

TPWKY

This is Exactly Right.

Erin Welsh

"July 29, 1847. The mate continued to grow worse and the mistress was unceasing in her attention to him. The day was exceedingly hot and sultry and I could not have remained on deck but the captain spread an awning over it which kept the cabin cool. We lay at some distance from the island, the distant view of which was exceedingly beautiful. At the far end were rows of white tents and marquees resembling the encampment of an army. Somewhat nearer was the little fort and residents of the superintendent physician and nearer still the chapel, seamen's hospital, and little village with its wharf and a few sailboats. The most adjacent extremity being rugged rocks among which grew beautiful fir trees. At high water this portion was detached from the main island and formed a most picturesque islet.

But this scene of natural beauty was sadly deformed by the dismal display of human suffering that it presented: helpless creatures being carried by sailors over the rocks on their way to the hospital, boats arriving with patients some of whom died in their transmission from their ships. Another and still more awful sight was a continuous line of boats, each carrying its freight of dead to the burial ground and forming an endless funeral procession. Some had several corpses so tied up and canvassed that the stiff, sharp outline of death was easily traceable. Others had rude coffins constructed by the sailors from the boards of their berths or should I say cribs. In a few a solitary mourner attended the remains but the majority contained no living beings save the rowers. I could not remove my eyes until boat after boat was hid by the projecting point of the island round which they steered their gloomy way. From one ship a boat proceeded four times during the day, each time laden with a cargo of dead. I ventured to count the number of boats that passed but had to give up the sickening task."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

Yeah. So that is from a diary that somebody published called 'Famine Ship Diary: The Journey of a Coffin Ship' and it's written by someone named Robert Whyte but that's a pseudonym. And it tells the story of Grosse Isle which is a place in Canada where a lot of ships sailed to from Ireland during the famine and typhus was absolutely out of control in Ireland, on the ships, and it's estimated that more than 20,000 people died from 1847-1848 on these so-called coffin ships.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

And also in Canada when they landed. And a lot of people who died were mostly people coming from Ireland but also the doctors and the priests and clergymen and so on who attended them. So yeah, it's really heartbreaking.

Erin Allmann Updyke

Wow. God that's awful, Erin.

Erin Welsh

Yeah. Hi, I'm Erin Welsh.

Erin Allmann Updyke

And I'm Erin Allmann Updyke.

Erin Welsh

And this is This Podcast Will Kill You.

Erin Allmann Updyke

Welcome, we're starting strong clearly to our fifth season.

Erin Welsh: Yeah, this is Episode 86 which marks the beginning of our fifth season. Feels like it was just yesterday that we recorded alcohol.

Erin Allmann Updyke: Was it? Kind of was.

Erin Welsh: Kind of was. But we're excited to be back and we're excited to do this episode, this topic.

Erin Allmann Updyke: Yeah.

Erin Welsh: I mean this is a big one, it almost rightly belongs in our first season.

Erin Allmann Updyke: Mm-hmm. I think it was a strong first season contender and it's just taken us four extra seasons to get here.

Erin Welsh: It's gonna be a very interesting episode I think.

Erin Allmann Updyke: I think so too.

Erin Welsh: I gained a new appreciation for lice.

Erin Allmann Updyke: I can't wait to talk about lice in more detail than people want.

Erin Welsh: I know! Lice are so fascinating.

Erin Allmann Updyke: They're so interesting.

Erin Welsh: I think this just goes to show that we got our PhDs in the right fields.

Erin Allmann Updyke: Uh-huh. I was thinking the same thing.

Erin Welsh: We are true vector-borne disease ecologists at heart I think.

Erin Allmann Updyke: We really are, yeah.

Erin Welsh: Okay, so Erin.

Erin Allmann Updyke: Yes?

Erin Welsh: What time is it?

Erin Allmann Updyke: It is quarantini time!

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

Erin Allmann Updyke: This week we're drinking The Soused Louse.

Erin Welsh: The Soused Louse. I love it. And in The Soused Louse is basically it's like a bourbon eggnog, or you can do rum if you want, I'm gonna do bourbon.

Erin Allmann Updyke: Yeah.

Erin Welsh: And I've never made eggnog before in my life, like I've only ever just gotten it from the store. But I made it for the first time and it is really delicious.

Erin Allmann Updyke: I've never had eggnog that I've enjoyed so I would like to try your eggnog, please.

Erin Welsh: (laughs) Okay. But yeah, part of the reason that I wanted to do an eggnog for this is because Herald Cox I think his name was a researcher at Rocky Mountain Labs in Hamilton, Montana which we talked about in our Rocky Mountain spotted fever episode. And he developed a typhus vaccine in egg yolks and so I thought you know what, let's do an eggnog. And also this episode's supposed to come out December, so perfect.

Erin Allmann Updyke: Feels like a good seasonal bev. So we'll post the full recipe for that quarantini as well as the nonalcoholic version, our placeborita, on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) and all of our social media channels.

Erin Welsh: We will. And I just wanna add that don't feel compelled to homemade eggnog. There are tons of options out there at the store and there are tons of non dairy options and vegan options as well. So take your pick, really. It works with it all.

Erin Allmann Updyke: Everyone can enjoy an egg-ish nog.

Erin Welsh: Yeah, egg-ish nog. Okay, other podcast business.

Erin Allmann Updyke: As always [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) is our website and it's pretty great, you should check it out. We have links to our Goodreads list and our [bookshop.org](http://bookshop.org) affiliate account, we have links to Bloodmobile, our music, who's also on Spotify. We've got links to our Patreon, we've got merch, so much cool merch. Did you get your holiday gifts yet? Erin, what am I missing?

Erin Welsh: Honestly I don't know, I'm just glad that you went through so many of them that I was like she's got it, she's got it covered probably.

Erin Allmann Updyke: Oh, transcripts!

Erin Welsh: Oh, transcripts. Yeah see, I don't wanna say I wasn't paying attention but I just had full confidence in you, how about that?

Erin Allmann Updyke: Oh thanks, I really appreciate that.

Erin Welsh: So before we begin I just wanna thank everyone who suggested topics to cover for this season.

Erin Allmann Updyke: Yes.

Erin Welsh: We got so many amazing requests so I think that we can essentially keep doing this podcast until the end of time.

Erin Allmann Updyke: For ever and ever.

Erin Welsh: Because literally hundreds and hundreds of suggestions.

Erin Allmann Updyke: Yes.

Erin Welsh: And really good ones.

Erin Allmann Updyke: Really good ones. And we also heard from listeners who really wanted to hear more in our diabetes episode about obesity and fatphobia and in our alcohol episode people wanted to hear more about addiction. And both of those are huge topics that we're hoping to tackle in future episodes.

Erin Welsh: Yeah, absolutely. We wanted to give them the time that they deserve and so devote entire episodes to those.

Erin Allmann Updyke: Yeah, exactly.

Erin Welsh: So keep an ear out. Okay.

Erin Allmann Updyke: Well with that, should we do it?

Erin Welsh: Yeah I think we should. Let's take a quick break and then tell me all about typhus.

Erin Allmann Updyke: Okay.

TPWKY: (transition theme)

Erin Allmann Updyke: So if you just hear the word 'typhus' listeners, not Erin who just researched typhus for a long time, you might think one of a few different things. You might actually think of typhoid.

Erin Welsh: I know, there were a few times when I had to correct in my notes that said typhoid and I'm like why am I doing this?

Erin Allmann Updyke: Yep. We covered typhoid in the season opener of our last season and this isn't that. So typhoid and typhus are two different groups of fevers. But then even if you are thinking about typhus, there's at least three different diseases that are called typhus. There's murine, scrub, and epidemic varieties and they all have additional names, just to really keep things interesting. In this episode today we are not going to cover all of these forms of typhus but although we're only focusing on one of these typhus fevers, the truth is that by the end of this episode you will actually know kind of a lot about all of the different kinds of typhus fevers just because while these three diseases differ both in terms of their causative agents and their transmission routes and their ecology and epidemiology, they're quite different. But in terms of the actual disease or illness that they cause, they're not all that different.

Erin Welsh: That's really interesting.

Erin Allmann Updyke: I know.

Erin Welsh: Like convergent disease characteristics.

Erin Allmann Updyke: Well the truth is they're just caused by really similar pathogens, so let's get into it briefly.

Erin Welsh	Okay.
Erin Allmann Updyke	I'll quickly mention the other two and then we'll get into the meat of the episode which is epidemic typhus. So first there's scrub typhus which is also called bush typhus, both of those are not great names. But they're caused by a bacterium known as <i>Orientia tsutsugamushi</i> , and I might have pronounced that horribly. But this form of typhus is transmitted by the bites of infected mites, larval mites which you may know of as chiggers.
Erin Welsh	Uh-huh, very familiar.
Erin Allmann Updyke	Too familiar with them.
Erin Welsh	Yeah, intimately familiar thanks to Kentucky and Panama and sitting in the grass when I should not have.
Erin Allmann Updyke	Never sit in the grass. So that's scrub typhus. There's also murine typhus which is also called flea-borne typhus or very confusingly endemic typhus.
Erin Welsh	Very confusingly, indeed.
Erin Allmann Updyke	Mm-hmm. So this is a disease caused by <i>Rickettsia typhi</i> which is also confusing cause typhi and...anyways.
Erin Welsh	Yeah.
Erin Allmann Updyke	It's caused by a bacterium called <i>Rickettsia typhi</i> and this form of typhus is transmitted by the feces of fleas, aka flea dirt as we learned in our <i>Bartonella</i> episode. And then there is epidemic typhus. And epidemic typhus is what we're going to focus on today. Epidemic typhus is also aka louse-borne typhus and this form is caused by the bacterium <i>Rickettsia prowazekii</i> . So this typhus, <i>Rickettsia prowazekii</i> , is transmitted by the poop, the feces. Is it also called dirt? I'm not sure. Of lice. And we're gonna get into more detail, like deep detail about that transmission cycle in just a second. But just to kind of wrap up these other typhi fevers. So scrub typhus and murine typhus are similar diseases and in truth the pathogens are very similar. So murine typhus is also caused by a <i>Rickettsia</i> and often you see murine or endemic typhus and epidemic typhus grouped together into what are called typhus group rickettsioses. So these are very similar diseases, endemic or murine typhus tends to be a less severe disease for the most part.
Erin Welsh	And is <i>Orientia</i> , is that a group that's closely related to <i>Rickettsia</i> ? Okay.
Erin Allmann Updyke	That's what I was just gonna say, yeah. So scrub typhus caused by an <i>Orientia</i> bacterium is in the same family of <i>Rickettsia</i> , so it's a different genus but very similar in truth.
Erin Welsh	Okay. Like intracellular, super reduced genome. Okay, cool.
Erin Allmann Updyke	Exactly, yep. I think it's a little bit larger of a genome than a <i>Rickettsia</i> but it's still an intracellular. And the disease looks very similar, can also be very severe but historically as you'll get into Erin, epidemic typhus has caused the most severe and widespread disease worldwide.
Erin Welsh	Way more than I had even thought before I started.
Erin Allmann Updyke	Yeah, exactly. Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: So that's what we're going to focus on today. *Rickettsia prowazekii*, like I said transmitted by the feces of the human body louse, *Pediculus humanus corporis*, one of our old friends from *Bartonella*, right.

Erin Welsh: Mm-hmm.

Erin Allmann Updyke: And I'm gonna go into more detail about the human body louse and I know you are too, Erin.

Erin Welsh: I'm excited.

Erin Allmann Updyke: Me too. Because it's so interesting as a vector for a few reasons and I don't think we really got into this in *Bartonella* cause we were covering so much ground but I know that we did talk in our *Bartonella* episode about just how host-specific this insect is. Lice are so specific to their individual host species that the human body louse is a separate louse than the human head louse.

Erin Welsh: Asterisk.

Erin Allmann Updyke: Well separate subspecies.

Erin Welsh: Asterisk.

Erin Allmann Updyke: Oh, okay. Oh my gosh, you're killing me here.

Erin Welsh: I know, I'm sorry.

Erin Allmann Updyke: All right. Well anyways, historically they have been which is intense.

Erin Welsh: Yeah.

Erin Allmann Updyke: And part of this intensity lies in the fact that lice are really very fragile creatures. So they can live up to 4-12 weeks and body lice generally live in and on our clothing for the entirety of their life cycle. But they're incredibly sensitive to temperature and humidity so if their host, i.e. us humans, for example comes down with a fever, lice will flee their hosts.

Erin Welsh: So I have a quote about lice fleeing their hosts. When Thomas Becket died in the 12th century and his body was laid out for the public funeral, onlookers noted that as his body cooled, the lice living in his clothes began to crawl out and quote "boiled over like water in a simmering cauldron and the onlookers burst into alternate weeping and laughter."

Erin Allmann Updyke: Oh no, no, no, no, no.

Erin Welsh: Yeah.

Erin Allmann Updyke: That's a lot of lice, Erin.

Erin Welsh: That's a lot of lice.

Erin Allmann Updyke

Ew. Okay. Well with that lovely image in mind, lice are also very susceptible to dehydration. So in addition to human body temperature, humidity is really important. So their poop which again is what contains the infectious bacteria is really, really dry and powdery which is an image that I never had thought of but their poop is only like 2% water.

Erin Welsh

Wow. They're very efficient little creatures.

Erin Allmann Updyke

Extremely. I looked it up for reference and our body poop is like 75% water.

Erin Welsh

Okay, come on. We gotta do better than that.

Erin Allmann Updyke

That's pretty good. (laughs) Anyways, that was a long divergence but all of that is to say that lice living in and on our clothes, they have to blood feed all the dang time, like 5 times a day everyday for weeks on end and while they're doing that, in our bloodstream they pick up these Rickettsia. Now then what happens is that these bacteria can infect the louse gut lining, the cells that line the lice's gut, their epithelial cells directly. They replicate in the gut cells of the lice and then they burst out of those cells which is how the bacteria gets into the feces and then is transmitted to us when we scratch that dry, flaky poop into all of our bite wounds or rub it into our eyes or nose, etc.

However this whole bursting out of the epithelial cells thing also goes the other way in the louse, causing blood, like our human blood that they just sucked up to enter the body cavity of the lice because the Rickettsia just burst open their fragile, tiny gut. The lice that are infected then become visibly red because they're full of blood that's no longer in their guts, it's just in their body cavity and they die within a week of infection.

Erin Welsh

Yeah.

Erin Allmann Updyke

I had no idea that this disease kills the vectors that it uses to maintain its life cycle.

Erin Welsh

It's really interesting and I have included a very touching quote about the poor louse and its unfortunate journey when it encounters typhus bacterium.

Erin Allmann Updyke

That's exactly how I felt. I was like, this poor louse!

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

Well I think you'll really like it, I'm saving it for later but I think you'll like it.

Erin Allmann Updyke

I can't wait for it. But also spoilers, keep that whole infecting the lining of something and then bursting out of that thing in mind, that's a spoiler for human disease too.

Erin Welsh

Okay. And so for humans, in order to get infected it really just has to be like you said you can either rub it in a cut or stick it up your nose or in your eyes, so it really is like pretty infectious in that way?

Erin Allmann Updyke

Yes it is and this is a disease that thrives when humans are in very close contact, sharing their clothing or having close bodily contact in short enough time frames that either these lice or their poop can then be transmitted person to person and complete the life cycle.

Erin Welsh

Right, okay.

Erin Allmann Updyke

But yes. So it also even if the lice dies, all of that fluid from that dead louse is infectious as well. So scratching the lice bodies themselves into your body can cause infection.

Erin Welsh

And do we know anything about the infectious dose?

Erin Allmann Updyke

You know, I don't. I didn't see that anywhere.

Erin Welsh

Okay.

Erin Allmann Updyke

There's a few things that I just simply did not find, we'll get to them. That was one of them. But once we humans are infected, the incubation period, so the time from that infection to when we show symptoms is usually 10-14 days which is actually kind of a long time. And then after that symptoms generally start with 1-3 days of just feeling cruddy, like nonspecific malaise, just feeling bad before the more kind of typical symptoms which start with a fever.

Erin Welsh

A fever.

Erin Allmann Updyke

Of course.

Erin Welsh

Always.

Erin Allmann Updyke

This Podcast Will Kill You season opener.

Erin Welsh

Aka it started with a fever.

Erin Allmann Updyke

And this fever usually persists throughout the course of illness until a person either dies or recovers, so it's not like a fluctuating fever, it's just you have a fever and it's gonna stay like that.

Erin Welsh

And is it a high fever or is it a mild fever? Like it really depends?

Erin Allmann Updyke

It really depends, yeah.

Erin Welsh

Okay.

Erin Allmann Updyke

It kinda varies.

Erin Welsh

And so does that suggest that the Rickettsiae replicate better at fever temperatures or is it a defense of do we know?

Erin Allmann Updyke

Ooh, very good question. That I don't know. That I don't know the answer to. What a good question.

Erin Welsh

Thank you.



Erin Allmann Updyke

But in addition to fever there's also usually a pretty sudden onset of a very severe headache and it's also common to have abdominal pain. But otherwise, other than those things, symptoms are very nonspecific. Everything from myalgias which are muscle aches, arthralgias which are joint pain, maybe you'll have some chills because you have this fever, maybe anorexia or lack of hunger, not eating anything cause you're just feeling really bad. If it's left untreated, about 80% of people will go on to have central nervous system involvement which can be very severe, it can be delirium or seizures or coma which can lead to death. And very commonly rashes are apparent. But the thing about these rashes is it's not like a single rash, you know like with Lyme disease it's like, 'Oh, the classic bullseye!'. It's nothing like that. In some people they'll have these red splotchy patches interspersed with areas that if you press on them they'll blanch which means they'll go to white.

Erin Welsh

Oh, yeah.

Erin Allmann Updyke

But then it also can either progress to or just start out as these smaller red spots that don't blanch when you press on them or you can have petechiae which are like pinpoint red to purple little spots all over, teeny tiny little dots all the way up to larger purplish splotches.

Erin Welsh

Okay and is that like a stage of the disease type of thing?

Erin Allmann Updyke

Not from what I can tell. And what's interesting is that if you look at older studies, older studies of typhus will say 100% of people or a very high percentage of people all have some kind of rash at some point. But some reports, more recent reports say only 20-40% of people have a rash. Unsurprisingly it's likely because, especially more recent studies that have come out of Africa, rashes in darker skin, and we've talked about this a lot on this podcast, are either not present or not apparent or not appropriately identified. And so a lot of these studies especially out of Africa have been ones that have reported a lot lower incidence of these rashes associated with epidemic typhus. And even the things like whether something blanches, turns back to white, that's the definitions that we use and that's not gonna happen in the same way on darker skin as it does on lighter skin. So that's the rash which isn't specific to begin with. But that's generally the course of epidemic typhus. Now overall pre antibiotics, before we had any kind of treatment, mortality rates were estimated to be as high as 60% which is very, very high.

Erin Welsh

That's ridiculously high.

Erin Allmann Updyke

Mm-hmm. Now with antibiotics they are estimated to be as low as 4% which is still very high.

Erin Welsh

It's still very high.

Erin Allmann Updyke

And the reason that epidemic typhus leads to death or the way that it tends to lead to death can be in a few different ways. One, it can be because of shock and we'll talk about that a little more in a just a second. The other thing is from these neurologic manifestations which can lead to coma and lead to death. And overall the biggest risk factors that lead to who is more likely to die vs survive and epidemic typhus infection are two biggest things: older age and malnutrition, so poor nutritional status is very strongly associated with severe infection and death compared to good nutritional status. Now before I get into the pathophysiology cause I know you have a lot of questions, I can see them on your face, I do wanna say another interesting thing about epidemic typhus and that is that it actually leads to a chronic infection that can then be reactivated many years, like up to 40 years based on one source that I read, 40 years after initial infection. And this is not from re-exposure but just from reactivation of a latent infection.

Erin Welsh

It sounds a lot like chickenpox.

Erin Allmann Updyke

It does.

Erin Welsh

And how chickenpox remained in small populations, yeah.

Erin Allmann Updyke

The nerves. Now I was trying to get a handle on what percentage of people does this happen to, I do not know. I'll just say that. Form what I can gather though it seems like if this disease is untreated, nearly everyone that survives the initial infection could potentially maintain a latent infection.

Erin Welsh

But if you are treated with antibiotics or through vaccination or something, there is very low chance of that Rickettsia surviving.

Erin Allmann Updyke

Right, exactly.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah so if you're treated then it should clear the infection but if you're untreated and survive it seems like that's the population that goes on to develop this latent infection. And then the risk factors for reactivation are kind of the same things that we see for reactivation of a lot of different diseases, so like times of stress or immune compromise like another illness or cancer or some other form of immunosuppression or even just advancing age. So this whole chronic reactivation disease, this is called (BRILLS INSERT) disease, it gets a whole new name of course.

Erin Welsh

I'll explain why.

Erin Allmann Updyke

Oh great. I mean it makes sense honestly.

Erin Welsh

Yeah, yeah.

Erin Allmann Updyke

But it generally looks very similar in terms of symptoms to initial infection but tends to be a lot more mild which makes sense cause your body has seen it before.

Erin Welsh

Right, right.

Erin Allmann Updyke

But we clearly have questions obviously, so let's get to my favorite part of the biology which is how the heck does this happen in our bodies, why are these the things that we see? Aka the pathophysiology.

Erin Welsh

Yeah, I wanna hear this.

Erin Allmann Updyke

Me too. Well I wanna tell it to you. (laughs) So Rickettsias, I know Erin you know a lot about these already but listeners may also remember from our Rocky Mountain spotted fever episode, Rickettsias are these obligate intracellular bacteria which means they have to enter our host cells in order to be able to replicate within our cells.

Erin Welsh

Very much like a virus in that way.

Erin Allmann Updyke

Very much like a virus. So when we get infected from louse - did we decide it's called louse dirt?

Erin Welsh

Louse dust?

Erin Allmann Updyke

Louse dust, I like it. When we get infected from louse dust either from rubbing it into our skin or our eyes, the bacteria enter our bloodstream as well as our lymphatic system and they travel to infect our endothelial cells. All of the Rickettsias do this and every listener of this podcast probably knows what endothelial cells are by now because I feel like we talk about them all the time.

Erin Welsh

But if this is your first episode...

Erin Allmann Updyke

It is, if this is your first one, endothelial cells are the cells that line our blood vessels, so they're the inside lining of your arteries and veins and capillaries. Rickettsia prowazekii tends to infect the endothelial cells specifically in our small capillaries. Why you may ask?

Erin Welsh

Yes. Why is on my face.

Erin Allmann Updyke

I don't actually know but I have suspicions, okay.

Erin Welsh

Okay.

Erin Allmann Updyke

These are not very mobile bacteria. They can't really move on their own, they just kind of go with the flow and capillaries are where flow is the slowest and the area between endothelial cells is really, really small. Like our red blood cells have to really squeeze to get through our capillaries so I suspect that that is where they are most able to use their little adhering proteins to just grab onto those endothelial cells and then get in.

Erin Welsh

Okay.

Erin Allmann Updyke

What interesting though is that a lot of other Rickettsia species tend to infect larger and more medium-sized vessels and I don't know why that is but in any case, Rickettsia prowazekii likes our tiny capillaries, it's found a nice little niche there. They enter our cells and inside our cells they multiply and multiply and multiply. But they're not really mobile so they're not doing anything inside of our cells, they're not even moving around within our cell, they're just replicating so much that eventually they fill up our cells and literally burst them open, releasing tons of new Rickettsias to go on and infect the neighboring endothelial cell just like in the louse, Erin.

Erin Welsh

I mean that makes complete sense.

Erin Allmann Updyke

So clearly this causes destruction of the linings of our capillaries and potentially other vessels, it's not exclusively capillaries.

Erin Welsh

Okay.

Erin Allmann Updyke

This is gonna cause leaking, so vascular permeability. And this, dear friends, is one of the hallmarks not just of this Rickettsia but Rickettsia in general. So it's widespread, systemic inflammation and leakage of our vessels. This is called vasculitis. So this can happen on a small scale and lead to micro hemorrhages, little tiny leaks from our tiny little capillaries or it can happen on a larger scale and lead to macro hemorrhages.

Erin Welsh

And so is this why we see the rashes that we see?

Erin Allmann Updyke

I think that's a large part of the rashes, yes.

Erin Welsh

Okay.

Erin Allmann Updyke

Absolutely. And why they can be so variable as well, okay. And this leaky blood and this tissue damage also stimulates a lot of inflammation so then you have white blood cells and other inflammatory markers coming to the region. And all of this inflammation can actually stimulate thromboses, so our body trying to clot off our blood so that we don't hemorrhage, see our hemophilia episode for more on that process.

Erin Welsh

For about the clotting cascade, mm-hmm.

Erin Allmann Updyke

But in this case what that leads to is then these little areas of thrombus or clot in these tiny, tiny little vessels surrounded by inflammation that then leads to cutting off of blood supply in certain areas, especially in our brain since this is a bacteria that by traveling through our blood vessels is able to make it's way past our blood-brain barrier and infect the endothelial lining of the small vessels of our brain.

Erin Welsh

Ooh.

Erin Allmann Updyke

Right? So it cuts off blood flow to parts of our brain.

Erin Welsh

Oh that is really bad and that explains a lot. Okay.

Erin Allmann Updyke

And so this actually leads to a very specific finding called typhus nodules that are basically little blood clots in the wall or near the wall of these small blood vessels in our nervous system that are then surrounded by a whole bunch of inflammation. And that's kind of a characteristic finding of a typhus infection in the brain.

Erin Welsh

Okay. And so you said that because it travels in the bloodstream it really can go anywhere in the body. And so is it just kind of random? Does the inflammation ever cut off the spread of it to the brain or to other parts of the body? You know what I mean?

Erin Allmann Updyke

Yeah, it's a good question. I think in general with these kind of bloodborne infections that travel in the bloodstream, they often go first to areas of really high blood flow so places like the brain, the liver, the spleen, and you do see a lot of involvement of those areas but I think eventually and theoretically this could go kind of everywhere.

Erin Welsh

Okay.

Erin Allmann Updyke

So it also probably depends too on where the initial site of infection is and how far it has to travel and what specific route it ends up on.

Erin Welsh

Yep, okay. Cool, interesting.

Erin Allmann Updyke

Yeah. So that's why though mortality is often caused by both shock in this case because of the volume lost from these leaky vessels or from the nervous system damage that can lead to then coma and death.

Erin Welsh

Wow. And 60%.

Erin Allmann Updyke 60% if untreated, yeah. It's terrifying.

Erin Welsh Wow. I mean that's horrific, yeah.

Erin Allmann Updyke Yeah. The good news is we do have treatment so it's a very treatable disease and it's actually quite easy to treat with either a one time dose or a very short course of antibiotics. And from what I can tell it still works really well, not a ton of concern for resistance from what I can tell. But the other thing that's incredibly important even if you're treating with antibiotics is that you have to get rid of the lice.

Erin Welsh Right.

Erin Allmann Updyke So antibiotics are not enough, you also have to be able to wash clothing in hot enough water to be able to kill the lice or leave the clothing and the bedding that are infested unused for at least a week so that they all die. So that's a huge part of both the treatment and prevention of epidemic typhus.

Erin Welsh That make sense, yeah.

Erin Allmann Updyke Oh also just as a side note, this is a human-specific disease except that there's some weird cases involving flying squirrels.

Erin Welsh Yeah, I'm gonna talk about that a little bit.

Erin Allmann Updyke Cool, I figured but I thought I should just mention that yeah, flying squirrels are like a reservoir.

Erin Welsh I know. Of all of the animals, I was like huh?

Erin Allmann Updyke I know! It's so random.

Erin Welsh Yeah, it's very interesting.

Erin Allmann Updyke Yep. But that, Erin, is the biology of epidemic typhus.

Erin Welsh Well do you wanna hear about the history?

Erin Allmann Updyke I can't wait, can you tell me everything?

Erin Welsh I will right after this break.

TPWKY (transition theme)

Erin Welsh To set the tone for the history section I wanna start with a quote about typhus from a book called 'Rats, Lice, and History' by Hans Zinsser, as in Brill-Zinsser.

Erin Allmann Updyke Oh!

Erin Welsh

Quote: "Soldiers have rarely won wars. They more often wipe up after the barrage of epidemics and typhus, with its brothers and sisters, plague, cholera, typhoid, dysentery, has decided more campaigns than Caesar, Hannibal, Napoleon, and all the inspector generals of history. The epidemics get the blame for defeat, the generals get the credit for victory. It ought to be the other way around."

Erin Allmann Updyke

I love that quote and I also love that we have now covered every one of those diseases.

Erin Welsh

I know, I know. I was looking at that and I was like wow.

Erin Allmann Updyke

Wow.

Erin Welsh

We could probably throw a few more in there too, to be honest.

Erin Allmann Updyke

Yeah. Malaria.

Erin Welsh

Malaria, yellow fever.

Erin Allmann Updyke

Yellow fever.

Erin Welsh

I mean trench fever for that matter.

Erin Allmann Updyke

Yeah.

Erin Welsh

Didn't really decide many wars but we could definitely make a case for other ones.

Erin Allmann Updyke

I think we did.

Erin Welsh

I think we did.

Erin Allmann Updyke

I think you did. Anyways.

Erin Welsh

This idea is a common theme for our podcast, right. Like wars and unrest directly and indirectly lead to the emergence and spread of infectious diseases both among soldiers as well as civilians. We've talked about dysentery loving a disaster, we've read some descriptions of the latrine conditions that led to typhoid outbreaks during the American Civil War, we've described how global movements during WWI helped spread the 1918 influenza pandemic in our very first episode, and we've even talked about the human body louse in that same war spreading trench fever, also accompanied by some very descriptive quotes of body lice and the problems with them.

Erin Allmann Updyke

Very descriptive.

Erin Welsh

But it's taken us this long, I still can't get over it, to talk about typhus which as you now know is 60% mortality among untreated people, it ranks among plague, cholera, to all of those other ones in its ability to absolutely devastate a village or a city or an entire country. The historical impact of it is huge. When we think about the death toll from a war or from a famine or even from just an epidemic alone, I think that many of us probably imagine people dying for example in combat on D-Day, right, or in bombings from the blitz, or maybe directly from starvation in the Holodomor, or directly from bubonic plague during the Black Death because that's often how we learn about historical events.

But even if that compartmentalization or assigning deaths to this cause and that cause, even if that's a useful way to learn, that's not really the way it happens. Alongside death and war is death and pestilence, death and famine. I mean this is why the four horsemen of the apocalypse which are most often represented as pestilence, famine, war, and death, it's why they ride together. They don't take turns showing up and then like, 'Okay peace out, it's your turn now.' It's a partnership.

Erin Allmann Updyke

True.

Erin Welsh

The firsthand account that I read described a typhus outbreak in ships of Irish immigrants fleeing during the Great Famine of around 1845-1852. In that famine there were an estimated 1 million excess deaths and the majority were not deaths directly from starvation but from infectious diseases including typhus. And that same thing has happened time and time again in wars where casualties from infectious disease outweigh those from battle. And I realize, like I fully realize that right now I'm presenting a micro history of typhus which is maybe a bit hypocritical about teaching things in isolation. So I really wanted to start off this section by saying that I hope you take away from this episode an appreciation for the enormous and horrible impact that typhus has had and also to ask you to remember that while I'm talking about typhus in Napoleon's soldiers or typhus in concentration camps, typhus was not acting alone. It worked side by side, aided and abetted, with other infectious diseases as well as human-created miseries like war and concentration camps and famine. So now that that's out of the way I can finally get to the meat of it by first asking not where typhus came from, but where did lice come from?

Erin Allmann Updyke

Yes! Where?

Erin Welsh

We've already talked about how fascinating we think lice are so it was really fun to get to read more about them for this episode. And I think I might have touched on some of this from our Bartonella episode but I'm gonna go over the basics as well as offer a self-correction, potential self-correction.

Erin Allmann Updyke

Okay.

Erin Welsh

So *Rickettsia prowazekii* is transmitted by the body louse, as you said, which is generally considered a different species or at least subspecies than the head louse. And it's been hypothesized that the body louse diverged from the head louse when humans started wearing clothing around 72,000 years or so, give or take, which is I think what I said also in the Bartonella episode. But after doing more lice reading for this episode I learned that the story might be a bit more complicated.

Erin Allmann Updyke

It always is, isn't it?

Erin Welsh

It always is. First of all, body lice and head lice can interbreed and produce fertile offspring under experimental conditions.

Erin Allmann Updyke

Okay, all right.

Erin Welsh

Yeah, that's one way that scientists often decide whether things represent different species or not but it's not like the only criterion. Secondly there are no consistent morphological differences between the two and species or subspecies identification usually depends on where on the body the lice was found, so if it was found on a the head it's a head louse, if it's found on the body or on the clothing it's a body louse. Under experimental conditions, researchers seem to have been able to raise body lice from head lice, like they take a population of head lice and then they raise them under body lice conditions and you have what looks like a body louse.

Erin Allmann Updyke

Interesting.

Erin Welsh

Yeah. But there are some behavioral and physiological differences between the two, namely in that the body louse has evolved to live in clothing and lays its eggs in clothing which head lice do not do. And there are also size differences and sometime color differences between the two although again those are not consistent. And until recently it was thought that body lice and head lice were indistinguishable genetically but more recent research has led to a molecular tool that can differentiate between them.

Erin Allmann Updyke

Yeah.

Erin Welsh

And this finding has led to the thought that body lice and head lice aren't two different species or even subspecies but that they represent two different ecotypes and that's the result of a difference in the way that their genes are expressed at some point during development or growth. I don't really know about the life stages of lice but...

Erin Allmann Updyke

Fascinating.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. Cause I was reading that they have different feeding patterns which they think leads to differences in vector competence, why body lice transmit a lot of things and it's thought that head lice generally don't even though they can, like you said, in the lab. And also the ecotype thing, there's differences in their immune responses to infection with things which then would make body lice more capable of getting infected with bacteria than head lice.

Erin Welsh

Yeah! It's really interesting and I probably should do some more digging on this but I wonder if it's just like a suite of genes that are turned on in one vs the other that has basically over time, once humans started wearing clothing, it wasn't necessarily a one time divergence between the two but a continual divergence where head lice populations especially an over infestation are feeding into body lice populations. It's like I don't know what environmental cue it could be, maybe intense population pressure or something in the head lice infestation that maybe one of them turns on those switches for the other genes and is like, 'Hey I'm a body louse now, I prefer a little bit cooler, I'm gonna lay my eggs out here, I'm gonna feed this way, it was nice to know you guys.'

Erin Allmann Updyke

Yeah, yeah. Fascinating, Erin.

Erin Welsh

Yeah. So it might be semantics whether we call them subspecies or different species or ecotypes or whatever but I just find that whole part incredibly interesting.

Erin Allmann Updyke

I do too!



Erin Welsh

Yeah, yeah. Okay so all of that nitty gritty info aside, humans have been parasitized by lice for millions of years and that's very typical of lice, they tend to be very species specific, they're often used to track the evolution of different mammalian species, each species tends to have their own louse species. And because of this high degree of specialization, human lice have basically followed the distribution of their host, meaning that they're globally distributed and they've been that way for a long time. And even though a lot of things are working against the preservation of lice in fossils, we do have some archeological evidence to back this up, to back this global distribution up. The oldest head louse was found on a hair from 8000 BCE in northeastern Brazil and the oldest found in the Old World came from roughly 7000 BCE in Israel. Combs for head lice have been found from around 6500 years ago in Ancient Egypt and lice have been found on mummies in Egypt, China, the Aleutian Islands, Greenland, and parts of South America. And I know this is a lot about lice so I wanna read that amazing other quote that I alluded to earlier before I move onto *Rickettsia prowazekii*.

Erin Allmann Updyke

Ooh, yes. Okay.

Erin Welsh

So this is also from Hans Zinsser, his book 'Rats, Lice, and History' is a goldmine, it's a very bizarre book. Let's just say that much. It literally was like 12 chapters not about typhus or rats or lice.

Erin Allmann Updyke

Oh okay. It was about history, I guess?

Erin Welsh

Yeah, in a chapter title he would apologize for like, I promise, this is the last divergence. It's great. It was written in 1935 I think, 32, 35. Okay, quote:

"The louse shares with us the misfortune of being prey to the typhus virus. If lice can dread, the nightmare of their lives is the fear of someday inhabiting an infected rat or human being. For the host may survive but the ill-starred louse that sticks his haustellum through an infected skin and imbibes the loathsome virus with his nourishment is doomed beyond sucker. In 8 days he sickens, in 10 days he is in extremis, on the 11th or 12th day his tiny body turns red with blood extravasated from his bowel and he gives up his little ghost. Man is too prone to look upon all nature through egocentric eyes, to the louse we are the dreaded emissaries of death. He leads a relatively harmless life, the result of centuries of adaptations. Then out of the blue an epidemic occurs, his host sickens and the only world he has ever known becomes pestilential and deadly. And if as a result of circumstances not under his control his stricken body is transferred to another host whom he in turn infects, he does so without guile from the uncontrollable need for nourishment, with death already in his own entrails. If only for his fellowship with us in suffering, he should command a degree of sympathetic consideration."

Erin Allmann Updyke

I love it.

Erin Welsh

Isn't that so good? I have so many quotes from this, I loved that so much. And gives up his tiny ghost?

Erin Allmann Updyke

His tiny ghost! Can't you picture it?

Erin Welsh

I can, or his little ghost, sorry. It's so cute.

Erin Allmann Updyke

It's so adorable.

Erin Welsh

Yeah that book did definitely convince me to like lice more as well, like appreciate their incredible biology.

Erin Allmann Updyke

Right? Yeah.

Erin Welsh

And feel a little bit sympathetic.

Erin Allmann Updyke

I mean it's killing them too.

Erin Welsh

Yeah. Well anyway, let's turn to typhus.

Erin Allmann Updyke

Let's.

Erin Welsh

So where did typhus come from? Great question. We don't know. (laughs)

Erin Allmann Updyke

(laughs) What are you me or something?

Erin Welsh

So from what I can tell it's still debated whether *Rickettsia prowazekii* came from the Old World or the New World. For a lot of human history the disease was grouped in with other fevers or not distinguished from typhoid. And like we said, that's a very common thing. The origin of the words are essentially the same. Typhoid actually comes from typhus which comes from the Greek word 'typhos' meaning smoky or hazy and that's meant to describe the neurological effects the disease can have. And I also wanted to just because one more little thing about lice here, there are a lot of words that we use in common English sayings that are a reference to lice. So like nitwit, lousy, or a lousy night's sleep meaning that you were bothered by all the lice on you.

Erin Allmann Updyke

Itching.

Erin Welsh

Nitpicking, going over something with a fine-toothed comb, and chatter which I think we mentioned in the Bartonella episode.

Erin Allmann Updyke

I don't remember that.

Erin Welsh

Like to pick chats I think or to chat would be to sit there and remove lice. And so they would call it chatter, to hang out with a group of people.

Erin Allmann Updyke

Maybe you did say that and I just don't remember. Oops.

Erin Welsh

Honestly, yeah. There are a lot of episodes that I'm like, we did that? I don't remember doing that.

Erin Allmann Updyke

No recollection, yeah.

Erin Welsh

Yeah. But reading back through ancient or historical writings and trying to figure out what might or might not be typhus is super tricky as you might expect. Some people point towards some of Hippocrates' writings describing typhus or maybe the Athenian Plague in the 5th century BCE as described by Thucydides or maybe from a battle in Spain in 1083 CE which would put the origin as Old World. But those are pretty hand-wavy and a disease that sounds much more specific to typhus doesn't show up in Europe until the very end of the 15th century, as early as 1448 I think, maybe 1492 in Grenada when 17,000 soldiers died of a disease that sounds a lot like typhus. And then again the same similar disease shows up in the 1550s in Spain. Quote: "A new disease unknown until the time of the civil wars in Grenada appeared in Spain in the year 1557 and depopulated the greater part of our peninsula. It did not begin to decline until the year 1570."

And around the same time or a few years before there are descriptions of what was clearly typhus in Mexico and the disease continued to pop up in epidemic form every time there was a drought or famine up until the 1900s. And I feel like either of those examples could be used to say, 'See? It's clearly Old World origin,' or 'See? It's clearly New World origin.' So what can the Rickettsia tell us about itself? As we probably discussed in our Rocky Mountain spotted fever episode, Rickettsiae are these super small and bizarre bacteria, they're really closely related to mitochondria, the powerhouse of the cell, and they're very tricky to culture in a lab. And for a long time researchers were unable to find a nonhuman reservoir for Rickettsia prowazekii but then people began finding antibodies to the Rickettsia in some domestic animals such as donkeys in parts of Africa. But it wasn't always consistently found, so that seemed like an incidental infection, that didn't really seem like that was the source.

Erin Allmann Updyke

Yeah.

Erin Welsh

But as you mentioned, Erin, one place where it does seem to be more consistently found and I'm talking about antibody prevalence rates of 40% or so-

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah, the southern flying squirrel which is found in the eastern half of the US and down into parts of Mexico.

Erin Allmann Updyke

I mean it's just so random.

Erin Welsh

It is and I wanna know more about it but yeah, that right there says to me okay, that's a big check in the New World origin column. But I'm still not convinced because of the timing of those outbreaks. So like somehow it just spread in the population? Are they affected by it? A lot of exposures in the eastern US seem to be associated with the southern flying squirrel.

Erin Allmann Updyke

Yeah.

Erin Welsh

It's just strange.

Erin Allmann Updyke

It's very strange, I don't get it.

Erin Welsh

But in a way it also makes sense because I think we talked about with the Rickettsia rickettsii also finding a nonhuman reservoir is challenging to do but small rodents do seem to be very good candidates for the nonhuman reservoir. So I don't know.

Erin Allmann Updyke

But of all the small rodents.

Erin Welsh: I know, I know.

Erin Allmann Updyke: There's no association with humans, there's no...you know? Or at least not a strong one.

Erin Welsh: I mean maybe there is, yeah. Maybe there's something in the biology that somehow it just happens to work that way.

Erin Allmann Updyke: Yeah, yeah, yeah.

Erin Welsh: Or maybe we're just not looking enough. That's also a possibility.

Erin Allmann Updyke: Definitely a possibility.

Erin Welsh: So yeah, I mean maybe we don't have a satisfactory answer right now for where exactly *Rickettsia prowazekii* came from but it seems that once it showed up it spread around the world pretty easily, especially under conditions like war and famine and unrest which seemed fairly consistent throughout the 1600s, 1700s, 1800s, a lot of the 1900s. And wherever it originated it would always find the vector to be able to transmit it, right, because body lice were already globally distributed.

Erin Allmann Updyke: Right.

Erin Welsh: Analysis of dental pulp, our fave, from remains in a mass grave in France from a siege in 1710-1712 shows evidence of *Rickettsia prowazekii* infection. And it was also found again in dental pulp in the remains of some of Napoleon's soldiers in a mass grave in Lithuania from the 1812 campaign.

Erin Allmann Updyke: It's amazing what ends up in dental pulp.

Erin Welsh: They also found Bartonella which I may have even mentioned those papers in the episode, I'm not sure.

Erin Allmann Updyke: Yeah.

Erin Welsh: Again, I have no recollection of previous topics. But the second finding, the one of Napoleon's soldiers, it lends support to the idea that typhus along with other diseases may have been a major contributing factor to Napoleon's decision to retreat during the Russian campaign. And I don't see how he would have had any other choice because listen to these numbers.

Erin Allmann Updyke: Oh dear.

Erin Welsh: Of Napoleon's 500,000 soldiers, half a million soldiers-

Erin Allmann Updyke: Whoa.

Erin Welsh: -that marched to Moscow in 1812, 3000 returned. Yeah, out of 500,000. 3000 returned.

Erin Allmann Updyke: That is incredibly depressing.

Erin Welsh: And an estimated 20% of the mortalities were due to typhus.

Erin Allmann Updyke: 20% due to typhus alone is the estimate?

Erin Welsh: Typhus alone. I mean typhus aided and abetted by all these other things as well.

Erin Allmann Updyke: Right, right, malnutrition and other things.

Erin Welsh: But yeah.

Erin Allmann Updyke: Oh my.

Erin Welsh: Yeah, it's a lot. And not long after this, Napoleon's ill-fated campaign to Moscow, typhus began to be distinguished as a separate disease from typhoid although confusion seemed to linger, like it had been differentiated once before but people were still not sure. Is this typhus? Is this typhoid? It's fever. Generally it was just fever.

Erin Allmann Updyke: Fever, yeah.

Erin Welsh: But it also gained some more descriptive names such as ship fever was a common one, jail fever, camp fever, and so on to describe the typical circumstances under which epidemics occurred. Because it's important to remember that although body lice were prevalent across the globe, it's not like typhus was constantly occurring, it wasn't like a childhood illness, it wasn't like oh you're just gonna get it and it's endemic here, right. It needed a spark which was usually provided by someone who had active typhus or who had Brill-Zinsser disease and then it needed fuel which was impoverished, crowded settings and malnutrition to then lead to this devastating and deadly epidemic.

Erin Allmann Updyke: Right.

Erin Welsh: Even before the so-called coffin ships left Ireland for North America like in our firsthand account during the Irish Famine, typhus was running rampant across the country. I'm gonna read another quote. Quote: "Never had conditions been so fatally favorable to the rapid spread of lice as in the famine winter of 1846 through 1847. The people were filthy, they had sold every stitch that would fetch the fraction of a penny and they were wearing the same rags day after day and night and day. Their bedding had been sold and they slept covered with rags and old coats. To heat water or wash themselves or their clothes was out of the question, they were eating their food half or wholly raw because they had no money to buy fuel. Indeed after months of starvation, even the strength to fetch water had disappeared. Once infection had been brought into a district it spread with lightning rapidity among the crowds brought together for relief. A brush in passing was enough to transfer the fever-transmitting louse or its dust-like excrement to a new victim and one fever-stricken person could pass on infection to 100 others in the course of a day."

Erin Allmann Updyke: 100?

Erin Welsh: I mean it's easy to imagine, right.

Erin Allmann Updyke: Yeah.

Erin Welsh

And so that quote is from Cecil Woodham Smith who is the author of the book 'The Great Hunger'. And in this book they estimate that about 10 times as many people died of disease than of starvation during the Irish Famine.

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah. But those deaths of course probably would not have occurred or at least in those numbers without the lack of food or rather the lack of access to food because it was a complicated history but food was still being produced and exported from Ireland during the famine.

Erin Allmann Updyke

That's a whole other episode.

Erin Welsh

That's a whole other episode, yeah. And as you hear in our firsthand, those who fled or were sent away by their landlords for North America, they often met a similar fate. I highly recommend reading more about this, about Grosse Isle, Canada and the typhus epidemic that occurred there in 1847. There's also a great short story called 'Ship Fever' by Andrea Barrett in a book of short stories about science. I really enjoyed it, I read it a couple years ago. And there's one, like the titular story or whatever takes place on Grosse Isle and it's so good. And we'll link to it on our website.

Okay but anyway, if you pick virtually any conflict or ecological disaster during the 1700s and 1800s you can be sure that typhus was there. It was present during the American Civil War although according to one paper I read it wasn't as prevalent as you might expect. It was in Mexico associated with drought or crop failure, it was during the Thirty Years' War, I mean you could list tons of different instances. And it's not difficult to see why typhus flourished so well in war and in famine and especially in northern climates or cooler seasons. Like let's say you're one of Napoleon's soldiers or let's say you're an impoverished immigrant fleeing the famine in Ireland. If the way you kill lice, like you said treatment alone is not enough, you have to kill the lice. And so if the way you kill lice is washing your clothes frequently, how do you do that when you're on a ship?

Erin Allmann Updyke

You don't.

Erin Welsh

How do you prevent yourself from becoming reinfested?

Erin Allmann Updyke

You don't.

Erin Welsh

I mean are you even lucky enough to have one change of clothes? And if you're a soldier constantly on the move, let's say you have a few changes of clothes, how are your clothes gonna dry? Do you have soap? Aren't they just gonna freeze in the Russian winter and then never actually dry?

Erin Allmann Updyke

And even just drying them alone isn't enough.

Erin Welsh

Right.

Erin Allmann Updyke

You have to wash them in hot enough water or dry them in hot enough conditions or leave them like I said completely unworn for at least 5 days which-

Erin Welsh

It's impractical.

Erin Allmann Updyke

Yeah.

Erin Welsh

And I think that also kind of serves as a good reminder of how ubiquitous body lice were. It was just normal to have body lice.

Erin Allmann Updyke

Right.

Erin Welsh

And if you look at a disease like typhus which has all but ceased to cause epidemics today which Erin, I know you'll talk more about the numbers. But I think it's easy to subconsciously think well people just didn't know how it was transmitted, germ theory hadn't been developed yet, we have so much more knowledge and medical technology to prevent diseases like typhus today so we'll never have to worry about it. And to a certain extent that's true, right, knowing more about how it's transmitted certainly helps to prevent its spread and being able to treat it or vaccinate against it has also helped to reduce the mortality associated with typhus. But how does that knowledge help or that technology help when you lack access to medical care or even the ability to regularly wash your clothes or have multiple changes of clothes?

Erin Allmann Updyke

Right.

Erin Welsh

Typhus outbreaks, like many other infectious diseases, are not just a matter of bad luck or being in the wrong place at the wrong time or not knowing how to protect yourself from the disease. They arise and spread in circumstances often way beyond your control. And that's what I just kept getting from reading about typhus, just this sense of total helplessness and horror in these typhus outbreaks. The fever appears and there's simply nothing you can do but wait for it to get to you, even if you know that it's an infectious disease and that it's transmitted by body lice. Sometimes it's just that knowledge doesn't help you.

Erin Allmann Updyke

Right.

Erin Welsh

So when did we learn those things? Well in 1909 Charles Nicolle published his observation that the disease was transmitted through body lice for which he was awarded the Nobel Prize in 1928, although it wasn't until 1938 I think that people realized it wasn't the bite of the louse but rather the feces of the louse that transmits the pathogen. And the causative agent of typhus, *Rickettsia prowazekii*, was discovered really by several people but it was named in 1916 by Henrique da Rocha Lima, a Brazilian doctor whose colleague Stanislaus von Prowazek died of typhus while investigating it just like Howard Ricketts who also died of typhus if you remember back to our Rocky Mountain spotted fever episode.

Erin Allmann Updyke

I do remember that, yeah.

Erin Welsh

And Ricketts died while investigating typhus in Mexico in 1910. And so da Rocha Lima named the bacterium to honor these two researchers who lost their lives while studying the thing that killed them which is sad.

Erin Allmann Updyke

Yeah.

Erin Welsh

And around the same time that da Rocha Lima named the bacterium, two researchers named Weil and Felix developed the first serological test for the disease and more info seemed to be rolling in. Brill disease as it was first known had been described by Nathan Brill in the 1910s as he worked as a doctor treating Eastern European residents in New York's Lower East Side. It was a mild disease that he described which is why he didn't consider it to be typhus initially.

Erin Allmann Updyke

Right.

Erin Welsh

And it seemed especially prevalent among older people mourning the loss of a spouse, so he actually called it bereavement disease.

Erin Allmann Updyke

Oh fascinating.

Erin Welsh

Yeah. Which I can imagine that being a hugely stressful and traumatic experience that would reactivate.

Erin Allmann Updyke

Exactly, exactly what I was gonna say, yeah.

Erin Welsh

But later it was shown by Hans Zinsser to actually be this reactivated form and so hence Brill-Zinsser.

Erin Allmann Updyke

Fascinating.

Erin Welsh

But again even with all of this new knowledge being gained about the disease and the bacterium, it continued to cause devastating epidemics. During WWI in many countries in Eastern Europe such as Poland it turned endemic to epidemic among both civilians as well as soldiers. In Serbia in 1914 after the Austrian invasion, typhus broke out and caused a massive epidemic with an estimated 500,000 cases of which 120,000 were fatal.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

During this epidemic more than half of the physicians in Serbia died or were incapacitated by typhus.

Erin Allmann Updyke

Whoa.

Erin Welsh

Overall during WWI it was estimated to have infected between 20-30 million people and once the war was over it's not like typhus just went away. Russia especially was in a great deal of turmoil and unrest with the Russian Revolution beginning in 1917 even before WWI ended cause there was just chaos. And typhus took advantage of that. Between the years 1917-1921 it's estimated that around 25 million people in Russia became infected with typhus and 2.5-3 million died.

Erin Allmann Updyke

Whoa.

Erin Welsh

Those numbers, they surprised me because I didn't realize, I just didn't realize. And it was this huge epidemic in Russia along with the enormous number of typhus infections during WWI that inspired many people to start working on a typhus vaccine and several countries had entire research organizations devoted to this which shows just how terrified of the disease that people were and rightly so. So one of the most prominent of these typhus researchers in the years after WWI was a man named Dr. Rudolf Weigl. Dr. Weigl was born in what is now the Czech Republic and lived most of his life in Lwów which was then part of Poland, now it's part of Ukraine. At his lab in Lwów he made great strides with developing a vaccine for typhus that didn't entirely prevent the disease but it did make it much less deadly if you contracted it.



But he faced a problem that was common to anyone researching typhus or other rickettsial diseases. Rickettsiae were notoriously difficult to maintain and culture in lab settings and it was also hard to get enough material to make the vaccine, the manufacturing side of it was hard. Mice and guinea pigs didn't really seem to become infected with *Rickettsia prowazekii* so they weren't a great solution. And so faced with this challenge Weigl came up with another solution. Use the louse as the maintenance animal. Grind up infected lice and then inject that into the butts, like through the butts of uninfected lice to infect them to then make more infected lice, you get to make more vaccine.

Erin Allmann Updyke

Yeah.

Erin Welsh

Which that seemed to work actually.

Erin Allmann Updyke

Through the butts, that's so specific.

Erin Welsh

I know. Well it was something about the chitin or whatever the material was was hard enough that you could actually inject it in there without destroying this fragile little louse.

Erin Allmann Updyke

Without hurting it, yeah. Okay, that makes sense. I believe it.

Erin Welsh

Yeah, that's pretty cool.

Erin Allmann Updyke

Yeah.

Erin Welsh

But how do you get enough lice to make enough vaccine?

Erin Allmann Updyke

Uh oh.

Erin Welsh

Yeah. For that you need a louse colony and for that you hire louse-feeders.

Erin Allmann Updyke

No!

Erin Welsh

Yes. This was an actually job created by Weigl and it's very cool, I'm gonna get more into it now and later. But essentially you strapped little boxes containing lice to your legs or arms and allow the lice inside those boxes to feed for a set amount of time.

Erin Allmann Updyke

Okay.

Erin Welsh

And if you happen to be one of those lucky louse feeders you would be feeding up to 30,000 lice at a time apparently.

Erin Allmann Updyke

Oh my.

Erin Welsh

Which would produce enough vaccine material for 300 people in one week.

Erin Allmann Updyke

Wow, okay.

Erin Welsh

That's pretty good, I feel like it syphilis a pretty noble job.

Erin Allmann Updyke

Yeah.

Erin Welsh: It was also decent paying and I would say relatively safe.

Erin Allmann Updyke: Okay.

Erin Welsh: Because if you had never had typhus before you were only allowed to feed the uninfected lice.

Erin Allmann Updyke: Okay.

Erin Welsh: And if you had had typhus then you could earn a bit more money by feeding the lice that were infected. But it did lead to some unfortunate side effects like blood loss and allergic reactions on occasion. But still.

Erin Allmann Updyke: Yeah.

Erin Welsh: By the 1930s Weigl's lab had become the world's typhus lab. People came from all over to study his louse colony and to learn how to make the Weigl vaccine. Basically he would put as many as 50 lice into what was called the Weigl clamp where their little lice butts were perfectly positioned for being injected with a slurry of their infected dead friends.

Erin Allmann Updyke: Oh my gosh.

Erin Welsh: (laughs) And then those infected lice fed on more human blood and then they were dissected, their intestines removed and the homogenized, then centrifuged, then diluted with saline and phenol which would kill the bacteria, and then boom, there's your vaccine.

Erin Allmann Updyke: Wow.

Erin Welsh: It's basically just mushed up louse intestines.

Erin Allmann Updyke: Yeah, louse intestines inactivated.

Erin Welsh: Yeah, inactivated.

Erin Allmann Updyke: Yeah.

Erin Welsh: As the years went on the need for louse-feeders grew as the need for the vaccine grew, especially as it became clear that war was on the horizon. And even before WWII began, Jewish academics in Poland faced many challenges, often being completely prohibited from working in academia. In 1937 for instance, a law was passed that Jewish people had to remain standing in university classes in Lwów and Weigl for his part rejected these policies for example by saying, 'Well I'm not gonna sit down until they can sit down' which is something that many of his colleagues were either too afraid or too prejudiced to do. But war was inevitable and German forces invaded Poland on September 1, 1939 followed by Soviet troops. And Poland was partitioned between the two.

During first the Soviet occupation and then the Nazi occupation of Lwów, Weigl was forced to keep working at his institute producing typhus vaccine. When so many other Polish intellectuals were being deported or imprisoned or just outright killed by both Soviet and Nazi troops, why were Weigl and his lab still there? Not just allowed to work but forced to work. Well it's because typhus was a terrifying threat and so Weigl's work was viewed as invaluable. And under German occupation Weigl's institute grew rapidly where it served as often the only means of survival for many Polish people who faced death, starvation, or deportation. Weigl went out of his way to hire hundreds of people as louse-feeders, often Polish intellectuals or Jewish people, people who were under incredible threat from Nazi occupation. And it's not certain exactly how many Polish people ended up working at the institute as louse-feeders but it's been estimated between 1200-3000.

Erin Allmann Updyke

Wow.

Erin Welsh

Which is a lot.

Erin Allmann Updyke

I also feel like this is one of those rare instances in this podcast where he's using humans in his research in a more ethical way.

Erin Welsh

Yeah, absolutely.

Erin Allmann Updyke

Like he's paying people, like it's a job.

Erin Welsh

Well I didn't include this but I also read that he was really hesitant or resistant to doing human trials of the vaccine. So he had developed this vaccine in theory but he was like, 'I don't wanna test it on anyone, it's dangerous to do.'

Erin Allmann Updyke

Yeah.

Erin Welsh

And so his research assistants took it upon themselves.

Erin Allmann Updyke

Wow.

Erin Welsh

One guy injected his wife with the vaccine and then let an infected louse feed on her. I was like excuse me, that's a bit extreme. (laughs) But yeah, so other people did the - I don't know if we can call them clinical trials but he did seem genuinely concerned.

Erin Allmann Updyke

Yeah.

Erin Welsh

And it is one of the rare instances. However don't speak too soon because there will be-

Erin Allmann Updyke

I've been waiting for it.

Erin Welsh

Yeah, yeah. The other shoe will drop.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah so all of these people, this was their lifeline, right, working as louse-feeders. And while feeding the lice people often sat around and chatted, exchanging ideas about philosophy or mathematics or I read one description about why salt is used to make ice cream but it's also used to melt roads, like melt ice on roads, so how does that work? And there are some great pictures of the louse feeding and some of these common areas where people are just sitting around with louse cages on their bodies. I'll try to post those. But the conversation during the louse feeding, it wasn't always about philosophy or even trivial things. About half of the feeders were actively working in the resistance and the louse feeding was a great cover, right, it allowed them to get out of the house and also to have free time for underground activities. And the institute wasn't just a place for resistance talk but also resistance action. Workers would sabotage the typhus vaccines intended for German soldiers, making them much less potent while tens of thousands of full strength doses were smuggled out of the lab and into the Jewish ghettos where lice infestation was incredibly high.

Erin Allmann Updyke

Wow. Oh my goodness.

Erin Welsh

Yeah. And just to illustrate again cause I think it's difficult to imagine how extreme infestation could be. So this is a quote from Henryk Szpilman, I know that I messed up that pronunciation and I'm sorry, describing lice in the Warsaw ghetto in his memoir 'The Pianist'. The lice, quote, "crawled over the pavements, up stairways, and dropped from the ceilings of the public offices. Lice found their way into the folds of your newspaper, your small change. There were even lice on the crust of the bread you had just bought. And each of these verminous creatures could carry typhus."

The black market vaccines from Weigl's lab did help save thousands of Jewish people from a death due to typhus but few of these people survived the concentration camps that they were ultimately sent off to. So I don't think that I've adequately described yet just how terrified the Nazis were of typhus and how they used this fear as an excuse to enact horrific policies. Because typhus wasn't seen as this universal threat from this bacterium or this louse, anyone could be impacted, it was of course blamed on Jewish people. Nazis used typhus as part of the justification for the construction of Jewish ghettos and public health orders for bathing and delousing often had this undertone of antisemitism, like beards were ordered to be shaved for instance.

And just to note that there are no new evil ideas under the sun, this was not the first time that an ethnic group was blamed for the spread of typhus and that typhus was used as an excuse for genocide and murder. For instance during WWI there had been brutal medicalized torture carried out on prisoners of war or political prisoners and also just straight up genocide, like when nearly 50,000 Armenian refugees were placed into concentration camps and most were murdered with typhus often used as an excuse. And upon entry into the Nazi concentration camps during WWII, people had to undergo disinfection and quarantine because the Nazi soldiers were incredibly scared of the disease spreading to them, hence the stripping and shaving and chemical baths. A single louse was sometimes used as an excuse to torture hundreds of people but these quote "sanitation efforts" did next to nothing to stop the spread of the disease among those imprisoned in the concentration camps and prisoner of war camps.

To illustrate, by November 1941 the German army had captured 1.5 million living Soviet prisoners of war and placed them in labor camps across Europe where 15,000 died of typhus each day. Yeah. With additional deaths due to starvation and cold and likely other infectious diseases. And this massive increase in typhus prevalence put Germany in a typhus panic by 1942 and they looked beyond vaccines for help to prevent the spread. Zyklon B was developed as a disinfectant for lice, as like a delousing agent, and it was found to be extremely successful in killing the lice but it was also found to be extremely toxic to humans. Of course this toxic side effect was included in the report of the chemical for the final analysis of this is where we stand in its development.

And Heinrich Himmler happened to read this report and he was like, 'Wait a second, I know where we can use this.' And so it gave him the idea to use it in gas chambers in concentration camps, like the fact that it was deadly to humans. And so Zyklon B gas which was originally developed as a delousing agent to prevent the spread of typhus was used to mass murder millions of people at Auschwitz and at many other concentration camps. I know, I'm sorry, this is a super difficult and sad and frustrating history to hear but I think it's important to learn and remember.

Erin Allmann Updyke

Yeah. You know when you learn or at least when I learned about the Holocaust you hear about diseases in abstract, like yes conditions were poor and infectious diseases rampant but to hear about it in more concrete terms, I think it's important context.

Erin Welsh

Yeah, exactly. Well put. I struggled with trying to articulate this in my notes and I was just like we need to learn about this. Yeah. So there's one more sad tidbit that I wanna share because I think again it's important to learn this history and then I'm gonna talk about maybe not uplifting but an inspiring part of the story. Despite all of these like I said sanitation efforts, despite all of this fear surrounding the spread of typhus in concentration camps, the disease continued to spread there, throughout the entire war. And I learned in researching this episode something I didn't know which was that Anne Frank likely died in a typhus epidemic that killed 17,000 people at Bergen-Belsen in the last months of WWII. Again like you said, we learned about these diseases in abstract, oh typhus killed this many people and typhoid killed this many and dysentery killed this many. But it's placing it in the context.

Erin Allmann Updyke

Yeah.

Erin Welsh

So there are no good estimates that I could find for the total number of people who died of typhus in concentration camps or prisoner of war camps during WWII but I'm sure that it's a staggering number. All right so now for a last maybe slightly less depressing bit of WWII history. There was a Polish physician and biologist named Ludwik Fleck who worked alongside Weigl in his laboratory during the 1920s. And like Weigl he worked on typhus vaccines and typhus biology but unlike Weigl, Fleck was Jewish and so was eventually excluded from academia entirely, like just prohibited from working there. And so he started a private lab and he remained connected to the academic community as much as possible.

And in many ways he was way ahead of his time than his peers in terms of the use of statistics in his research and also in his philosophical approach to science. He was interested in the sociology of science in the way that people thought about scientific questions, the philosophical matter of what is sickness and what is health? Where is that line drawn? And he felt very strongly that advancements in science and medicine were not made by one person but by a community working together, a concept that would inspire Thomas Kuhn when writing his 'The Structure of Scientific Revolutions' a couple decades later. And Fleck was also concerned with the growing division between science and the humanities and with the fact that as scientific knowledge grew it became more inaccessible to non-scientists. So I think we can really appreciate as a science podcast, we can really appreciate that last part in particular.

Erin Allmann Updyke

Yes.

Erin Welsh

But as a Jewish researcher in Nazi-occupied Poland, he was not free to express any of these thoughts really. And this is a very condensed version of Fleck's story and if you want to read more I will recommend a book called Dr. Weigl's fantastic laboratory. But anyway, during the occupation he was commandeered by SS doctors who first had him work at a Jewish hospital where he began working on a typhus vaccine to try to give to the Jewish patients that he treated and also smuggle it out to the ghettos as well. But unfortunately the Nazis grew suspicious that he was trying to help people and so they sent him and his family to first Auschwitz and then Buchenwald, not as prisoners per se although they were prisoners in everything but name, right, couldn't move freely. They always had the threat of death hanging over them.

But he was sent there to conduct research on typhus, specifically a vaccine. Horrifying medicalized torture plans were drawn up initially by the SS doctors in charge of course and there was medicalized torture carried out during WWII absolutely but thankfully those specific plans were not something that Fleck had to carry out. Rather he was tasked with making a vaccine for typhus to administer to Nazi soldiers. And he did was he was asked. But this vaccine was a vaccine in name only, it wasn't real. It didn't do anything.

Erin Allmann Updyke

Are you serious?

Erin Welsh

Yeah. He and some his colleagues who were in the know were making a fake vaccine that was just absolutely nothing that they sent out to the German troops while at the same time making a real vaccine that they administered to the people who were imprisoned in the camps.

Erin Allmann Updyke

Wow.

Erin Welsh

And they kept up the charade when anyone suspected them of not sending a real vaccine, like people would come back and be like, 'Hey, people are still getting sick, this vaccine isn't working.' And so then they had a little vial of real vaccine on the ready to be like, 'No, here it is, go ahead, test it, do what you want with it.' And they did this. I really liked really about that act of resistance. And they kept this up for quite a bit of time and the truth about this vaccine sabotage came out in the Nuremberg Trials for the Nazi doctors. And when they learned about it they were shocked and outraged, they were like, 'You haven't shown any humanity, how could you do that to us?' And literally when they said that people in the courtroom just laughed. They were like you haven't shown humanity because you gave fake vaccine to people who were literally carrying out genocide? Okay.

Erin Allmann Updyke

Wow.

Erin Welsh

Okay so going back to what I feel like is becoming the theme of the history section, in WWII people knew what the causative agent of typhus was, they knew how it was transmitted, they could test for it, they could vaccinate against it even, but yet it still infected and killed an untold number of people. People from whom treatment or vaccines were withheld intentionally, people who were forced to live in conditions that were absolutely perfect for the spread of typhus. Outside of the concentration camps typhus wasn't nearly as prevalent as it had been during the first world war. Most American troops for example were protected by the vaccine developed by Harald Cox at the Rocky Mountain Biological Labs in Hamilton, Montana. And shortly after the war chloramphenicol and other antibiotics were found to be effective against typhus which did help bring down the mortality rate. But again, typhus lingers. Like it still lingers. It infected and killed many people in the gulag in the Soviet Union for instance and it often pops up when large groups of people are displaced due to conflict or ecological crisis.

So I think I have three take-home points from this, at least three, I mean probably more that I'll realize but whatever. Number one, typhus is much more devastating and has had much more of an impact than I realized before doing this episode. Like wow, yeah. And number two, it just reinforces again the idea that medical technology and knowledge alone doesn't prevent disease. And three, that typhus may seem like a disease of the past, like a disease just in the history books but it's still here and it's unlikely to go away forever. It can and has popped up in these times of conflict, of food shortages or ecological disasters and more of those are on the horizon.

Erin Allmann Updyke

Yeah.

Erin Welsh

And I don't really get the sense that we're prepared for that. So Erin, what's going on in the world of typhus today? How was that segue?

Erin Allmann Updyke

Oh gosh, Erin. Let's try and figure it out together.

Erin Welsh

Okay, I like that. I can do that.

Erin Allmann Updyke

Right after this break.

TPWKY

(transition theme)

Erin Allmann Updyke

It turns out, Erin, it is incredibly difficult to get solid numbers on epidemic typhus. Like honestly more so than I think any disease that we've covered so far.

Erin Welsh

Whoa.

Erin Allmann Updyke

The World Health Organization doesn't even have a page or a facts sheet on typhus or any of the typhus fevers. I am shocked at how tough it was. I do not have for you global estimates, period. That's period.

Erin Welsh

Okay.

Erin Allmann Updyke

Okay.

Erin Welsh

Like I can't tell if that's reassuring or disturbing or both at the same time.

Erin Allmann Updyke

Well I think it's both. So let's talk about the numbers I do have. So from 1980-1990, so in that 10 year period, there were just over 20,000 cases reported worldwide from at least one source that I found. So at least we have those numbers, right. But like you mentioned, this is a disease that tends to happen in clusters, in these outbreaks under certain circumstances. So in 1997 there was an outbreak largely in Burundi that caused an estimated over 100,000 cases.

Erin Welsh

Wow. Yeah, that's an incredible number.

Erin Allmann Updyke

This is 1997. We have treatment and yet the case fatality rate in that outbreak is estimated to be 15% which is devastating.

Erin Welsh

It just goes to show again, it's like what does that knowledge do if you can't actually apply it?

Erin Allmann Updyke

Right. Exactly, exactly. And to try and get more recent numbers I found a bunch of papers looking at largely this group that I mentioned at the very top of the episode, these typhus group rickettsioses. So there's a number of epidemiological studies or review papers that I found that were trying to get at the epidemiology of these typhus group rickettsioses. So one of them was looking at these typhus rickettsioses in China from 2005-2017 and that paper determined that there was a total of 29,000 cases reported in that 12 year period but it didn't distinguish between epidemic typhus and what they called endemic or this flea-borne or murine typhus. But it noted that just based on the epidemiologic patterns, most of these cases fit the seasonal distribution and the kind of ecological distribution of endemic typhus, not epidemic typhus.

Erin Welsh

Okay.

Erin Allmann Updyke

So that doesn't give us a lot of information about what we're focusing on for this episode but suggests that the majority of typhus rickettsioses in China from 2005-2017 was not epidemic typhus, so very low numbers if any potentially. On the contrary a similar dataset in the US that was looking at data just from one healthcare insurance group from 2003-2016 identified just over 1700 cases of typhus rickettsiosis, again this is just one healthcare group in the US but around the same period of time. And in that case over 50% of those were actually determined to be epidemic typhus and about 40% were endemic or flea-borne typhus and the rest maybe some other rickettsiosis. So that's quite different.

Erin Welsh

Yeah.

Erin Allmann Updyke

Another study that was looking at febrile illness in kids in Kenya, so this is just in children and this is just sort of a cohort study, this is from 2011-2012. They found that 1.5% of kids that came in with a fever tested positive for typhus group rickettsiosis. But again, this doesn't distinguish between epidemic and murine or endemic typhus. Yeah. And that paper also only had 360 kids so it's low numbers to begin with.

Erin Welsh

And the treatment for those two things is the same, right?

Erin Allmann Updyke

It is, yeah.

Erin Welsh

Okay.

Erin Allmann Updyke

The treatment for all of the rickettsioses is the same as well as scrub typhus too. So that's at least convenient.

Erin Welsh

That is quite convenient, yeah.

Erin Allmann Updyke

And another paper from the early 2000s that was looking at northern Africa, I was trying to get as global as I could, I didn't do a great job but a paper that was looking in northern Africa found no cases of epidemic typhus and all of the cases they detected that reacted as positive for *Rickettsia prowazekii* turned out actually to be *Rickettsia typhi* so it was all the endemic or murine typhus in that one study. So none of that gives us very much information to work with to try and understand anything close to an annual number or anything like that.

Erin Welsh

Well so okay, people are clearly still infected or becoming infected occasionally.

Erin Allmann Updyke

Right.



Erin Welsh

So is that evidence of Brill-Zinsser disease or is it just the fact that the conditions aren't often met?

Erin Allmann Updyke

Right, it's so many good questions, Erin.

Erin Welsh

Yeah.

Erin Allmann Updyke

So in the US most of the sporadic cases are associated with flying squirrel. So bizarre but true. In other places it's very possible that maybe there's a case of Brill-Zinsser that then becomes a couple sporadic cases of epidemic typhus actually transmitted by lice. But because conditions aren't perfect don't result in a huge epidemic. But we just don't have the numbers to know. And then it's also hard because in truth our diagnostics are not great and so really getting a handle on is it endemic typhus or is it epidemic typhus, you can look at the clinical picture like is it a less severe disease or is it more severe but that's not perfect and a lot of times the tests that we have will cross-react with a number of different rickettsiosis. So in a lot of parts of the world we don't have great diagnostics, we're not getting down to that nitty gritty.

Erin Welsh

And if the treatment for the two is the same-

Erin Allmann Updyke

Then does it matter?

Erin Welsh

Yeah, I mean it does in the epidemiological sense but for a doctor treating a patient-

Erin Allmann Updyke

Right, it doesn't. Exactly.

Erin Welsh

Does not.

Erin Allmann Updyke

Well it does though if there are lice, right.

Erin Welsh

True.

Erin Allmann Updyke

So let's talk about that for a second.

Erin Welsh

Yeah, I was gonna say how many people have lice? Body lice, head lice, etc.

Erin Allmann Updyke

I don't have a number on how many people have it.

Erin Welsh

That would be a hard number to get but yet.

Erin Allmann Updyke

That would be incredibly more difficult than typhus. (laughs)

Erin Welsh

Yeah.

Erin Allmann Updyke

But like you said Erin, lice are absolutely globally distributed. Body lice infestations occur worldwide and predominantly they tend to affect areas or populations that don't have access to either change their clothes daily or to clean and dry their clothes in a way that actually kills the lice that are living there. So very frequently outbreaks of lice infestation will follow large scale disasters like you talked about a lot in the history section, Erin. Natural disasters, war, political upheaval, refugee camps. In urban settings body lice are also very prevalent among those experiencing homelessness. And I think I touched on this in our Bartonella episode but in studies in the US and Europe anywhere from 5-30% of unhoused people are found to be suffering from body lice.

Erin Welsh

Yeah.

Erin Allmann Updyke

And what all of these situations have in common of course is things like crowding and poor sanitation which lead to very efficient person to person transmission of body lice and persistence and transmission of these lice on clothing. So I think there's a lot of things that contribute to epidemic typhus especially although I want to point out that scrub typhus, one paper that I read suggested that it's possibly the single most neglected disease of all time. So I was like ooh, very interesting.

Erin Welsh

Well and I definitely think we should do an episode on it at some point in the future.

Erin Allmann Updyke

Yeah, it's very interesting. It's a very interesting one just in terms of how little people study it. But I think some of the big things that contribute to epidemic typhus being relatively understudied, definitely I would assume though I don't have numbers on it, underfunded compared to a lot of other diseases today despite it being such a massive problem historically is because I think it's very easy to ignore the most vulnerable populations who are the ones that are most likely to be affected by epidemic typhus in the case of an outbreak, right.

Erin Welsh

Right.

Erin Allmann Updyke

And it is in fact these most vulnerable populations, forcibly displaced migrants of which there are an increasing number year after year. And we talked in our dysentery episode about how many hundreds of millions of people live without access to sanitation and clean water facilities. If you don't have access to that, how are you going to keep lice off of your clothing?

Erin Welsh

Right.

Erin Allmann Updyke

Right?

Erin Welsh

Yeah.

Erin Allmann Updyke

And it's essentially inevitable at this point that even barring any political instability or wars that may break out, climate change is going to result in increasing numbers of displaced people as the frequency and severity of natural disasters continues to increase. So yes.

Erin Welsh

Yes, yes, yes.

Erin Allmann Updyke

Epidemic typhus might not E. coli a problem right at this moment for much of the world however-

Erin Welsh

We can not get comfortable with that thought.

Erin Allmann Updyke

No, we really can't. We really, truly can't.

Erin Welsh

And we shouldn't be comfortable at this moment anyway considering the fact that there are people who if typhus were to break out would be very susceptible, very vulnerable.

Erin Allmann Updyke

Exactly because we know that things like malnutrition and all of these other things that go along with increasing your risk for severe disease or death, all of those things go hand in hand. It's really like tornado's perfect storm of the kinds of situations that lead to these epidemic typhus outbreaks.

Erin Welsh

Yeah. I think that we often touch on the devastation that climate change could have and it is in a more abstract sense, right. Every time that we talk about it we're like well it's gonna cause food instability, it's gonna cause a large movement of people, it's gonna cause etc etc. But part of me wonders whether we're in this nice little dip in the history of typhus, right. Right now it declined rapidly and there's not really much going on but it's really hard to see any way that it would stay at such low levels in the future.

Erin Allmann Updyke

Honestly this Season 5 opener is going to be akin to our Season 1 opener where people listen to it several years later and are like, 'Oh, how did you guys predict that?' Which is so interesting though because it's one that I never learned a lot about it in any of my epidemiology classes or in anything, you know. It's epidemic typhus. And I mean it is treatable so there's that.

Erin Welsh

Right.

Erin Allmann Updyke

But are you going to be able to get not only antibiotic treatment but also delousing treatment available to everyone in the midst of a disaster? No, you're not. It's not realistic.

Erin Welsh

It's not realistic, yeah. And I think it's interesting too like I read this somewhere and I think Erin you and I were talking about this but most typhus experts around the world today have never seen an actual case of epidemic typhus.

Erin Allmann Updyke

Right, yeah. Maybe you've seen endemic typhus, maybe scrub typhus.

Erin Welsh

Yeah, not likely epidemic typhus. Yeah. This is a very big episode which we always say.

Erin Allmann Updyke

Hopefully we've helped someone make a case for funding.

Erin Welsh

Yeah. I mean I think that's not the only answer but I think it is a big answer to understanding not just basic research like where did *Rickettsia prowazekii* come from? Are body lice and head lice two different things?

Erin Allmann Updyke

Right.

Erin Welsh

That basic foundational knowledge but also applied information and programs to help delouse and to help keep people from being so susceptible to louse-borne diseases.

Erin Allmann Updyke

Right. And because I don't think that this was made clear because you talked a lot about the various vaccines that have existed in the past, no vaccine exists today.

Erin Welsh

Oh right, yeah.

Erin Allmann Updyke

Period.

Erin Welsh

I was going to ask but I kind of assumed. I feel like that's been the case for a few historic vaccines.

Erin Allmann Updyke

A lot, yeah. And it's really because there have, like you said, been a lot of various different vaccines that have shown varying degrees of effectiveness but none of them have been safe or effective enough to be licensed currently and because of lack of funding and lack of a perceived market there is no vaccine currently.

Erin Welsh

Lack of a perceived market...

Erin Allmann Updyke

Yeah.

Erin Welsh

Well.

Erin Allmann Updyke

On that note.

Erin Welsh

Yep, in typical TPWKY fashion we really started off with a depressing episode. But it's important again.

Erin Allmann Updyke

I think it's a really interesting one in so many different ways.

Erin Welsh

It is.

Erin Allmann Updyke

So at least there's that.

Erin Welsh

Well okay, on that note, shall we do sources?

Erin Allmann Updyke

We should, yeah. We shall.

Erin Welsh

Okay. I had a few books and a bunch of papers. The first book is 'The Fantastic Laboratory of Dr. Weigl' by Arthur Allen and that's all about like I said Dr. Weigl and Dr. Fleck and it's a really interesting read, very thorough look at a very small part of history which is fascinating. And then also that collection of short stories called 'Ship Fever' by Andrea Barrett. 'The Great Hunger: Ireland 1845-1849' by Cecil Woodham Smith. And the firsthand account came from 'The Ocean Plague' by Robert Whyte. And then of course I have to mention one of the most classic books in disease history, the history of disease, even though it's not a great history of disease book but it's an interesting book. Anyway it's called 'Rats, Lice, and History' by Hans Zinsser. And I have a ton of papers, I'm gonna put them all on the website so please take your pick of them.

Erin Allmann Updyke

Yeah. I also had a very large number of papers for this episode. I have affair number on both scrub and murine typhus so if this episode left you hungry for more on those there's a bunch of papers on both the biology and epidemiology of those. I think one of my favorite papers just on the general biology of typhus was just called epidemic typhus and that was published in The Lancet Infectious Diseases in 2008. But there were a whole bunch more including all of the epidemiological studies that I mentioned at the end. So you can find all of our sources from this episode and every one of our 85 other episodes on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com).

Erin Welsh

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

Erin Allmann Updyke

Thank you to the Exactly Right network of whom we're so proud to be a part. Have you listened to all of the other Exactly Right podcasts yet? You should.

Erin Welsh

You should. And thank you to you, listeners, for tuning into our season opener, we hope you liked it.

Erin Allmann Updyke

It's gonna be a good season.

Erin Welsh

I think it is. I know it is. I feel it is.

Erin Allmann Updyke

And an extra thank you to our patrons, we love you so much.

Erin Welsh

We truly, truly do. Okay well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.