

Erin Welsh

"On July 19th during dinner, announcement was made of the departure of Sister Rogers after an illness of eight days. This was the beginning of a great time of sorrow for Bethabara and for me. A strange kind of fever had broken out amongst us and most of those living in Bethabara had it in more or less a serious form. My doctor was much worried for the usual treatment for fever gave little relief. Of those who left us, Sister Rogers was the first but not the last. Next came Catherine Sidle and it seemed almost impossible that only a few short weeks before she had traveled south with us. Her husband missed her sadly and it was only a few days later that he returned from a visit to Bethania, oppressed by the feeling of utter weariness which we were learning to recognize as the first symptom of the disease. He did not seem very ill at first but when hope was expressed for his recovery he shook his head and so it was.

And then my Martin. Perhaps because of his unremitting efforts for others, he was seriously ill from the first. He saw what was coming. His pain was intense as it always was in the earlier stages of the fever. His request was, 'Stay by me and hold my hand, hold it tight.' And when the fever mounted, when the terrible red splotches broke out on his body, when delirium came, he still felt my presence and was quieted as I held his hand in mine, spoke gently to him, or sang some of our best-loved hymns. Then he became unconscious of pain or weariness but we were still hand in hand when the call came that took him back to the eternal home. Others were laid to rest beside him but I was stunned and rebellious and nothing seemed to matter much. The fever that took Martin from me persisted until late in the fall, though with decreasing violence and we heard that it was prevalent in many parts of North Carolina and Virginia."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

Whoa.

Erin Welsh

Yeah.

Erin Allmann Updyke

That's a sad story.

Erin Welsh

It's really sad. So that is from an account from 1759 and I found it in a paper referenced in a book that I read. The paper is titled 'A 1759 spotted fever epidemic in North Carolina'. Before we go any further it's debated, like the whole purpose of this paper is to say this might be an instance of spotted fever or Rocky Mountain spotted fever, it's not certainty.

Erin Allmann Updyke

Okay.

Erin Welsh

But I liked the account so much that I wanted to read it.

Erin Allmann Updyke

It was a really good account.

Erin Welsh

Right? It's heartbreaking.

Erin Allmann Updyke

By everything that was in the account it certainly could be Rocky Mountain spotted fever.

Erin Welsh

There are a few things, as we'll talk about, that seem a little bit off to me. I mean the fact that was it contagious? It seemed to strike all at once, that's not contagious.

Erin Allmann Updyke

Yeah, that's the one thing.

Erin Welsh

Anyway, so yeah.

Erin Allmann Updyke Okay.

Erin Welsh Maybe we should pump the brakes because Erin, what are we? This is This Podcast Will Kill You. I'm Erin Welsh.

Erin Allmann Updyke And I'm Erin Allmann Updyke.

Erin Welsh Welcome. Wow, we did that all weird and backwards.

Erin Allmann Updyke Yeah, that was backwards but we're professionals.

Erin Welsh Oh totally. We've done this before, right?

Erin Allmann Updyke We've done this before. 50... Oh I lost count already!

Erin Welsh This is 55 or 56.

Erin Allmann Updyke No!

Erin Welsh Yeah.

Erin Allmann Updyke I thought it was 52. (laughs)

Erin Welsh (laughs) Antibiotics was last week!

Erin Allmann Updyke Oh gosh.

Erin Welsh Well this week we are covering Rocky Mountain spotted fever or-

Erin Allmann Updyke Rickettsia rickettsii.

Erin Welsh Yes, spotted fever group rickettsia.

Erin Allmann Updyke I am very excited about this episode, Erin.

Erin Welsh I didn't start out that way but I've come around and now I'm thrilled.

Erin Allmann Updyke I have known that this was going to be a great episode since we literally decided to make a podcast, okay.

Erin Welsh Oh okay. Can I guess the two reasons why?

Erin Allmann Updyke Okay, yeah, please guess them.

Erin Welsh Are there two reasons why, first of all?

Erin Allmann Updyke No but please guess them. (laughs)

Erin Welsh (laughs) Okay number one is because the quarantini name.

Erin Allmann Updyke So what's our quarantini name, Erin?

Erin Welsh Nice segue, Erin. Oh my god, we're being so obnoxious. Okay. Our quarantini is Cold As The Rocky Mountain Spotted Fever.

Erin Allmann Updyke That's the most clever name that we could come up with, it's so good. We came up with that quarantini literally the same moment that we came up with a podcast idea.

Erin Welsh Yeah, it was on our list that very first day.

Erin Allmann Updyke Original.

Erin Welsh At the picnic, or at the barbecue.

Erin Allmann Updyke Yeah, exactly.

Erin Welsh What are the quarantini names?

Erin Allmann Updyke So in this quarantini of course you have to have Coors Light, not sponsored.

Erin Welsh Because the logo is Cold as the Rockies, just in case anyone has forgotten.

Erin Allmann Updyke And basically we're making a shandy out of it.

Erin Welsh Yeah.

Erin Allmann Updyke Super simple.

Erin Welsh Summertime, delicious.

Erin Allmann Updyke We'll post a full recipe for that quarantini as well as a nonalcoholic placeborita on our website thispodcastwillkillyou.com and all of our social media channels.

Erin Welsh Yes we will.

Erin Allmann Updyke So Erin, what's the second reason that you knew I was gonna be excited about this episode?

Erin Welsh Because we get to tell the story of Brett possibly having Rocky Mountain spotted fever.

Erin Allmann Updyke Genuinely forgot about that.

Erin Welsh What?

Erin Allmann Updyke I mean I didn't forget about that I just forgot that aspect of it. I keep remembering it-

Erin Welsh I think that was a formative moment of our friendship.

Erin Allmann Updyke: Oh it absolutely was. I will never forget the moment, okay. I just meant I forgot that we were gonna get the opportunity to talk about it.

Erin Welsh: Right, right. Okay so why did you think it was gonna be such a great episode from the very beginning of the podcast?

Erin Allmann Updyke: Oh mostly the quarantini name.

Erin Welsh: Oh yeah.

Erin Allmann Updyke: Yeah, yeah.

Erin Welsh: Excellent.

Erin Allmann Updyke: But as I was researching for this episode, I also was having a really busy week and I was like oh gosh, I have to do research. But then the very first paper that I came across to do research for this episode, the first line of the biology section, I was like oh this is gonna be a good one. Erin, I had to google two words in the first sentence.

Erin Welsh: (laughs) What were they?

Erin Allmann Updyke: 'Fastidious' and 'pleomorphic'.

Erin Welsh: Ooh!

Erin Allmann Updyke: Yeah, it's a good sentence, I'll read it to you later.

Erin Welsh: Also I have to say that the book that I read, the very first line of the chapter... So you know how chapters start with a quote from whatever? It literally made me go oh, this is gonna be good. And I put it in my notes.

Erin Allmann Updyke: Ooh! Look at us both, we're the same person.

Erin Welsh: Oh man.

Erin Allmann Updyke: Oh my gosh, that's really funny.

Erin Welsh: So do we get to just do the episode now or do we have business?

Erin Allmann Updyke: I think so. We've got new merch coming out soon.

Erin Welsh: Yeah, keep an eye out for that.

Erin Allmann Updyke: We're very excited.

Erin Welsh: It's literally the most exciting thing, we love it.

Erin Allmann Updyke: Yeah.

Erin Welsh: Love is not a strong enough word.

Erin Allmann Updyke: What's a stronger emotion? Really love. Okay, I don't think we have any other business to attend to Erin, so let's take a short break and then get into the biology of this.

Erin Welsh: Oh my gosh, let's do it.

TPWKY: (transition theme)

Erin Allmann Updyke: Okay so here it goes. Quote: "Rickettsia rickettsii is a fastidious, small, pleomorphic, gram-negative coccobacillus."

Erin Welsh: Okay, okay.

Erin Allmann Updyke: I feel that description, it's why people don't like reading scientific papers.

Erin Welsh: Oh for sure.

Erin Allmann Updyke: And the reason that it made me excited for this episode is because I was like I really like that this is how... If you read that you'd be like (snoring) snooze, I don't wanna learn anymore. So now I'm gonna take that and make it a lot more exciting and tell you why you should be excited about Rickettsia rickettsii. Okay?

Erin Welsh: Oh yes, please.

Erin Allmann Updyke: So here's what that boring sentence means. We're talking today about a very, very tiny, like so tiny that it lives inside of our cells bacterium that is very difficult to grow in medium. And the reason it's difficult to grow is cause it lives inside of cells.

Erin Welsh: Is that the fastidious part?

Erin Allmann Updyke: That's what fastidious means, yep.

Erin Welsh: Okay.

Erin Allmann Updyke: When you're talking about fastidious organisms. And the pleomorphic part means that not every single coccobacillus, not every single cell looks exactly like every other, so they kind of when you look at them stained inside of another animal cell, they look like a bunch of little and bigger dots, if that makes sense. Okay?

Erin Welsh: Why?

Erin Allmann Updyke: That's a really good question that I don't know because they divide the same way that anything else divides, right, which is by fission.

Erin Welsh: That's fascinating.

Erin Allmann Updyke: All right so let's get into the disease that Rickettsia rickettsii causes, Rocky Mountain spotted fever. So this is a tick-borne disease, okay.

Erin Welsh

Woo-woo!

Erin Allmann Updyke

Woo-woo! We get excited about these. So humans get infected, humans are essentially dead end hosts, okay. So we're not part of the normal life cycle necessarily of this pathogen. But humans get infected when we are bitten by an infected tick, specifically in a number of different species but most commonly in most of the US it's *Dermacentor variabilis*, that's the dog tick, the American dog tick. But there's also the Rocky Mountain wood tick, *Dermacentor andersoni*, those live in the Rocky Mountains in Canada; the brown dog tick, *Rhipicephalus sanguineus* in Mexico; and of course Erin, *Amblyomma cajennense*.

Erin Welsh

Or *Amblyomma mixtum*.

Erin Allmann Updyke

I was waiting for you to go correct, correct, correct me.

Erin Welsh

As I got corrected at an academic conference, yes. It is now *Amblyomma cajennense* species complex.

Erin Allmann Updyke

Okay, great. And is that throughout Central America, that species complex?

Erin Welsh

Yes, Central and South America.

Erin Allmann Updyke

All right. So now we also know where this disease is found, right. This is a disease of the New World essentially, so North America, Central America, and then down into South America. Okay? And like many other tick-borne diseases, in order to get infected the tick does have to be attached for a relatively long period of time, usually a minimum of 4-6 hours but sometimes up to 24 hours. And the reason that the tick has to be attached for a long period of time is because although these bacteria are already in the salivary glands of the tick, when they're in the tick - I'm getting excited. When they're in the tick, they're basically not in a virulent state.

Erin Welsh

Right.

Erin Allmann Updyke

So then they have to bite a host and then something happens within the salivary glands of the tick to reactivate these bacteria and make them virulent, make them able to actually infect our cells.

Erin Welsh

It's so amazing and weird.

Erin Allmann Updyke

And we don't know how it happens.

Erin Welsh

Oh my gosh, yeah. You're right. This is a thrilling disease.

Erin Allmann Updyke

Yeah. Absolutely thrilling. Okay. I didn't know that either before researching this and I think that's just super fascinating. Okay. So then you have activation, it somehow becomes virulent again, and then it will exit the salivary glands and then enter underneath our skin. Okay? So because we know that this is the life cycle, right, how does the tick then get infected? How do we end up with infected ticks? As it turns out there's two ways that a tick can become infected. One is the way that we know of ticks getting infected from past tick-borne disease episodes and that is that a tick takes a bite of an infected host and then in that blood meal they suck up some bacteria, okay? And then those bacteria go on to replicate and like many tick-borne diseases, once a tick is infected they remain infected for their entire life. So even if they get infected as a larva, then when they transition to a nymph they remain infected, when they transition to an adult they remain infected. But here's where it gets interesting.

Erin Welsh: I know where you're going and I love it.

Erin Allmann Updyke: I know you do. Infected female ticks transmit transovarially and lay infected eggs.

Erin Welsh: Oh yeah.

Erin Allmann Updyke: So you can have larval tick bombs that burst out already full of Rickettsia just waiting to infect their first blood meal host.

Erin Welsh: Let's put an asterisk on this.

Erin Allmann Updyke: Oh great. Well I actually have a question for you about this.

Erin Welsh: Okay.

Erin Allmann Updyke: Because my understanding from what I read, and you are much more of an expert. If you guys didn't know, listeners, by the way, Erin literally did her PhD research on Rickettsias in Central America.

Erin Welsh: On pathogens in ticks in Central America which happens to be a lot of Rickettsias.

Erin Allmann Updyke: Did you hear her trying to asterisk her way out of that?

Erin Welsh: Well I'm not an expert.

Erin Allmann Updyke: Okay. So my question is my understanding is that for humans it's really only adult ticks that go on to infect humans. Is that just behavioral? Is that just because these tick species don't tend to bite us unless they're adults or is that something to do with infectious dose? Why is that?

Erin Welsh: Honestly I don't know.

Erin Allmann Updyke: Oh okay.

Erin Welsh: Possibly behavioral. So different tick species will have different host preferences overall. So this tick species might like deer and mammals more and this tick species might like reptiles more. But even within a tick species you see a lot of differences in terms of what they like to feed on at different stages.

Erin Allmann Updyke: Okay.

Erin Welsh: And so there's a trend, it's not 100% but there is a trend where as you go to the older life stages, so like from larva to nymph to adult, the host range narrows. And part of that is a mate-seeking phenomenon because if you're trying to find a mate, you wanna be like all right, I wanna get on this horse because I know that other adult ticks of my species are gonna be on this horse.

Erin Allmann Updyke: Right.

Erin Welsh: But you might not be like oh, or maybe that squirrel or maybe that monkey or maybe that sloth. You're gonna be focused in.

Erin Allmann Updyke: Right.

Erin Welsh: Anyway. So it might be behavioral. As far as the bacterial load overall across the life stages, that might be a factor. But another factor might be that if you're an adult tick, you've taken two blood meals and so just the chance that you have acquired the pathogen is greater than if you have taken just one blood meal as a nymphal tick.

Erin Allmann Updyke: Okay. Right, right. That makes sense.

Erin Welsh: Yeah.

Erin Allmann Updyke: Okay.

Erin Welsh: But the asterisk that I wanna add to the transovarial transmission-

Erin Allmann Updyke: Please.

Erin Welsh: Is that it's fairly rare for *Rickettsia rickettsii*, like it doesn't happen all that often and actually the *Rickettsia rickettsii* negatively affects the reproductive output of the tick, the female tick.

Erin Allmann Updyke: Oh yeah.

Erin Welsh: So that's good news in a way. So if you look at horizontal transmission, so getting it from an infected animal vs transovarial transmission or vertical transmission, getting it from mom, it's much less likely to get it from mom. And then the third way that might be possible is co-feeding.

Erin Allmann Updyke: Oh. Does co-feeding mean the same thing for ticks as it does for kissing bugs?

Erin Welsh: Probably, two bugs feeding close to one another and then they-

Erin Allmann Updyke: Oh no.

Erin Welsh: Oh, what does it mean for kissing bugs?

Erin Allmann Updyke: Sometimes the adult kissing bugs will come back to the nest and then the nymphs will feed on the adult from their blood meal.

Erin Welsh: That's beautiful and horrifying.

Erin Allmann Updyke: Yeah, it is.

Erin Welsh: That's my aesthetic. Literal life blood.

Erin Allmann Updyke: Co-feeding. So then if you have say an infected adult feeding very close by to another uninfected nymph, then they could-

Erin Welsh: Right.

Erin Allmann Updyke: That's fascinating!

Erin Welsh: Oh yeah, that happens with tick-borne encephalitis virus as well I think occasionally. You do get co-feeding events and this is really important when you have cocurrent stages existing or emerging. So if you have larvae that are emerging at the same time as nymphs.

Erin Allmann Updyke: Yeah. Very cool. Well that was very fascinating. Okay so now we understand fully the transmission dynamics of this bacterium. So let's talk about what happens if you get infected, okay? What are the symptoms? It starts with, Erin, wait for it, with a fever.

Erin Welsh: Ooh! (laughs)

Erin Allmann Updyke: Okay. So in general the incubation period after you get infected is about 7 days on average, it can range from about 2-14 and the first symptom is often a rather sudden onset of fever, pretty substantial malaise and body aches, and very commonly a headache which very often people will describe as the quote "worst headache they've ever had" is what one paper said.

Erin Welsh: Interesting.

Erin Allmann Updyke: I will say in med school we don't learn Rocky Mountain spotted fever as the worst headache you've ever had, you learn that for a brain bleed but that's okay. The point is it's a very severe headache, it's not just like I feel a little dehydrated headache, it's like a bad headache.

Erin Welsh: Okay.

Erin Allmann Updyke: You can have a lot of other pretty nonspecific symptoms as well, things like anorexia because your stomach doesn't feel good, anorexia meaning you just don't want to eat, not like an eating disorder, nausea, vomiting, abdominal pain is fairly common. So especially early on in the course of this disease, it's very potentially easy to mistake it for a kind of viral syndrome, okay. You feel crappy but it's very nonspecific. And then comes the third of what's often called the classic clinical triad of Rocky Mountain spotted fever. There's actually two different triads which I think is silly depending on what paper you read. Okay. Within two weeks of a tick bite, almost always in like 80-90% of cases you see this third symptom and that is the spots of Rocky Mountain spotted fever.

Erin Welsh: There we go.

Erin Allmann Updyke: It's a rash. This rash starts out as small, what are called macules which just means flat red spots, little ones, maybe less than the size of your pinky nail. And these tend to start on your wrists and your ankles. They're a blanching rash, it doesn't itch usually, it doesn't hurt. So if you press on them then the color would drain from them, okay.

Erin Welsh: Oh, that's a blanching rash, wow. Cool.

Erin Allmann Updyke: Yeah.

Erin Welsh: New word.

Erin Allmann Updyke New word. Then this rash which starts on your ankles will begin to spread. It'll spread up approximately, like up your arms and up your legs to your trunk but it also spreads down, down to your palms and your soles which you may remember from our episode on syphilis, it is a very uncommon place to have a rash. The palms of your hands and the soles of your feet really don't get rashes except in a few infectious diseases.

Erin Welsh Okay. It's was syphilis.

Erin Allmann Updyke Syphilis.

Erin Welsh Hand, foot, and mouth?

Erin Allmann Updyke Mm-hmm, coxsackievirus.

Erin Welsh And Rocky Mountain spotted fever?

Erin Allmann Updyke Rocky Mountain spotted fever!

Erin Welsh Is that it?

Erin Allmann Updyke That's it. You can get fungal infections on your palms or soles, you could get contact dermatitis and things, but in terms of infection diseases those are the three big ones.

Erin Welsh And it would be all, both hands, both feet?

Erin Allmann Updyke Both hands, both feet, exactly. Yeah.

Erin Welsh But it's not itchy.

Erin Allmann Updyke Not itchy usually.

Erin Welsh And not painful.

Erin Allmann Updyke Not painful.

Erin Welsh Well that's nice.

Erin Allmann Updyke Yeah. Well not really.

Erin Welsh Oh. I spoke too soon.

Erin Allmann Updyke You spoke too soon. Okay. So this rash is now spreading. By the end of about a week of having this rash, the rash becomes raised. So it's now what we call maculopapular, so it has red flat spots with little dots, raised bumps in the middle. And then in the center of these lesions you can sometimes get petechiae which are little pinpoint purple spots that usually are a sign that you're having some kind of issues with your blood clotting. And so that is kind of the general course of disease. It doesn't sound that bad, right?

Erin Welsh Well that was a leading question.

Erin Allmann Updyke I mean it doesn't though, right? It's like headache, fever, you're feeling crappy, you get a rash. But then as it turns out, this disease is about... Okay, without treatment and before we had treatment for it it was on average about 25% fatal. But that fatality rate ranged a lot from about 20% to maybe up to 85% depending on where geographically you got infected.

Erin Welsh Yep.

Erin Allmann Updyke So this is a highly fatal illness.

Erin Welsh Right. If your average, if your lower level is still over what did you say?

Erin Allmann Updyke 25%.

Erin Welsh Yeah. If the average is 25%, I mean think about the other ones that we've had that have been 25%, it's not that many.

Erin Allmann Updyke Right, exactly. That's a huge case fatality rate.

Erin Welsh Yeah.

Erin Allmann Updyke So the question is what are you dying from, right? You've got a rash, how is this killing you?

Erin Welsh Well I feel like the petechiae or whatever the blood clotting issue, that might be an indication.

Erin Allmann Updyke Yeah, so that's one sign. So let's talk about kind of the actual pathophysiology of how this makes you sick, what's going on when you have this rash, okay? So this is a tick-borne disease so like many other tick-borne diseases, when that tick spits the bacteria underneath your skin, those bacteria travel through your lymphatic system to end up in their host cells. And even though this is a bacterium it acts a little bit more like a virus in that it has to invade our cells, it's an intracellular bacteria, in order to replicate. It does not have the machinery to replicate outside of a host cell, much like a virus.

Erin Welsh Isn't it thought that Rickettsia might be closely related to mitochondria?

Erin Allmann Updyke Yes, I believe so. They think that mitochondria came from something, whether a precursor to Rickettsia or something similar because they're like... Yep, yes.

Erin Welsh I just think that's so cool.

Erin Allmann Updyke Oh it's so cool. It's so cool. Their genomes are tiny. Okay. So in the case of Rickettsia rickettsii, the cells that they invade, the cells that they replicate in are our vascular endothelium. So those are the cells that line our blood vessels, okay. The inside lining of our blood vessels.

Erin Welsh Okay.

Erin Allmann Updyke Do you see where we're going with this?

Erin Welsh I mean yeah, unfortunately.

Erin Allmann Updyke

So what happens when they enter our cells and start to replicate? They do a very good job replicating, they replicate by fission. They also have these ways of moving from cell to cell to cell without necessarily damaging our cells directly as they move from cell to cell. So they can kind of just spread along your blood vessels, just jumping from cell to cell to cell. And because they're in your blood vessels, they are literally anywhere and everywhere in your body because everywhere needs blood, right. And then they start to cause direct damage to the cells that they infect and they do this in a few different ways. One is free radical-induced injury which I feel like we're experts on now after our radiation episode. Okay. And then they also release a number of different enzymes that cause damage to these cells. So if you are damaging the cells that line your blood vessels, what do you think is going to happen to the fluid that is supposed to be in your blood vessels?

Erin Welsh

Well it's gonna create a little leaky pipeline.

Erin Allmann Updyke

A little leaky pipeline Erin, exactly. Okay. So this cell damage causes exactly that. Not frank hemorrhage, okay, it's not gross enough damage that you're gonna be bleeding out necessarily.

Erin Welsh

Who's Frank Hemorrhage? (laughs) I'm sorry. Did you like that?

Erin Allmann Updyke

(laughs) I really did. So not actual hemorrhage but this damage does cause increase in the permeability of that membrane essentially. So that means you're going to get fluid, plasma leaking out. This is going to also cause you to lose protein because as you damage that membrane, proteins are usually kept in your blood vessel in part by charge differences, so you mess up that membrane, you mess up those charges, so then protein can leak out more easily which then just draws more liquid out with it.

Erin Welsh

So it's like this cascading, horrible, positive feedback loop.

Erin Allmann Updyke

Exactly, exactly. And let's talk about positive feedback loops, okay. Because like we talked about in the radiation episode, when you have this free radical damage that happens to these cells, our body mounts a response to that right and that's an inflammatory response. And in responding to that, part of what our body does to try and fight off the inflammation and damage that's caused by things like free radicals and these enzymes is that they will vasodilate our blood vessels in order to get more white blood cells to the areas that they need to be to try and fix this damage. That vasodilation means you have more flow which means you have more vascular permeability which means you have more leakage. So this will eventually lead to edema, so swelling outside, liquid outside of our blood vessels and eventually hypovolemia where you don't have enough volume in your blood vessels.

On top of that if it happens to be important organs like your brain or your lungs that get involved in this, this is called a vasculitis where you have inflammation of your blood vessels. If it's somewhere like your brain or your lungs, you don't have a lot of good lymphatic drainage to drain that fluid away, so you have pressure that builds up because of that in that interstitial space. So what's interesting about this is that none of the papers that I read really clearly outlined what the exact cause of death tends to be in Rocky Mountain spotted fever but it is essentially organ failure. What organ it is that ends up failing kind of just depends on what organ happens to be the most affected.

Erin Welsh

Okay.

Erin Allmann Updyke

A very large proportion of people have hepatomegaly on necropsy or on autopsy after they've passed, so your liver is very commonly involved at least in fatal cases. Many people also have renal failure, so kidneys might fail. Your lungs can certainly be involved, so you could die maybe from just not being able to breathe, from respiratory failure because of all the fluid around your lungs. But there's not a one single thing that tends to be the ultimate cause of death necessarily. But pathophysiologically we know that it's this diffuse vascular damage that leads to hypovolemia, so not enough volume and eventual shock. So yeah.

Erin Welsh

Terrible, terrible.

Erin Allmann Updyke

Really, really terrible. Another thing that I did want to point out that I think is really, really important about this disease is that the mortality rates still today, it's non trivial. It usually hovers around 5% even with treatment and there is very good treatment for this, doxycycline, a few days worth clears infection. But delays in diagnosis are strongly associated with poor outcomes, so not getting to a doctor fast enough or a doctor failing to make the correct diagnosis or get the treatment initiated quickly is very strongly associated with a vastly increased risk of death. And especially in the US this disproportionately affects black individuals. And there was a limited amount of discussion in the papers that I read as to why exactly that is, whether it's people not seeking care and things like that. But my guess and some of the papers also said this is that we are really bad at diagnosing rashes on black skin.

Erin Welsh

Yeah.

Erin Allmann Updyke

It's a huge issue.

Erin Welsh

Yeah.

Erin Allmann Updyke

When you google pictures of this, I haven't seen a single picture of Rocky Mountain spotted fever on a black-skinned person.

Erin Welsh

Yeah, I came across that as well in the research and how it's historically been like that as well.

Erin Allmann Updyke

Yeah and I mean it's not just for this but this is a very fatal disease that's also very treatable if you diagnose it properly. And so the thing is we don't have good tests, like laboratory tests to diagnose this. It's a clinical diagnosis which means you make that diagnosis based on history and physical findings including a rash.

Erin Welsh

Right.

Erin Allmann Updyke

So if we don't know what a rash is supposed to look like because no one's taking pictures of it, it's not in our textbooks, etc, then people are dying unnecessarily which is a huge, huge failure of the medical system.

Erin Welsh

Absolutely.

Erin Allmann Updyke

So yeah. That's the biology of Rocky Mountain spotted fever!

Erin Welsh

Well it's a terrible disease. And that's a point that I saw made in a lot of different papers in terms of how important this disease is and how overlooked it tends to be despite the fact that things like landscape change and climate change are going to greatly shift our exposure, our risk, you know.

Erin Allmann Updyke: Yeah and I mean it's the kind of case where it directly results in people dying.

Erin Welsh: Yeah.

Erin Allmann Updyke: But it's a difficult thing because it is so rare and I think that we'll talk later about where you see this geographically but I think a lot of people maybe don't know or don't know to think of it when they're listing their differentials in their head. It could easily look like a viral illness, it's like oh you've got a fever and a headache and you're feeling crappy. You know?

Erin Welsh: Right. And in the history section I don't talk much about the name itself but if you look at so many different rickettsial diseases, particularly the arthropod-borne ones, they tend to have location-specific names.

Erin Allmann Updyke: Yeah.

Erin Welsh: And so in one place it's Rocky Mountain spotted fever, in another place it's something else. So you have all over the world different species of pathogenic Rickettsia called by different names and that has created a lot of confusion, particularly with Rocky Mountain spotted fever, since we're talking about it.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yes it occurs in the Rockies in the western States but the Eastern Seaboard is like-

Erin Allmann Updyke: Bam!

Erin Welsh: South America.

Erin Allmann Updyke: Bam.

Erin Welsh: Central America.

Erin Allmann Updyke: Bam.

Erin Welsh: It's there too. So there was a huge push at one point to just call it spotted fever or spotted fever group rickettsia but that never really caught on, so RMSF is what it is.

Erin Allmann Updyke: Yeah. Well tell me more, Erin, about this history. How did we get here? Where did this thing come from?

Erin Welsh: Okay I cannot wait. We will take a quick break first.

TPWKY: (transition theme)

Erin Welsh: Erin, you started off biology with a quote and I laughed because I'm starting off history with a quote.

Erin Allmann Updyke: I love it.

Erin Welsh: You started off with the quote from the first paper you read and I'm starting off with that quote from the book from the very beginning. Okay, here we go. "The unwritten history of the investigational work in connection with Rocky Mountain spotted fever, if written, would read like a romance." Right?

Erin Allmann Updyke: Ooh I wanna read this.

Erin Welsh: Can you see why I was like, what? What is this? Okay so yeah, why is that?

Erin Allmann Updyke: Yeah.

Erin Welsh: Hopefully I'll tell you. Hopefully I'll do a good enough job that you'll understand what that quote means, I'm not sure that I do. Anyway. Before researching this, I didn't know there's quite a bit of lore or fame or infamy around Rocky Mountain spotted fever research. There was a movie called Green Light starring Errol Flynn from 1937 and one of the subplots, it tells the story of the researchers involved on the Rocky Mountain spotted fever project.

Erin Allmann Updyke: What?

Erin Welsh: Yeah! And the disease itself plays a major role in the 1947 movie Driftwood. I haven't seen either of these so I can't vouch for their accuracy or how much romance they have in them or whatever. But I have now read about the history of Rocky Mountain spotted fever, especially the history of its research and that does contain a fair amount of drama and romance. To start the story we don't have to go all that far back, actually. So the firsthand account that I read at the beginning of the episode, as I mentioned it's from 1759 but like I said it's not 100% accepted to be Rocky Mountain spotted fever.

Erin Allmann Updyke: Right.

Erin Welsh: In any case there were likely cases of RMSF, Rocky Mountain spotted fever, scattered throughout the Americas for hundreds of years at least but the real story begins only in the late 1800s. We don't have written records for anything earlier.

Erin Allmann Updyke: Right, yeah.

Erin Welsh: So around this time, starting in maybe the 1860s or the 1870s, a mysterious illness was seeming to pop up in the Bitterroot Valley in Montana. So this, if you can picture Montana in your head-

Erin Allmann Updyke: Okay.

Erin Welsh: Go to the far, far west, kind of the southwestern part of the state.

Erin Allmann Updyke: Okay.

Erin Welsh: If you know where Missoula is, it's like the very north end of the valley.

Erin Allmann Updyke: I don't know where that is but I can picture Montana.

Erin Welsh

Okay. So this valley, the Bitterroot Valley, runs about 95 miles long and it's sandwiched inbetween the Bitterroot Mountains and the Sapphire Range with the Bitterroot River winding its way through the valley. Historically the Salish Tribe of the Flathead Nation lived in Bitterroot Valley and while the region experienced some settlement throughout the 1800s, Lewis and Clark passed through in 1805, it lagged behind other parts of the west. But then the discovery of gold in California and the increasing number of Mormon settlements in Utah eventually led to people striking out to find a piece of land of their own. In the second half of the 19th century, Montana grew enormously in popularity. The Bitterroot Valley in the second half of the 1800s in particular was super popular because it had these ample resources for lumber and fertile farmland, for livestock and apple orchards were really popular. And as you can guess the increasing number of white settlers meant that more land had to be found. So what was the natural solution to this problem?

Erin Allmann Updyke

Genocide?

Erin Welsh

Well at least forcible removal.

Erin Allmann Updyke

Okay.

Erin Welsh

So the government removed the Salish for whom this was their ancestral home.

Erin Allmann Updyke

Of course.

Erin Welsh

And so in the 1870s with the Salish driven out, the land of the Bitterroot was ripe for clear-cutting and apple farming and it was also apparently ripe for the emergence of a seemingly new tick-borne disease. All this clear-cutting to make room for orchards and farms led to proliferation of scrub habitat which was great for sheep grazing but also great for mice and other small mammals which happened to be excellent blood meal hosts for ticks. The first case of what we now know as Rocky Mountain spotted fever that we can trace back for sure occurred in 1873 in Montana.

Erin Allmann Updyke

Consequences, man.

Erin Welsh

Yeah, right?

Erin Allmann Updyke

Consequences for our actions.

Erin Welsh

(laughs) And this case was not a one-off. So from that first case more followed and not just in Montana. Colorado, Oregon, Idaho, Wyoming, a lot of other places grew aware and wary of the disease, rightfully so. And I have to include another side note here. So for a while it was thought that the Salish Indians had warned the incoming white settlers of Rocky Mountain spotted fever by saying certain canyons in the spring in the Bitterroot were full of evil spirits. But this is no longer thought to be in relation to the disease.

Erin Allmann Updyke

Oh okay.

Erin Welsh

So rather at least in this book it was thought that the disease probably wasn't super prevalent before the white settlers clear-cut the land and allowed for the super proliferation of ticks. And so anyway, with this alarming rise of an extremely fatal disease combined with the daughter and son in law of the Montana governor dying of the disease, the state feared that they would lose out on prospective land buyers because of this pesky fatal illness. And so they told the Montana State Board of Health to do something. And that's exactly what they did starting in 1902 by appointing two young pathologists name Louis Wilson and William Chowning to see what they could figure out about the disease. And that same spring a bacteriologist named Earl Strain suggested a connection between the disease and a tick bite because he was there touring to kind of see what can I figure out about this disease and he visited someone who had Rocky Mountain spotted fever and noticed a tick embedded in the genitals of the sick person.

Erin Allmann Updyke

Ooh. Very interesting that he just happened to see a tick because almost certainly if that person was suffering from Rocky Mountain spotted fever and they happened to have a tick, that tick was not in fact the perpetrator of their illness.

Erin Welsh

I think it speaks to the high levels of infestation around the Bitterroot at the time.

Erin Allmann Updyke

Right. And that would explain why you had such a huge increase in cases if you were just getting bit left and right. And genitals.

Erin Welsh

Well and if you think about the occupations of people who were settling in Bitterroot at this time, you're outdoors.

Erin Allmann Updyke

Right, exactly.

Erin Welsh

You're outdoors especially during that time of year.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so it's almost unavoidable.

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

So Wilson and Chowning took note of Strain's observation when they were planning their research season which they had to do basically right away because Rocky Mountain spotted fever season is actually pretty short which is great news if you're at risk for the disease but a little bit challenging if you're researching it. Joys of fieldwork. And they covered their bases. They performed autopsies, they did epidemiological surveys, lab studies. And what they found was concerning. Between 1895 and 1902 there were 88 cases in the Bitterroot Valley with 64 deaths.

Erin Allmann Updyke

Wow.

Erin Welsh

So it's a 72.7% mortality rate. And they concluded that it was not contagious from person to person and not a result of melted snow water which was the leading hypothesis at the time.

Erin Allmann Updyke

Okay. Well good thing.

Erin Welsh

Right? It would be hard to avoid melting snow water.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so they suspected instead that it was caused by a protozoan that they had found in some of the tick samples that they had dissected and stuck under a microscope.

Erin Allmann Updyke

Interesting.

Erin Welsh

And so by the end of this first season of their research they had a nice little disease ecology cycle all laid out: the wood ticks transmitted the protozoan to humans and ground squirrels, aka gophers, were the disease reservoirs. This was an untested hypothesis but that didn't stop reports of it in the news because people were hungry for information about it. They were like we wanna know how to protect ourselves. But just knowing or thinking that ticks were responsible for the disease didn't really do that much because ticks were absolutely everywhere in the spring in the Bitterroot and so the only way to avoid them would be to not live or work there which was not the solution that the state was looking for. And the only practical step in their eyes which wasn't really practical at all was to eliminate the ticks themselves or the gophers that were thought to be the hosts.

Erin Allmann Updyke

Oh gosh.

Erin Welsh

So in the spring of 1904 the residents of the Bitterroot took this to heart. They burned and they burned vegetation and they set out poisoned grain to kill the gophers which actually killed a lot of game animal, game birds and other animals. And they also got a bunch of sheep to eat the grass, the tall grass that they thought was the ticks' habitat.

Erin Allmann Updyke

Oh dear.

Erin Welsh

But it's nearly impossible to get rid of ticks.

Erin Allmann Updyke

You need opossums, Erin.

Erin Welsh

We need opossums.

Erin Allmann Updyke

Just set loose the opossums! Just kidding, don't do that.

Erin Welsh

I feel like maybe we shouldn't gamble, throw the ecological die in that way. So the next best thing though was just to remove a tick as soon as you saw it attached, right. And people were encouraged to treat it like a venomous snakebite, dab some carbolic acid on the site of the bite right away, so then people had a lot of acid burns, accidental spills, infections, etc. I mean basically the bottom line is that though these efforts had led to some fundamental knowledge being gained, the application to prevention simply wasn't there.

Erin Allmann Updyke

Right.

Erin Welsh

And so more help was called in in the form of Charles Wardell Stiles. Does that name sound familiar to you?

Erin Allmann Updyke

Yeah, it sounds very familiar. What else did he do?

Erin Welsh

Hookworm.

Erin Allmann Updyke Oh that's right, Erin!

Erin Welsh He discovered or identified the second species of hookworm in the Americas.

Erin Allmann Updyke Awesome.

Erin Welsh Yeah and I think he played a role in, I don't remember, but I think he played a role in determining that it was the cause of the widespread anemia in the South.

Erin Allmann Updyke Ah and he's Harry Styles' great grandpa.

Erin Welsh Exactly, exactly. (laughs)

Erin Allmann Updyke I'm so hip. Just dropping those names.

Erin Welsh Oh my god. Okay anyway, so Stiles set out to basically test the ground squirrel tick protozoan life cycle that Wilson and Chowning had laid out. He was enthusiastic about the hypothesis early on but he was a little bit close-minded when it came to any challenge to the accepted dogma of the time which was, and this is news to me, but apparently for a while it was believed that arthropods could transmit protozoa but were not capable of transmitting bacteria other than accidentally, like a fly could accidentally give you an infection-

Erin Allmann Updyke Right, cause they stepped in poop or something.

Erin Welsh Exactly. But mosquitoes and ticks and whatever weren't capable of actually completing the life cycle. I don't know why.

Erin Allmann Updyke Of a bacterium. That's so interesting.

Erin Welsh Yeah. So when he searched for this supposed protozoan in the ticks and the blood of the victims, he came up empty handed again and again. But instead of saying well this ticks may have something to do with it but the protozoan probably doesn't, he openly refuted and dismissed the existing hypothesis.

Erin Allmann Updyke Oh dear.

Erin Welsh And he started to say like, 'Oh you know what? These residents are overreacting, ticks aren't involved, it's probably snow melt all along.' And in a way this contemptuous criticism actually was beneficial for the research of Rocky Mountain spotted fever because it drew such attention from other researchers including a pathologist from the University of Chicago named Howard Taylor Ricketts.

Erin Allmann Updyke Ricketts.

Erin Welsh Ricketts. Ricketts set up a correspondence with Chowning saying that he believed their hypothesis had gotten unfair treatment by Stiles. And Chowning was like, 'I agree. Also I've been doing some site experiments in my spare time including a little bit of medicalized torture.'

Erin Allmann Updyke Oh great.

Erin Welsh

So he had obtained quote "consent" from two people to attach ticks to them which had been feeding on a man who died of Rocky Mountain spotted fever.

Erin Allmann Updyke

Oh.

Erin Welsh

They both got sick with the disease and recovered and so Chowning was like, 'Must be ticks.' So anyway when he told Ricketts about this, Ricketts just didn't acknowledge it apparently.

Erin Allmann Updyke

Okay.

Erin Welsh

He didn't denounce him but he didn't acknowledge it and he was like, 'I'm gonna do my own research.' And so he went to Montana.

Erin Allmann Updyke

Okay.

Erin Welsh

But the state had no money to give him and so he and Wilson and Chowning had to find their own way to pay, they cobbled together a bunch of resources. And in 1906 Ricketts set up a laboratory in a tent on the grounds of the Northern Pacific Hospital in Missoula. So he was just like in a tent. And that spring and summer proved very productive for Ricketts and another researcher named Walter King who joined in on the research. But it must be said that this wasn't a super collaborative project. Each one of these men for the most part, maybe Chowning and Wilson worked together, but Ricketts and King were very much like, 'This is my project and I want to do it my way and I want publication priority and I want blah, blah, blah.' So anyway. And so first Ricketts and King found that they could cause the disease in a guinea pig by injecting serum into the animal and they could sustain the infection by alternating infecting a guinea pig and then a monkey and then a guinea pig and then a monkey which then enabled year-round research.

Erin Allmann Updyke

Okay, that makes sense.

Erin Welsh

Yeah. Then at the very end of the spotted fever season, both Ricketts and King demonstrated that ticks can cause infection and they did this by attaching a tick to a guinea pig and then disease resulted. And this was a super exciting finding but it came at just the wrong time for them because it was the end of the season and soon there would be no more ticks to be found. Back in Chicago and Washington, Ricketts and King tried to keep these tick experiments going by advertising in Montana papers for anyone who could find a tick, a live tick, to send it their way. At one point they offered a financial incentive of \$10 in gold for anyone who could deliver 50 or more live ticks.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

Citizen science! But they never got any, they had to wait until the spring.

Erin Allmann Updyke

Okay.

Erin Welsh

And mid April 1907 saw the first victim, a 26 year old lumberman whose family refused to allow Ricketts to draw any blood. Ricketts was peeved about this and so he asked the secretary of the State Board of Health to do something about it. And so he drew up an official-looking document saying that the family must cooperate with the investigation. And then he told Ricketts, 'Hey, don't let anyone get too close a look at this because in truth I have no authority to issue it.'

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

And people wonder why there's deeply rooted mistrust-

Erin Allmann Updyke

In the medical establishment.

Erin Welsh

And the government.

Erin Allmann Updyke

And research, yeah.

Erin Welsh

And research. And authority, yeah.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

So anyway in 1907 Ricketts concentrated on finding out the pathology of the infection in ticks, still without knowing what the causative agent was. And he determined that a small proportion of female ticks could transmit the pathogen to their offspring, so larval ticks could be infectious.

Erin Allmann Updyke

Awesome.

Erin Welsh

Which is a great finding. And then in January of 1909 he seemed to finally hit the jackpot when he published a paper in which he described the teeny tiny bacillus, coccobacillus, that was the causative agent of Rocky Mountain spotted fever. He had detected ample amounts of the bacteria in the eggs of infected females and while he was unable to culture the bacteria he was confident in his finding.

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

I mean it's pretty cool.

Erin Allmann Updyke

That's very, very cool.

Erin Welsh

And his achievements, like people were psyched about this. Cause he had done microbiological research, he had done ecological research, he had done some medical research. So his achievements won him praise and opportunities left and right and even the state of Montana recognized his work by writing in a Bill in 1909 that would fund a bunch of his research on Rocky Mountain spotted fever over the next couple of years.

Erin Allmann Updyke

Wow.

Erin Welsh

Unfortunately though the funds were suspended when the state realized that they had allocated more money than they were going to collect in revenue. And so Ricketts' work was put on hold.

Erin Allmann Updyke

Oh man.

Erin Welsh

And even though his colleagues in Montana encouraged him to stick around, to get private funds to bridge the gap, Ricketts was like, 'No, I've got so many opportunities here, I'm going to Mexico to solve the question of another spotted fever-like disease, typhus.'

Erin Allmann Updyke

Ah!

Erin Welsh

So then he went down to Mexico City but it was only after he arrived in Mexico City in December of 1909 when he learned that the big puzzle pieces of typhus had already been put together. The vector, animal model, it was a lot of the stuff that had drawn him to study it was already discovered, identified, done.

Erin Allmann Updyke

Wah-wah.

Erin Welsh

But he gamely stayed on and tried to figure out the causative agent which he suspected might be very similar to Rocky Mountain spotted fever. So then in early 1911, Ricketts got word that it finally looked like the Montana funds were coming through and he was super happy but he was not incredibly eager to leave despite, you know, he was working under very dangerous conditions. There was no protection against typhus, in his letters to his friends he wrote like, 'My wife is very upset with me, she's very scared for me, if she knew what I was doing she'd be wanting me to come back.'

Erin Allmann Updyke

Furious. Yeah.

Erin Welsh

But he wanted to see the project through to the end. And so just as tick season was starting in Montana, just as he was trying to get up there, he came down with typhus and died May 3, 1910 at the age of 39.

Erin Allmann Updyke

No!

Erin Welsh

Yeah. His death was a huge blow to spotted fever research and it also established a very tragic pattern.

Erin Allmann Updyke

Uh oh.

Erin Welsh

If the first decade of the 1900s was characterized mostly by research on the causative agent and medical treatments for Rocky Mountain spotted fever, the second decade looked towards the tick for answers. By the late 19th century when the focus on Rocky Mountain spotted fever was heating up, entomology and medicine were two totally different fields, particularly in North America. Research combining the two was conducted only rarely such as with yellow fever research in Panama, for instance. Largely entomologists played the role of helping combat agricultural pest arthropods or doing academic foundational biology research. And medical doctors and researchers dealt with human diseases, how it worked in the body, how to control it. And there often wasn't a lot of opportunity for overlap. Rocky Mountain spotted fever however required a full understanding of the vector tick's ecology like its life cycle, hosts, behavior, etc as well as the characteristics of the disease, bacteria, pathogenesis, etc.

And you might instinctively think that public health researchers or physicians and entomologists working together would be the best way to make progress but then maybe you forgot about ego. After Ricketts met his untimely end, there was maybe a bit of a vacuum in the Rocky Mountain spotted fever research arena in Montana. The secretary of the State Public Health Department whose name was Tuttle appointed a physician named McClintic to continue work on the project. But then when he arrived he found an entomologist named Robert Cooley had rudely started on a bunch of control efforts on his own. And neither was willing to cede any ground for publication priority or research area and apparently neither was willing to work together.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh	I know.
Erin Allmann Updyke	Just get over yourselves.
Erin Welsh	Get over it. So the physician McClintic believed because it's a human disease, it's a physician or a public health problem. And the entomologist was like no, it's a tick-transmitted disease so that calls for a tick control expert.
Erin Allmann Updyke	No, it's all of these. Just work together! Ugh.
Erin Welsh	I know, it just goes on and on. This sparring over funds, it actually spilled over to the federal level and resulted in Cooley, the entomologist, losing support for his work.
Erin Allmann Updyke	Oh my goodness.
Erin Welsh	So then McClintic who was the physician was like, 'Alright, I'm gearing up to do some tick work, setting up giant vats to dip the livestock in to try to prevent tick infestations on livestock, and I'm gonna initiate a massive project to identify the reservoir of the bacterium.' But that second project was mostly just destroying all small wild mammals like pine squirrels, yellow-bellied chipmunks, woodrats, woodchucks, weasels, badger, and of course the infamous gopher.
Erin Allmann Updyke	Cool, cool, cool.
Erin Welsh	That's not the way you do it, by the way. Control ticks. That doesn't work.
Erin Allmann Updyke	No.
Erin Welsh	And so while he was able to rule out several of the species as playing a major role in the infection cycle such as badgers, he had a hard time finding a single smoking gun species responsible for the disease. And he would never find it because he died of Rocky Mountain spotted fever in 1912.
Erin Allmann Updyke	Oh my god.
Erin Welsh	Just a year after starting his research in Montana.
Erin Allmann Updyke	Oh that's sad.
Erin Welsh	It's really sad. Once again, spotted fever research in Montana was left without a leader. Maybe this was an opportunity for a fresh start, to bring together physician and entomologist.
Erin Allmann Updyke	I have a feeling it's not gonna happen, Erin.
Erin Welsh	No, it didn't happen. The budget and the land would be split. The north part of the valley went to the US Bureau of Entomology with Cooley in charge and the south part of the valley would be designated as US Public Health Service land.
Erin Allmann Updyke	Kind of an interesting way to do it.

Erin Welsh: Isn't it so fascinating? Yeah.

Erin Allmann Updyke: Who did better?

Erin Welsh: Well, great question. So the entomologists on the north side of the valley were set on just livestock dipping.

Erin Allmann Updyke: Okay.

Erin Welsh: And basically taking cattle, submerging them into acaricide or a pesticide to kill the ticks.

Erin Allmann Updyke: Right.

Erin Welsh: And so these entomologists were like, 'Alright, this is the key, killing small rodents, that's wasted effort.' And the public health folks on the other hand were like, 'No, we're gonna dip and kill small mammals and also not allow cattle to feed on the western side of the river,' which was the only side that was infected, by the way. Yeah. And so whether the dipping was actually effective was called into question as well. So from 1913 to 1918, the number of ticks supposedly declined 80-90% while the number of cases had been reduced from 11 to 3. But these numbers are far from conclusive.

Erin Allmann Updyke: Right.

Erin Welsh: Like 11 to 3 is super...

Erin Allmann Updyke: Could just be seasonal variation or whatever, yeah.

Erin Welsh: Exactly, exactly. And eradication which was the promised end of these projects was not on the horizon. The tick must be destroyed. Killing small animals wasn't doing it, dipping cattle wasn't doing it, maybe a vaccine could work.

Erin Allmann Updyke: By the way that's our title.

Erin Welsh: (laughs) The tick must be destroyed.

Erin Allmann Updyke: The Tick Must Be Destroyed!

Erin Welsh: Before Ricketts died he published his preliminary findings of this bacterium but the debate continued with still the protozoan leading the pack.

Erin Allmann Updyke: Gosh.

Erin Welsh: I know. The pathologist S. Burt Wolbach, like Wolbachia-

Erin Allmann Updyke: Oh! That's exciting.

Erin Welsh: Yeah. He decided to give it a shot. And he also observed teeny tiny bacteria-like things in the ticks, their eggs, and the blood of humans and animals that had spotted fever.

Erin Allmann Updyke: Okay.

Erin Welsh

But he wasn't sure that they were actually bacteria cause he was like it doesn't make sense, they live entirely within the cells of the animals. So this has got to be some new kind of microorganism somewhere inbetween protozoa and bacteria.

Erin Allmann Updyke

I mean yeah, not wrong.

Erin Welsh

He's not wrong. And even though he was pretty certain he had discovered the causative agent which he called *Dermacentroxenus rickettsi*, others weren't convinced chiefly because he was unable to culture the organism in media in a lab.

Erin Allmann Updyke

Of course he was!

Erin Welsh

And he was like, 'Listen, I understand that these postulates are important but we have to evolve, we're learning new things, maybe we should look up different criteria.' Yeah, he was right.

Erin Allmann Updyke

He's right.

Erin Welsh

But then the discovery of the causative agent of typhus forced researchers to accept that these intracellular microbes might actually be real and maybe a new type of microbial life or at least a new version of what we've already seen.

Erin Allmann Updyke

Cool.

Erin Welsh

And eventually the name that Wolbach had given for the spotted fever bacterium was changed to *Rickettsia rickettsii*, giving rise to a whole new genus of pathogenic intracellular bacteria.

Erin Allmann Updyke

Cool.

Erin Welsh

So by the 1920s the causative agent of Rocky Mountain spotted fever had been discovered and the life cycle had been outlined. But this knowledge didn't translate into lives saved, yet again. Rather the incidence of the disease as well as its mortality seemed to be on the rise. For instance in 1921, all 11 cases of Rocky Mountain spotted fever died, land prices reflected this, they were dropping from \$125 per acre to \$15 per acre in some places. Also \$15 per acre, can you even imagine?

Erin Allmann Updyke

We should have bought. We should have bought, Erin.

Erin Welsh

I should have bought.

Erin Allmann Updyke

We really missed out.

Erin Welsh

We did. (laughs) And tourism obviously plummeted, no one wanted to go to a place where you could catch spotted fever.

Erin Allmann Updyke

And 100% of you would die?

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

And matters were only made worse when the first state bacteriologist Arthur McCray died of Rocky Mountain spotted fever in 1919.

Erin Allmann Updyke

Oh my gosh Erin, how many people are gonna die from this?

Erin Welsh

There's more.

Erin Allmann Updyke

Okay.

Erin Welsh

So panic was at an all-time high so the state finally acquiesced to providing funds to create a laboratory whose main focus was to stop the problem of spotted fever. The quote "Schoolhouse Lab" was established in an abandoned schoolhouse a couple of miles from Hamilton, Montana in the Bitterroot Valley. There lab and ecological facilities were built or cobbled together where researchers could actually do the work that they had been doing in their spare time in makeshift tents and distant university labs for years. And to head this new research venture two people were appointed: physician Roscoe Spencer and entomologist Ralph Parker.

Erin Allmann Updyke

Parkeri, all right.

Erin Welsh

Another physician and another entomologist.

Erin Allmann Updyke

Are they gonna work together this time?

Erin Welsh

Well this is where the romance comes in. Just kidding. (laughs) At first the old time rivalry between these two professions seemed like it was gonna rear its ugly head yet again. Before they arrived in Montana it was like oh what about publication priority, what about this, what about that? But then they met in person and they were like, 'Let's work together, all of our research will be published jointly.' Isn't that nice? I like that.

Erin Allmann Updyke

And that is how you do it.

Erin Welsh

That's how you do it. So Parker, the entomologist, he had set his sights on big picture ecological studies, like huge, how do we find out the links between ticks and these animals and spotted fever and the behavior and seasonality and all of these. Just the most fun questions, right? And Spencer is like, 'I'm gonna do a vaccine.' And so there had been some research by Hideyo Noguchi at the Rockefeller Institute that was promising in terms of spotted fever vaccines and in 1923 Noguchi had declared that he had developed an effective vaccine, it just needed to be tested in humans. So who better to volunteer than some of the laboratory staff at the Schoolhouse Lab in Hamilton?

Erin Allmann Updyke

For sure.

Erin Welsh

Where incidence of the disease was disturbingly high. The vaccine was not without side effects but it seemed to be effective in at least reducing the severity of illness if exposed to the disease.

Erin Allmann Updyke

All right.

Erin Welsh: But because the efficacy of Noguchi's vaccine remained doubtful, Spencer, the physician involved in the project, continued his own work on a vaccine, work which ended up being delayed because tularemia, another disease, started popping up in the Bitterroot Valley.

Erin Allmann Updyke: Oh my gosh, this does not make me want to visit this part of Montana.

Erin Welsh: Oh my gosh, what? First of all...

Erin Allmann Updyke: Okay.

Erin Welsh: That was not the image I was trying to portray with this history and I feel now very bad about it cause it is absolutely beautiful. And yes there are ticks but we know a lot more about Rocky Mountain spotted fever, we know a lot more about how to protect ourselves, and if there is ever an area where the physicians are probably keyed into signs and symptoms-

Erin Allmann Updyke: Yeah, that makes sense. You'd get doxycycline if you walked in and said, 'I have a fever' probably.

Erin Welsh: You're like, 'I went hiking in the Bitterroot.' Here's some doxycycline.

Erin Allmann Updyke: Here you go. Just kidding, you don't give it prophylactically. But anyways.

Erin Welsh: Okay, tularemia pops up. Both Spencer and Parker, the heads of the project, became ill and they wouldn't be the last to fall during this work.

Erin Allmann Updyke: Oh no. Erin, I don't know if my heart can take this.

Erin Welsh: I'm so sorry.

Erin Allmann Updyke: You said romance, this is not that.

Erin Welsh: I think it was like romance meant in the way that was like tragedy.

Erin Allmann Updyke: Oh yeah, those are two different categories of film.

Erin Welsh: (laughs) I don't know, are they? I think a tragic movie could be romantic at the same time and vice versa. Romeo & Juliet.

Erin Allmann Updyke: Yeah, I don't like that one. Anyways.

Erin Welsh: Regardless, let's learn more about the fallen researchers.

Erin Allmann Updyke: Okay.

Erin Welsh: Student research assistant William Gettinger died in 1922 of spotted fever. Field assistant George Henry Cowan who had worked for over a decade on the disease die in 1924. And another student researcher named Albert Kerlee died in 1928 of spotted fever. In 1925 alone 6 people working at the Schoolhouse Labs became infected with either spotted fever or tularemia.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

The Schoolhouse Lab was notoriously and deservedly so an incredibly dangerous place to work because there was no biocontainment facilities and spotted fever-ridden ticks were crawling all over the place.

Erin Allmann Updyke

Oh no.

Erin Welsh

They would have rabbits that they would infect and then the ticks would just be... Like the tick falls off and then it could go and get up on a lab worker.

Erin Allmann Updyke

Oh dear.

Erin Welsh

Dogs wandered in and out, bringing ticks with them. I mean they didn't have the best facilities.

Erin Allmann Updyke

Right, right.

Erin Welsh

Part of it was funds. There's a lesson here and it's about funding disease research.

Erin Allmann Updyke

As usual.

Erin Welsh

There's a famous book called 'Microbe Hunters' by Paul de Kruif that tells the romantic and swashbuckling tales of early microbiologists and microbe hunters. And it includes the story of the Rocky Mountain spotted fever researchers which enraged the residents of the Bitterroot because it portrayed them all as cowering in their cabins, hiding from this dreaded disease. But I mean people were rightfully scared of spotted fever and so when Spencer rolled out testing of his vaccine in 1925, both workers at the lab as well as residents eagerly volunteered. And it seemed effective in at least reducing the duration and severity of the illness.

Erin Allmann Updyke

Okay.

Erin Welsh

So overall, retrospective studies showed that vaccinated people had a 75% lower fatality rate than those who were unvaccinated.

Erin Allmann Updyke

What? That's amazing.

Erin Welsh

Yeah, yeah. But the hazardous working conditions remained a concern and so the state finally put together funds to build new facilities. But where should they go? Should they move to Missoula where the University of Montana was located? But maybe that was too far from the field and so we should keep it close to Hamilton? So it was decided that it would be built on the east side of the river in Hamilton which had always been spotted fever-free.

Erin Allmann Updyke

Oh no.

Erin Welsh

This caused quite a bit of a stir as people became concerned that the disease would become established on the east side or that infected ticks would escape or children playing in the yards of the lab would get infected. But tons of special precautions were put in place including a moat and heavy-duty sterilization procedures.

Erin Allmann Updyke

Whoa.

Erin Welsh

And work began. Ultimately the residents of Hamilton warmed to the lab and they would occasionally lead out-of-town visitors through the building and then that became problematic because the researchers were like, 'You're putting yourselves at risk, we need to shut this down. You need to sign in, you need to have somebody supervising this.' But anyway the availability of a vaccine also allayed some of these fears. But the vaccine was not a permanent solution because in order to make it researchers had to collect or rear thousands of ticks, get them infected, and then grind them up and then turn that into a vaccine.

Erin Allmann Updyke

Oh that's what they were using, okay.

Erin Welsh

And there wasn't much work that had been done on streamlining the production process and nor would there probably be since the market for the vaccine was relatively low, only in the western states.

Erin Allmann Updyke

Right, yeah.

Erin Welsh

Or was it?

Erin Allmann Updyke

Oh.

Erin Welsh

So throughout the 1930s a mysterious typhus-like illness was noted along the Eastern Seaboard of the US as well as in Brazil and it seemed to be associated with a tick bite. And while initially it was thought to be a disease distinct from spotted fever, like doctors would say, 'Oh I would say this is spotted fever if I were in Montana'. But ultimately microbiological research showed it to be one in the same. And this development was pretty crucial since it came around the same time as the Great Depression was sinking its teeth into everything, including scientific research funding. So funding for the Rocky Mountain Laboratory was threatened and in response to this one person, on researcher replied, quote - and I'm including this quote because I think it's relevant to today and always: "If the government should discontinue this activity in the light of our present knowledge, the persons responsible for such action would in my opinion be morally responsible for the deaths which will occur as a result of the lack of material. I may add that only a few days ago a request was received from the army for a large quantity of this material to be used for the protection of its forces in the field."

Erin Allmann Updyke

Sounds strangely familiar in our current climate. And that's all I'm gonna say about that.

Erin Welsh

That's like the government doesn't wanna fund this anymore but yet they want it. So anyway.

Erin Allmann Updyke

Okay.

Erin Welsh

Fortunately, maybe this is cause for optimism-

Erin Allmann Updyke

There's a fortunate?

Erin Welsh

The funds were preserved.

Erin Allmann Updyke

Okay.

Erin Welsh

The lab stayed in place and actually some civilian conservation course, CCC camps, which was part of Roosevelt's new deal, were established in the Bitterroot to help collect ticks and to do this research for vaccine production. So they had tons of people coming in to work there which was actually also a problem because there wasn't enough vaccine to vaccinate the newly arrived workers.

Erin Allmann Updyke

Oh my.

Erin Welsh

So until the mid 1930s research at the Spotted Fever Lab in Hamilton had focused on just that, hence its name which was the Spotted Fever Lab, maybe some dips into tularemia. But developments in the mid 1930s would greatly expand its role and give it the name Rocky Mountain Laboratory.

Erin Allmann Updyke

But Rocky Mountain Labs is still a thing today.

Erin Welsh

Oh yeah. These are its roots.

Erin Allmann Updyke

Yeah, I never knew that. And when you said Rocky Mountain Labs earlier, I don't know how I never would have made a connection between Rocky Mountain spotted fever and Rocky Mountain Labs. I never made that connection before.

Erin Welsh

Oh my gosh. And it's so wild because that's always been... Well throughout my PhD I was like oh that's my dream place to work, I wanna work on Rickettsias in RML in beautiful Hamilton. But I didn't know any part of this history and I also didn't know the incredible significance that this lab has had not only on Rocky Mountain spotted fever research but as we're about to find out, even more research.

Erin Allmann Updyke

Ooh, tell me.

Erin Welsh

Okay. So in 1936 a researcher at Rocky Mountain Laboratory named Harold Cox had been experimenting with different ways to grow Rickettsia outside of ticks.

Erin Allmann Updyke

Ooh.

Erin Welsh

Because he was like, 'I wanna put together a better method of vaccine production.' One day he ran out of the tissue that he had been using mid-experiment and rather than scrapping the whole thing, he reached for some yolk sac that he had put in the fridge.

Erin Allmann Updyke

You have that just laying around.

Erin Welsh

I guess. Well they were doing egg membrane whatever.

Erin Allmann Updyke

Right, right.

Erin Welsh

And the next day he found it teeming with Rickettsia and he was like, 'Oh my gosh, what?' He wrote to everyone, people were super skeptical and then they saw it in person and they were like, 'Are you kidding me? Good job. Good job.' And this accidental discovery had huge implications but not just for spotted fever research but other rickettsial diseases and I know that we haven't done a typhus episode but typhus is really bad.

Erin Allmann Updyke

Yeah.

Erin Welsh

I mean you talk about one of the big killers of especially like wartime and any sort of civil unrest areas, typhus was massive.

Erin Allmann Updyke

Yeah. It's still around.

Erin Welsh

It's still massive.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. So typhus was a huge one. So spotted fever, yeah, across the US and into Central and South America, incidence of it ran pretty low. Of course it was very deadly and so that was a huge cause for concern but of even more interest was the big killer typhus.

Erin Allmann Updyke

Right. Yeah.

Erin Welsh

Especially as WWII began and as US soldiers began to be stationed in regions where it was endemic. Cox's yolk sac method provided a cost efficient way to produce the volume of vaccines that had long been sought after. This discovery turned Rocky Mountain Laboratory into a national vaccine factory for typhus and yellow fever and others during WWII. It turned into just pumping out vaccines.

Erin Allmann Updyke

Wow, I did not know that.

Erin Welsh

And it played such a hugely important role during WWII that there were armed guards from armed forces there around the clock 24/7 to make sure that nothing happened to the lab. In old Hamilton, Montana, tiny town. So anyway, super cool. And then while at Rocky Mountain laboratory, Cox also developed the complement fixation test which allowed for diagnosis of rickettsial diseases.

Erin Allmann Updyke

Wow.

Erin Welsh

That's a big deal!

Erin Allmann Updyke

That's a very big deal.

Erin Welsh

So Rocky Mountain Lab.

Erin Allmann Updyke

Rocky Mountain Lab.

Erin Welsh

The discovery of antibiotics that were effective against rickettsial diseases in the 1940s and the 1950s took some of the urgency out of the preventative or treatment research programs for spotted fever. Researchers could now focus on understanding the physiology of Rickettsia and the microbiology of these bizarre, tiny bacteria. And the miracle of antibiotics as we had discussed a few episodes ago led to this unfortunate decline in some of the more fundamental medical entomology research that had been the hallmark of the Rocky Mountain Laboratory in its early decades. With the combination of a vaccine and antibiotics, fear of spotted fever declined throughout the 50s and the 60s despite the fact that it continued to pop up in new locations and with increasing incidence. Like if you look at a chart of the cases over time, it's like increasing, increasing in the late 1800s/early 1900s and then plummets. And then throughout the 60s and 70s it's like on the rise.

Erin Allmann Updyke

Oh, just wait Erin. Just you wait.

Erin Welsh

Okay. I'm very interested.

Erin Allmann Updyke

Okay.

Erin Welsh

And then budget cuts in the 1970s eliminated the medical entomology research program at Rocky Mountain Lab. And I don't know if it's back up or not, I should have checked that. And the tick collection was shipped to the Smithsonian. Work on Rickettsia continued and Rocky Mountain Laboratories is still a hugely important site of research in general, as you mentioned. And a few more pieces of the spotted fever puzzle fell into place during this time. For instance the recent resurgence in cases in the 1970s was traced to the encroachment of humans into previously wooded areas, à la Lyme disease.

Erin Allmann Updyke

À la Lyme.

Erin Welsh

Surprise, surprise. And most interestingly the longstanding mystery of why the east side of the Bitterroot River remained protected from the west side was solved.

Erin Allmann Updyke

Okay.

Erin Welsh

By Willy Burgdorfer.

Erin Allmann Updyke

Burgdorferi?

Erin Welsh

Of our Lyme disease episode, *Borrelia burgdorferi*, yep.

Erin Allmann Updyke

Lyme disease! What?

Erin Welsh

Okay.

Erin Allmann Updyke

Willy Will!

Erin Welsh

I'm so excited that I get to tell you this.

Erin Allmann Updyke

Oh I'm so excited too because I really was expecting this story to go, 'And then they built a lab and then released infected ticks and now they're everywhere.' Like that's 100% what I expected.

Erin Welsh

So that's not what happened. And here's why. So he discovered that on the east side of the river he was doing a bunch of microbiology assays of these ticks and he discovered that they were infected with Rickettsia but it was a nonpathogenic one and the Rickettsia in those ticks prevented Rickettsia rickettsii, the pathogenic one, from colonizing the ticks. Interference phenomenon.

Erin Allmann Updyke

Okay. Oh my god, I'm getting chills.

Erin Welsh

I know, I know. So researchers had long made the observation that animals freely pass from the east side to the west side of the river, animals are found on both sides, it didn't make sense.

Erin Allmann Updyke

Right.

Erin Welsh

So if a tick that is infected with this non pathogenic Rickettsia bites an animal that is infected with spotted fever, Rickettsia rickettsii, that spotted fever can't establish in that tick.

Erin Allmann Updyke

Right.

Erin Welsh

Because the other bacteria is just already there. And so this bacteria also has better transovarial transmission. So it will not hurt the tick as it's passed from female tick to eggs.

Erin Allmann Updyke

This is so interesting, Erin.

Erin Welsh

Tick biology is so amazing.

Erin Allmann Updyke

It really is very cool.

Erin Welsh

It's so amazing.

Erin Allmann Updyke

That is so bizarre.

Erin Welsh

So this interference phenomenon, it's been discussed this type of thing, we've talked about it with Wolbachia and maybe we haven't but we've referenced it at least or alluded to it in terms of finding certain microbes that can prevent pathogenic ones from establishing in a vector.

Erin Allmann Updyke

Yeah, we talked about it with dengue fever.

Erin Welsh

Oh yeah, yeah.

Erin Allmann Updyke

Oh my gosh, wow.

Erin Welsh

So anyway, Burgdorfer, yeah. So even though Rocky Mountain spotted fever has been heavily studied for over 100 years there's still a lot that we don't know about it, particularly when it comes to the disease reservoirs, strain differences, geographic differences, climate change. The list goes on and on and on. Seasonality. Fortunately for researchers now it's a lot safer than it used to be to study and I repeat again, I hope, hope, hope I haven't discouraged anyone from visiting the Bitterroot Valley because you definitely should do so, it's gorgeous, it's amazing, and anyway.

Erin Allmann Updyke

And you could go see Rocky Mountain Labs.

Erin Welsh

And you could go see the infamous, the famous, the amazing Rocky Mountain Labs. Okay well Erin, tell me what's going on with Rocky Mountain spotted fever today.

Erin Allmann Updyke

Oh I'm really thrilled to after that history. We'll take one quick break first.

TPWKY

(transition theme)

Erin Allmann Updyke

I'm gonna start off not where I expected to start off because I want to ask you questions, Erin.

Erin Welsh: Okay.

Erin Allmann Updyke: I wanna start off with the vaccine. We don't have one, Erin.

Erin Welsh: No.

Erin Allmann Updyke: There is none.

Erin Welsh: The one that they had developed, the Parker-Spencer vaccine, it's not been used for several decades now.

Erin Allmann Updyke: Yeah.

Erin Welsh: And I think ultimately it caused some side effects and possibly infection in some people.

Erin Allmann Updyke: That makes sense if they were just grinding up ticks, then that would...

Erin Welsh: Yeah. It seems like Rickettsia in general are a tricky bunch to make vaccines for.

Erin Allmann Updyke: Yeah, I don't know but we don't have a vaccine. Honestly from what it sounds like, and I'm sure that this is the case, it's largely just because of a lack of funding and a lack of interest not just from a research standpoint but from a pharmaceutical standpoint. There are not enough cases essentially per year to produce a vaccine, it's not financially viable, for better or for worse. It is true that patients who survive infection do mount a very good and long-lasting immune response and we've also identified a number of the surface protein antigens so it's certainly theoretically possible to develop a vaccine. I usually use Google Scholar, that's my preferred search website for finding my papers.

Erin Welsh: Yeah.

Erin Allmann Updyke: And when you search 'Rocky Mountain spotted fever vaccine', the first entire page of results, there is not a single paper from past 1990 on that page.

Erin Welsh: Yeah. Yup.

Erin Allmann Updyke: Yup. And some of them are from 1925, they're probably some of the ones referenced in your book.

Erin Welsh: Oh my gosh! Parker-Spencer!

Erin Allmann Updyke: Yeah, right. But that doesn't mean that no one's doing research on it, I did find a recent paper that was looking at and did develop an effective wholesale vaccine that they tested in dogs. I will link to it but I wouldn't read that paper again, it was very depressing, they killed a lot of dogs.

Erin Welsh: Oh my god.

Erin Allmann Updyke: Yeah. But they made a vaccine.

Erin Welsh: Oh.

Erin Allmann Updyke

So anyways, that's the current research. Let's talk about the epidemiology.

Erin Welsh

Yes.

Erin Allmann Updyke

All right. So in the United States, Rocky Mountain spotted fever has been a nationally notifiable disease since the 1920s. Since 2010 they've been calling it a different name and therefore reporting it a little bit differently. It's now reported as spotted fever rickettsiosis. And the reason is we don't have a good way to differentiate the clinical syndrome that is caused by *Rickettsia rickettsii* from the clinical syndromes that are caused by a number of other rickettsial pathogens including *Rickettsia parkeri* which we briefly said those words earlier, rickettsial pox, and a few others. So kind of that's the background I think to keep in mind as I'm gonna talk about these numbers because this gets really interesting, okay?

Erin Welsh

Okay.

Erin Allmann Updyke

So let's talk about you said that cases were increasing through the late 1990s or through the late 1900s, right, after that drop off. Well if you look at the graphs of cases since the year 2000 it's terrifying.

Erin Welsh

It is.

Erin Allmann Updyke

It's an exponential growth curve which everyone is now very familiar with, we've all seen a lot of those these days, okay. The number of cases has increased steadily just about every year, 2018 was a little better than 2017 but in 2017 there were over 6000 cases reported and that's up from under 500 in the year 2000.

Erin Welsh

What? Okay, I'm so embarrassed because this is literally what I did my PhD on. But I did it in Panama.

Erin Allmann Updyke

Yeah you did it in Panama, it's okay. It's fine, okay, you didn't need to know these numbers. But here's the question. We're seeing these huge increases in cases, how many of these are the very deadly Rocky Mountain spotted fever vs other *Rickettsia*? And it's really hard to say. And also how much of it is are we getting better at recognizing it, are we getting better at reporting it or are there an increase in infections? I think this is me thinking but also based on what I read, it's likely a combination of both as usual, but the increase is so large over such a short period of time, like we're talking 20 years right, from 2000 you have under 500 cases to over 6000 in 17 years. That's massive. And this is a disease that's been notifiable since the 1920s.

Erin Welsh

Yeah.

Erin Allmann Updyke

And our diagnostic tools are not much better today than they were 20 years ago, okay. The case fatality rate has drastically, dramatically decreased since the 1940s, since the introduction of tetracyclines for treatment.

Erin Welsh

Yeah.

Erin Allmann Updyke

So in clinical reviews worldwide, even after tetracyclines were introduced for treatment, case fatality rates still usually are about 5-10%, usually around 5%. But the current case fatality rate in the US according to surveillance data is as low as 0.5%.

Erin Welsh

That's excellent.

Erin Allmann Updyke

It is excellent but it bears the question is this Rocky Mountain spotted fever or is this something else? So let's look in other parts of the world, what's going on there. Well turns out that's hard to do. There's not very good surveillance data for much of the rest of the world but I did find some really good data for Mexico. So in Mexico throughout the 2000s, the incidence of disease has also been increasing, also dramatically. I don't have an exact number. However unlike in the US the case fatality rate has also been increasing rather than decreasing.

Erin Welsh

Really?

Erin Allmann Updyke

The aggregate case fatality rate has been between 14-18% depending on the region in Mexico but in some years the case fatality rate has been as high as 40%.

Erin Welsh

Ooh.

Erin Allmann Updyke

So then I think there's a lot of questions as to what is this. Does this mean that we're looking at different diseases or does it just mean that we're looking at drastic differences in lack of availability of good diagnostic tests, delays in reaching a doctor to get diagnosis or to get treatment. Another issue is that a large proportion of cases not just in Mexico but also in the US are in children cause kids are running around outside getting bitten by ticks.

Erin Welsh

Right.

Erin Allmann Updyke

And usually tetracyclines aren't used as treatment for children because it can permanently damage and discolor your teeth. So a lot of physicians might be hesitant to prescribe doxycycline for kids but it turns out that for Rocky Mountain spotted fever it's a short enough course that doesn't actually increase the risk of tooth discoloration. But maybe you don't know that and so then a kid is delayed in getting the appropriate treatment or receives the wrong kind of treatment, so then you have North America increase in case fatality rate. But overall it's less than 1% of spotted fever group rickettsioses that are reported in the United States are actually lab confirmed.

Erin Welsh

Okay. So it's all based on the triad of..

Erin Allmann Updyke

Clinical. Yeah, exactly. Oh and the other triad piece is often tick exposure. So some people say the triad is fever, rash, tick exposure or history of tick exposure vs fever, headache, and rash.

Erin Welsh

Oh right, rather than the headache.

Erin Allmann Updyke

But not everyone reports tick exposure, right, and that doesn't mean they weren't exposed, they just might never have known it.

Erin Welsh

Comforting thought.

Erin Allmann Updyke

Yeah. So that's spotted fever group rickettsiosis, Rocky Mountain spotted fever today. We never told Brett's story. (laughs)

Erin Welsh

Okay now we need to tell Brett's story. Cast your mind back to 2013, 2014.

Erin Allmann Updyke

2014?

Erin Welsh	The summer.
Erin Allmann Updyke	The summer of 2014, okay listen, listeners.
Erin Welsh	The rainy season in Panama.
Erin Allmann Updyke	Everyone.
Erin Welsh	June.
Erin Allmann Updyke	As we mentioned, Erin Welsh did her research on tick-borne disease in Panama, that was what her thesis was on. Our lab is a disease ecology lab, we studied tick and other vector-borne diseases, okay.
Erin Welsh	My focus in particular, well my focus was the general ecology of ticks and their pathogens as it related to the climate gradient across the isthmus and seasonality in different animals and blah, blah, blah. But in all the research proposals I ever wrote during my PhD, I always mentioned <i>Rickettsia rickettsii</i> .
Erin Allmann Updyke	Of course.
Erin Welsh	Because it is present there and it is a cause for concern, so you wanna understand where they are, what the ticks are, and you wanna increase awareness of a tick bite and a rash and a fever and a possible headache.
Erin Allmann Updyke	So June of 2014, Brett, my now husband, and I flew back from Panama after my first field season down there to California to stay with family for a short time. And on the plane ride back he started feeling crappy, okay. He felt unwell. We made it back to my brother's house and I believe he had a fever but I'm sure we didn't have a thermometer but he felt sick, like he just really didn't feel good. And I was like, 'Gosh, I hope you didn't come down with something.' But he had no respiratory symptoms, he wasn't coughing, he didn't have a sore throat, any of the normal kind of things I would associate with flu or a cold. He just felt achy, he felt unwell, he had a headache, a fever. And this lasted for a couple of days and then he went to the bathroom.
Erin Welsh	(laughs) Did you tell him that you were gonna tell this story?
Erin Allmann Updyke	Yes I told him, don't worry.
Erin Welsh	Okay good.
Erin Allmann Updyke	He goes, 'I knew as soon as you said you were doing Rocky Mountain spotted fever.'
Erin Welsh	He's like, 'I've been waiting for this for three years and it's finally here.'
Erin Allmann Updyke	Three years. So then he came out of the bathroom and he said, 'I just pulled something off of the top of my butt crack.' And I was like, 'What?' And he was like, 'Yeah, there was a bunch of blood and some black stuff.' And I said, 'What?' And then I grabbed his arms and on his wrists was a rash, a red, blanching, macular rash that did not hurt and did not itch and he also had one on his legs that he hadn't even fully noticed up to this point.

Erin Welsh

Oh my god. Brett!

Erin Allmann Updyke

And then he said, 'I pulled this thing off the top of my butt, I squished it, there was blood and black things and I threw it in the toilet and I flushed.' And I said, 'You just flushed a tick. You have a Rickettsia, you need to first of all go to the doctor and second of all I can't believe that you threw the tick in the toilet!'

Erin Welsh

I was devastated.

Erin Allmann Updyke

Oh we all were. Our whole lab knows this story. He's also probably gonna be like, 'You told it entirely incorrectly' but I didn't. This is how it happened.

Erin Welsh

Listen. Yeah. This is the myth as I know it now at this point, it's legendary status.

Erin Allmann Updyke

It was classic. I will say I can't remember if he had the rash before he pulled the tick off or if I didn't see the rash until after he told me about pulling the tick off. But as soon as he told me about that I looked and he had this rash and I was like this is either Rickettsia rickettsii and you're going to die or it's a lesser one but either way you need to go get treatment. And he wouldn't listen to me until we went to go visit his parents and I had to tell his mother and she's the one who forced him to go to the doctor and get treatment because he wouldn't listen to me. So thank you Chris because otherwise he might be dead.

Erin Welsh

Oh my gosh.

Erin Allmann Updyke

So he went to the doctor and he said that he told the doctor that he thought he had Rocky Mountain spotted fever and this is why and apparently the doctor went and took his phone and then came back in with his phone and was like, 'Well we can do a test but I think I should just give you some antibiotics.' And Brett was like, 'Yep.' And he was better in a couple of days.

Erin Welsh

Well I am very glad that Brett was better. I am still puzzling over where you picked it up because you had just been scuba diving or something.

Erin Allmann Updyke

We had been at Coiba. So it could have been Coiba cause we had hiked around that a little bit but also it could've just been in Gamboa because we went up to the ridge or whatever.

Erin Welsh

Oh well yeah.

Erin Allmann Updyke

We'll never know because he threw the tick in the toilet. Even yesterday when I told him we were gonna tell this story on the podcast, he was like, 'I should have just thrown it in the trash.'

Erin Welsh

I know. I know, Brett. You had killed it, dead and good. (laughs) It could have been my entire dissertation right there.

Erin Allmann Updyke

Right? At least that's a case report. We could have been co-authors, Erin.

Erin Welsh

We can still be co-authors on a paper.

Erin Allmann Updyke

Whoops.

Erin Welsh

I know.

Erin Allmann Updyke

Okay. Don't tell Brian. So that's our story.

Erin Welsh

That's our story. You know Erin, I feel like it lived up to my expectations, my hype for this episode. I had a great time.

Erin Allmann Updyke

Me too!

Erin Welsh

I feel like it was back to our roots in a way.

Erin Allmann Updyke

Yes, it really did. It felt good, it felt good.

Erin Welsh

I was a little bit afraid to do something that was very close to my PhD and then I realized this doesn't have anything to do with my PhD. (laughs)

Erin Allmann Updyke

(laughs) Well sources?

Erin Welsh

Sources, yes. I mostly used a book called 'Rocky Mountain Spotted Fever: History of a 20th Century Disease' by Victoria Harden which told the complete story, it was great. And then a couple of papers and I will include those on our references page on our website.

Erin Allmann Updyke

I read through a number of fun papers about the biology and a few good ones on the epidemiology, we'll post all of our sources on our website thispodcastwillkillyou.com under the EPISODES tab. You can find all of our sources for this and every single one of our episodes. Yeah.

Erin Welsh

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

Erin Allmann Updyke

And thank you everyone for listening!

Erin Welsh

Yes, thank you. We hope that you enjoyed this one as much as we enjoyed talking about it.

Erin Allmann Updyke

We really enjoyed this one, so we hope that you guys did too.

Erin Welsh

With that, until next time, wash your hands.

Erin Allmann Updyke

You filthy animals!