

Ummat Somjee

Hi, I'm Ummat and when I was a graduate student I was doing fieldwork in Panama. It was just this amazing place with tropical birds and I loved the fieldwork I did, I had to hike up these rivers in the forest and find these insects and it was so diverse and amazing. But it was also tropical so we were getting bit by insects, we were getting water in our food, we were dealing with a lot of animals and things. And there was five of us living in this house, it was pretty crowded. Five of us and a cat. And then one morning I woke up exhausted. I had a fever the night before and these awful dreams and a headache. And I knew that something was up and so I just rested that day and I tried to kind of nourish myself, have a lot of water, have a lot of food. And I felt better. By the afternoon I was even able to take a walk and everything. I said okay, maybe this is just a short term thing, everything will be fine. And then that night it was worse.

I had this awful fever, really, really bad headaches, and in the morning I was just feeling awful. And so I didn't have a car at the time and luckily I got a friend of mine to drive me to a clinic. And so I got to the clinic and I explained my symptoms and they're like well this sounds like dengue and we're gonna test your blood. And so they took a blood test and they didn't find dengue. So they sent me home and told me that this is probably some virus or something and you should probably just recover on your own, just take lots of water, vitamins, just take care of yourself. And so I said okay. But the disease just progressed and so I started getting more fevers and the next day I was really awful. But it would be also kind of cyclical, so I would feel better and think it's improving and then suddenly it would hit me again and I would get these fevers and headaches and be sensitive to light.

So two days after I went to the clinic I woke up and my sister just happened to be visiting and I was showing her the tropics, I was showing her my field site. And so we woke up in the morning, I was not feeling great but I was feeling okay. And so we drove up to the Canopy Tower, saw some beautiful tropical birds. And I remember driving back and just suddenly being extremely sensitive to light, slowly feeling this weakness coming over my body, this fever coming. And by the time I got back I was in bad shape, I kind of hobbled to bed and my head was killing me. And luckily I had a friend who who said I think we should go right to the hospital right now, this is really bad. And we got to the hospital and I remember just having a hard time kind of even walking to hospital reception in the emergency room and stuff and remember somebody bringing me a wheelchair. And I was like I don't need that wheelchair. But as soon as they brought it to me, I did sit down in it and I was like whew, okay. I definitely did need that wheelchair.

And I remember my friends talking to the doctors and stuff and they immediately took a blood test. That was the moment when I knew things were way more serious than I had initially thought. I saw the doctor's expression and he came up with this paper and he said this is a critical situation, some of my liver enzymes were off the charts, we need to get to the ICU immediately. So I got immediately admitted to a bed in the intensive care unit, they had monitored my heart rate, my blood pressure and everything. And then I was under 24 hour surveillance. Every 20 minutes somebody would come and check on me because apparently that's how critical the situation was. So it progressed so quickly, at least from my perspective. And I remember just being extremely uncomfortable and confused. And so I did improve slightly when I was in the intensive care but it still wasn't good and they still couldn't figure out what it was.

And so I stayed in the hospital and I just remember there was this routine, somebody would come and take a lot of blood from me and then I would spend my time in my room and I'd be very comfortable. I was still getting these headaches, this fever, but I'd also started getting pain in my stomach. I'd never experienced this before but apparently my liver was extremely swollen and so my stomach had become tight and tender and it was kind of terrifying thinking that a single organ has swollen to a level where it's distending your body a little bit. And I spent almost two weeks in that hospital and they still couldn't figure out what it was. I was not getting any positive tests, they were prescribing me kind of general antibiotics but eventually I started to feel a little better. I'd lost a lot of weight, I was weak but after about two weeks I was released from the hospital. But I was still very weak and it really bothered me that we didn't know what it was. I mean is this something that was dormant that could come back again and resurge, something this serious? I really wanted to know. It's just not knowing was really, really stressful.

And so I ended up going to Canada, I'm a Canadian citizen and I went to Canada and I called the hospital beforehand and it turns out they had a tropical medicine program going on there with the med students. When I called them and told them my situation, they put me in touch with this doctor who's teaching this course. And it turns out they don't get a lot of tropical disease patients in Canada. So I was talking to him about all the stuff I had read and trying to figure out what what I had. And he asked me if it was okay if I could participate in trying to help figure out what was going on. And so he had a bunch of these med students around the bed and it was like an episode of House or something, one of those medical dramas where they try to figure out what you have. And different medical students gave their hypotheses, experienced doctors said well maybe that's something you should pursue or maybe that's not right because of these chart readings or something. And they were trying to figure out what it might be to try to look for antibodies or some indication of what I had.

And so then I left the hospital and I was recovering slowly and then it wasn't until three months later I got a call and one of the medical students figured it out, it was leptospirosis. And so when I found out that it was leptospirosis, now I had a diagnosis, I could start thinking about what the mode of transmission was. And I remembered when I was living in that house with those five people and that cat, that cat didn't like me very much. And I would go on these runs on pipeline, on this road, this muddy road and I'd leave my shoes outside. There was this one time this cat peed in my shoes and I didn't realize until I was walking around and I could smell something weird. And it was an outdoor cat too so it was probably grabbing all sorts of rats and rodents outside and also a potential vector for leptospirosis. So that time I also happened to have this cut in my foot. And so there's this possibility that it was this direct blood transmission that got me infected. But yeah, so that's the story of me getting leptospirosis.

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

I remember that so vividly and it was terrifying.

Erin Allmann Updyke

It sounds awful. I remember hearing about it after the fact.

Erin Welsh

Yeah. Well Ummat, I'm so glad that you are better and that everything eventually turned out okay.

Erin Allmann Updyke

Yeah. And with us. Yeah.

Erin Welsh

And also thank you so much again for sharing your story because for those of you who are longtime listeners, you may have recognized Ummat's voice from Season 1 when he provided the firsthand account for malaria.

Erin Allmann Updyke Let's hope, Ummat, that there's no more diseases that we need to have you provide a firsthand account for.

Erin Welsh Let's hope. Hi, I'm Erin Welsh.

Erin Allmann Updyke And I'm Erin Allmann Updyke.

Erin Welsh And this is This Podcast Will Kill You.

Erin Allmann Updyke And today we're talking about leptospirosis.

Erin Welsh Leptospirosis. Yeah.

Erin Allmann Updyke Can I make a quick confession? I just want to say this off the bat.

Erin Welsh Of course.

Erin Allmann Updyke I don't know why but leptospirosis, legionella, and leishmaniasis constantly confused in my brain.

Erin Welsh Interesting.

Erin Allmann Updyke Those three and now we've covered all of them.

Erin Welsh That's like me and Gerard Butler and Clive Owen, they're the same person.

Erin Allmann Updyke They actually are the same person so that's very valid.

Erin Welsh So now you don't have to worry about getting them confused anymore because this is just, we're done.

Erin Allmann Updyke Right, right.

Erin Welsh I'm really excited for this episode because when I was going through emails to be like okay, what do people want to hear? I was so surprised at the number of requests for leptospirosis.

Erin Allmann Updyke Yeah.

Erin Welsh And one of the reasons it seems like is because this this is a disease that affects not just humans but also many animal species.

Erin Allmann Updyke Yep.

Erin Welsh And it's so much more prevalent and important than I think I realized even after watching Ummat go through this horrible ordeal.

Erin Allmann Updyke Yeah, I think it's easy to think of this as a disease of the tropics or as a disease of other places but it's a worldwide pathogen as we'll talk about. And I think a lot of pet owners and veterinarians are probably a lot more familiar with it than maybe the general public.

Erin Welsh: Yes, totally.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: I'm excited. It's going to be good.

Erin Welsh: First things first.

Erin Allmann Updyke: It's quarantini time.

Erin Welsh: It's quarantini time. What are we drinking this week?

Erin Allmann Updyke: We're drinking I Smell A Rat.

Erin Welsh: And why are we drinking I Smell A Rat?

Erin Allmann Updyke: It turns out Erin that rats are a very important part of the overall distribution and prevalence and life cycle of Leptospira.

Erin Welsh: And I also want to say just right here that we are not trying to intentionally further the stigma against rats.

Erin Allmann Updyke: Don't blame the rats.

Erin Welsh: Don't blame the rat. Rats are just one piece of the puzzle, many other animals do this. But the title was too good to pass up.

Erin Allmann Updyke: Yeah because who doesn't want to drink I Smell A Rat? I mean really.

Erin Welsh: I mean once you hear the recipe though you're definitely going to want to drink it.

Erin Allmann Updyke: Please tell me what is in it.

Erin Welsh: It is a shrub. It's a mango habanero mint shrub. So this is like a drinking vinegar, you muddle all of these fruits and ingredients together with sugar, let it sit, and then you can use that as a great base for a cocktail like this one with tequila for instance. Or you can use it as a placeborita as well with no alcohol.

Erin Allmann Updyke: Yeah!

Erin Welsh: Delicious either way. And we will post the full recipe for I Smell A Rat the quarantini as well as the placeborita on our website thispodcastwillkillyou.com as well as on all of our social media channels.

Erin Allmann Updyke: And on our website thispodcastwillkillyou.com you can find all of the best website-type things you can find.

Erin Welsh: You think people even need to hear this at this point?

Erin Allmann Updyke: I don't know really. Just check out our website, it's there.

Erin Welsh: Yeah, I like that. Erin, I am so ready to learn. So can we take a quick break and get started?

Erin Allmann Updyke: Let's do it.

TPWKY: (transition theme)

Erin Allmann Updyke: Leptospirosis is a disease caused by a bacterium in the genus *Leptospira*. These are spirochaetes which means those little twirly corkscrew dudes like a few other pathogens we've covered like *Treponema*, the causative agent of syphilis; *Borrelia* which causes Lyme disease. Have we done any others?

Erin Welsh: I was trying to think of that and I can't come up with any more.

Erin Allmann Updyke: Me neither, those are the two I remember.

Erin Welsh: Yeah.

Erin Allmann Updyke: So this spirochaete it turns out is not just one bug, it's not just one species. And it seems like from what I could read the classification and species definition seems to be in flux currently.

Erin Welsh: Yeah.

Erin Allmann Updyke: So different papers have a lot of different numbers cited but it seems like there's over 60 different species, I think that's the consensus, in the genus *Leptospira*. And importantly this includes more than 300 serovars. Asterisk, a note Erin, I would like to talk about this a little bit more.

Erin Welsh: Okay.

Erin Allmann Updyke: Because in our episode on salmonella we talked about the idea of species and subspecies and serovars and in that episode I feel like I did a very bad job of trying to define what serovars actually are. And when it comes to leptospirosis and salmonella and a lot of other bacteria, serovars are really important epidemiologically a lot of times in distinguishing was this outbreak all from this source or from that source, etc. So I wanted to give a little bit of a better definition of what a serovar actually is in this case. Basically serovars are determined based on the surface antigens, so differences in those surface proteins and things which of course are some of the main things that our bodies use to recognize various pathogens, right.

Erin Welsh: Right.

Erin Allmann Updyke: And so serovars are like strains or isolates that differ in their surface antigens. In the case of leptospirosis there are over 60 different species, not all of which are pathogenic, but which include over 300 serovars, at least 200 or over 200 of which are pathogenic.

Erin Welsh: It seems like more are being discovered all the time.

Erin Allmann Updyke I am not surprised. So anyways, I hope that was at least a little more helpful than my description in the salmonella episode.

Erin Welsh It was, it's really interesting.

Erin Allmann Updyke Yeah.

Erin Welsh Before we move back to leptospirosis, I just want to take a moment to share something about salmonella.

Erin Allmann Updyke Yeah? Love it.

Erin Welsh A listener reached out to us and you know how in the salmonella episode we were like is it pronounced Daniel Sal-mon or Daniel Sam-mon?

Erin Allmann Updyke Yeah!

Erin Welsh The person who salmonella is named after. So someone tweeted at us and said it's pronounced Sam-mon because he is one of her ancestors which is so thrilling.

Erin Allmann Updyke That's awesome! Oh, I love that. I feel like we've had a couple times where people have emailed us saying, 'I'm related to one of the people you talked about.' And I don't know why it thrills me.

Erin Welsh 100% every single time. It's so cool.

Erin Allmann Updyke My heart is beating quickly. I love it.

Erin Welsh Back to leptospirosis.

Erin Allmann Updyke Back to leptospirosis. All right, if you're related to anyone... No, okay. So anyways, that's the pathogen. A lot of different species, a lot of different serovars. Like I said up top, this is a pathogen that is found worldwide. And while it is more prevalent or at least more common in the tropics, this is mostly just because it can be an environmentally transmitted pathogen. This is something that can persist in the environment for weeks to months in the water and in the soil and the climate in the tropics is just a little better suited for *Leptospira* growth and survival. But this is a bacterium that can infect almost any mammal, pretty much all mammals. Some of them, some mammal species are very good reservoirs which means that they can harbor this bacterium mostly in their kidneys at really high levels for months at a time and pee it out all over the place, often without showing any symptoms or getting sick at all. Other species are less great reservoirs and they may get sick to varying degrees but what's really important is that this can infect literally almost any mammal, including marine mammals which I always find fascinating.

Erin Welsh Yeah, yeah. Question. You are saying this bacterium, do you mean the genus overall or are there species differences in terms of which animals are best reservoirs for which species or serovars?

Erin Allmann Updyke Great, great, great, great question. Yes, there are differences where some species or some serovars are maybe more common in certain animal species and others are more common in other species. But of the pathogenic species of *Leptospira*, they have been shown in the lab to infect nearly any mammal if you expose them to it.

Erin Welsh	Any given <i>Leptospira</i> pathogenic species.
Erin Allmann Updyke	Right, exactly.
Erin Welsh	Gotcha.
Erin Allmann Updyke	So I probably shouldn't be saying 'this bacterium'. This genus.
Erin Welsh	Okay.
Erin Allmann Updyke	These pathogenic spirochaetes.
Erin Welsh	Yeah.
Erin Allmann Updyke	But excellent question. So when it comes to humans, we generally get exposed either through direct contact with infected domestic animals like cattle or dogs, or more commonly through exposure to infected water sources or infected soil. And exposure happens in a variety of ways. These spirochaetes can corkscrew their way in through any little cuts or abrasions on our skin, they can enter directly. If you get infected water in your eyes or your mouth, they can enter through your mucus membranes. Even if you swallow a bunch of contaminated water or drinking water sources become contaminated, you can get infected that way as well. And that is true for animals as well, so that's the way that all other animals are also being infected, through abrasions on their skin or through their mucous membranes.
Erin Welsh	Which makes sense about high infection rate in some animals because if you just imagine dogs, a lot of dogs love drinking out of puddles.
Erin Allmann Updyke	My veterinarian when my dog was a puppy was like, 'Oh we could vaccinate for <i>Leptospira</i> , is your dog a puddle licker?' And I was like are not all dogs puddle lickers? So yes, if you have a puddle licker, they will be exposed.
Erin Welsh	A puddle licker. Unbelievable.
Erin Allmann Updyke	So these highly mobile little spirochaetes, once they get into our bodies corkscrew their way directly into our bloodstream and begin to replicate. They cause a bacteremia which is bacteria in our blood, that's all that means, over the course of usually about a week or so. And then once those bacteria reach high enough numbers, and what's fascinating about leptospirosis is that the amount of bacteremia can be incredibly high, we're talking millions of bacteria per milliliter of blood which is very high, even before you show any symptoms. And this is way higher than what we would see from a bacteremia in an <i>E. coli</i> or something without our body's freaking out about it.
Erin Welsh	Why is that? Why does it produce such a high bacteremia?
Erin Allmann Updyke	Well it seems like our bodies our very good at detecting and mounting a response to very low levels of antigen from something like <i>E. coli</i> but essentially just don't even recognize leptospirosis antigen until it's at very, very high levels. What?
Erin Welsh	Interesting.

Erin Allmann Updyke

I know. Right? Then after they get to these very, very high levels in our blood, these bacteria start burrowing their way through our endothelial cells that line our blood vessels and into various organs. And that is usually the point at which symptoms will tend to start to appear. So the total incubation period is anywhere from 7-14 days, could be as long as a month and rarely is shorter than that.

Erin Welsh

Okay. And once these bacteria leave the blood and start burrowing and finding their way to organs and whatnot, does that mean that they straight up leave the blood? Would you be able to detect them in the blood?

Erin Allmann Updyke

Excellent question. They don't leave the blood entirely but these are still difficult bacteria to detect because like other spirochaetes that we've talked about on this podcast, they don't gram stain very well and so they're just not as easy to pick up. And I do think that the amount of bacteremia tends to go down once they enter our organs.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

Okay. That plays a relevant role in the history section.

Erin Allmann Updyke

Oh I bet. I can't wait.

Erin Welsh

Bacteremia.

Erin Allmann Updyke

Okay, all right. Spoilers. Or just foreshadowing.

Erin Welsh

Foreshadowing, yeah.

Erin Allmann Updyke

When it comes to animals, various animal species that get infected, they can remain infected and primarily in the proximal tubules of the kidney, which is just so interesting that this pathogen loves that particular part of a kidney, for literally months in some cases up to a year. And then because they're in the tubules of the kidney where your kidney is making urine, this pathogen is just being shed beautifully at very high levels in the urine. So for some animals this process can be completely asymptomatic and for other animals including dogs and in some cases including cattle, they can also get sick from leptospirosis. And what's interesting is that especially in the case of dogs, which there's maybe more detailed clinical information at least that I could find on dogs compared to some other animals, the disease actually can look a lot like the disease in humans. So let's talk about what those symptoms actually look like. First of all, this is something that even in humans can be entirely asymptomatic.

Erin Welsh

You could just be shedding bacteria in your urine.

Erin Allmann Updyke

Shedding.

Erin Welsh

Okay.

Erin Allmann Updyke

And importantly for humans, some papers call humans dead end hosts. We're not truly dead end hosts but transmission from humans to humans is very, very, very, very rare. We can potentially shed *Leptospira* in our urine but it tends to be at much lower levels than something like a rat.

Erin Welsh

Okay, so the general route of infection and course of infection where the bacteria go from point A to point B and so on is the same across these mammalian hosts but the symptoms that they show is different and the amount that they excrete is different.

Erin Allmann Updyke

Absolutely.

Erin Welsh

Interesting.

Erin Allmann Updyke

Yep. I know.

Erin Welsh

Okay.

Erin Allmann Updyke

But even in humans it can be asymptomatic and I tried to get a handle on how often and that was very difficult to do. A couple of studies that I read suggested that up to 70% of the time people tested seropositive for leptospirosis but couldn't recall any febrile disease in the months prior. So it's kind of hard to say. Could it be that someone just is still sero-positive but they had an infection a couple of years ago that they just don't remember? I don't really know. But we do know that in animals and in humans it can be asymptomatic and that's really important when we're trying to control or reduce the prevalence of a disease.

Erin Welsh

Right.

Erin Allmann Updyke

But when there are symptoms, here's how it usually starts. It starts with a...?

Erin Welsh

Fever!

Erin Allmann Updyke

Yeah! It sure does. Usually it's a sudden onset of fever along with chills. Usually there's a pretty severe headache that develops and body aches, generalized muscle aches. And the number of pathogens that we've covered even in this season alone that start out that exact same way is a lot. So this is something that especially in the early stages is a very non specific disease that can easily be mistaken for a number of other viral or bacterial infections.

Erin Welsh

Yeah.

Erin Allmann Updyke

Interestingly with leptospirosis, in contrast to the other spirochaetes we've seen, you tend to not have any rashes or skin findings early on and that's because of the way that leptospirosis goes straight into the bloodstream rather than having any skin manifestations. Usually you'll also then start to see GI symptoms like nausea, vomiting, maybe some diarrhea. And in a lot of cases that might be where this disease ends. So you might get pretty sick but it will be self-limited and then you'll recover. But when this progresses to a severe illness and this can happen over the course of a few days and sometimes people get a little better and then have a biphasic illness where then they get better and then start to get worse again. And at that point whether you just progress immediately or have this biphasic illness, this progression to severe leptospirosis is when we start to see signs of real organ dysfunction.

So what does that mean? It means we see signs of liver damage like jaundice, yellowing of the skin, and icterus, yellowing of the eyes. This happens from build up of bilirubin because of the damage to your liver as well as hemolytic anemia. So this bacteria can cause breakdown of your red blood cells that also contributes to the jaundice. A lot of times you'll have dysfunction in various other blood cells as well, so you can have a lot of signs of bleeding because of a decrease in your platelets. So it might be mild like little purple spots on your skin called petechiae or can be very severe and have massive gastrointestinal bleeding or pulmonary hemorrhage, so bleeding into your lungs that can be fatal. In fact if you do see that pulmonary hemorrhage, it's an up to 50% mortality rate at that point. So this is something that can progress to a very, very severe illness.

Erin Welsh

Okay, question.

Erin Allmann Updyke

Give it to me.

Erin Welsh

How is it causing all of these different symptoms?

Erin Allmann Updyke

Great question. We'll get there.

Erin Welsh

Okay. My other question then is about who has these symptoms?

Erin Allmann Updyke

Yeah.

Erin Welsh

Are there characteristics that determine or play or seem to play a role in whether someone has an asymptomatic or a mild or a moderate or a severe case of this?

Erin Allmann Updyke

Yeah, that's another great question. The older people are, the more likely that they are to progress to severe disease. I didn't see a ton of data on if the same is true in people who are very young. But I'll talk more in just a little bit about how much specific host factors likely play a role in the severity of infection. And we truly don't know what those specific host factors are at this point.

Erin Welsh

And do the different serovars and species play a role too?

Erin Allmann Updyke

Potentially yes. But again, we don't have great, great data on this serovar. There's a couple of serovars, Icterohaemorrhagiae, I think that's it, is one that is known to be of very important human significance because it can cause pretty severe infection. But there's so many serovars and we just don't have a ton of data. So we'll get into a little bit more detail on how it's causing these specific findings. When it comes to the pulmonary hemorrhage, it really is that this bacteria ends up causing damage directly in your lungs that then causes that bleeding to the point where you essentially can drown in your own blood.

Erin Welsh

How is it causing that damage?

Erin Allmann Updyke

So it's damaging the endothelial cells, it's damaging the lining of our blood vessels, it's reducing our platelets so it's not allowing for our blood to clot, etc.

Erin Welsh

Okay. Gotcha.

Erin Allmann Updyke

Yeah. So that's the liver and the lungs and blood and blood vessels. But one of the other main target organs of leptospirosis of course is the kidneys. And so when this progresses to severe disease it often results in what's called Weil's disease which essentially can cause progressive kidney damage to the point of kidney failure. Kidney failure of course can be extremely fatal unless you have access to dialysis. And access to dialysis can drastically reduce the mortality rate in the case of severe kidney failure when it comes to leptospirosis. So it's a lot, it really can affect all of our organs. It can infect the heart and cause cardiac involvement, it can cause myocarditis, it can cause an aseptic meningitis, so it can get into the CSF or at least cause enough inflammation in our brain and spinal cord. That headache that presented at the beginning can become incredibly severe. But overall a lot of these symptoms can be really difficult to distinguish from viral hemorrhagic fevers like dengue fever for example, or from things like scrub typhus which we technically haven't covered yet.

Erin Welsh

Right. No, we have not. But I remember. It comes up again.

Erin Allmann Updyke

Oh good. Symptoms can last a pretty varied amount of time. When they get severe, they can persist for potentially weeks and even in the case when symptoms are not that severe, there is some suggestion of post-leptospirosis type syndrome with things like fatigue, persistent headache, myalgia that can potentially last for months.

Erin Welsh

If you get leptospirosis and recover, do you have immunity towards it in the future? And is there a cross-protection with different serovars or different species?

Erin Allmann Updyke

What a great question, Erin. That is such an important question because basically if you circle on that question long enough, you ask can we make a vaccine? Do we have a vaccine? Etc.

Erin Welsh

Right, yeah.

Erin Allmann Updyke

You get at least some immunity. How much cross-protection there is on different serovars, unclear. How long that immunity might last, again unclear. There is some data that suggests that waning immunity over time in people who maybe lived in an endemic area and were exposed as young people and then get exposed again as they're older, are susceptible again. So it doesn't seem to be something where you're immune for the rest of your life forever. We do mount immunity to it in a way that offers at least some protection against severe infection.

Erin Welsh

Okay.

Erin Allmann Updyke

But obviously this is a huge range in disease severity. And you kind of already asked the question of what is the underlying pathology of this? Why do some people get so sick, other people don't get so sick? And it boils down to three major things which we've already touched on but I'll go in a little bit more detail. One is those virulence factors of the particular *Leptospira* species or serovar that you get exposed to. So some that are more or less host specific might cause disease in certain animals and not in others. And some with particular virulence factors on them might be more or less virulent than others. The second factor is the inoculum, so how much pee-contaminated water did you guzzle down or how many spirochaetes did you end up with initially?

Erin Welsh

Right.

Erin Allmann Updyke

And the third is my favorite, the most difficult, the host factors. It's a very nebulous category. In the case of leptospirosis what it seems to boil down to is our cytokine-related immune response. So cytokines are proinflammatory agents, right, these are proteins and stuff in our body that we make and secrete in response to an infection in order to get the rest of our immune system on high alert to go look for and eliminate this problematic spirochaete. But as we've talked about time and again on this podcast, if our body goes on too high of an alert, if we get too intense about this inflammation, then we can end up with tissue damage that's not even directly due to the pathogen but due to these inflammatory cytokines and all of the other immune response that they stir up. So while we don't know a lot of the details on this, we think that that's a huge part of the pathogenesis especially of severe leptospirosis is this intense inflammatory and cytokine response that is generated. And that's what's causing a lot of these severe manifestations, that's what's causing the damage to our lungs, that's what's causing the damage to our liver, that's what's destroying our red blood cells and our platelets and causing us to bleed to death.

Erin Welsh

Okay, interesting.

Erin Allmann Updyke

Yeah.

Erin Welsh

Seems like there's a lot more work to be done in that field.

Erin Allmann Updyke

Absolutely. We don't have enough data just yet to say for sure what specific cytokines are being upregulated or causing the most damage when it comes to this very severe vs not so very severe infection. But I will link to a couple of papers that have more detail on what we do know about particular cytokines.

Erin Welsh

Question about diagnosis.

Erin Allmann Updyke

Oh great!

Erin Welsh

So like you mentioned, this disease can be confused with many other diseases, it has kind of these nonspecific symptoms. And what would make someone suspect leptospirosis, number one? And number two, you said it's difficult to test for because it doesn't show up very well on gram stains. How do you then test for it? What are the samples you would take?

Erin Allmann Updyke

Beautiful questions, Erin. So how you would suspect it would be of course if someone is having these symptoms that I described, like these laboratory abnormalities that we see, jaundice, signs of kidney failure. But also if they have a history of something that would make us think they've had an exposure to potentially contaminated environmental sources. If they've been white water rafting, if they've been jumping off of cliffs into freshwater sources, or if they work in a field like a rice paddy or something like that. So occupational exposures or recreational exposures, that might make us think maybe this is leptospirosis. It might be higher on your list to think about in areas where leptospirosis is more common and less likely that you'll think about it in places where it's less common but it's important that it exists everywhere. So probably overlooked in some places. How you diagnose it can be really tricky. So it's hard to diagnose on culture alone but that is the gold standard, it is possible to do, it's just more tricky. So there's PCR tests that you can use but those of course aren't accessible everywhere across the globe because they're difficult and expensive. So it's mostly based on serologic testing, so looking for antigens or looking for antibodies against leptospirosis.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. And there is treatment which is the best news. A number of different antibiotics work but especially in severe cases it's also really important to have access to supportive care, like potentially emergent dialysis if someone progresses all the way to kidney failure and things like that.

Erin Welsh

In terms of antibiotics, you said that the first stage was this extreme replication in the bloodstream, just tons and tons of bacteria. And then that's asymptomatic.

Erin Allmann Updyke

Yeah.

Erin Welsh

And then when they move into the organs is when people would tend to probably go seek treatment. Does the massive die-off of bacteria at that point hurt anything about you and your organs?

Erin Allmann Updyke

What a good question. That's like a thing that can happen with a lot of other spirochaete diseases. Not that I read.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah but that's a really interesting question, especially for spirochaetes.

Erin Welsh

Okay.

Erin Allmann Updyke

Because they are still replicating the whole time, they don't just stop replicating once they make it into our organs.

Erin Welsh

Okay, of course.

Erin Allmann Updyke

They just keep on going.

Erin Welsh

Yep, chugging away.

Erin Allmann Updyke

Keep on trucking on. So that's kind of the disease in humans. Because this is a pathogen like I said that can infect essentially any mammal, it does cause slightly different disease in different animal species. But the spectrum, especially in things like dogs can tend to be pretty similar. So there can be asymptomatic infection and then there can be this severe disease that often still has fevers, jaundice, nausea, vomiting, liver failure, kidney failure. So it's very interesting to me how it tends to affect a lot of the same organs and then a lot of what you see might be very similar.

Erin Welsh

Yeah.

Erin Allmann Updyke

That's leptospirosis.

Erin Welsh

Alrighty.

Erin Allmann Updyke

So tell me Erin, where did this thing come from? How did we figure it out?

Erin Welsh

Yeah, I will do my best right after this break.

TPWKY

(transition theme)

Erin Welsh

I found it really interesting to read about the history of leptospirosis because I feel like although this is not the flashiest of diseases that we've covered, it hasn't caused these widespread epidemics and left destruction in its wake like something like smallpox or plague for instance.

Erin Allmann Updyke

Right, right.

Erin Welsh

But the story of leptospirosis is a classic tale of observation and discovery. It really sort of highlights the golden age of germ theory. And I think that what surprised me most about the history of leptospirosis was not how we learned about the transmission cycle or the causative agent of leptospirosis but how much things haven't really changed. But I guess I'm getting ahead of things, so let's start at the beginning.

Erin Allmann Updyke

Okay.

Erin Welsh

Leptospirosis has existed for millennia and it seems to have been globally distributed for quite some time. So that's about as precise an answer as you're going to get for where did this thing come from? That's about as precise as I could find.

Erin Allmann Updyke

Okay then.

Erin Welsh

Yeah. And part of that is because of how many different *Leptospira* species and serovars there are that can cause infection in humans and other animals. And so it's hard to say when *Leptospira* emerged or when it evolved and where it evolved.

Erin Allmann Updyke

Okay.

Erin Welsh

And it's also hard to say when humans were first exposed and which particular species or serovars were responsible because those are also things that would have likely varied geographically and maybe those serovars aren't even around anymore. And in the scientific literature discussing the history of leptospirosis, generally speaking researchers refer more to the disease leptospirosis rather than a particular pathogen.

Erin Allmann Updyke

Yeah, I found that really interesting.

Erin Welsh

I found that interesting too. And I think that just speaks to the importance... Well, I think it speaks to two things really. One is the importance of the group of pathogenic species rather than any one individually at least historically.

Erin Allmann Updyke

Yeah.

Erin Welsh

And I think the other thing is that maybe it just kind of speaks to the fact that we don't maybe know that much about the different serovars and their impacts. I don't know.

Erin Allmann Updyke

Yeah and they're just so hard to culture, I think they're a difficult bug to work with.

Erin Welsh: It seems like it, yeah. And that's of course not to say that the differences among *Leptospira* species or serovars isn't important medically or in terms of public health. Of course like I'm always saying on the podcast, tracing the evolutionary relationships among these bacteria can greatly help in understanding things like transmission routes or reservoir species or disease-causing abilities. Information that like you talked about Erin for some or even many leptospirosis species isn't that well known.

Erin Allmann Updyke: Yeah.

Erin Welsh: In general the pathogenic *Leptospira* are thought to have evolved from non pathogenic species that just live in the environment which some *Leptospira* species still do.

Erin Allmann Updyke: They sure do.

Erin Welsh: And historically that's how this group of bacteria was divided, along lines of is it pathogenic or is it not pathogenic? And that is in the classification, I think that division is still really important in terms of public health and medicine but I'm talking about classification systems.

Erin Allmann Updyke: Right.

Erin Welsh: But more recently that division into those two groups turned into three groups, essentially saprophytic meaning living on decaying material and nonpathogenic, intermediate in terms of pathogenicity, and pathogenic. And some researchers are now arguing that this isn't the best way to classify *Leptospira* because it just takes into account one characteristic of these bacteria rather than looking at, I don't know, their entire genomes for instance.

Erin Allmann Updyke: Right. Yeah.

Erin Welsh: But as far as I can tell that's still under discussion and probably won't be resolved-

Erin Allmann Updyke: By the time this episode comes out?

Erin Welsh: Yeah, certainly not.

Erin Allmann Updyke: Yeah. It was really interesting how much it seemed to still be in flux.

Erin Welsh: Yeah.

Erin Allmann Updyke: The whole classification of *Leptospira*.

Erin Welsh: Absolutely. And not just the classification but just learning more about the ecology and which species are playing a role, there are new serovars that are constantly being discovered, which species can cause disease, that's still kind of being learned. No, that one is just an environmental bacteria. Oh wait a second actually...

Erin Allmann Updyke: Oops, actually...

Erin Welsh: Yeah. The bottom line of all of this seems to be that *Leptospira* is diverse, many different species and serovars can cause disease, and there are so many research opportunities for understanding more about these pathogens from a public health perspective. So if anyone needs a Masters or PhD you project, go for it.

Erin Allmann Updyke

Yeah, do it. I love it. We support you.

Erin Welsh

But that's just the bottom line for the ecology evolution of these bacteria. What about the human history part of it?

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

Given how widespread *Leptospira* are and how many of them can cause disease in humans and other animals, it's likely of course that leptospirosis has affected humans for millennia. As long as humans have been humans. Although there's an asterisk there, I didn't read anything specifically about the historical distributions of these pathogens, I'm not sure if it's known. But one paper I read suggested that an epidemic that occurred around 1616-1619 in the area that's now eastern Massachusetts could have been leptospirosis. It hit the Native American populations living in the area particularly hard with the death toll estimated to be as low as 1/3 of the local population to as high as 90%.

Erin Allmann Updyke

Whoa.

Erin Welsh

And since the Europeans living in the area weren't as badly affected, some researchers have suggested that rats on the ships introduced leptospirosis to the region.

Erin Allmann Updyke

Got it.

Erin Welsh

But also there's a huge laundry list of other diseases that it could have been.

Erin Allmann Updyke

Right.

Erin Welsh

And we may never know what it actually was. So leptospirosis is one of the suggested options. As with many other diseases that we've covered on the podcast, changing patterns in human settlement or any other practices that would have increased contact with rodents, especially rats, sorry rats, would have made catching the disease more likely. And if you look through historical medical literature, there are many, many mentions of things that could be leptospirosis or have retrospectively been decided to be leptospirosis. Like you said Erin, jaundice is of course one of the primary symptoms of leptospirosis and references to jaundice go back thousands of years. Whether or not that jaundice was caused as a result of leptospirosis is anyone's guess.

Erin Allmann Updyke

Yeah. There's so many things that can damage your liver.

Erin Welsh

So many things. There is this passage though in the Hippocratic texts that some people believe maybe about leptospirosis. Quote: "When jaundice supervenes in fevers before the seventh day, it is a bad symptom unless there be watery discharges from the bowels."

Erin Allmann Updyke

Interesting.

Erin Welsh

Yeah. I don't know. I mean I'm sure that leptospirosis was around.

Erin Allmann Updyke

Yeah. How interesting.

Erin Welsh
Yeah. And medical texts from Ancient China discussed diseases referred to as rice field jaundice or rice harvest jaundice. And the descriptions of those diseases seem very similar to leptospirosis. And also old Japanese medical texts describe lepto-like diseases called autumn fever or seven day fever. In Europe and Australia there were diseases known as cane-cutter's disease or swineherd's disease, and Schlammeieber, mud fever.

Erin Allmann Updyke
Oh okay.

Erin Welsh
I doubt I pronounced that remotely correctly. And all of these terms were used before anyone figured out what caused these diseases or whether they were even related.

Erin Allmann Updyke
Right.

Erin Welsh
We should have some sort of jingle for when I mention Napoleon's name.

Erin Allmann Updyke
Yeah!

Erin Welsh
Because here he is again.

Erin Allmann Updyke
Oh, I can't wait. Doo-doo-doo-doo-doo! Here he comes on his horse!

Erin Welsh
Napoleon. There we go. Oh Napoleon. His infamous troops in Cairo, Egypt during the early 1800s may have experienced an outbreak of leptospirosis which they called jaundice fever. Also I have to shout out our chlamydia episode where I talked about trachoma and Napoleon's troops in Egypt and I just at this point need to make a list of diseases that these poor troops were subjected to during their time under Napoleon.

Erin Allmann Updyke
I would love that.

Erin Welsh
We should have just done a series on diseases of Napoleon.

Erin Allmann Updyke
Yeah, where all we do is list them because it would take two hours.

Erin Welsh
But even before germ theory was a thing, what would be later known as leptospirosis had recognizable patterns. And you can tell that from some of these early nicknames. So one was that it was commonly associated with certain occupations and that these occupations and hence the occurrence of this disease were often associated with wet marshy areas, they were kind of geographically restricted.

Erin Allmann Updyke
Right.

Erin Welsh
And this tight link especially between certain areas or certain times of year and this disease made it like a shoo-in for miasma theory which was this pre-germ theory idea that proposed that diseases and disease outbreaks for the result of bad air. And it's easy to see how that would have been a reasonable explanation for leptospirosis because it did occur in certain areas and it did occur in certain professions and it didn't really occur in large epidemics the way something like influenza or smallpox did. And importantly avoiding those areas or removing the source of the bad air, like draining water around mines, it decreased the incidence of the disease. So even before people knew that cane-cutter's disease or swineherd's disease or rice harvest disease were the same things, people were able to limit their exposure to it.

Erin Allmann Updyke

That's amazing.

Erin Welsh

So interesting, yeah.

Erin Allmann Updyke

Yeah. I love it when those kinds of things happen in these episodes, Erin.

Erin Welsh

Me too. But leptospirosis wasn't alone in causing jaundice and a fever and occurring in certain marshy environments. There's also yellow fever, infectious hepatitis, louse-borne relapsing fever. And it wasn't until the late 1880s that leptospirosis or at least one manifestation of it was officially distinguished from the rest of these possible causes of infectious jaundice. In 1886 a German physician named Adolf Weil described a disease that involved jaundice alongside splenomegaly, renal dysfunction, conjunctivitis, and skin rashes. He called it infectious jaundice. His characterization of this disease stuck but the name obviously did not. A couple of years after his paper was published another researcher named it Weil's disease. And like happens so often, giving this disease a name, giving it a description increased awareness of it substantially.

And soon papers were being published describing outbreaks of the disease in coal miners or sugar cane cutters, association with rainfall or swimming in certain areas. But even though people were able to recognize patterns in where and when this disease occurred and in whom, without a causative agent identified those were just patterns without a mechanistic explanation. And you were also a little bit limited in your ability to do anything. For that satisfying understanding of how all the pieces eventually fit together and whether the cases of Weil's disease in England were caused by the same pathogen as those in Japan for instance, we needed a causative agent. And to get that we have to wait almost 30 years after the clinical description of Weil's disease.

Erin Allmann Updyke

Wow!

Erin Welsh

Yeah. So 1886 was Weil's disease. And 1915 I believe was when leptospirosis was identified, was when *Leptospira* identified.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

Yeah. So why was there so long a wait? And none of the papers I read really went into that great detail about why but I think it could have been many different things. So even though this period, the last decades of the 1800s and the first few decades of the 1900s was this golden age of germ theory and pathogen discovery, that doesn't mean that all diseases received equal attention.

Erin Allmann Updyke

Right.

Erin Welsh

I mean if you think about it again, leptospirosis is not a big name marquee disease which isn't to say it doesn't deserve that attention but at the time there were things like plague or syphilis or tuberculosis that people were trying desperately to figure out because of the death toll, because of the number of people that were infected with those diseases. Leptospirosis definitely attracted interest but it maybe didn't get the focused attention that some of these flashier diseases did. But one thing was working in lepto's favor which is that spirochaetes, the kind of spiral-shaped bacterium that causes lepto, these had already been discovered and recognized to cause disease, the most important of which at the time was syphilis. And so people had spirochaetes on their radar and they should have maybe been able to pluck these little guys out as the cause of leptospirosis. Except for this quirk that you mentioned. Spirochaetes don't stain well so they're really difficult to isolate, they can be difficult to culture, and what the eventual discoverers of Leptospira noticed was that - well they blamed it on this anyway - is that after this huge influx of bacteria in the bloodstream, those levels drop. And they were like if you don't catch it then then it's going to be really difficult to isolate leptospire.

Erin Allmann Updyke

That's not unlike malaria or something.

Erin Welsh

Exactly.

Erin Allmann Updyke

Where you have a lot of difference in even just times of day on when you have a high enough burden in the bloodstream to be able to pick it up.

Erin Welsh

Exactly, yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

And I think that's what they said. They were like yeah, we didn't see it in the bloodstream. And so if you test a blood sample of someone who is super duper sick, especially considering the microbiology technology that was around in the 1910s.

Erin Allmann Updyke

Right. And I want to say because like I mentioned how something like E. coli might be at low numbers, you can grow those other bacteria out in culture from blood. So even if you only have a tiny bit of it, you can grow it to be more. But that's really difficult to do with Leptospira. So if you can't see it right away, it's a lot harder.

Erin Welsh

Yep. Yeah, that's a really important point too.

Erin Allmann Updyke

Yeah.

Erin Welsh

So how did people eventually discover what was causing Weil's disease? Seems super difficult.

Erin Allmann Updyke

Yeah.

Erin Welsh

They went looking for it specifically, it wasn't just one of those serendipitous discoveries. A couple of researchers in Japan named Ryukichi Inada and Yutaka Ito had an interest in Weil's disease for years. And an outbreak of the disease among coal miners around 1914-1915 led them to run some experiments to see if they could isolate a pathogen from an infected person. And I also want to point out that their interest was not purely scientific, not like oh here's this curious little disease, let's see if we can find a new pathogen. At the time mortality rates of Weil's disease at their clinic averaged 32%.

Erin Allmann Updyke

Oh my.

Erin Welsh

Which is incredibly high.

Erin Allmann Updyke

That's really terrifyingly high.

Erin Welsh

Exactly. And so they wanted to do whatever they could to try to control the outbreaks by finding the source. They looked for bacteria in blood, urine, feces, you name it, in people who had Weil's disease. And when they didn't find anything, they took some blood from these infected individuals and injected it into monkeys, rabbits, rats, guinea pigs. And the guinea pig turned out to be the unlucky or lucky one, depending on your perspective. It developed many of the symptoms that were characteristic of Weil's disease and when they dissected the animal's liver, they found it to be teeming with spirochaetes which they named *Spirocheta icterohaemorrhagiae*.

Erin Allmann Updyke

Yep, okay.

Erin Welsh

Yep. Later of course *Leptospira*. Almost immediately after they published their findings in 1915, researchers in Germany also isolated leptospirosis from infected individuals. But the real first placed finisher, even though he didn't know it, may have been A. M. Stimson who observed spirochaetes in the blood of someone that had been diagnosed with yellow fever. He figured that what he saw, these little squiggly bacteria that looked like question marks, hence the name he gave them, *Spirocheta interrogans*, was causing yellow fever. For a long time people were like it must be a spirochaete that's causing yellow fever. It wasn't as we know but in retrospect he did end up being the first to describe a bacterium that later researchers would link to leptospirosis.

Erin Allmann Updyke

Interesting.

Erin Welsh

The similarity in symptoms between leptospirosis and yellow fever and not to mention their association with wet marshy areas also made diagnosis sometimes confusing and that could have potentially contributed to the delay in identifying both the causative agent of Weil's disease and the yellow fever virus. Anyway, soon after Inada and Ito and colleagues identified the causative agent of Weil's disease, they next set their sights on uncovering everything they possibly could about this pathogen. And they did a hugely impressive job. From culturing it in the lab to characterizing the timeline of infection, early vaccination studies to understanding the transmission route of the pathogen.

What they did was set a really strong foundation for understanding the disease and for growing future research, especially research that was focused on prevention. Because as we know, if you want to stop a disease from spreading you at the very minimum have to know how it spreads in the first place. Which for leptospirosis by the time of the causative agent's discovery was still under debate. They knew it was in wet marshy areas and associated with water so could it be mosquito-borne like yellow fever? Several people seemed to think so and it was a reasonable explanation given the geographic and climate variables associated with outbreaks. And some researchers even successfully carried out experiments with mosquitoes transmitting leptospirosis to lab animals. But it was likely that the mosquitoes were acting as mechanical vectors, just depositing infected blood clinging to the mouthparts into the animal.

Erin Allmann Updyke

Yeah.

Erin Welsh Weil himself thought it was something that you ingested while others thought vertebrate animals played a large role. Inada and Ito and colleagues demonstrated that the leptospire could be transmitted through the healthy unbroken skin of a guinea pig.

Erin Allmann Updyke Yeah.

Erin Welsh Though broken skin was more reliable. I had no idea it could be through unbroken skin.

Erin Allmann Updyke It can be, yeah. Usually it's broken skin but especially if you're exposed for a long period of time and especially with wet skin, wet skin really increases permeability essentially. So then yeah, it can be unbroken skin.

Erin Welsh Wow, okay.

Erin Allmann Updyke Sorry.

Erin Welsh Yeah. Well they also showed that it could cause infection through ingesting it.

Erin Allmann Updyke Yeah.

Erin Welsh But where did it come from? They got the idea to look at rodent kidneys and urine after a different team of researchers observed spirochaetes in the kidneys of field mice while working on scrub typhus.

Erin Allmann Updyke Oh cool.

Erin Welsh Yeah. And so they were like, you know what? All right fine, gather all of the rodents that we possibly can, house and wild rats, and then look in their kidneys. And boom, they found a bunch of their spirochaetes, Spirocheta at the time, icterohaemorrhagiae, and they noticed that the leptospire seemed restricted to the kidneys and that the rats seemed in excellent health.

Erin Allmann Updyke Until they took out their kidneys.

Erin Welsh Prior to their dissection. And that pointed towards their role as reservoirs. And this didn't actually surprise too many people, possibly because A) rats have been maligned for centuries, but also during trench warfare in WWI, cases of Weil's disease shot up particularly in areas with high rat populations.

Erin Allmann Updyke Okay, yeah. So they were like I suspected it!

Erin Welsh Oh yeah, of course it's the rat. Which is sad for rats. Rats are great by the way. Anyway, all of this clinical and epidemiological and ecological knowledge about leptospirosis, which is a lot, I mean that happened in a very short time span, just a few years.

Erin Allmann Updyke Yeah.

Erin Welsh

And that's pretty remarkable. And even though antibiotics weren't yet available to help treat the infection, understanding the transmission cycle was enough to enact control measures in some places. And throughout the following decades into the mid 20th century and beyond, people continued to find out more about this group of pathogens, like how long it can survive in water and under what conditions, what pH is best, what temperature, which animals play a role in the transmission of the disease in certain areas, how disease progression or severity could be tied to certain species or serovars, and also linking all of these previously separate diseases or separate named diseases into one big picture name, leptospirosis.

Erin Allmann Updyke

Yeah.

Erin Welsh

And another big development was understanding that other animals may not just be asymptomatic carriers or reservoirs but that many of them suffered severe infection from these bacteria as well, like domestic cattle, pigs, and dogs. The early history of leptospirosis may not be as flashy as some of the diseases or topics that we've covered on this podcast and there don't really seem to be at least that I could find any major fireworks discoveries during the rest of the 20th century. But that doesn't mean at all that this disease is not hugely important because despite how much we've learned about this group of pathogens and despite having effective treatment and knowledge of prevention, it's still a huge problem globally, as you're about to talk about Erin, and since it has such close ties to things like weather and temperature, we can expect to see big shifts as a result of climate change and land use change. So Erin, can you tell me where we stand with these pathogens of one health importance today?

Erin Allmann Updyke

I would love to. Let's take a quick break and I'll get into it.

TPWKY

(transition theme)

Erin Allmann Updyke

Erin, I know that you know and have very recently felt just how difficult it is to get numbers on some of these topics that we cover. And I'm always still somehow shocked at just how difficult it can be and that was the case for leptospirosis. Very, very hard to get an estimate of what the true burden of disease is as well as looking at the distribution of that burden because of course it's not equal across the globe. So this is a pathogen that is worldwide, everywhere except the arctic where everything is frozen. But it is most common in the tropics and it's very common both in rural areas associated with things like agricultural or mining exposure like you talked a lot about. But also in urban, especially poor urban areas where you have lack of access to sanitation and potentially high rat burdens. But to look at actual numbers, if you look at the World Health Organization website you won't really find any numbers because they don't have any fact sheets on leptospirosis. All of their information is from 2003.

Erin Welsh

That's almost 20 years ago.

Erin Allmann Updyke

Yeah. And now there's not a page. The links to World Health Organization lepto, it goes to Page 404 Not Found.

Erin Welsh

Interesting.

Erin Allmann Updyke

I know. I was shooketh, as they say. PAHO which is the Pan American Health Organization, so for the Americas, has some information. The CDC has a page on it. There are probably a lot of other country-specific public health agencies that have data but it's hard to go through every single country. So there are two numbers that I found which are wildly different as to global estimates of leptospirosis. Some papers and the PAHO website estimate about 300-500,000 cases of leptospirosis globally every year.

Erin Welsh: Which is a huge number.

Erin Allmann Updyke: Yeah. Well a paper from 2015 that was trying to estimate the global prevalence as well as mortality from leptospirosis, granted this is from 2015 so it's a little bit outdated, but they estimated a million cases annually and just under 60,000 deaths every year.

Erin Welsh: That's a lot.

Erin Allmann Updyke: It's a lot. And this was really just an estimate of severe cases, cases that are bad enough that people are getting very sick and ending up in the hospital. And again a lot of times this can be asymptomatic. So how many cases are there? Potentially even more.

Erin Welsh: Yeah. Wow.

Erin Allmann Updyke: Yeah. And there is a lot of data to suggest that the overall burden of leptospirosis is likely going to continue to rise because of shifts in things like climate change that might worsen storms and flooding events which are really high risk for leptospirosis outbreaks.

Erin Welsh: Yep.

Erin Allmann Updyke: As well as like you said land use changes that might increase urbanization in a way that also puts people at increased exposure to rats and contaminated water sources, etc. So it's not good news looking forward, especially with how little data we have to begin with.

Erin Welsh: I think I'm still surprised at this.

Erin Allmann Updyke: Same. I was actually shocked because a lot of papers say this is on the scale of things like schistosomiasis, of things like leishmaniasis, of things like cholera. And I feel like we don't think of it in that way. I think a lot of people think of leptospirosis as a disease of animals.

Erin Welsh: Or as recreational exposure.

Erin Allmann Updyke: Yeah, exactly. Which it is, that's totally true.

Erin Welsh: Sure, absolutely.

Erin Allmann Updyke: But it's also just a global serious disease. When it comes to animal infections by the way, it's even harder to get a sense of what the magnitude of the problem is worldwide, as you can imagine.

Erin Welsh: Yeah.

Erin Allmann Updyke: There are a lot of really interesting papers that look at the overall diversity of animal species that have been shown to be infected. I mean it really just boils down to all of them. If you try it, they will infect. But it's really hard to get a handle on what percentage of domestic dogs would test positive or how many cattle every year are getting sick from this, how much milk production is lost because cattle gets sick? We just don't have that kind of information. I did find one paper that was looking in the United States at hotspots of leptospirosis within the US and one thing that stuck out to me from that paper is that at least from data from the early 2000s, it did seem like seroprevalence in dogs was increasing. Which is not great.

Erin Welsh: Why is it increasing?

Erin Allmann Updyke: I have no idea.

Erin Welsh: And there's a vaccine available for dogs as well.

Erin Allmann Updyke: Great question. Yes, there's a vaccine. There's a vaccine for humans too and for animals including dogs. Most of the vaccines, as far as I can tell all of the vaccines that are currently available are whole killed spirochaetes of some of the more common serovars depending on what area you're in.

Erin Welsh: Okay.

Erin Allmann Updyke: So you asked very early on Erin, how much cross-protection do you get? What kind of an immune response are we talking about? And because the vaccines that exist are just for particular serovars, they're not universal. So they don't cover every given Leptospira serovar.

Erin Welsh: Seems like a great candidate for an mRNA vaccine.

Erin Allmann Updyke: Yeah. There's a lot of research mostly on recombinant vaccines actually. But an mRNA one could be interesting.

Erin Welsh: Okay.

Erin Allmann Updyke: But recombinant vaccines would allow you to put a whole bunch of different antigens essentially, antigen components on one little vaccine and then give that so you could get immunity to a whole bunch of different serovars.

Erin Welsh: And who gets vaccinated against leptospirosis?

Erin Allmann Updyke: Such a great question. I had a really hard time figuring that out. In the US definitely dogs, like my puddle licker is vaccinated. So domestic animals, livestock can get vaccinated. In terms of humans I think it's relatively uncommon except perhaps during outbreaks or maybe in occupational settings in particularly high risk environments it might be that people are vaccinated. But in general I didn't even know that there was a human vaccine, I don't think it's very common. Yeah. But that is what I know about the status of leptospirosis worldwide.

Erin Welsh: It's such an interesting... I truly cannot believe how overlooked this is. I can't get over it.

Erin Allmann Updyke: I really felt similarly about this. Yeah. I want there to be so much more information.

Erin Welsh: Yeah.

Erin Allmann Updyke: Yeah. Well, sources?

Erin Welsh: Sources.

Erin Allmann Updyke: Okay.

Erin Welsh

I have several, I'm going to shout out two in particular. One is a 2015 book called 'Leptospira and Leptospirosis' which the editor of that book is Ben Adler. Then there was a paper from 2001 by Kobayashi and that is titled 'Discovery of the Causative Organism of Weil's Disease: Historical View.'

Erin Allmann Updyke

I had a lot of different papers. A couple of actually book chapters that I wanted to shout out, two different chapters, one on leptospirosis in humans and one on animal leptospirosis both from the book 'Leptospira and Leptospirosis' from 2015, so those were great chapters. And then I had a lot on the genetic diversity and serovar diversity of Leptospira and at least some data on the epidemiology. So you can read for yourself. We post all of our sources from this episode and all of our episodes on our website thispodcastwillkillyou.com.

Erin Welsh

We sure do. Thank you so much again to Ummat for sharing your story again.

Erin Allmann Updyke

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

Erin Welsh

Thank you to the Exactly Right network.

Erin Allmann Updyke

And thank you to you, listeners. We liked doing this episode. I hope that you really enjoyed it. Thanks for listening.

Erin Welsh

Yeah. And a special thank you as always to our wonderful, generous patrons. We appreciate you so very much.

Erin Allmann Updyke

So much.

Erin Welsh

Okay well, until next time, wash your hands.

Erin Allmann Updyke

You filthy animals!