it caused, and its association with wet years, even noting that, quote, "the dengue-like fever in man would in all probability fail to attract serious attention in view of the fact that in such years the incidence of malaria would be unusually high." End quote.

Erin Allmann Updyke: Yeah. So they're like it's-

Erin Welsh: Obscured. Yeah.

Erin Allmann Updyke: Right. It's here but it's not as big of a deal as the other stuff, so no one's looking at it.

Erin Welsh: Right.

Erin Allmann Updyke: Yeah.

Erin Welsh: And it's also like everyone's getting sick from these other things and so it kind of flies under the radar.

Erin Allmann Updyke: Right, right, right.

Erin Welsh: Yeah.

Erin Allmann Updyke: Okay, makes sense.

Erin Welsh: And so but with that similarity to malaria pointed out, they made an educated guess that the Rift Valley fever virus was transmitted like malaria by mosquitoes.

Erin Allmann Updyke: Love that.

Erin Welsh: Yeah. But it was also clear that mosquitoes were not the only way you could get exposed to the virus. First you had the four who worked on the virus including Daubney and Hudson get sick, along with so many people who worked with sheep in the field, presumably from handling samples or directly interacting with the sheep themselves. But then the disease started to crop up in laboratory researchers a long way from Kenya, especially those who performed necropsies on the lambs. And the first known death from Rift Valley fever in humans was recorded in 1933 or 1932 from our firsthand account.

Erin Allmann Updyke: Okay.

Erin Welsh: This death though would stand out as somewhat of an anomaly for the four or so decades that followed the publication of Daubney and Hudson's paper. From the 1930s to the 1970s, Rift Valley fever caused nearly two dozen epizootics throughout Africa, first spreading from East Africa to South Africa, and infections seemed limited to livestock only. Few human cases were noted and no deaths. And these weren't necessarily small outbreaks. One epizootic in Kenya from 1950-1951 led to 500,000 sheep infections and 100,000 deaths.

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah.

Erin Allmann Updyke

That's like I feel like when you hear numbers like that, it's just so hard to imagine that much death and devastation honestly.

Erin Welsh

It is. And like livelihoods ruined.

Erin Allmann Updyke

Absolutely ruined, yeah.

Erin Welsh

Was it possible that in an epizootic like this, just no one was looking for human cases and they were just mild or asymptomatic? I mean potentially, likely. But researchers screened some of the people that were handling animals during the outbreaks and found really low levels of antibodies to the Rift Valley fever virus, suggesting that they weren't getting infected at all.

Erin Allmann Updyke

I have so many questions, Erin.

Erin Welsh

I know. Because this isn't the way things stayed.

Erin Allmann Updyke

Yeah.

Erin Welsh

Right? Like this epizootic happening every few years causing a few mild human infections, if any, but lots and lots of animal infections and death. That was going to be a thing of the past. The first signal that something changed came in 1974 and 1976 when South Africa saw half a million animal infections and the first human deaths due to Rift Valley fever virus in South Africa. This time not from laboratory workers and more human infections than had ever been reported. 110 lab diagnosed cases and 7 deaths.

Erin Allmann Updyke

Wow.

Erin Welsh

But this outbreak would quickly be overshadowed by another, resulting in a total paradigm shift for this disease that would shape our understanding of the virus and its relevance in public health. Between 1977-1979, Rift Valley fever ripped through Egypt which had never seen a case before. In fact no cases outside of sub-Saharan Africa had been seen before this. Officials estimated that half of all susceptible animals in the country were infected.

Erin Allmann Updyke

Whoa.

Erin Welsh

Yeah. Which absolutely devastated the Egyptian economy. As if that wasn't bad enough, the disease also caused extensive morbidity and mortality in humans, with an estimated 200,000 human infections and 600 deaths.

Erin Allmann Updyke

Yeah. I mean so different than these early outbreaks that you're discussing.

Erin Welsh

So, so different. And even in the past outbreaks when there had been some human infection, they were mild.

Erin Allmann Updyke

Right. And small comparatively.

Erin Welsh

And small.

Erin Allmann Updyke

Yeah.

Erin Welsh

Small numbers, yeah. But this outbreak in Egypt, there was hemorrhagic disease, there was encephalitis, there was ocular disease, all of these extreme manifestations of the virus that you described. And with this outbreak came the realization that this was more than a potentially devastating disease for livestock. Rift Valley fever also posed a serious threat to humans. This became more and more apparent over the following decades, first in 1997-1998 with a devastating epizootic and epidemic in Kenya after rainfall exceeded 60-100 times the normal amount-

Erin Allmann Updyke

Wow.

Erin Welsh

Resulting in livestock losses up to 70% on some farms and an estimated 89,000 infections and 478 deaths in humans. Then Rift Valley fever continued to expand its geographic range with the first cases of Rift Valley fever outside of Africa happening in Saudi Arabia and Yemen in 2000, where it caused 880 lab confirmed cases, the real number is likely much, much higher, and 123 deaths. Since then Rift Valley fever has settled into this new pattern, causing occasional epizootics and epidemics after periods of unusually heavy rainfall, often resulting in hundreds if not thousands or tens of thousands of human cases and deaths as well as severe economic losses due to livestock mortality. And so circling back to those two questions that I asked at the start of this, why did Rift Valley fever become deadlier and cause larger outbreaks over the past 50 years or so, and what can that tell us about future outbreaks?

Erin Allmann Updyke

Yeah.

Erin Welsh

The answer to those questions is complicated because we've got so many interconnected factors at play, right. We've got the virus itself, how likely it is to mutate or reassort or recombine, how often it gets an opportunity to become more virulent. We've got the vectors, how abundant they are, which species are in which areas, whether different species are equally good at transmitting the virus, whether different species tend to bite humans or livestock more readily, how often they feed, how long their eggs which could potentially contain the virus last between epizootics in the environment. We've got the hosts, how many sheep are in a certain area, how controlled their movements are, how susceptible they are, whether the animals have been vaccinated, when lambing happens, importation of animals from affected regions to ones where the virus has never appeared, how many humans live or work near outbreak areas, whether they have access to protective equipment when handling infected animals, whether this region has the resources to monitor outbreaks and take steps to prevent or control the disease if it appears. I'm not done.

Erin Allmann Updyke

There's more. I know there's more.

Erin Welsh

Because then there's the environment.

Erin Allmann Updyke

Right.

Erin Welsh

Rainfall amount, humidity, temperatures, soil type. Some soils retain water better than others which in turn has an effect on mosquito habitat, the propensity of certain areas to flood. Vegetation density and type which also affects mosquito breeding habitats and grazing, deforestation, irrigation, dams, El Niño events, wind, and so many other factors.

Erin Allmann Updyke

Well wildlife.

Erin Welsh: Wildlife, yes. What potential hosts-

Erin Allmann Updyke: What other hosts are around besides your livestock?

Erin Welsh: Yeah.

Erin Allmann Updyke: And what kind of density and what kind of environments, what kind of mixing? What species of mosquito are biting them vs you vs your livestock? It is an unbelievably complicated... This is why we don't have predictive models. That's the... Spoiler.

Erin Welsh: Well we do, that's the kind of cool thing. I mean no but like we do and we don't, right.

Erin Allmann Updyke: Right.

Erin Welsh: Do we have perfect models? There's no such thing.

Erin Allmann Updyke: Right.

Erin Welsh: We're never going to have the amount of data. Ecology is just too noisy. There's too much going on, it's too difficult to collect, things are changing too much. Drawing a straight line from cause to effect is impossible.

Erin Allmann Updyke: None. Doesn't exist, yeah.

Erin Welsh: I mean yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: Just not really a feasibility. But even with all of these moving parts, there are some ways that we are able to see what the future might look like. And it also might help us to answer some questions about the past. Why Rift Valley fever became more deadly and more likely to cause human deaths about 50 years ago, I mean it's probably a mix of those moving parts, maybe mutations or reassortments of the virus, increased rainfall events because of climate instability, increasing herd sizes, and crucially movement of infected animals across large geographic areas especially from endemic to naive areas. More virus equals more infections equals more opportunities to become deadlier. We don't have a perfect roadmap for how this happened. But putting together the drivers of these past outbreaks or some factors associated with these past outbreaks can give us clues about the future. So there's a cool paper from 2024 by Chemison et al that talks about how they created a model using climate data to see if they could accurately predict past Rift Valley fever outbreaks across Africa.

Erin Allmann Updyke: Okay.

Erin Welsh: And it is Just like primarily climate data.

Erin Allmann Updyke: Okay.

Erin Welsh

But their model did a pretty good job which is exciting in itself. But what this also means is that you could tell this model, okay, this is what the climate is projected to look like in the next 10 years for this region or that region or even the next year or the next 5 years, whatever you want. And you could see how those different climate scenarios or climate change scenarios could impact the risk of Rift Valley fever outbreaks.

Erin Allmann Updyke

Right.

Erin Welsh

Broad strokes right now seems to be that things will get wetter in affected regions which means more outbreaks potentially. And so you could say, okay, next year what is it going to look like potentially for rainfall? And you could place higher alert. And so then if an outbreak does start to happen, are there things that you can do to cut that outbreak short?

Erin Allmann Updyke

Right. What are the plans that you put in place knowing that this is going to be a wetter year, knowing that that's going to increase the risk of transmission. How do you then deal with it?

Erin Welsh

Right, right. And so these models are not perfect but they can help to create early warnings to focus resources during certain areas at certain times in places where resources typically are often very limited. To see where Rift Valley fever might spread as the climate changes, like you'll see some papers that are like Rift Valley fever in Europe, is this where it's going to be now? And these models can be updated as we learn more about this virus, about the climate, about the hosts, about the mosquitoes, about everything.

Erin Allmann Updyke

Yeah.

Erin Welsh

They are a really important part of our tool kit but they're not the only thing. So speaking of which, Erin, I was hoping that you could tell me where we are with Rift Valley fever today and whether there's maybe a human vaccine in the works.

Erin Allmann Updyke

We'll talk about it right after this break.

TPWKY

(transition theme)

Erin Allmann Updyke

So like you mentioned, Erin, when you were talking about where we first saw this virus and how it has spread, this is a virus that's endemic at this point in animals and/or mosquitoes across eastern Africa, all the way into southern Africa, honestly across the entire continent into Western Africa and has gone north into Egypt and caused a few outbreaks on the Arabian Peninsula. Looking at the World Health Organization's outbreak reports, because they have disease outbreak news reports and this is absolutely one of the viruses that gets reported on if there are any human cases, the most recent outbreaks that they reported were actually a couple of years ago which I was a little bit surprised about. There haven't been any that they reported thus far, as of the time of recording, in 2023 or 2024. The most recent outbreak that the World Health Organization reported on was in Mauritania in 2022. And in this outbreak, there were 47 cases confirmed in humans. Almost all of them were people who worked with animals of some kind, many animal breeders. But of those 47 cases, 23 people died.

Erin Welsh

Wow.

Erin Allmann Updyke

Which is a case fatality rate of 49%. In this outbreak, of the animals that they tested there were nearly 300 animals that were positive for Rift Valley fever virus, 24% of those animals died. And these were a mix of cattle, camels, and small ruminants. If we look back at past outbreaks, in 2021 there was an outbreak in Kenya that had 32 confirmed human cases and 11 deaths which is a case fatality rate of 34%. There was an even larger outbreak in Mauritania in 2020 with at least 75 people confirmed positive, over 200 people were suspected to be infected, and at least 25 deaths. And what I was thinking in looking through all of these individual outbreaks, and again you can link to all of these on the World Health Organization website, there's a number more dating back to like the 2010s, that these are very high case fatality rates.

Erin Welsh

Yeah.

Erin Allmann Updyke

Very high compared to what we have seen in the past and very high compared to what all of the sources that I read would lead you to expect. When we talk about 1%-2% of cases or even 8%-10% of symptomatic cases being severe and 50% of hemorrhagic cases ending in death, right. That's the numbers that I cited earlier.

Erin Welsh

Yeah.

Erin Allmann Updyke

So what is going on here? Like does this mean that in these outbreaks the cases that we are able to report, that the World Health Organization is reporting, are those cases only the tip of the iceberg?

Erin Welsh

Probably.

Erin Allmann Updyke

In a case... Yeah, that's possible. I did some Erin math to try and get a handle on what that would mean. So if we look at the outbreak in Mauritania in 2022, we had 47 people that were confirmed to be infected and 23 people who died. If we think that that means that those cases were only the people who had severe infection, if we tried to Erin math that outbreak, then we would estimate that that outbreak could have been as large as like 4700 people who were infected. If we were expecting that only 1%-2% of all people who are infected had severe symptoms and 50% of people with severe symptoms, that would be those 47 people, 50% of those people would end up dying. That's my Erin math of the situation. Does that make sense?

Erin Welsh

Yes.

Erin Allmann Updyke

We don't have any data to suggest that that is what happened, at least that has been reported that I have seen. So I'm not trying to say that these cases are actually, these outbreaks are actually thousands more than we think but that is one possibility. The other possibility is that case fatality rates are indicative of much more severe illness than we have seen in the past. And if so, why? Is that because the virus is changing? Is that because something was happening with hosts who were infected at the time? I don't know. But there was a paper from PLOS Neglected Tropical Diseases that was the systematic review and meta-analysis of all the case reports from the last few decades. They looked at like 32 different studies. And they found an overall 21% fatality rate among those who had symptoms of disease. So it seems like the mortality rate may be on the rise from Rift Valley fever. And we don't, as far as I read, understand what exactly might be driving that.

Erin Welsh

Which is Very interesting because, as we talked about, the virus is not directly transmitted human to human.

Erin Allmann Updyke

Exactly, it is not. And there still has been no evidence that that has started.

Erin Welsh

And so what is going on in the environment? Like it must be something that is happening to increase the virulence. Is there a corresponding increase in virulence in the affected animal species?

Erin Allmann Updyke

And it's hard because it's already so virulent.

Erin Welsh

Right. How can you go up from 90%?

Erin Allmann Updyke

Right, yeah. So no. And I haven't seen data that suggests that it's killing more animals. It's certainly still killing hundreds, tens of thousands if not hundreds of thousands in many outbreaks. But yeah. So it's very interesting. It's going to be important I think to watch what is actually happening. And I think too, I'm sure, that especially for these last few years of outbreaks there will be more papers coming out that maybe look at a larger swath of the population where these outbreaks occurred to try and get sense of like what is the seroprevalence in that population? How big were these outbreaks really? In some studies that have looked across endemic areas, there have been seroprevalence studies that have estimated anywhere from like 6%-8% of humans and 8%-12% of livestock show evidence of prior infection. So this virus is out there circulating even when we're not necessarily seeing it cause epizootics or outbreaks in humans. So what do we do about it all?

Erin Welsh

Yeah. I was just about to say is there a vaccine in the works?

Erin Allmann Updyke

Yeah. There are many.

Erin Welsh

Okay.

Erin Allmann Updyke

So there are two already, at least two and there might be multiple versions, but there are two that exist for animals, for livestock. Neither of them are perfect. The live vaccine is very effective. A single dose of the live vaccine is very effective but it has a lot of drawbacks. It tends to cause spontaneous abortion in animals if they are pregnant.

Erin Welsh

Okay.

Erin Allmann Updyke

Because it is a live vaccine.

Erin Welsh

Yep.

Erin Allmann Updyke

Even though it's less virulent. You also can't give that vaccine during an outbreak because it can actually end up amplifying the outbreak.

Erin Welsh

Right.

Erin Allmann Updyke

And there's always a risk because it's a live vaccine that it would then kind of mutate back closer to the wild type and then cause disease outbreaks amongst animals or humans. So those are the big drawbacks of the live vaccine. There is also an inactivated vaccine. They require multiple doses, I think at least three doses, which makes them more difficult to implement in a lot of areas. And they just don't provide quite as long lasting of protection. But they also don't have the drawbacks that the live vaccine has. So unsurprisingly this is one of the main areas of research is developing a vaccine, especially one that could be used for both livestock and humans. There's at least one that's being studied right now in both the UK and in Uganda, or at least when this paper was published in 2022 it was being studied in these areas in both livestock and humans, that was using a viral vector very similar to some of the COVID vaccines that we saw that used like a viral vector as a vaccine. But there's also like a whole bunch of different vaccine candidates that people are studying. We don't have any that I saw that are super close to being ready for use in humans.

Erin Welsh

Okay. That's disappointing.

Erin Allmann Updyke

Yeah but maybe by the time this episode comes out, there will be a new paper that changes that that. Because I mean as of a couple of years ago, they were definitely studying it.

Erin Welsh

Yeah.

Erin Allmann Updyke

And I think that with all of the advancements that we've seen in vaccine platforms since COVID, I think that we are very likely to see the development of vaccines for viruses like Rift Valley fever because of what a huge impact it has on livestock, on economics, and on human health and public health. So there is a vaccine that some veterinarian laboratory personnel have gotten.

Erin Welsh

Okay.

Erin Allmann Updyke

There is a vaccine that people have gotten when they are at very high risk for infection but it's an animal vaccine that has never been licensed or approved for use in any country.

Erin Welsh

Interesting. Okay.

Erin Allmann Updyke

Yeah. Someone's like I've been vaccinated. That's very cool, it's not approved. So yeah, that's Rift Valley fever. I feel like it is one that should get more press than it has gotten perhaps. Like it made me more nervous than I...

Erin Welsh

Absolutely. I feel like yes, it is a scary and potentially very impactful disease in a public health context. But also just as a livestock disease, it's so economically devastating and traumatizing.

Erin Allmann Updyke

Yes.

Erin Welsh

Because just again, from one day to the next or like one week to the next-

Erin Allmann Updyke

Yeah.

Erin Welsh

You could lose your entire herd, your entire livelihood.

Erin Allmann Updyke

Right. It's I mean absolutely devastating the size of some of these outbreaks. And we'll link to some papers that have kind of details on all of the dozens of outbreaks that have happened over even just the past 20 years. I mean some of them have been hundreds of thousands of livestock.

Erin Welsh

Yeah.

Erin Allmann Updyke

It's just I mean horrific.

Erin Welsh

Unfathomable. Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

Well speaking of sources, shall we share some sources?

Erin Allmann Updyke

Let's share so you can read some more.

Erin Welsh

Okay. I'm gonna shout out three in particular. By Baba et al from 2016, 'Has Rift Valley fever virus evolved with increasing severity in human populations in East Africa?' By McMillen and Hartman from 2018, 'Rift Valley Fever in Animals and Humans: Current Perspectives'. And that modeling paper that I mentioned in the last bit of the history by Chemison et al from 2024, 'Ability of a dynamical climate sensitive model to reproduce historical Rift Valley fever outbreaks over Africa'.

Erin Allmann Updyke

I have a number of papers, a couple that I wanted to give a shout out to. One was that PLOS Neglected Tropical Diseases paper, it was from 2022. It was titled 'Clinical manifestations of Rift Valley Fever in Humans: Systematic Review and Meta-Analysis'. Another was from the Journal of Veterinary Research from 2021 called 'Rift Valley Fever: A Growing Threat to Humans and Animals'. And there was a number of other ones. So we will post the list of all of our sources from this episode and every single one of our episodes, you can get so deep on the neuropathophysiology on our website thispodcastwillkillyou.com under the EPISODES tab.

Erin Welsh

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

Erin Allmann Updyke

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Erin Welsh

Thank you to everyone at Exactly Right.

Erin Allmann Updyke

And thank you to you, listeners. I hope that you enjoyed this episode.

Erin Welsh

Yeah. I hope you learned something new. That's always my hope. I certainly did.

Erin Allmann Updyke

Always. It's our favorite thing is to learn new things.

Erin Welsh

It truly, truly is.

Erin Allmann Updyke

Yeah.

Erin Welsh

And a special thank you to our wonderful patrons. We appreciate your support so, so very much. It really means a lot to us.

Erin Allmann Updyke

It really does. Thank you.

Erin Welsh

Well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.