

TPWKY

This is Exactly Right.

Erin Welsh

"Every September, like many, I feel sick and frightened around the anniversary of the 9/11 attacks. But it was the weeks following September 11th that would forever change my life. During that time I was the victim of terrorism when I opened a letter containing a lethal amount of anthrax. Around September 18th, 2001 I headed to work as a desk assistant at NBC Nightly News. One of my jobs was opening Mr. Brokaw's mail. There was one letter that looked as if it were written by a child. Something seemed unusual, I had never seen a letter containing a granular substance. I mentioned this strange letter to my friends. Nothing happened for about 10 days, then one Friday night my throat began to swell up. A cold, I thought. But it worsened over the weekend. My glands were soon enormous. Monday morning came and my face was barely recognizable. I went to the doctor who said it was a reaction to my Accutane medication and I should rest in bed. A few days later I went back to work but I still felt a bit off.

A week or so after I was sick Mr. Brokaw's assistant became sick. Both of our symptoms were unusual. Authorities became involved. When Bob Stevens died at the American Media building in Florida at the end of September, the pieces slowly began to come together. I soon learned why I had been sick: anthrax poisoning. Like Mr. Brokaw's assistant I had contracted cutaneous anthrax. The events over the next few months changed my life. I had carried anthrax back on my clothes and had contaminated my home. I chose to have all of my things destroyed. I lost my most personal belongings, all my precious pictures and mementos. I worried I might die. I'll have to see doctors the rest of my life. I'll never have an overall sense of security again, that's what I lost. But what I gained was the deep, true appreciation for my family, friends, and coworkers whose support was incredible."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

Whoa.

Erin Welsh

Yeah. So that was an account of Casey Chamberlain written in 2006 and I will post the link to the full account on our website. And it was in regards to the 2001 anthrax letters.

Erin Allmann Updyke

I remember that.

Erin Welsh

Oh yeah, I remember that too. 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

Obviously today we're talking about anthrax.

Erin Welsh

Obviously yes, yes we are. This is such first season type of material, Erin.

Erin Allmann Updyke

It's big. It's a big one.

Erin Welsh

It's a big one. And it makes me kind of happy that we've already done some of the enormous ones because I think now at this point I would be so perfectionistic and so, 'Oh gosh, I didn't get this and oh I should talk about this too' and the episodes would be like 8 hours long.

Erin Allmann Updyke

I mean is that not what we're about to get into?

Erin Welsh: Okay yeah, it's gonna be pretty long. But it's gonna be fun, it's gonna be really interesting. The scope of this is huge.

Erin Allmann Updyke: Massive.

Erin Welsh: And we've got some very exciting guests to bring on.

Erin Allmann Updyke: We really do.

Erin Welsh: We really do. But first-

Erin Allmann Updyke: But first-

Erin Welsh: It is-

Erin Allmann Updyke: Quarantini time! You know I always check my imaginary watch when I say that?

Erin Welsh: Oh I like it. Does that mean it's always quarantini time on your imaginary watch?

Erin Allmann Updyke: Yes it is. (laughs)

Erin Welsh: So what are we drinking this real quarantini time, non-imaginary quarantini time?

Erin Allmann Updyke: We're drinking Spore Me Another. Get it?

Erin Welsh: What is in Spore Me Another?

Erin Allmann Updyke: It's basically a stout float.

Erin Welsh: Yeah. And you can kind of go wild with it, like coffee stout, milk stout.

Erin Allmann Updyke: Chocolate stout.

Erin Welsh: Chocolate spicy chili stout, I don't know.

Erin Allmann Updyke: Whatever.

Erin Welsh: Whatever. And whatever ice cream you want. I have chocolate chip cookie dough currently so that's what I'm doing.

Erin Allmann Updyke: Yum.

Erin Welsh: Yeah. We will post the full recipe for the quarantini and the nonalcoholic placeborita on our website thispodcastwillkillyou.com as well as all of our social media channels. So make sure you follow us to make yourself a Spore Me Another.

Erin Allmann Updyke: Yeah, exactly. What other business do we have today, Erin?

Erin Welsh Well we can just go through the usual suspects. Check out our website thispodcastwillkillyou.com. You can find things like all of our sources for each episode there as well as transcripts, alcohol-free episodes, links to our Goodreads list, bookshop.org affiliate account, music by Bloodmobile, our awesome, cool merch, there's Patreon links. There's honestly so much more, go check it out.

Erin Allmann Updyke And you can also listen to this episode and all of our past and future episodes on Amazon Music, Apple, Stitcher, or wherever you get your podcasts.

Erin Welsh All right, should we dive in?

Erin Allmann Updyke Let's do it. Right after this break.

TPWKY (transition theme)

Erin Allmann Updyke So anthrax. We touched on this ever so briefly in our sweating sickness episode.

Erin Welsh Yes.

Erin Allmann Updyke Which probably honestly just angered people, they were like, 'What? That's all?'

Erin Welsh Well and that's why we're doing it right now so that you get the full picture.

Erin Allmann Updyke Exactly. Yeah. So anthrax really is the name of the disease that is caused by this particular bacterium. But I just wanna say up front that there's a really good chance that I'll probably just say anthrax at some point when I'm referring to the bacteria. So just bear with me.

Erin Welsh Oh I'm gonna do that a lot.

Erin Allmann Updyke Okay, good.

Erin Welsh Probably.

Erin Allmann Updyke So we'll both just do that and make someone angry.

Erin Welsh Yeah.

Erin Allmann Updyke But anyways, the bacterium which causes anthrax is known as *Bacillus anthracis*, this is a gram-positive, spore-forming, rod-shaped little bacterium. And we'll talk a lot more about the importance of those spores as we go through this episode.

Erin Welsh Oh yeah.

Erin Allmann Updyke They're the most important thing. And this bacterium is related to a pretty large group of other bacterium in the group known as *Bacillus cereus*. But for the most part what I think is so interesting is that *Bacillus anthracis* is one of the most genetically monomorphic, meaning there is not a lot of genetic variation in this species across the entire globe.

Erin Welsh It's kind of bananas.

Erin Allmann Updyke

It really is. Like this is a bacterium that is very ubiquitous, it's found across the whole globe and yet if you grab one anthrax bacterium from Siberia and another from North America, they're gonna be so similar. It's fascinating. And for the most part this is the only species in the large B. cereus group that usually causes serious disease in humans. But there is a serovar of B. cereus that can cause a disease very similar to anthrax and we'll probably touch on that a little bit more later in this episode. But where I wanna start is with the life cycle of this pathogen because by going over its life cycle we'll learn who tends to get infected or affected by anthrax and we'll learn how it's transmitted and then we can get into how it actually causes all of the damage and then what those symptoms look like in humans. Okay?

Erin Welsh

Sounds good.

Erin Allmann Updyke

So Bacillus anthracis spores are where we're gonna start. These spores exist in the soil and on vegetation, like I said, pretty much worldwide. They can persist in a huge range of environmental conditions across the globe for years or in some cases decades or maybe centuries. These spores don't really replicate probably - asterisk, we're not sure.

Erin Welsh

Asterisk.

Erin Allmann Updyke

They just mostly hang out in the environment. And then at some point they're ingested, most commonly by herbivorous mammals, especially large ungulates like cattle or zebras or hippos or antelope or goats, whatever. And then because these herbivores often eat things like spiky grasses for example, they might have small abrasions throughout their gastrointestinal tract. And these spores can then enter into the animal's bloodstream through these little openings, these little cuts in their mucosal lining. Once those spores are introduced into the bloodstream they're promptly engulfed by macrophages which are white blood cells. And that is where the trouble starts. The spores inside these macrophages are activated back into full-fledged bacteria and they begin to replicate, often in the lymph nodes which is where these white blood cells are traveling to. And these bacteria that are replicating burst out of macrophages, they travel throughout the bloodstream, they replicate and replicate and cause overwhelming infection that almost inevitably leads to the death of the host.

Erin Welsh

It's sad.

Erin Allmann Updyke

It's absolutely devastating. And in many species of animal this generally happens so suddenly that very often the first symptom of infection in a herd is just the sudden death of one animal followed by many more. And it happens so quickly. Incubation period is often as short as 36-72 hours.

Erin Welsh

How? It's so fast.

Erin Allmann Updyke

So fast. And what's important is that when the host dies, in so doing they release billions, billions of vegetative bacteria, so the anthrax bacteria. Upon contact with the air in the environment, these bacteria sporulate, they form those spores again, they are released into the environment, and thus complete their life cycle.

Erin Welsh

It's just like botulism where we were like, 'Why does it kill you?'

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

It's because it needs to kill you in order to be transmitted.

Erin Allmann Updyke

It has to. Exactly. Exactly! Fascinating. Okay so obviously my favorite question to try and answer is how? How can this kill so quickly?

Erin Welsh

Yeah Erin, how?

Erin Allmann Updyke

Okay, let me tell you. So *Bacillus anthracis*, anthrax, has a couple of different virulence factors which are the things that bacteria have that make us sick or animals sick and allow them to be pathogenic. They have one virulence factor that makes a capsule, so it's like a little capsule that surrounds the bacteria that makes it really hard for immune cells to actually engulf and get rid of those bacteria via phagocytosis.

Erin Welsh

Oh okay.

Erin Allmann Updyke

So that's one but it's not the most important. Well it is essential but the other ones are more exciting. The other virulence factor they have encodes two different exotoxins. We've talked about toxins a fair amount on this podcast but it's been I think kind of a little while. So as a refresher, toxins are generally usually proteins that bacteria or other organisms can make that cause us harm in some way. In the case of *Bacillus anthracis* there's two different exotoxins which are called edema toxin and lethal toxin.

Erin Welsh

Ooh. Let me guess what the second one does.

Erin Allmann Updyke

Yeah, yeah you're right. And so each of these two different toxins is made up of two proteins. They're each made up of one part a protein called protective antigen, PA, and then lethal toxin is made up of PA plus lethal factor which is another protein, and then edema toxin is made up of the PA plus edema factor which is another toxin. And they do like what you said, like what it sounds like they do. The protective antigen part of each of these toxin protects the toxin itself and makes sure that the toxin can make its way into our cells. And then you have edema factor which causes a lot of inflammation and swelling and lethal factor which causes mostly cell death, especially of white blood cells.

Erin Welsh

What's the mechanism of cell death?

Erin Allmann Updyke

I knew that you were gonna ask so let me scroll to my 'specific questions Erin is going to ask me' section. It's via a caspase-1-dependent cell death program known as pyroptosis.

Erin Welsh

I almost wish I didn't ask.

Erin Allmann Updyke

I know! I know. So these specific mechanisms of action of both lethal toxin and edema toxin are absolutely fascinating and they've been studied in great detail, I have a ton of papers that people can read if they wanna know this specific cell like receptor by receptor detail of how these work. But essentially to go over just the broad strokes of it for the sake of this podcast, the toxins both together have actions both in the early phase of infection where these toxins serve to downregulate and suppress our immune response. This is what allows for *Bacillus anthracis* to persist and replicate within our bodies so that you have a huge number of bacteria in the blood.

Erin Welsh

Oh okay.

Erin Allmann Updyke

And then later in the course of infection these two toxins together create the edema, so the swelling, vascular collapse, and eventually shock that does lead to death which like you said Erin is pretty much an essential part of the natural history of this pathogen.

Erin Welsh: And it's also like for at least in the 20th century there was the prevailing thought that pathogens will evolve to be more mild, that's just the way evolution works, and this is case in point that does not happen.

Erin Allmann Updyke: Yeah.

Erin Welsh: Not necessarily.

Erin Allmann Updyke: I mean not for a pathogen like this, right.

Erin Welsh: Yeah, right.

Erin Allmann Updyke: For something where the host has to survive in order to transmit, yes. But this is not a directly transmitted pathogen, this is essentially an environmentally transmitted disease.

Erin Welsh: It's fascinating. This is why mode of transmission and virulence I think are just still two of the most fascinating topics or one of the most fascinating topics.

Erin Allmann Updyke: Oh I agree, absolutely amazing. Last point I wanna make about these virulence factors, and this gets back to what we were talking about with this new serovar of *Bacillus cereus* that we've seen. Both of these virulence factors, so the capsule and the two toxins, both of them are required in order for anthrax to be pathogenic, like to cause anthrax, but both of these virulence factors are encoded on plasmids which are circular little pieces of DNA that are not part of the main genome.

Erin Welsh: Right.

Erin Allmann Updyke: Which means they can be passed back and forth from bacterium to bacterium.

Erin Welsh: But how often does that happen, the passing back and forth?

Erin Allmann Updyke: It's a really good question, especially in a bacterium like *Bacillus anthracis* which for the most part we think doesn't replicate well in the environment, how often is it going to be even coming in contact with other bacteria to be transmitting and passing plasmids? I don't know the answer to that, it's a really interesting question though.

Erin Welsh: So I know there has been some evidence that they form biofilms but I don't know if that's just from like one individual bacterial cell.

Erin Allmann Updyke: Yeah and from what I understand, while *Bacillus anthracis* can't in theory replicate in the soil, like they don't need to be inside of a host to replicate necessarily, they're really bad competitors.

Erin Welsh: Right.

Erin Allmann Updyke: So for the most part in the environment, even if they could try and replicate, they're just not good at it and so they get out-competed.

Erin Welsh: Okay. Cool.

Erin Allmann Updyke

Yeah. Fun question, Erin. Okay. So now what does this actually look like in humans?

Erin Welsh

Yeah.

Erin Allmann Updyke

That's what we usually talk about on this podcast. And how do humans get exposed? There are a few different ways that humans can become infected. There's three main routes that you can get infected: cutaneous anthrax when spores enter through breaks in your skin, you can get gastrointestinal anthrax if you ingest the spores very similar to how most animals become infected, or you can inhale the spores which results in inhalational anthrax. So let's go through each of these one by one. The cutaneous form worldwide by far is the most common in humans, something like 90-95% of cases worldwide are cutaneous anthrax. So this is when spores enter through a cut in your skin. Just like in animals, like I described for the main transmission cycle or main life cycle of this pathogen, the replication still happens in macrophages. But in the case of cutaneous it tends to be those macrophages that stay locally in the skin surrounding where the spores were introduced or in nearby lymph nodes. So let's say you get a cut on your arm, then maybe you'll get swelling in the lymph nodes under your armpit.

Erin Welsh

Okay.

Erin Allmann Updyke

The first symptom that you usually see is just a little bump, that's it, just a little bump. It's generally painless but it's often quite itchy and this happens anywhere from 1-12 days after exposure. But usually that little bump starts to get swollen, like all around it there starts to be some swelling, more than you would expect from something like a regular bug bite. And the this bump gets surrounded either by small little vesicles, little fluid-filled blisters all around the bump or one large, 1 or 2 centimeter blister that kind of encompasses that initial bump.

Erin Welsh

Anyone right now who has a bug bite is staring at it intently.

Erin Allmann Updyke

I know. (laughs) It's gonna get worse, I keep going.

Erin Welsh

Hopefully your bug bite won't.

Erin Allmann Updyke

And this blister, it's filled with clear fluid. So it looks at first especially a lot like the kind of blister that you might get on the back of your heel after you walk all day in new shoes, you know those really taut, fluid-filled blisters?

Erin Welsh

Oh I'm familiar.

Erin Allmann Updyke

But unlike those blisters on your heel, it is surrounded in a wide margin by what they call gelatinous edema.

Erin Welsh

Oh boy.

Erin Allmann Updyke

So swelling that makes your skin feel like there's jello underneath it.

Erin Welsh

That is disturbing.

Erin Allmann Updyke

Mm-hmm.

Erin Welsh

(laughs) You're just like, 'Mm-hmm, yeah it is'.

Erin Allmann Updyke

Often people might also have some low grade fever, maybe they're feeling kind of crappy, and then this vesicle, this blister enlarges and eventually it pops just like the blister on your heel except that this blister leaves an ulcer, a pretty sizable one potentially. And this ulcer progresses into a black eschar which is kind of like a really, really gnarly-looking scab.

Erin Welsh

Okay.

Erin Allmann Updyke

That's the best way I can describe it, it's like completely black. It's basically entirely dead, necrotic tissue that's pretty characteristic of cutaneous anthrax.

Erin Welsh

How deep is that?

Erin Allmann Updyke

Good question. Not necessarily that deep but they can be quite large, like encompass a pretty large area. They don't tend to scar.

Erin Welsh

Oh interesting, okay.

Erin Allmann Updyke

Yeah. But what's much worse even is the edema. So the swelling is still present and often it continues to grow and especially if the lesion instead of on your arm was near your face or your neck, the swelling can get so intense that it can block your airway.

Erin Welsh

Oh my god. And it's still gelatinous?

Erin Allmann Updyke

Yeah, it's like a gelatinous... (laughs) Your face.

Erin Welsh

(laughs) I'm just imagining pressing down on my skin and just feeling like jello underneath it.

Erin Allmann Updyke

Yeah.

Erin Welsh

That would be very alarming to say the least.

Erin Allmann Updyke

Very alarming. Very alarming is a good description.

Erin Welsh

Yeah.

Erin Allmann Updyke

And while cutaneous anthrax is the least lethal of the three forms and in many cases these eschars heal over the course of 2 to 3 to 6 weeks, especially if this edema is near the face or neck it can be fatal because of just how much swelling you get or if this extends beyond just a local infection and does cause a more systemic infection. So if cutaneous anthrax is untreated, mortality ranges from 5-20% although I have seen estimates as high as 30% or more. With antibiotics though mortality is less than 1%. So that's good.

Erin Welsh

Excellent. Which antibiotics by the way? I can't remember.

Erin Allmann Updyke

Oh a whole range of antibiotics.

Erin Welsh

Okay.

Erin Allmann Updyke

You can use penicillin, you can use clindamycin, you can use doxycycline. All kinds.

Erin Welsh: That's good.

Erin Allmann Updyke: Yeah.

Erin Welsh: Resistance?

Erin Allmann Updyke: Very little.

Erin Welsh: Great.

Erin Allmann Updyke: Yes.

Erin Welsh: Figured.

Erin Allmann Updyke: So moving onto the next most deadly form and that would be gastrointestinal anthrax. In a lot of ways you can actually think of gastrointestinal anthrax as cutaneous anthrax but in your guts.

Erin Welsh: So jello guts.

Erin Allmann Updyke: Jello, yeah. Guts, not exactly. But kind of. Let me go into detail.

Erin Welsh: Okay.

Erin Allmann Updyke: So gastrointestinal anthrax is really how anthrax is spread in its enzootic cycle, right. Herbivores are most often infected while grazing on grass or ingesting soil that's contaminated with anthrax spores. So while humans could be infected that way, most commonly humans get infected with gastrointestinal anthrax by ingesting meat that is contaminated with the spores. And there are two different forms of gastrointestinal anthrax depending on where the spores enter your body and break through your mucosa. Either oropharyngeal, so in the back of your throat, or truly intestinal, in your intestines. But pathologically both essentially result in ulcer formation, not dissimilar to the ulcers that you see on the skin but as you can imagine ulcers in your throat or your intestine are a much bigger problem than on your skin because they can lead to perforation.

Erin Welsh: Yeah.

Erin Allmann Updyke: (laughs) Your face.

Erin Welsh: Sorry it just sounds really painful.

Erin Allmann Updyke: It's not great.

Erin Welsh: I know you said the ulcer is not painful, right.

Erin Allmann Updyke: That's what they say, I don't know. They look awful.

Erin Welsh: Gosh.

Erin Allmann Updyke: So supposedly they're just itchy.

Erin Welsh: It just still seems highly uncomfortable.

Erin Allmann Updyke: I'mma get more uncomfortable.

Erin Welsh: Wonderful.

Erin Allmann Updyke: Okay.

Erin Welsh: That's what this podcast is about.

Erin Allmann Updyke: So remember when I said that often the bacteria travel to your lymph nodes and you get a lot of swelling in your lymph nodes. If this happens in your guts, you get swelling or lymphadenopathy in the lymph nodes in your throat potentially if we're talking oropharyngeal infection, or in the mesentery which is the connective tissue that holds your guts in place. We have a ton of lymph nodes in there and if those become severely inflamed and very swollen, that can lead to potentially intestinal obstruction. It can also lead to ascites which we've talked about a fair number of times on this podcast but that's basically the buildup of fluid in your abdomen because the blood vessels and the lymph nodes, the whole lymph system that should drain fluid gets congested because of all this swelling. You can, through these ulcers or through just ischemia because of all the swelling, you can get perforation of the bowels which is a pretty serious emergency.

And because we're talking about becoming infected through the mucosa, so through a cut in your gastrointestinal tract rather than through your skin which is quite thick, this disease is far more systemic than cutaneous anthrax. So it makes its way into your bloodstream much more easily than from our skin. And for that reason the mortality rate is much higher, it's usually 25-60% if untreated.

Erin Welsh: I have a question.

Erin Allmann Updyke: Yes, Erin.

Erin Welsh: So you mentioned that Bacillus anthracis is not a good competitor. Does any of that potentially have anything to do with the gut microbiome and not being able to establish there? Or is it not really that because it's perforations in your gut?

Erin Allmann Updyke: Yeah so that's a really interesting question. I haven't read anything on this, I don't know that there's been studies on it so I can't answer it with data but I can tell you based on what I know of the life cycle. It enters our gut as spores, it's not establishing an infection in our gut.

Erin Welsh: Okay.

Erin Allmann Updyke: So it's not gonna be competing with any other bacteria that live in our gut that are commensals. And what's really interesting about this pathogen is that even though it's not intracellular, so it doesn't live its life inside of our cells, it does necessarily have to enter macrophages, we think, in order for the spores to reactivate and become replicating bacteria again.

Erin Welsh: Okay. So it's able to sort of sneak in under the guise of macrophages and then get to high enough volume or whatever.

Erin Allmann Updyke	Exactly.
Erin Welsh	Interesting, okay.
Erin Allmann Updyke	Yeah.
Erin Welsh	Cool.
Erin Allmann Updyke	And I do also think it's interesting that for the most part it does need, we think at least, it needs a break in the mucosal lining, it can't just like other bacteria we've talked about on this podcast do, it can't burrow its way through our mucosa on its own, it has to enter through a wound of some kind that's already there. And so I wonder if that plays a lot into why different animals are differentially susceptible based on what they're eating and how likely they are to have some kind of...
Erin Welsh	How much roughage is in their diet?
Erin Allmann Updyke	Exactly.
Erin Welsh	How much Cap'n Crunch they ate? Just these abrasions everywhere.
Erin Allmann Updyke	(laughs) That's so true. That's really, really interesting. Okay anyways, that's gastrointestinal anthrax. Do you have any more questions about that one?
Erin Welsh	I don't think so.
Erin Allmann Updyke	Symptoms, you have abdominal pain, nausea, vomiting, fever, diarrhea, and then you pretty much die very rapidly.
Erin Welsh	And you die because of all the same things. Is it diarrhea, what?
Erin Allmann Updyke	Yeah, we're gonna talk a little bit more about the mechanisms when we get to the next form which is the deadliest form which is inhalational anthrax.
Erin Welsh	The most terrifying, yes.
Erin Allmann Updyke	Absolutely the most terrifying. And the reason that most people who have heard of anthrax are probably most terrified of it because they think of anthrax and they think of bioterrorism and that means that they're thinking of inhalational anthrax, whether they know it or not. So the inhalational form, in this form you have a biphasic illness, so you have two different parts to this infection. The first part happens about 1-6 days after exposure. It starts pretty nonspecifically. Fever, I feel cruddy, my muscle ache, maybe I have a cough since I inhaled something into my lungs, maybe some chest pain. And then within 2-3 or 4 days your fever will increase but you'll become short of breath, you won't be able to breathe, you can't get in enough air, you might get cyanosis - cyanosis is when your skin turns blue because you literally don't have enough oxygen. Often your lymph nodes in your neck will get so swollen that those will further obstruct your windpipe so then when you breathe in it might sound like (wheezing) which is called stridor.
Erin Welsh	Yeah.

Erin Allmann Updyke

And about half of people will progress to complications like meningitis because these bacteria have crossed the blood-brain barrier. If you get meningitis it's essentially 100% chance that you're gonna die even with treatment. But even if not as this bacteria replicates throughout your body, because of those toxins what happens is that you very rapidly progress to shock. So shock we've talked about a lot but it's essentially there's a lot of ways that it can happen but what it means is that you're not getting blood and oxygen perfusing your tissues. So in this case it can happen kind of in a lot of different ways, you're losing a lot of fluid because of these toxins and their actions both on your blood vessels and also on your lymph system essentially just causing a lot of swelling and in some cases actual bleeding and bleeding out of places that you're not supposed to bleed. So in general with inhalational anthrax, whether because of the meningitis or whether because of the shock, death usually happens within 24-36 hours of that second stage of the illness.

Erin Welsh

Okay. That's terrifying, horrifying.

Erin Allmann Updyke

It's very horrifying. And what happens in inhalational anthrax and the difference between inhalational anthrax and cutaneous and gastrointestinal anthrax is that in the case of inhalational, when these spores are inhaled they're engulfed by macrophages that live in the bottoms of our lungs, the little alveoli which are where gas exchange happens. And these macrophages take those spores to a set of lymph nodes that are right along the center of our chest called the mediastinum and that is where they germinate and begin to replicate. And from there they very rapidly produce a huge, huge amount of bacteremia, so tons of bacteria that are able to go throughout your whole bloodstream, a huge amount of toxin and then the shock and the death. So this is an inhaled spore, so it's a quote "lung thing" but it's not really a lung disease.

Erin Welsh

Right, it's just the avenue of entry.

Erin Allmann Updyke

Exactly, right. So in general mortality rate in some outbreaks has been as low as 46%, that's with really good treatment.

Erin Welsh

As low as 46%.

Erin Allmann Updyke

Yeah, that was the US in 2001.

Erin Welsh

Right.

Erin Allmann Updyke

The death rate was 46%. But it's usually as high as 85-95%. And like I said if it progresses to meningitis, it's nearly 100%. It's treatable especially early on in the infection but often, especially if it progresses to meningitis, antibiotics alone often aren't enough because of the high level of toxemia because of the toxins themselves. So yeah, really briefly there's also actually a fourth route that has been documented pretty rarely but that is injectional anthrax.

Erin Welsh

Yeah.

Erin Allmann Updyke

And this has been documented in several places throughout Europe because of contaminated heroin which is very scary. And the reason that this is different than just cutaneous anthrax even though it's a needle going through the skin is that it ends up producing a deeper soft tissue infection which is more likely to result in systemic infection and therefore has a higher mortality rate because it's introduced much deeper than just a superficial skin infection would be.

Erin Welsh

Gotcha. So it's not the needle, it's the heroin itself.

Erin Allmann Updyke

Right, yeah. It's been from contaminated heroin, not from needles that were dropped in soil or something like that.

Erin Welsh

Right, right. Wow.

Erin Allmann Updyke

Yeah. It is treatable in animals and in humans so that's exciting and there is a vaccine technically.

Erin Welsh

Yes, yes. That's true.

Erin Allmann Updyke

For animals and for humans. But it's not a great vaccine for animals or for humans.

Erin Welsh

Low protection or what?

Erin Allmann Updyke

Yeah. For reasons that we don't fully understand it doesn't produce super long lasting immunity so even for animals they have to get boosters like every year. For humans the vaccines that we have, at least the one that we have in the states, you have to get a dose at time zero and then again at 2 weeks and 4 weeks and then 6 months and then 12 months and then 18 months and then every year after that.

Erin Welsh

That's a lot of... Yeah, compliance must be challenging to achieve on that.

Erin Allmann Updyke

Yeah. It definitely can be. So speaking of the anthrax vaccine and animals, we wanted to bring on a very special guest to help us explore a huge area of this disease and this microbe that we've really just barely touched on so far and that is the impact of anthrax on domestic and wild animals. You know Erin, so that we don't have to just speculate about how much Cap'n Crunch a cow vs a deer is eating. So we consulted an expert. We were so thrilled to get to chat with Dr. Johanna Salzer, Veterinary Medical Officer at the CDC. So we'll let her introduce herself.

Johanna Salzer

So I'm Johanna Salzer, I'm a Veterinary Medical Officer in Bacterial Special Pathogens Branch at the US Centers for Disease Control and Prevention. I serve as both a veterinarian and an epidemiologist.

Erin Allmann Updyke

Yay! We're so thrilled to get to talk to you today. So we wanted to ask you because you are both a veterinarian and infectious disease epidemiologist researcher, we wanted to ask you about anthrax in animals. So could you tell us a little bit about what the course kind of in general of anthrax as a disease looks like in animals other than humans?

Johanna Salzer

Sure. So anthrax affects different animal species differently. So there are some animals that are more affected and have more severe disease than others. So usually when we think about anthrax and animals we think about herbivores so cattle, sheep, goats, and wild herbivores such as zebras and buffalo and other antelope. And in these animals when they either ingest or inhale the *Bacillus anthracis* spore, they have a pretty rapid onset of disease and pretty severe. And so usually the first sign of disease in these animals is actually sudden death. And so usually the first sign that you have an outbreak of anthrax in a herd is when animals are found dead. And the carcasses present with lack of rigor mortis or reduced rigor mortis and dark blood that can be oozing from the mouth or nostrils or anus, a marked bloating, and often this rapid decomposition of the carcass.

Erin Welsh

Interesting.

Erin Allmann Updyke

That's awful.

Erin Welsh

Yeah. So looking now more specifically, are there any big differences in how this disease happens among different animal species? Like are some animals more susceptible or seem to be more susceptible or is it just a difference in exposure risk?

Johanna Salzer

Yeah. So some animals are considered more resistant. So species like pigs, dogs, cats, carnivores, some of your scavengers. Actually some of the animals that would maybe feed on a carcass are the animals that if they are infected they have less severe disease and it's more rarely fatal.

Erin Welsh

Interesting.

Erin Allmann Updyke

That's fascinating. So I mean because this is a disease that can cause these really massive outbreaks and like you were saying just really rapid death and decomposition of the carcasses leading to further outbreaks. What do control efforts kind of look like and entail once an outbreak has been identified and how does that control differ for an outbreak maybe in livestock vs wildlife?

Johanna Salzer

Yeah so the two primary tools that we have for controlling anthrax are livestock vaccination and vaccination programs for anthrax, especially in areas that are known to be endemic. So vaccination, it had been done in wildlife but it is pretty challenging, right, cause most of the time it would involve darting of an animal. And then proper carcass disposal when you do have an animal that's suspected or confirmed to have died of anthrax. The carcass disposal, so the recommendations are either to incinerate or burn a carcass and if that's not possible then to bury. And even with livestock this can be a challenge. There are places where anthrax is endemic that there's just not much topsoil, you're not able to actually physically bury an animal or perhaps there's a burn ban or other reasons you wouldn't burn a carcass.

With wildlife it's even a bigger challenge because you have to find the carcass fairly quickly before scavengers do and that's often nearly impossible with wildlife. And wildlife, they're also larger carcasses, right. You're talking about elephants or hippos, buffalo. One of the outbreaks that we recently consulted on in Namibia, some the recommendations were just to bury the carcasses when possible and just to minimally move them to try to prevent further environmental contamination.

Erin Welsh

In places where there's mixed cattle and wildlife grazing, I know that that's been happening a lot like integrated farms, would that practice increase the risk to domestic animals or decrease the risk almost to the wildlife because maybe an anthrax outbreak could be identified more quickly even if there are more susceptible individuals? I was just thinking about how that practice might affect either the risk or control measures for anthrax in those animal populations.

Johanna Salzer

Yeah I mean that is a perfect example of where vaccination and good vaccination programs are our strongest weapon against anthrax. You're asking, Erin, if identifying a wildlife case early then could trigger vaccination in livestock?

Erin Welsh

Mm-hmm.

Johanna Salzer

Yeah and I think that actually is the case in Texas where you do have a lot of wildlife mingling with livestock. From a veterinary perspective one of the things I most love about working on anthrax is because it is one of those diseases much like rabies that if you could protect the animal and prevent the disease in animal, you protect people. And anthrax, working on anthrax in livestock specifically and protecting livestock also in turn can not only protect people but also wildlife which is one of the things that I find so fascinating about anthrax. It really, much like rabies, the connectivity is so tight between human and animal health. And with anthrax you also have this environmental piece where you have to have the right environmental conditions for the spore to survive, too. So it's kind of the poster child for one health and using a one health approach to disease control.

Erin Welsh

Thank you so much Dr. Salzer for taking the time to chat with us. It was so fantastic and we really appreciate it.

Erin Allmann Updyke

Yeah we do, it was absolutely thrilling. So Erin, after all of that, what can you tell me about the history of anthrax? Like where did this come from and how did we get here?

Erin Welsh

I can't wait but let's take a quick break first.

TPWKY

(transition theme)

Erin Welsh

For many of us, especially those that remember watching the news coverage in 2001 on the anthrax letters, more on that later, anthrax holds a very specific meaning: that of a bioterrorism agent. And that reputation or perception of anthrax hasn't diminished over the years despite the fact that anthrax poses a much more real threat as a disease of livestock and wildlife than it has as a bioweapon so far. And the bioweapon angle itself, that's relatively new. Throughout its very long history, anthrax has been many things. A punishment from the heavens, an agricultural disease, an occupational hazard, and now a potential weapon of bioterrorism. So my goal for the history section is to take us through these different faces of anthrax. And let's begin at the beginning, the evolutionary origins.

Erin Allmann Updyke

Yes!

Erin Welsh

So as you mentioned, Erin, *Bacillus anthracis* is kind of a funky little pathogen, it's not super diverse, it reproduces clonally primarily. And actually this incredible lack of diversity meant that it was only in the past few decades or so, past two decades or so with the development of next generation sequencing technology that researchers were able to get a full picture of its evolutionary history and relationships among different strains or clades. Before it was too difficult.

Erin Allmann Updyke

Yeah, cause they were just too similar across...

Erin Welsh

Exactly, yeah.

Erin Allmann Updyke

Fascinating.

Erin Welsh

So what did they find? Well first of all they found that *Bacillus anthracis* likely evolved several tens of thousands of years ago.

Erin Allmann Updyke

Okay.

Erin Welsh: I couldn't actually find a very good estimate of when it first emerged or diverged. But in any case several researchers believe that it evolved from an insect pathogen or insect commensal.

Erin Allmann Updyke: Ooh, like some of the closely related...

Erin Welsh: Exactly, Bacillus thuringi-

Erin Allmann Updyke: Thuringiensis.

Erin Welsh: Thuringiensis, thank you. So yeah, it evolved from this insect pathogen or commensal and it diverged from Bacillus cereus after acquiring those virulence plasmids.

Erin Allmann Updyke: Okay.

Erin Welsh: It's thought that Bacillus anthracis emerged in Sub-Saharan Africa but the location of where it spread from and then this burst of diversification is likely to have happened somewhere in the Fertile Crescent which is where the domestication of livestock primarily happened.

Erin Allmann Updyke: That makes sense.

Erin Welsh: Makes sense.

Erin Allmann Updyke: Yeah.

Erin Welsh: And it's unclear exactly how this bacterium got to the Americas but there are a couple of hypotheses which are not mutually exclusive. So one introduction could have come during the Holocene by ungulates traveling over the Bering land bridge and then down into the Americas. And another source of introduction is thought to be European trappers who brought it into the eastern US. But overall like you said anthrax is a very slow-moving creature evolutionarily, accumulating mutations slowly. And this quality of anthrax has made it a lot easier to trade not only its history but it also has great forensic value in tracing the source of an anthrax bioweapon such as in the case of the 2001 anthrax letters. So like pinpointing exactly where this particular strain came from.

Erin Allmann Updyke: Ooh.

Erin Welsh: This is pretty interesting.

Erin Allmann Updyke: Yeah.

Erin Welsh: But anyway, I'm getting ahead of myself a little bit. And so now that we've got the evolutionary history out of the way, let's check in with ancient history and anthrax.

Erin Allmann Updyke: Yes! This really is like a first season...

Erin Welsh: It super is. I'm overwhelmed. Anthrax seems like it was definitely known in ancient times. The fifth and maybe sixth biblical plagues, the plague of livestock and the plague of boils respectively which always makes me think of Brooklyn 99, the plague of boils. (laughs) Anyway. Those have often been held to be anthrax as well as rinderpest, like I know that I mentioned these biblical plagues in the rinderpest episode.

Erin Allmann Updyke

Yeah.

Erin Welsh

And in ancient writings in India from 500 BCE or so describing the diseases of animals, anthrax seems to be one of those diseases described. It was also known in Ancient Greece and in Ancient Rome the poet Virgil wrote about animal plagues, one of which sounds an awful lot like anthrax. Here's a quote for you: "A terrible plague once sprang up there and raged on through the warmer part of autumn, not only destroying one flock of sheep after another but killing animals of all kinds. Nor did the victims die an easy and uncomplicated death. After a burning fever had raged through an animal's veins and shriveled its flesh, the fluids again became abundant and virtually dissolved the bones."

Erin Allmann Updyke

Ew, yeah.

Erin Welsh

Sounds rough no matter what it is.

Erin Allmann Updyke

Rough and right.

Erin Welsh

Could have been anthrax. And one of Virgil's plagues supposedly wiped out almost half of both the human and animal populations of Rome and the disease continued to be a major problem in the area for centuries, popping up over and over again. This tendency of anthrax, which is like to haunt certain farms or regions, gave rise to almost a mythology around the disease and I meant that generational knowledge was required. So families or villages had to remember where the bodies were buried, so to speak, and pass that information down so that future generations could avoid grazing livestock in those areas.

Erin Allmann Updyke

Not even so to speak but like literally.

Erin Welsh

Literally, yeah. Not even so to speak. Yeah. Actually side note, I saw a really cool paper about how the spots where carcasses are actually end up being an attractant to animals because if an animal dies of anthrax, that nutrient influx into the soil will actually help plants grow better and faster, thus attracting other animals, thus influencing the transmission chain.

Erin Allmann Updyke

At what time frame though? Cause I was reading about how for the first year-

Erin Welsh

The second year.

Erin Allmann Updyke

The second year.

Erin Welsh

Yes! The first year it's avoidant, the second it's attractant, the third year the preference goes away.

Erin Allmann Updyke

Fascinating.

Erin Welsh

I know, I know.

Erin Allmann Updyke

Cause it seems like after two years is when infectivity goes down so that second year is when... Ooh!

Erin Welsh

It's crucial. Evolution, ecology. It's just magical. But this tendency to haunt certain areas led to for instance in France some of these areas being referred to as 'the cursed fields'. So widespread trade of animals and animal products ensured that these cursed fields could spring up anywhere and by around 1000 CE, anthrax was really well established throughout the Old World. Germany and the British isles experienced major outbreaks of anthrax in the 10th, 13th, and 14th centuries and these epizootics resulted not only in the deaths of livestock but also in the humans and dogs and birds and other animals that fed on the cattle carcasses or they ended up starving due to food shortages or nutritional deficiencies.

Erin Allmann Updyke

So does that mean that anthrax moved around the world from livestock trading?

Erin Welsh

Exactly, yeah. Well livestock trading and fur trading and wool and so on.

Erin Allmann Updyke

Wow!

Erin Welsh

So this is what's so interesting to me is that for a lot of diseases that are human-specific, they moved around the world due to human travel but it was almost an inevitability. But with anthrax I feel like we really lent a helping hand.

Erin Allmann Updyke

Right. What? This is blowing my mind right now, actually.

Erin Welsh

Yeah, I mean it turns out this is one of the Big Ones, like capital 'B', capital 'O'.

Erin Allmann Updyke

Oh man. (laughs)

Erin Welsh

I mean it has really had a huge impact on history and ecology and it's just really fascinating to me. Let me give you an example.

Erin Allmann Updyke

Oh please.

Erin Welsh

In 1613 in Southern Europe, a massive outbreak of anthrax is estimated to have killed around 60,000 people and untold numbers of livestock.

Erin Allmann Updyke

What?

Erin Welsh

Over the next 100 years, so between the 1600s and 1700s, anthrax outbreaks seemed to grow stronger and deadlier in some ways which probably definitely had something to do with this increased movement and trade. And one of these places of trade was the New World. Even if anthrax had been brought over across the Bering land bridge around 10,000 years ago, it greatly spread in prevalence and outbreak intensity following European colonization. It seems that anthrax began to be perceived as a problem in the New World by the 1500s but the biggest and most devastating outbreak of what was likely anthrax didn't occur until the 1770s in what is now Haiti. In this outbreak an estimated 15,000 people died of anthrax-

Erin Allmann Updyke

What?

Erin Welsh

And untold thousands of cattle and other livestock also perished. And a major component of this anthrax outbreak that contributed to its deadliness was the fact that an earthquake occurred in the middle of the outbreak, making food even more scarce than it was before. And so out of desperation people began to eat the livestock that had died of anthrax which of course led to even more cases.

Erin Allmann Updyke: Yeah I feel like it's important to also point out that cooking the meat doesn't kill the spores.

Erin Welsh: Oh no, these spores are like-

Erin Allmann Updyke: They're like prions practically.

Erin Welsh: I know.

Erin Allmann Updyke: Yeah.

Erin Welsh: Nevertheless they persisted.

Erin Allmann Updyke: Yeah.

Erin Welsh: A hardcore spore. (laughs) Oh my gosh. Okay. So although this 1770 outbreak of anthrax may have been the most devastating it certainly wouldn't be the last. But before I go into more of those, let's talk names real quick.

Erin Allmann Updyke: Okay.

Erin Welsh: I'm not gonna go through all the different names because there are very many but I will go over some of the patterns that we have seen in these names. And so one is that they often called out that grazing animals were most commonly infected, so like cow sickness, goat sickness, etc. And another is that the skin condition caused by anthrax, which is the most common manifestation as you pointed out, also made an appearance in many of the names.

Erin Allmann Updyke: Okay.

Erin Welsh: And the word 'anthrax' itself comes from the Greek 'anthrakos' meaning coal or carbuncle. And many other names call out the black color that can often result from the anthrax skin condition.

Erin Allmann Updyke: Right, yeah. It's a very characteristic lesion.

Erin Welsh: Yeah. And the Latin word 'anthrax' also means carbuncles or malignant boils. The French word for the disease was 'charbon'.

Erin Allmann Updyke: Like carbon.

Erin Welsh: Yeah, coal or charcoal. And the whole body forms of anthrax though were of course called by many different names because no one yet knew that the diseases were linked.

Erin Allmann Updyke: Right. That's what's so interesting about these ones that have such varied manifestations.

Erin Welsh: Yeah.

Erin Allmann Updyke: Like who connected cutaneous anthrax to inhalational anthrax?

Erin Welsh: Oh well I'm gonna tell you that.

Erin Allmann Updyke

Oh good!

Erin Welsh

I can tell you his name, I can tell you how he did it. And another characteristic or another parallel was that many of these names included a reference to the spleen in the disease's name, so like in South Africa the disease was referred to as spleen illness and in German, spleen fire or inflammatory death of the spleen. Is that where a lot of macrophages are?

Erin Allmann Updyke

It's a giant lymphoid organ.

Erin Welsh

There we go. As I've talked about before, the names that people use for a disease can tell us about the importance of the disease to humans or what they saw as its defining characteristics. And maybe it was because of the economic importance of livestock, the fact that humans could also become ill, or the terrifyingly random and rapid way it killed, it's pretty clear that anthrax in all of its various forms was not an overlooked disease. By the 1700s, widespread global trade and population growth had led to, among other things, increasing urbanization and industrial specialization. And that also included textile production. So rather than wool or leather products being processed at the same place where the farms were, they were sent to textile mills where many people worked the animal products. Wool, hides, skins, etc began to be transported long distances. And Erin, can you guess who hitched a ride?

Erin Allmann Updyke

Anthrax spores.

Erin Welsh

Exactly. At some of these busy textile mills in France, a physician named - and I'm gonna need your help with this pronunciation, Erin - Nicholas Fournier.

Erin Allmann Updyke

Yeah, that was great.

Erin Welsh

Perfect. Fournier started to notice that some of the workers began to show signs of illness similar to those experienced by the animals where the materials came from. And the rate of these conditions was substantially higher than it was in the general population and it wasn't just inflamed skin that these workers were experiencing but also the GI symptoms or the full body manifestations of anthrax. Fournier, inspired in part by his older colleague, began to question whether these diseases with different names, thought at the same time to all be distinct diseases, were really all the same thing.

He noticed a common thread binding the affected people together. They all had some connection to animal hair or animal parts, either eating or working or cleaning, whatever. Some sort of connection. And he published his findings and his description of anthrax in a booklet that may not have been very popular at the time of publication but it would go on to greatly influence other researchers and physicians and veterinarians that came after him. And it would also mark him, at least in my eyes, as pretty dang ahead of his time because all of these observations and hypotheses that he was making were taking place in the mid 1700s.

Erin Allmann Updyke

Wow.

Erin Welsh

The birth of germ theory was still about 100 years away.

Erin Allmann Updyke

That is truly remarkable.

Erin Welsh

Yes. It reminds me a lot again of the botulism dude, I can't remember his name. Remember? He made all of these amazing achievements.

Erin Allmann Updyke: Yeah, he's the one who did all of the things, like discovered the pathogen, did the test, did the thing, found a treatment, found a use, blah, blah, blah.

Erin Welsh: Everything.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah, he was cool. If only I could remember his name. (laughs) Like I said, limited space here. Okay. But speaking of germ theory, shall we jump 100 years into the future?

Erin Allmann Updyke: I just wanna give Fournier like a second more credit because I am still blown away.

Erin Welsh: Okay, a moment of appreciation for Fournier.

Erin Allmann Updyke: Nice job, dude.

Erin Welsh: Okay.

Erin Allmann Updyke: Okay. (laughs)

Erin Welsh: (laughs) There's no way we're gonna get away with not laughing about that one. Okay. Anthrax actually played a pretty huge role in the development of germ theory.

Erin Allmann Updyke: What?

Erin Welsh: Yes! This is again where I was like, what? This bacteria has so much beneath the surface.

Erin Allmann Updyke: Okay, keep going.

Erin Welsh: Okay. Bacillus anthracis was one of the first bacterial species actually that was really intensively studied. It was used as one of the first case studies to develop Koch's postulates.

Erin Allmann Updyke: What?

Erin Welsh: To understand the ecology of the disease and the role that the environment played.

Erin Allmann Updyke: What?

Erin Welsh: And to develop a vaccine.

Erin Allmann Updyke: Why don't I know any of this, Erin? It feels like I should know this.

Erin Welsh: I think it was all overshadowed by 2001. Yeah. But yeah I think also there's a question in that as to not just why don't you know all this but why anthrax? Why was it so heavily studied?

Erin Allmann Updyke: I mean cause it was killing people and their cows?

Erin Welsh

Those are a couple of the reasons. So definitely yeah, it caused these huge epizootics that led to loss of life, loss of wealth, etc. It was terrifying, just a very threatening disease in terms of the symptoms and the mortality rate and also how it seemed to appear randomly, so like untangling that mystery would have placed it at high priority. Another reason though is that anthrax cases continued to rise in people who worked with animals or animal products, not just livestock farmers but tanners and butchers and wool-sorters as well.

Erin Allmann Updyke

Ooh yeah, definitely.

Erin Welsh

And number four, this is a very practical reason but the anthrax bacillus is actually quite large.

Erin Allmann Updyke

Yeah, it's big.

Erin Welsh

Yeah so it was large enough to be easily seen under a mid 1800s microscope and it also turns out it's pretty easily stained as well. But still the discovery of the anthrax bacillus begins probably earlier than you might expect in the 1850s.

Erin Allmann Updyke

What?

Erin Welsh

This is like before germ theory really, it's like the very, very beginning of germ theory. In that time, so like 1849-1850, a French and a German researcher both observed the bacteria independently at nearly the same time and priority doesn't really matter but it still led to this huge controversy in both France and Germany, trying to lay claim to who first discovered the anthrax bacillus. And I think it's interesting because this controversy between France and Germany was just a preview of the contentious rivalry that would emerge between the French Louis Pasteur and the German Robert Koch when it came to anthrax and all other things microbiology.

Erin Allmann Updyke

Oh yeah.

Erin Welsh

Okay so observing the rods in the blood of infected humans or animals was pretty easy, like those two earlier microbiologists did. But isolating those rods and growing them in a lab is a whole other story.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. And so by recognizing that the anthrax bacillus and other microbes were living things, early microbiologists were faced with the enormous hurdle of figuring out how to feed and shelter them, how to keep them happy enough to grow in an artificial setting outside of an animal.

Erin Allmann Updyke

Yeah.

Erin Welsh

And anthrax because it has this pretty unusual life cycle proved to be quite technically challenging.

Erin Allmann Updyke

Yeah, that's why it's surprising that it was one of the first.

Erin Welsh

Yeah. It's surprising that it was one of the first but I also think that the way that it was studied was rather ingenious.

Erin Allmann Updyke

Oh okay.

Erin Welsh

So Robert Koch, I'm not gonna go into too many details but what he did was he developed a culture slide, it had a little dip in it, that not only allowed the bacillus to live but it also allowed an observer to closely watch its every move. And this slide is how he was able to observe that the rods at the edge of the liquid suspension, those that were more exposed to air, they were undergoing shape changes.

Erin Allmann Updyke

Stop it.

Erin Welsh

Yes! They were turning into long filaments and they started to look granular.

Erin Allmann Updyke

Stop it right now.

Erin Welsh

In other words, they were transitioning into perfectly formed spores.

Erin Allmann Updyke

I am losing it right now. Okay but this is the 1800s and we're talking about looking through a microscope and watching a bacterium sporulate.

Erin Welsh

Yeah!

Erin Allmann Updyke

What the heck?

Erin Welsh

1876!

Erin Allmann Updyke

I'm dead now.

Erin Welsh

I know. Because the implications for that discovery were enormous. So not only did this answer a whole host of questions, why did the bacillus seem to disappear in blood and tissue samples after the animal died?

Erin Allmann Updyke

Because it did!

Erin Welsh

Because it turned into a spore. Why grazing animals seemed to be the most affected?

Erin Allmann Updyke

Because they ate so much of it in the soil!

Erin Welsh

And how on earth this bacterium survived in the soil and was able to cause seemingly random outbreaks?

Erin Allmann Updyke

Oh my gracious.

Erin Welsh

I mean it's amazing. So another reason why anthrax became a model organism is because Koch published his super detailed protocol for cultivating these anthrax bacilli.

Erin Allmann Updyke

That makes sense.

Erin Welsh

And so for that reason everyone was able to go out because like you said it's globally distributed or find a farm that had an anthrax outbreak, get some blood, and then work with it in the lab.

Erin Allmann Updyke

Yeah.

Erin Welsh

So it's really weird to think about now because A) anthrax is so deadly and B) we're like, that should be under high, it's like a highly controlled substance.

Erin Allmann Updyke

Right, it's like a biosafety level 3 or 4. You can't just do that.

Erin Welsh

You can't just do that. But they just did that. And so anthrax was used not only to develop Koch's postulates but also the principles that researchers would use to ensure that the bacterial species they were working on was indeed the species they thought it was, so things like morphology, lab requirements, staining principles, life cycle, illustrations. Like it was used as a model for all those things.

Erin Allmann Updyke

Wow.

Erin Welsh

And Koch's anthrax research also caught the eye of none other than Louis Pasteur. Among his many achievements, Pasteur is often credited with developing the first anthrax vaccine. But in doing the research for this episode I learned that he actually was not the first. The first was a veterinarian named Jean Joseph Henri Toussaint who used heat and chemicals to develop a strain of anthrax that would produce an immune response in an animal without killing it. Heat and chemicals, again ahead of its time. 1800s, late 1800s. He successfully tested his vaccine on 20 sheep and published his findings. And Pasteur came across Toussaint's vaccine work and decided to test it out. So in a public and highly publicized demonstration he injected anthrax into two groups of sheep, one that had been vaccinated and the other not. I mean newspapers came from all over, it's now been made into a movie, like this was a huge demonstration. And thank goodness it worked. All of the sheep who had not been vaccinated died and those that had lived.

Erin Allmann Updyke

Wow.

Erin Welsh

And this public demonstration was not only a very exciting demonstration of germ theory in action and the life saving power of vaccines but it also firmly placed Pasteur as the creator of the anthrax vaccine.

Erin Allmann Updyke

Cause he was like, 'I'm gonna do it loudest!'

Erin Welsh

Well not only did he do it loudest but he also was like, 'Oh no, my vaccine is way better, I used a much better thing. Toussaint's method is unreliable and unscientific' and blah, blah, blah. And poor Toussaint who was both less well known and less powerful than Pasteur was also suffering from a neurodegenerative disease that would go on to kill him at the age of 41. And so he didn't have the ability to really assert his claim to fame.

Erin Allmann Updyke

That's very sad, Erin.

Erin Welsh

Very sad. Pasteur did not create the first anthrax vaccine. Maybe that's the take home. No it's not really, there's lots of other take homes. But let that be one of them. So anyway, vaccine credit aside, the important thing was that there was now an anthrax vaccine and the administration of this vaccine to livestock all over the globe did a great deal to reduce the incidence of the disease. But it did still happen. And here is where I want to revisit anthrax as an occupational disease. At this point in anthrax's history it was still viewed primarily as a rural agricultural disease despite Fournier's work in the French textile mills of the 1700s because people just ignored that work straight up.

Erin Allmann Updyke

Okay.

Erin Welsh

But this characterization of anthrax as just agricultural, that was about to change. Okay. By the late 1800s the textile industry in Europe had become very centralized, even more so than 100 years prior with large factories where different types of wool and hair and skins would be imported from all over the world. In these factories a disease started to show up with increasing prevalence in the workers who would sort the wool. Woolsorters' disease as it was called.

Erin Allmann Updyke

Yeah.

Erin Welsh

One day you felt fine, the next you got a fever and pneumonia-like symptoms and then you collapsed and died. And during these outbreaks no one yet knew that woolsorters' disease was actually a type of anthrax. And that's because anthrax at the time like I said was still thought of just as a disease of agriculture and at the same time most anthrax cases tended to be cutaneous rather than inhalational.

Erin Allmann Updyke

Right, yeah.

Erin Welsh

And woolsorters' disease is inhalational. Remember how scrapie, which is the prion disease of sheep, increased in prevalence and geographical distribution because of the wool trade?

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. Anthrax also. So around this time which is also similarly when wool demand grew so much and scrapie became a huge problem and also more widely distributed, that high demand for exotic furs and wools grew so much that some farmers became more reluctant to lose out on a profitable fleece from a goat or sheep that died prematurely.

Erin Allmann Updyke

Oh no.

Erin Welsh

Perhaps from anthrax.

Erin Allmann Updyke

Oh dear.

Erin Welsh

Yep. And so they would shear the animal anyway and send off the hair which often still had bits of blood or skin attached.

Erin Allmann Updyke

Ugh.

Erin Welsh

Yeah. The wool sorter would then comb the wool using newly developed machinery which would often result in the dirt and dust and blood and skin particles turning a bit aerosolized.

Erin Allmann Updyke

Oh god.

Erin Welsh

Yeah, just like a haze of anthrax.

Erin Allmann Updyke

Yuck. Oh god.

Erin Welsh

And I think to us now woollsorters' disease may seem like an isolated problem limited to a very small part of the population but that wasn't the case at all. Wool sorters made up a huge part of the occupational community and to give you some sense of how much of an impact occupational anthrax had during this time, consider these stats from Italy: between 1890 and 1904, 36,436 cases of anthrax were registered among tanners, brush makers, and wool workers with 7,308 deaths.

Erin Allmann Updyke

Whoa.

Erin Welsh

That's a lot.

Erin Allmann Updyke

That's a lot.

Erin Welsh

And so it makes sense then that there would be many epidemiologists hard at work on this problem. But among all of these epidemiologists, John Henry Bell may have been the most influential in getting woollsorters' disease to be widely recognized as a form of anthrax. He was also one of the first to push for workers rights or at least call out the responsibility of the employer in providing a safe work environment and minimizing the risk of disease.

Erin Allmann Updyke

Oh, get it.

Erin Welsh

As a physician Bell would often be called upon to perform autopsies on those who died of woollsorters' disease and he became increasingly frustrated with what seemed to him to be careless employers who refused to acknowledge their own responsibility in the disease. And so under cause of death he started to put things like 'employers neglect and not properly washing or disinfecting imported mohair'.

Erin Allmann Updyke

Whoa! Get it.

Erin Welsh

Yeah. And so employers don't wanna be blamed for the death of their employees. And also I think that his voice was loud enough and he was prominent enough in the community to really raise the alarm on this.

Erin Allmann Updyke

Wow.

Erin Welsh

And so in effect he started this activist movement among the wool sorters to protest these working conditions and to fight for protections from anthrax. And this also marked one of the first occasions of an infectious disease being recognized as an occupational hazard. So interesting.

Erin Allmann Updyke

So many pieces to this anthrax puzzle, Erin.

Erin Welsh

I know!

Erin Allmann Updyke

My gosh.

Erin Welsh

Practices like vaccination or increased sanitation of wool reduced the incidence of anthrax among these workers but it did still pop up and not just in the wool sorters. For instance early shaving brushes were made of animal hair and some of these carried anthrax spores on them.

Erin Allmann Updyke

Stop.

Erin Welsh

And so when somebody would use a brush on their face and they had tiny little cuts from shaving-

Erin Allmann Updyke

Tiny cuts, oh no.

Erin Welsh

Yeah, the spores would get in there and cause cutaneous anthrax.

Erin Allmann Updyke

No thank you.

Erin Welsh

And horse hair was often used as an ingredient in plaster and often or at least occasionally contained anthrax spores. By the early 1900s the perception of anthrax had evolved into one of both agricultural and industrial importance and several tools had been developed to combat the disease. Vaccines, which I'm not gonna go into the history of except to say that new and improved ones had been developed, better sanitation practices and serum were all variously used and seemed to make a pretty substantial dent in slowing transmission. Anthrax seemed to be turning into a disease of the past. Not quite. The world wars of the 20th century really showcased how inventive and cruel and brutal and relentless humanity could be when it comes to killing other humans. And one of these methods of murder happened to be bioweapons.

Long before the 2001 anthrax attacks in the US there had been previous attempts to develop anthrax into a bioweapon by nearly every country involved in these global conflicts. Anthrax has always been near the top of the list of potential bioweapon agents because of its high mortality rate, its relatively easy manipulation in the lab thanks to its model organism status, its durability, its ability to survive an explosion, and the existence of a vaccine which could protect those who were administering the bioweapon.

Erin Allmann Updyke

That is a gross part that I did not realize was a criteria for what makes a good bioweapon.

Erin Welsh

Yeah.

Erin Allmann Updyke

That's so gross.

Erin Welsh

Gross is the right word. Research was carried out in many countries to work on how best to use anthrax as a weapon, maybe in warfare with shrapnel bombs or as a massive civilian attack using high altitude bombs or atomizers, or maybe lace some anthrax in linseed cakes and then drop those into German fields where they would be eaten by the cattle, killing cattle and then humans that ate the cattle. It's a very specific example that I'm giving because that was an actual British operation called Operation Vegetarian during WWII.

Erin Allmann Updyke

Are you...

Erin Welsh

I know. Like I wrote this and I'm like am I reading this right? Yeah. Scientists dealt with things like the logistics of how high a bomb should be deployed to impact the widest area, which way the wind was going, or which form of the bacillus, should we do a liquid suspension or a spore form that would be most likely to cause death or be the most stable, or how to protect those deploying the weapon. So we know that people worked on anthrax as a bioweapon during these wars and researched it as a possibility but did anyone ever try it out? Well the first instance of anthrax being used as a bioweapon is often cited as a part of a WWI German sabotage program in which anthrax was supposed to be administered to Allied draft animals like horses, mules, reindeer, etc.

In 1917 German spy Baron von Rosen was captured in Norway and accused of smuggling a bioweapon, anthrax-filled glass capillaries concealed in sugar lumps. So these anthrax sugar cubes in 1998, they were analyzed and anthrax genetic material was found. So maybe there was something to it. However in 2017 a paper came out that suggests that those anthrax colonies were actually just lab contamination and so we'll never really know if the sugar cubes held anthrax or not.

Erin Allmann Updyke

Actually did or not.

Erin Welsh

But we do have solid evidence of weaponized anthrax being tested on humans from Unit 731. And so this is the infamous unit of the Japanese army that in WWII carried out bioweapons testing on human and animal subjects and also where no one was ever punished because the US made an immunity deal to get access to all their research in exchange for immunity. Cool.

Erin Allmann Updyke

Which is the polio where you talk a lot about that one?

Erin Welsh

Hantavirus I believe.

Erin Allmann Updyke

Hantavirus, that's right.

Erin Welsh

Anyway, thousands of people primarily in the historical region Manchuria were intentionally dosed with anthrax to observe how quickly it killed or the dose necessary, medicalized torture that mostly resulted in death. There were anthrax shrapnel bombs that were blasted at people tied to stakes nearby with different body parts exposed to test dose and site of entry.

Erin Allmann Updyke

What the actual...?

Erin Welsh

I know. And many, many other countries including France and England and Germany and Canada and the US performed similar horrifying experiments on weaponized anthrax on animal subjects throughout WWII. As you can expect, as we all expect, research into anthrax as a bioweapon did not cease with the end of WWII nor did it end in 1972 when nearly every country around the globe signed the Biological Weapons Convention which banned research, development, possession, and deployment of biological weapons. In 1979 in Sverdlovsk, Russia approximately 100 people, maybe more, fell ill and died within a few days of anthrax. Most of the people were workers at a ceramic plant located across the street from a biological research facility whose main project was, you guessed it, aerosolized anthrax.

Erin Allmann Updyke

Yeah, okay.

Erin Welsh

Well bioweapons with aerosolized anthrax as the main, yep. And the Soviet government claimed at the time that's ingestional anthrax, they just got it from eating tainted meat.

Erin Allmann Updyke

Sure.

Erin Welsh

And then they also happened to destroy all of the victims' medical records. And then later investigations though, like they invited American researchers to come in and investigate the source of this outbreak and that revealed that a filter that was preventing the fine anthrax powder from escaping the building had been removed and no one had noticed. And so the drying machines with this mound of anthrax were turned on, basically blowing these anthrax spores into the outside air.

Erin Allmann Updyke

Oh no.

Erin Welsh

Yeah. Downwind was as you can guess the ceramic plant. There's a whole book on this written by one of the American researchers who helped uncover the truth about this incident, it's called 'Anthrax: The Investigation of a Deadly Outbreak'. Looks fascinating, I didn't read it but I'll post it. Anyway around the same time as the Sverdlovsk incident an enormous outbreak of anthrax was taking place in what was then Rhodesia, now Zimbabwe, the largest epidemic of the last 200 years.

Erin Allmann Updyke

Oh my god.

Erin Welsh

Between 1978 and 1984, 101,990 cattle and 17,199 people were stricken with anthrax and nearly 200 people died.

Erin Allmann Updyke

Whoa.

Erin Welsh

This outbreak which was obviously economically devastating took place at a time of great civil unrest in the country and there has been a lot of speculation that the surge in anthrax cases was due to the intentional release of anthrax as a bioweapon. And while there's not a whole lot of physical evidence that that's the case, there is a good deal of circumstantial evidence and I'll post a great review that goes over this outbreak and all the different sort of hypotheses. Okay, this is a long episode, just a couple more bioterrorism incidents and then I'll throw it back to you.

Erin Allmann Updyke

Okay.

Erin Welsh

In 1993 in Japan a liquid culture of anthrax was sprayed from the rooftops by a religious cult but no one got sick because it turns out it was a strain of anthrax used to vaccinate animals and was therefore harmless. Yay! Great news. And then finally the 2001 anthrax letters. And I'm just gonna go over the basics here, like some very surface-level stuff because A) this episode is very long as is, and B) there might be a time in the future where I give this topic the time that it truly deserves which is my way of throwing in a very vague potential teaser.

Erin Allmann Updyke

Ooh, stay tuned!

Erin Welsh

(laughs) Yes, definitely stay tuned for more updates on that. But okay, the anthrax letters. The first victim of the anthrax letters was Bob Stevens, editor for tabloid published American Media in Boca Raton, Florida. On October 4, 2001, a couple of days after opening a letter that contained a threatening note, he checked himself into a hospital due to trouble breathing. The next day he died. A few days after his death one of his coworkers developed cutaneous anthrax. Then cases of anthrax started popping up in New York City news outlets, studios for NBC News and headquarters of the National Enquirer, all from letters containing anthrax spores. Anthrax letters arrived at US senators Tom Daschle and Patrick Leahy's offices and then postal workers in New Jersey and Washington, D.C. became sick with inhalational anthrax.

In total 22 people became sick due to these anthrax letters, 11 with cutaneous anthrax and 11 with inhalational anthrax. And 5 of those with the inhalational form died. Pretty quickly it seemed likely that the person responsible had access to a highly secure scientific facility where the deadly so-called Ames strain was kept and genetic testing also supported this which created this very strange situation, right, where like everyone who worked at USAMRIID which is United States Army Medical Research Institute of Infectious Diseases, much easier to say USAMRIID.

Erin Allmann Updyke

Yeah, the longest acronym of all time.

Erin Welsh

Yep. But everyone who was working there, they were treated as both suspect and they were also these essential assistants to the case because they would be the ones performing the genetic tests and the analyses that would reveal where the anthrax from the letters came from. It's like a really strange thing to think about.

Erin Allmann Updyke

Yeah that's bizarre.

Erin Welsh

Yeah. And the investigation itself into who was responsible for the anthrax letters, it has so many twists and turns and at least a couple of dead ends but years after the letters were mailed, super sensitive genetic tests were developed that allowed investigators to identify not only the strain of anthrax used in the letters but the specific flask where those spores had come from.

Erin Allmann Updyke

That is amazing.

Erin Welsh

I know! It's just such an interesting course of investigation.

Erin Allmann Updyke

Yeah.

Erin Welsh

The more technology you have and then I don't know. And also the characteristics of anthrax itself of the *Bacillus anthracis*, right, the fact that it's so clonal, the fact that it doesn't really evolve very much or is so consistent.

Erin Allmann Updyke

Right. Yeah you can identify it down to the flask, that's incredible.

Erin Welsh

Yeah, exactly. And it turns out that these anthrax spores had come from a flask at USAMRIID that was under the care of researcher Bruce Ivins. And Ivins motive was thought to be that he wanted to save the anthrax vaccine program which was in danger of being shut down. And so if there were suddenly a bunch of deadly anthrax cases then the need for the program would become clear or something. And throughout the investigation Ivins never confessed. I believe that there was no physical evidence found connecting Ivins' home or car to the anthrax envelopes and Ivins himself died of an acetaminophen overdose in 2008. But the circumstantial evidence does seem pretty strong and like I said, there's a lot more to this story that I didn't do it justice. And even if we never have a conclusive answer as to who sent those letters, one thing is for sure: the 2001 anthrax letters forever seared anthrax as a dangerous bioweapon in the minds of the public.

Erin Allmann Updyke

Yeah.

Erin Welsh

So what started out as an agricultural disease transformed into that of an occupational hazard and now a bioweapon. Since 2001 we've learned so much more about the ecology of this bacillus, how it infects wildlife, how it interacts with plants and may not be as dormant in the soil as we previously thought, how anthrax may not just be a disease caused by *Bacillus anthracis*, the role that necrophagous flies may play in transmission, the risk that a warming climate plays in expanding the geographical distribution of this pathogen.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

And so on and so forth. Clearly despite being one of the longest studied bacterial species, there are still many, many mysteries to uncover. So Erin.

Erin Allmann Updyke

Oh gosh.

Erin Welsh

Where do we stand with anthrax today?

Erin Allmann Updyke

Oh my goodness. I will try to bring us up to speed right after this break.

TPWKY

(transition theme)

Erin Allmann Updyke

Wow. Okay, those were a lot of questions that you left open for me, Erin. So let me just say off the bat I'm not gonna be able to answer those but we're gonna call in some backup. So historical analysis reveals, and I think this is really interesting, for every 10 anthrax cases in animals that leave anthrax carcasses essentially, that tends to result in 1 human cutaneous anthrax case. There is one case of human gastrointestinal anthrax for every 3000, just over 3000 anthrax-infected animals that are eaten.

Erin Welsh

Wow. Wait for every 3000 anthrax-infected animals that are eaten?

Erin Allmann Updyke

So we didn't get into this in the biology Erin but while we don't fully know exactly the infectious dose, it's estimated to be quite high especially for gastrointestinal and inhalational anthrax. Humans are actually probably pretty resistant to anthrax infection.

Erin Welsh

That is very interesting.

Erin Allmann Updyke

I know! Okay and we also know from historical data that in humans there are about 100,000 cutaneous cases for every enteric or gastrointestinal case that occurs worldwide.

Erin Welsh

Wow.

Erin Allmann Updyke

And inhalational anthrax today is extremely uncommon. Okay so that's what we do know. Globally overall we have a fairly poor understanding of global risk and incidence of anthrax but we do know, like I said, that human infection largely results from interactions with animals or animal products and so outbreaks in humans tend to occur both temporally and spatially in association with outbreaks in animals. And we also have a lot of good data that shows that in most parts of the world, widespread distribution of vaccines for domestic animals and livestock is really effective at reducing infection in animals and in humans. But like we've talked about in pretty much every episode of this podcast, our estimates of incidence and prevalence are only as good as the surveillance that we do. And in the case of anthrax even though in almost every country it's a global presence and it's a notifiable disease, we still just don't have excellent data in a lot of cases.

Erin Welsh

Okay.

Erin Allmann Updyke

And I think this is probably at least in part because it's not specifically a human disease and it can often infect wildlife, it's really hard to get a handle on something as big as that. Understanding everything from the course of the disease to the ecological characteristics in so many different ecosystems, it's a massive challenge.

Erin Welsh

Oh yeah.

Erin Allmann Updyke

So anthrax is really I think probably especially fun for us, Erin, because it's an environmental pathogen that really requires a large scale interdisciplinary approach to understanding and control. And because of that we wanted to talk to someone who is an expert in this type of interdisciplinary research when it comes to anthrax, understanding the disease dynamics in wildlife, evaluating the climate and environmental patterns in the distribution of anthrax, identifying the challenges and predicting outbreaks and most of all working across fields to most effectively control the incidence of this devastating disease. We were so lucky to get to chat with spatial epidemiologist Morgan Walker and we'll let her introduce herself right now.

Morgan Walker

My name is Morgan Walker, I am a spatial epidemiologist at the University of Florida. I work in Dr. Jason Blackburn's lab and we are housed jointly in the Department of Geography and the Emerging Pathogens Institute at UF. And my research focuses on the spatial and temporal patterns of diseases and disease spread especially of bacterial zoonoses which are bacterial diseases that can affect both animals and humans, one of which is anthrax.

Erin Welsh

Awesome.

Erin Allmann Updyke

Excellent.

Erin Welsh

Thank you so much for joining us, we're so excited to talk with you.

Erin Allmann Updyke

We're thrilled.

Morgan Walker

Thank you so much for having me.

Erin Welsh

So we wanna just start off by asking a very basic general question. What is the current worldwide distribution of *B. anthracis*? I know it's a big one. And so because there are presumably patterns in the distribution of this pathogen, we also wanted to ask you what are some of the environmental or climatic determinants of its distribution? What are some of the patterns that we see?

Morgan Walker

Yeah so it is definitely a big one, it's attributed pretty much globally. Some of the areas where it is endemic or where we typically see cases are areas like Central Asia, the Midwest of the United States extending up into the Northwest Territories of Canada, Sub-Saharan Africa, Southern and Eastern Europe, and Southeastern Australia. And part of the reason why it has such a wide range is because it can form a protective spore around it which makes it really hearty and really resistant to a variety of environmental and climatic conditions. But it survives best in soils with slightly alkaline pH, soils where there's high calcium concentrations, and in soils where there's lots of organic matter present, so fertile soils.

Erin Allmann Updyke

Excellent. So then what types of kind of environmental or ecological patterns do we know of that are tied to an increased risk of anthrax outbreaks either among animals or even humans?

Morgan Walker

That's a great question, it's something that we're definitely still researching and trying to figure out because if we have a better idea of why an outbreak happens we can do a better job predicting when they're going to occur and how intense they're going to be. There's not a clear consensus at this point what the mechanism is that leads to an outbreak because outbreaks have happened in such a variety of geographies and a variety of ecological conditions and to such a wide variety of animal species. But what we can say at this point is it seems to be that in the mid to high latitudes of the world the pattern that precedes an outbreak is there will be a wet spring followed by a hot, dry period and then there will be a rainfall event, so basically it will rain really hard. And then a few days after that rain event there will suddenly be cases popping up.

And we're still researching why is it that pattern leads to outbreaks but in areas like West Texas we see both on the ground and anecdotally when talking to land managers that those conditions seem to allow the populations of biting fly populations to explode. So we think that biting flies are mechanical vectors of the disease which essentially means that when a biting fly bites an animal that is actively fighting that infection and has *Bacillus anthracis* circulating through its bloodstream, it can get the bacteria on its mouthparts and then fly to another animal, bite it, and infect it.

Erin Welsh

That's such an interesting mechanism of dispersal cause it's like a vector but not a vector.

Erin Allmann Updyke

But not a vector. Yeah. (laughs)

Erin Welsh

In the way that we traditionally think of vectors.

Erin Allmann Updyke

Oh man.

Erin Welsh

Yeah. So I know that you said that we're still sort of working out the exact risk factors for an anthrax outbreak but how do we monitor how risk of exposure to anthrax changes over time? And then also how does that risk in general differ between let's say some groups of wildlife or some groups of domestic animals and humans as well? How does the risk change for those different groups?

Morgan Walker

Yes. So globally the use of active surveillance or continually monitoring risk in a population for anthrax is really limited especially because areas can go long time periods without seeing an outbreak so people get into a habit of not really worrying about it and so they're not actively monitoring. It's much more common to do sort of passive surveillance which means that on the animal side of things, if a land manager sees an animal that is exhibiting clinical signs of anthrax, they might have that animal tested or they might have that animal carcass tested if the animal actually succumbs to disease. And then on the human side of things, passive surveillance pretty much looks like waiting for humans to get infected to come into a clinical setting because they need to be treated and then that's how cases get reported. So almost all mammals are susceptible however the animals that we typically see dying of anthrax are herbivores, so that's why it's a big problem in livestock amongst cattle, goats, and sheep. Whereas carnivores actually very rarely succumb to anthrax. So it does differ amongst animal groups.

And then for humans, risk is definitely sort of dependent on occupation and behavior. So obviously if you're a land manager that's trying to handle an outbreak and dispose of carcasses, that's something that will put you at risk. But also it's not uncommon in certain areas of the world for people who are raising livestock, if they see an animal that's sick they might go ahead and slaughter that animal just so that they can try to recover some of the financial investment that they've spent. And then once they are slaughtering the animal, handling infected animal meat, that puts you at risk for cutaneous anthrax. And then if you go on to sell that meat and people eat it and it might be undercooked, they can also become infected that way.

Erin Allmann Updyke

Got it. So as a pathogen that spends part if not the majority of its life cycle in the external environment, like not being pathogenic necessarily, it seems very likely that global climate change is going to or maybe already has begun to impact the distribution of *Bacillus anthracis* in some way. So could you talk a little bit about what some of the models are predicting in regards to the impact of a warming climate on either a shift or expansion in the range of this pathogen and what might that mean for the kind of shifting landscape of risk?

Morgan Walker

Yes. So at this moment in time there's a lot of uncertainty in the face of climate change when thinking about *Bacillus anthracis*. Because there could absolutely be range expansion where we see that new areas are not suitable for other bacteria to survive but at the same time some models predicted there will be range contraction. Additionally some people hypothesize that outbreaks could become more intense because those weather patterns that I talked about earlier where there's a really wet spring and then a hot, dry period, that could happen more frequently or it can be on larger scales. But at this point it's really difficult to know exactly what's going to occur, we don't really have enough data and because anthrax, there's a lot of stigma around it so it's actually underreported globally so we're still kind of working on getting highly accurate maps of just where cases are occurring today. So projecting that into the future is something that's pretty difficult at this point to do.

Erin Welsh

Gotcha, gotcha. Yeah. Fortunately for *Bacillus anthracis* we do have various methods of control or prevention, sometimes treatment. So we have like a vaccine, we have antibiotics, and we have also just improved sanitation and monitoring measures. And so we wanted to ask sort of how do the use of these different control measures differ between wildlife and domestic animals for instance or just between animals in general and humans? So like for instance let's say that there's an outbreak in wildlife, how might different control strategies be used in that outbreak compared to one in livestock for instance?

Morgan Walker

Yes. So that is the good news, there are different control strategies and for livestock there is a vaccine that's very effective and it's been in use for decades and it's easy to administer. But the downside of that is that the vaccine is most effective 21 days after vaccination. So it might not be most effective to administer in the middle of an outbreak. And then additionally the vaccine has to be readministered annually so that is time consuming and can sometimes be difficult.

In terms of wildlife the vaccine is safe for wildlife, that is an off label use meaning that there haven't been many clinical trials done to confirm the safety and efficacy of the vaccine in wildlife but it has been used for a variety of species and seems to be effective. The problem with that is that the vaccine is an injectable vaccine, so if you can't get close to the wildlife in question, that makes it very difficult. You can dart, so if you have a dart and you put the vaccine in it and then you can shoot the animal, that is a way to administer it and that's sometimes used for wildlife that are on some of these closed ranches that have exotic wildlife species that are expensive animals, sometimes people try to do that. But they also have to weigh the risk of then you can potentially injure the animal with a dart vs administering the vaccine.

Erin Welsh

Right. Interesting, yeah. So with these different control strategies, does their effectiveness vary regionally?

Morgan Walker

Yes. Vaccine use is a strategy that varies regionally and by countries and sometimes even within countries. In the former Soviet Union for example they have a legacy of really high vaccination of livestock and so that's still in place in many countries in Central Asia and Eastern Europe. Whereas a lot of areas in for example Sub-Saharan Africa and South and East Asia, the amount of vaccinations going out to livestock are really low, sometimes around 0-5%. So one of the methods of control during an outbreak is proper carcass disposal, so it's very important to try to dispose of the carcass in a way that will minimize the amount of bacteria that gets leached out into the environment, how we recommend that people do that, best method is through burning and if you can't burn the animal thoroughly we recommend that people bury it. If you can't bury it we recommend decontamination with a bleach spray. But regionally, especially in areas if they're experiencing an outbreak in the hot, dry season, it might be too dangerous to try to burn the animal carcass because of danger of wildfires.

Erin Allmann Updyke

So with anthrax, it's one of these examples of a system that there are so many different angles where not only can you study it but you kind of have to because you have animal hosts, you have a human disease, you have the genetics or the microbiology of the pathogen itself but then you have the environmental aspects, you have all these different regional aspects of different cultural practices. It's so much and then there's like public health, big scale, on top of all that. So could you talk a little bit about how interdisciplinary research is just so crucial for a disease like anthrax and kind of what interdisciplinary research looks like in practice?

Morgan Walker

Yeah. So interdisciplinarity is really important for anthrax because as you know there are many different agencies and research groups and stakeholders all involved. And our lab aims to be a part of that practice by being involved in so many different pieces of the puzzle. So we do things from working outbreaks on the ground with land managers to then taking those samples that we collect back to the lab and doing diagnostics to whole genome sequencing to then mapping the outbreak and trying to analyze it to then also working with partners internationally to try to mutually educate ourselves about the disease and also to help inform them with prevention of the disease.

So there's definitely a lot of components that go into it and it's difficult to coordinate. And as many public health issues are, there's still a lot of progress to be made. As I mentioned, there's a lot of stigma around anthrax so it goes underreported globally and it's also really difficult to determine the exact distribution of vaccination and how many vaccines are going out to animals. So to more accurately understand where cases are occurring as well as vaccination, we really need more accurate reporting which takes interdisciplinarity and the cooperation between many different groups and agencies.

TPWKY

(transition theme)

Erin Welsh

That was so awesome, thank you so much Morgan and thank you to Dr. Salzer as well, that was just so great. I loved it.

Erin Allmann Updyke

Yeah. We're so lucky to get to have both of you on, thank you.

Erin Welsh

Yeah. All right. This was a really fun episode to do, it was super interesting, so many different angles.

Erin Allmann Updyke

Yeah. I feel like I learned a lot.

Erin Welsh

Yeah, absolutely. Speaking of learning a lot and learning a lot more, should we do sources?

Erin Allmann Updyke

Let's do sources.

Erin Welsh

Okay. So for this episode I have a lot of sources and I will list all of them on our website but I do wanna shout out a book that I used called 'Death in a Small Package: A Short History of Anthrax' by Susan Jones.

Erin Allmann Updyke

Yeah. I also had quite a number of sources, Erin. A couple that I wanted to give a special shout out to, there was a paper, it's a little old now from 1998 by the World Health Organization that is 'Guidelines for the surveillance and control of anthrax in humans and animals'. It's just a really nice kind of overview of just how broad anthrax is. And then a couple of really great papers by Dr. Colin Carlson really focusing on how important interdisciplinary research is for anthrax. So there's a paper from 2018 called 'Spores and soil from six sides: interdisciplinarity and the environmental biology of anthrax'. And Morgan Walker wrote an awesome paper that came out in 2020 called 'Ungulate use of locally infectious zones in a re-emerging anthrax risk area'. You'll find the list of all of our sources from this episode and every one of our episodes on our website thispodcastwillkillyou.com.

Erin Welsh

Yes you will. Thanks again so much to our absolutely wonderful guests, it was such a joy to chat with you.

Erin Allmann Updyke

Yeah. It really was. Thank you also to Bloodmobile who provides the music for this episode and all of our episodes.

Erin Welsh

And thank you to the Exactly Right network of whom we are a very proud member.

Erin Allmann Updyke

And thank you to you, listeners! You make this podcast worth making honestly.

Erin Welsh

Seriously, absolutely, 100% true.

Erin Allmann Updyke

Yeah.

Erin Welsh

And also a special shout out to our patrons, we love you and appreciate you like so much.

Erin Allmann Updyke

So much.

Erin Welsh

Okay well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals!