

Erin Welsh

Hey everyone. We're including a content warning for the firsthand account that we're about to read which includes a description of the death of an infant. To skip this, jump ahead about three minutes.

Erin Allmann Updyke

"Mrs. Cyril, Orchard Street, age 24 was delivered of her third child on Friday morning, September 2, 1859. It was a male child, fine and apparently healthy in every respect. From Friday til Wednesday, all was well. The court separated on Tuesday, the fifth day. On Wednesday the child was restless, cried, and kicked. On Thursday the mother reported that he cried all day, could not open his mouth, could not suck, and frequently stretched and was stiff. The next day, Friday, I saw him. Every few minutes he appeared as if struck by an electric shock. Every muscle was thrown into distorted action. I will not attempt to describe. This drawing tells.

The wrinkled forehead, the elevated brow, the closed eye, the dilated nostril, the rigid masseter, the fixed jaw, the closed mouth, the corrugated lips, the bubbling saliva, the retracted head, the shortened neck, the starting cervical muscles, the turgid veins, the arched spine, the raised chest, the troubled breathing, the catching diaphragm, the heaving abdomen, the separated arm, the squared elbow, the bent wrist, the clenched fingers, the in-curved thumb, the extended and separated legs, the bent down toes, the livid surface, the whole figure rigid as wood. A pitiful sight.

The paroxysm was renewed by a slight noise, the gentlest touch. A placid interval of a few minutes succeeded and then another fit followed. On examining the child the umbilicus was seen prominent, at least half an inch long, red and showing an unhealthy separating surface. The umbilicus continued to discharge. Emaciation rapidly advanced. The skin assumed a brownish hue and hung in shriveled folds of leathery texture. Peace and pain pursued their sickening interchange. The child gradually became more feeble and on the 10th day of the disease and the 15th of his existence, he sank by degrees exhausted."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

That was really difficult to read.

Erin Welsh

Absolutely horrible.

Erin Allmann Updyke

Yeah.

Erin Welsh

And thank goodness there's a vaccine.

Erin Allmann Updyke

Yeah. That was from an 1860 case description of tetanus infantum, aka neonatal tetanus or tetanus.

Erin Welsh

Yep. Hi, I'm Erin Welsh.

Erin Allmann Updyke

And I'm Erin Allmann Updyke.

Erin Welsh

And this is This Podcast Will Kill You.

Erin Allmann Updyke

And I'm sure you all know by now the subject of today's episode.

Erin Welsh

Yeah. Tetanus. It's a vaccine preventable disease that we haven't covered yet which is exciting.

Erin Allmann Updyke      Yep. And it's obviously going to be difficult at times because it's a really truly horrible disease.

Erin Welsh      Yeah. I mean absolutely horrific, devastating, awful.

Erin Allmann Updyke      Yeah, yeah. But there's going to be a lot of very interesting biology. I know there's going to be some fascinating history that I can't wait to learn about. And I have some thrilling things to talk about in the current events section. I am really excited, yeah.

Erin Welsh      Ooh I'm so intrigued.

Erin Allmann Updyke      So shall we get started on the important things?

Erin Welsh      Of course, of course we should. What time is it?

Erin Allmann Updyke      Quarantini time.

Erin Welsh      It is. And this week we are drinking The Rusty Nail which just so happens to be an actual cocktail.

Erin Allmann Updyke      It's a real drink.

Erin Welsh      It is. It has scotch and Drambuie and I think that's it.

Erin Allmann Updyke      And we're going to find a way to make the nonalcoholic version, our placeborita.

Erin Welsh      Yeah, it's going to be an interesting one to make a placeborita for but I think that it might not bear too much resemblance to a scotch in a scotch-based liqueur. But I think that's okay as long as it's delicious, right?

Erin Allmann Updyke      Yeah. I trust in you, Erin.

Erin Welsh      Okay, thank you. And we'll post the full recipe for this quarantini and non alcoholic placeborita on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com).

Erin Allmann Updyke      On our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) you can find all of the things. You can find our merch which is incredible, you can find a link to Bloodmobile who does all of the music for this podcast, you can find transcripts of all of our episodes and the sources that we use for every single episode. You can find our [bookshop.org](http://bookshop.org) affiliate account and our Goodreads list. You can find our Patreon. Really there's just so much there.

Erin Welsh      Yeah, you did a great job.

Erin Allmann Updyke      Thanks.

Erin Welsh      There's a lot there, go check it out. Can we dive into this?

Erin Allmann Updyke      Yes, I think that we ought to right after this break.

TPWKY      (transition theme)

Erin Allmann Updyke

So today we're talking about another Clostridium species, Clostridium tetani. We've covered this genus before of course in our botulism episode and then I mentioned it again in our C. diff episode, although C. diff was reclassified as Clostridioides. But anyways today it's Clostridium. Clostridium tetani is an incredibly widespread and hearty little bacterium. It's a rod-shaped, gram-positive, spore-forming bacterium that when it's making its little spores, if you look at it under a microscope, looks like a little matchstick or like a tennis racket. It's kind of cute because it makes it a little spore at the end.

Erin Welsh

Oh interesting.

Erin Allmann Updyke

And like its cousin Clostridium botulinum, this is an anaerobic bacterium which means it likes to grow without any oxygen. But because it's a spore former, these spores are incredibly hearty. They're very resistant to heat, to cold, to antiseptics, to oxygen. And so this is a bacterium that persists in the environment across the globe. It makes its home in the soil. But Clostridium tetani can also thrive in the intestines of various animals including humans.

Erin Welsh

I found that so interesting. And what is it doing there? Is it just a part of your gut microbiota? Are there any sort of negative effects or is it just really hanging out?

Erin Allmann Updyke

As far as I know at least they just hang out. I'll be honest I didn't do a lot of digging into what they're doing in our guts.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. But as this is a soil bacterium and as this is This Podcast Will Kill You and we're talking about the disease caused by Clostridium tetani, people are exposed through the soil kind of in general. Usually exposure to this bacterium tends to be from wounds, especially deep wounds or puncture wounds that come into contact with anything contaminated with this bacterium which again can live almost anywhere. So this can be anything from rusty nails to fence posts, thorns from a tree, even potentially bites if they are contaminated. Really any kind of deep wound because those kinds of wounds have pretty limited exposure to air which means limited exposure to oxygen. And so as tissue death occurs deep within that wound, the environment can become very anoxic which can allow for tetani spores that are present in the soil that contaminate that wound to germinate and grow.

Erin Welsh

Interesting.

Erin Allmann Updyke

Yeah.

Erin Welsh

I have a really dumb question.

Erin Allmann Updyke

Okay.

Erin Welsh

Anaerobic environment meaning there's no oxygen. There's oxygen carried by your blood. If you're bleeding is that an anaerobic environment?

Erin Allmann Updyke

It's a great question. So no. If you have active blood flow to an area, then that tissue is not going to become very anoxic. What can happen in deep puncture wounds is that the tissue can die deep within. And so once you have dead tissue, that tissue is not being supplied by your blood supply very well. So that is why it can become an anoxic. But that's a really good question, it's not a dumb question at all.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

I'm fascinated.

Erin Allmann Updyke

Yeah. That's why in theory any wound can become contaminated with *Clostridium tetani*. But not every wound is going to be as susceptible to actually harboring an active tetanus-generating infection, if that makes sense. Now I'll talk a lot in this episode about neonatal tetanus and the firsthand account that you heard was a description of neonatal tetanus. It's the same as regular tetanus in kind of what it does to the body but neonatal tetanus is often classified as specific because it happens with contamination of the umbilical stump, so the umbilical cord that's left when a baby is born. That's just kind of an open area that can very easily become contaminated and the base of that is dead and dying tissue because that's what's normally supposed to happen with an umbilical cord. And so that's why it's a place that's very easily... And then of course babies have almost no immune system so that helps as well.

Erin Welsh

Right, right.

Erin Allmann Updyke

So that's kind of how we get exposed. And just like with *Clostridium botulinum* and *Clostridioides difficile*, the story here is not the bacterium itself. It's also not the spores of this bacterium. The story of tetanus is the story of the toxins that this newly germinated bacterium can release within our body. So let's talk about them.

Erin Welsh

Yeah, these toxins are... Can I read a quote real quick actually? Can I interject a quote?

Erin Allmann Updyke

Please.

Erin Welsh

Okay.

Erin Allmann Updyke

Yes, please do.

Erin Welsh

I was hoping I was going to be able to use it somewhere. Quote: "An amount of tetanus, botulinus, or dysentery toxin weighing no more than the ink in the period at the end of this sentence-" presumably Times New Roman 12, "would be enough to kill 30 grown people. An ounce could kill 30 million tons of living matter, half a pound would be more than enough to destroy the entire human population of the world." I'm not sure when this was written but I think it probably would still be sufficient.

Erin Allmann Updyke

I love it. Okay I feel like I remember you reading that quote in our botulism episode.

Erin Welsh

I feel like I did too. Whoopsie.

Erin Allmann Updyke

I'm pretty sure you did. No, it's not a whoopsie. I'm really glad that you said that again because I was trying to classify how much because the numbers that we're going to talk about are so small and I was really worried that you were going to ask me to be able to and I'm really glad you just did it for me.

Erin Welsh

Why, how about that?

Erin Allmann Updyke

All right, so let's talk about those incredibly terrifying potent toxins, shall we?

Erin Welsh

Let's do it.

Erin Allmann Updyke

So exotoxins are proteins that bacteria make that can disperse throughout our body and cause an effect. We've talked about them a lot on this podcast. The toxin in *Clostridium tetani* is the causative agent of tetanus, not the bacteria themselves. This toxin, the tetanus toxin - tetani as a side note, it actually produces two different toxins. One is called tetanolysin and the other tetanospasmin. Tetanolysin we don't really understand at least from what I read, maybe it helps establish an infection or something like that. But tetanospasmin is tetanus toxin. So that's what we're going to talk about today. So this tetanus toxin is a neurotoxin just like botulinum produced from *Clostridium botulinum*. And so it specifically binds to our nerves and affects our nervous system. Let's recap what we learned in our botulism episode, shall we? Then we can do some compare contrast.

Erin Welsh

My favorite. I was so looking forward to this.

Erin Allmann Updyke

I know. I actually just took some notes. I copy-pasted some notes from my... It's gonna be great. It's a recap. Botulinum toxin blocks the release of acetylcholine at our peripheral nerve synapses, if that sounds familiar. So what that results in is a flaccid paralysis meaning a limp paralysis. Because the signals from our brain don't ever actually make it all the way to our muscles, so your muscles are paralyzed in this flaccid limp state rather than a contracted state. That happens when this botulinum toxin binds to our nerve cells at the neuromuscular junction which is the junction between our nerves and the muscles that they innervate and then blocks the release of the transmitters at that junction.

Erin Welsh

Okay.

Erin Allmann Updyke

Tetanus toxin does the exact same thing. It blocks the release of neurotransmitters in a synapse in a junction. But it does it in the inhibitory interneurons within our spinal cord. I'll explain.

Erin Welsh

Okay.

Erin Allmann Updyke

But the bottom line is that tetanus toxin has the exact opposite clinical effect. It causes a spastic paralysis or muscles that are paralyzed in a rigid or contracted state. So let's go through the steps, shall we?

Erin Welsh

Yeah.

Erin Allmann Updyke

What happens in the case of tetanus toxin is it binds actually to our nerve cells in the same exact place as botulinum toxin. It binds to our nerve cells at the neuromuscular junction, the NMJ, and it is internalized in those cells at the same place as botulinum. But while botulinum toxin acts, it exerts its effects right there at the neuromuscular junction, blocking the release of acetylcholine. What tetanus toxin does instead of acting right where it enters our cells, is it actually travels retrograde along our nerve axon à la rabies virus.

Erin Welsh

Oh yeah, okay.

Erin Allmann Updyke

If that sounds familiar. It travels all the way up our nerve axons, like from the muscle in your jaw for example all the way up the nerve into our central nervous system where the nerve came from. And then it enters the space in between. It travels through that intersynaptic space inside our central nervous system and enters another set of neurons in our spinal cord. And there it blocks the release of neurotransmitters the same way that botulinum does. But it just so happens that the neurons that it enters in our spinal cord are the inhibitory neurons that primarily release neurotransmitters whose primary job is to inhibit or block the firing of our motor neurons.

Erin Welsh

Okay. And so if they can't do their job then all those motor neurons are going pew-pew-pew and then that's where you get the rigidity and spasms.

Erin Allmann Updyke

Exactly, you just read my next line. It's perfect. So exactly. If you can't inhibit the inhibitors then your motor neurons are getting signals from your brain rapid fire which leads to this intense muscle rigidity, this spasm.

Erin Welsh

Okay. I have a question about wound location and course of disease and stuff like that.

Erin Allmann Updyke

Okay. Ooh yeah.

Erin Welsh

So the classic picture that I have of someone with tetanus, and I'll talk about this actual picture later on, is someone who is completely every single muscle is rigid.

Erin Allmann Updyke

Yeah.

Erin Welsh

Does that happen all the time? Does it happen in stages? For instance if you have a wound on your hand, does that mean that the hand will become rigid first?

Erin Allmann Updyke

Such a good question. In general, the course of tetanus is the same always. And in general the course is that the muscles that tend to be affected first are the facial nerves, so the muscles that are in your face like your jaw and your neck and your head. And then it tends to travel kind of downward and then affect your trunk and your limbs, etc.

Erin Welsh

Why is that?

Erin Allmann Updyke

That's a great question. I don't know and I don't think that we fully know. So the nerve pathways to our facial muscles are a lot shorter, like the distance from the central nervous system to those muscles, it is a lot shorter. But it doesn't matter where you get exposed if that makes sense. So say you get a wound on your foot, that tetanus toxin makes it in, makes it to your central nervous system and it seems to be that it's still the head and neck first and then the rest of the body after that. It is really interesting. I don't fully know why.

Erin Welsh

So bizarre.

Erin Allmann Updyke

I know. It is really, really interesting. Yep. And the same was true for botulism where it often went from the head down.

Erin Welsh

Right.

Erin Allmann Updyke

Yeah. So that is kind of how this toxin works. In general the incubation period, the time from when you are first exposed to when these symptoms start, it's quite variable. Most sources on average say like 3-14 days, some say 7-10. It really can just depend on where you get exposed, whether you're talking about an infant versus an adult, things like that. And like I said the symptoms do tend to follow this general progression. So they often start with this neck stiffness, difficulty opening the mouth, and then that progresses to the classic name for tetanus which is lockjaw. And that is from the spasm of the muscles of chewing, the muscles of the jaw that spasm shut. And then that continues to progress. There is a kind of characteristic facial posture called risus sardonicus.

Erin Welsh

Oh yeah.

Erin Allmann Updyke

And it's this really awful facial expression that's a very pronounced closed mouth, teeth bared grimace because all of the muscles of your face are just rigidly contracted. At this point the muscles of swallowing are very likely affected, so there's going to be some degree of dysphasia or difficulty swallowing. And as it continues to progress, the muscles of the trunk can become affected and this can lead to a rigid posturing that's known as opisthotonus which is again really, really awful if you see pictures of it. But it's this very rigid arched back with head jutting back because all the muscles of your spine, along your spine become contracted. At this point because of all of this contraction of all of these muscles, the chest wall is not very compliant. So that means that you can't breathe very well because the muscles between your ribs and your back, they're kind of in spasm so it can be really difficult to take in air.

Erin Welsh

Oh my goodness.

Erin Allmann Updyke

Yeah. There can also be kind of convulsions that happen similar to seizures that can happen on top of this generalized increase in muscle tone. So these spasms can look a lot like seizures. But if these spasms affect muscles like the larynx of the throat then they can lead to airway obstruction which can be life threatening. And one of the papers I wanted to read a quote from because I think it kind of sums up just how awful this really is. They said after this description of all of these symptoms, quote: "Consciousness is preserved, making tetanus a truly dreadful disease." End quote.

Erin Welsh

Oh no.

Erin Allmann Updyke

Yeah, yeah. So it's a really horrible disease.

Erin Welsh

Yeah. To say the least.

Erin Allmann Updyke

To say the least. And you can imagine there are a lot of different ways that people can end up dying from tetanus and just like with botulinum while there is treatment for the effects of tetanus toxin, we have tetanus IgG, like antibody treatment. The treatment, the main function is to bind and neutralize any of this toxin that hasn't yet bound into the central nervous system. But this can only do so much because once tetanus toxin is bound and internalized into our nerve cells there's nothing that we can do about it. It's permanent until our nerves essentially regenerate which is what has to happen. Those nerve terminals have to actually remake themselves to be able to then resend the signals that they need to send to inhibit muscle contraction.

Erin Welsh

So if you don't get that early enough it's...

Erin Allmann Updyke

Right.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. Tetanus toxin doesn't kill any of the nerve cells which I think is really important. But the neurons still do have to kind of remake those synapses in order to be able to work again properly. So you're not having to make entirely new nerves or anything like that but you can't stop the effects of the toxin that have already been integrated into our cells.

Erin Welsh

Right.

Erin Allmann Updyke

So on top of using treatments like the tetanus antibodies, you also have to treat the source of infection. So antibiotics or wound debridement if there is some kind of active wound that's still making more tetanus toxin. But really the most important thing in terms of treatment is supportive care and sedation. And one thing that's really interesting, although incredibly depressing still, is that after the advent of mechanical ventilation, so being able to intubate someone and breathe for them while this process is taking place in their body, this obviously helps keep people alive because they usually would die from respiratory failure with tetanus. But since we have invented that, we have found that tetanus wreaks even more havoc on the body than we realized. While botulinum really only affects the motor nerves, because tetanus goes into our central nervous system it causes a lot of autonomic instability as well that we didn't realize until we had mechanical ventilation to keep people alive long enough to see that process, if that makes sense.

Erin Welsh

Yeah.

Erin Allmann Updyke

And so it can cause a lot of blood pressure variation, it can cause heart rates to go really, really high and then drop really, really low because it basically is blocking your autonomic nervous system from being able to send signals appropriately. So it's a very difficult disease to treat with supportive treatment though it's not impossible, it's absolutely possible, it's just really complicated.

Erin Welsh

Jeez.

Erin Allmann Updyke

And so because of that, mortality rates for people who are unvaccinated, who have never been vaccinated can still vary really widely. One source that I read estimated anywhere from 10% -60% mortality for neonatal tetanus. And of course neonatal tetanus happens when babies are too young to be vaccinated. So in adults the mortality rate can vary from 8%-50% I read and it increases with age. So it's a very complicated disease to treat but it is entirely preventable which is amazing.

Erin Welsh

Yeah. Truly.

Erin Allmann Updyke

It really is. We have an incredibly effective vaccine that has very long lasting immunity and it is I think the cheapest vaccine to ever have been produced is one thing that I read. Yeah, I love that.

Erin Welsh

Cool.

Erin Allmann Updyke

And it's been around for a really long time. So that's the good news that we'll get to end this episode later with at least some happy news because of the vaccine. So that's the biology of tetanus, Erin.

Erin Welsh

It is just as, maybe more horrifying than I anticipated it would be.

Erin Allmann Updyke

Yeah, I know. It really is.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. I have a question for you, Erin. How on earth did this process evolve? Because okay, here's the thing Erin.

Erin Welsh

Yeah.

Erin Allmann Updyke

You mentioned up at the top just how potent this toxin is.

Erin Welsh

Right.

Erin Allmann Updyke

Right? It is so potent. I didn't even know this until researching but getting infected with tetanus, getting infected with *Clostridium tetani* and then surviving an infection does not provide you with immunity. Because the tetanus toxin is so potent that just the tiniest amount of it causes incredible symptoms but not enough to produce antibodies that we actually make enough of to then produce immunity. Whereas we know that we produce immunity because we have a great vaccine. And I mean that's incredible. And one source that I read said that the toxin may constitute 5% of the weight of this organism.

Erin Welsh

Whoa.

Erin Allmann Updyke

So they're making a ton of this toxin.

Erin Welsh

It is so bizarre and I am not certain that I have a satisfying answer. But I want to get into it with you.

Erin Allmann Updyke

Okay good.

Erin Welsh

So let's take a quick break and then I'll get started.

Erin Allmann Updyke

I can't wait.

TPWKY

(transition theme)

Erin Welsh

I found the history of tetanus to be so interesting for a number of reasons. First it checks a lot of the boxes for a classic TPWKY episode. Tetanus is an infamous disease, there are plenty of ancient descriptions, of course war plays a role, gets a mention.

Erin Allmann Updyke

Oh yeah.

Erin Welsh

And also we get to talk about the golden age of germ theory.

Erin Allmann Updyke

Yeah.

Erin Welsh

All that good stuff. Second, we've covered a couple of related pathogens before as you mentioned. And so it was kind of fun to compare the evolutionary histories or human histories of these, especially with *Clostridium botulinum*.

Erin Allmann Updyke

Yeah.

Erin Welsh

And third, there are parts of the history of tetanus that I feel provided an opportunity to think about how perceptions of a disease, especially who is most likely to get that disease can really find their way into how these diseases are written about historically. And I think that's good to keep in mind as we try to read between the lines and understand how people were observing disease and why. So let's get started.

Erin Allmann Updyke

I love it.

Erin Welsh

Where did tetanus come from? Great question. I wish I had an answer. I can tell you where the word tetanus came from which is the Greek verb 'tetanos' meaning to stretch. But from what I can tell, we don't really know where this pathogen originated in the world and when it spread around the world because it is globally distributed. Did its global distribution predate wide scale travel by humans? Maybe.

Erin Allmann Updyke

Maybe?

Erin Welsh

Maybe. It's a mysterious little pathogen. We do know though that humans have been exposed to tetanus for at least most if not all of written history and probably have been for all of our prehistory as well. But we'll get to that in a second because first I want to talk about some aspects of tetanus ecology and evolution. So like I said, we don't know where geographically tetanus emerged but we do know that it doesn't really seem to change all that much. Its genome is highly conserved which is actually I think something that we've seen for a few other spore formers which I think is cool.

Erin Allmann Updyke

Yeah. Anthrax, right?

Erin Welsh

Anthrax especially, yeah. Clostridium botulinum is less stable. But anyway the plasmid carrying the tetanus toxin gene is more variable but the gene itself-

Erin Allmann Updyke

Is not.

Erin Welsh

Is very stable which makes sense.

Erin Allmann Updyke

Yeah. That's so interesting though because with botulism there's more than a few different types of the toxin but with tetanus it's really just tetanus toxin.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

And with the botulinum toxin it's found in many different strains of Clostridium. Whereas yeah, the tetanus neurotoxin only in Clostridium tetani.

Erin Allmann Updyke

Yeah.

Erin Welsh

And like you said, these two neurotoxins are structurally and functionally similar but they seem to have followed different evolutionary pathways. And I think it's really cool to look at the ecology of these bacteria to see maybe why that might be or why these different characteristics of these two bacterial species, why they contribute to the patterns that we see in disease and outbreaks and sporadic cases, stuff like that. So both *Clostridium tetani* and *Clostridium botulinum* are anaerobic, soil dwelling, and they produced this deadly and potent neurotoxin. But why? Why do they do this?

Erin Allmann Updyke

Right.

Erin Welsh

Why Are You The Way You Are was the title of our botulism episode because we were like why, why, why? And we talked about how *Clostridium botulinum* will be picked up by a dabbling duck or something and then the toxin will kill the bird, that carcass becomes a great anaerobic replicating ground for the bacteria and also a great source of environmental contamination as other animals either nibble on the corpse or around the corpse or in the more dabbling ducks, then the soil, whatever.

Erin Allmann Updyke

Right. I remember that a lot.

Erin Welsh

Yeah. It was a very cool thing to visualize.

Erin Allmann Updyke

Right.

Erin Welsh

Like oh that's why this exists. And so having this deadly neurotoxin is key to the life cycle of *Clostridium botulinum*. By killing its host, it can now contaminate a big chunk of the environment and spread to other hosts. And the tetanus toxin isn't too much different really. It's a potent neurotoxin that can kill its host but one key difference is that the botulinum neurotoxin can survive ingestion and that's how it creates disease while the tetanus neurotoxin cannot. And this difference is why we see outbreaks in botulism in nature and in food poisoning outbreaks, whereas we mostly see isolated sporadic cases in tetanus.

Erin Allmann Updyke

Whoa. So it makes even less sense.

Erin Welsh

It makes even less sense but it also does make sense to a degree, right? So this is likely a costly toxin to make. It has to help the bacteria, it has to help *Clostridium tetani* to survive, to be transmitted, to help it complete its life cycle in some way.

Erin Allmann Updyke

Yeah.

Erin Welsh

I mean these are soil-dwelling microbes so they don't necessarily need hosts to live, to proliferate.

Erin Allmann Updyke

Right.

Erin Welsh

But it would be great if a host came along with a little cut on their foot and picked up some tetani spores and then that host after it died became another great breeding ground for more contamination. So it might be a combination of the fact that this is a very useful tool for the bacteria and also their spore formers.

Erin Allmann Updyke

Yeah.

Erin Welsh

So I don't know.

Erin Allmann Updyke: But the whole gut thing. That's just so interesting.

Erin Welsh: I know.

Erin Allmann Updyke: Because I feel like that was such a big part of the botulinum story where then you eat it and then you continue it, etc. And so to know that that's not part of the story here is really interesting.

Erin Welsh: Yeah. I mean I feel like this story makes sense still, like the toxin plays an important role but it isn't as satisfying.

Erin Allmann Updyke: Yeah.

Erin Welsh: Nearly as satisfying.

Erin Allmann Updyke: Right.

Erin Welsh: And maybe that's the lesson is that evolution doesn't always tell a satisfying story.

Erin Allmann Updyke: Yeah, doesn't always make sense.

Erin Welsh: Yeah, it doesn't always make sense. It doesn't follow logic. It just is what it is sometimes.

Erin Allmann Updyke: Right.

Erin Welsh: That being said if anyone listening is like wait no I know why this happens or you have a paper where you can show me exactly because I spent hours and hours on Google Scholar trying to find out the evolutionary ecology of this neurotoxin, please shoot us an email.

Erin Allmann Updyke: Yeah.

Erin Welsh: I would love to read it.

Erin Allmann Updyke: We have so many more questions.

Erin Welsh: Yeah. But the good thing about this relatively non exciting or maybe not satisfying evolutionary history and the super stable genome of *Clostridium tetani* is that this means that the vaccine is very widely and highly effective and we don't have to worry about the emergence of strains that the vaccine doesn't protect you against. Which is good because this disease is horrible. Absolutely horrible. Tetanus causes this visually dramatic and deadly infection. And so it should come as no surprise that it has been mentioned in so many ancient texts.

Erin Allmann Updyke: All of them.

Erin Welsh: All of them. It's really back to back classic TPWKY with trachoma and chlamydia last episode and now this.

Erin Allmann Updyke: Oh yes.

Erin Welsh	So we're going to run through these ancient medical texts again. So we've got the Edwin Smith Surgical Papyrus written around 1500 BCE, that mentions it. The Ancient Indian physician Sushruta from around 600 BCE made a possible reference to it. Early Chinese medical texts from around 400-200 BCE described it. And of course we've got the Hippocratic texts from around 400s BCE.
Erin Allmann Updyke	Of course.
Erin Welsh	Yep.
Erin Allmann Updyke	Yep.
Erin Welsh	Hippocrates and other contributors to the texts, because it wasn't just Hippocrates, actually wrote quite extensively about tetanus, both the local and systemic forms and included some very colorful descriptions of the disease. Quote: "A man who was struck from behind by a sharp dart a little below the neck had a wound which did not look serious because it did not go deep. But sometime later when the point had been extracted, the patient was seized with backward bending convulsions like those of a opisthotonus. His jaws were locked and any liquid that he attempted to swallow was returned through his nostril. He died on the second day."
Erin Allmann Updyke	Oh goodness.
Erin Welsh	And if you're looking for treatments, the Hippocratic texts have got you covered. Fat bird soup, vapor baths, cold water baths, pepper, hellebore, and of course you have to throw in some bloodletting.
Erin Allmann Updyke	Of course.
Erin Welsh	Of course. And over the next hundreds of years nothing really changed for tetanus. 700 years after the Hippocratic texts, Aretaeus of Cappadocia added his thoughts on the disease and you can really tell how badly he felt as a physician completely unable to help his patients. Quote: "An inhuman calamity, an incredible sight, a spectacle painful even to the beholder, an incurable malady." He listed treatment after treatment. Frankincense, the hair of a poli*, fleabane, turpentine, etc. And this variety just kind of goes to show again that nothing seemed to help. Classic tetanus like what you would see in an adult human wasn't the only thing that these ancient physicians noticed. There was also mentions of equine tetanus and neonatal tetanus, which was sometimes called trismus and not necessarily recognized to be the same thing as tetanus for hundreds of years.
Erin Allmann Updyke	Interesting.
Erin Welsh	From these ancient texts, I'm going to skip way ahead until the 1800s, kind of like I did also for chlamydia/trachoma because not very much happened in terms of tetanus until that time. I mean yeah, sure there were additional descriptions of it and case reports and shifting hypotheses as to what caused the disease but overall the way that it was characterized in the Hippocratic texts didn't change much. A tiny injury, like one instance I read from the bite of a tame sparrow in the 1700s.
Erin Allmann Updyke	Whoa.
Erin Welsh	I know, there's a lot to take in in that sentence.

Erin Allmann Updyke

Yeah there really is.

Erin Welsh

But this tiny injury could lead to a horrifically painful infection that was ultimately fatal a lot of the time with no reliable effective treatments.

Erin Allmann Updyke

Right.

Erin Welsh

Even in 1892 when doctors had slightly better tools to help with feeding and muscle relaxation, the mortality rate was 80% after four days.

Erin Allmann Updyke

Yeah.

Erin Welsh

For much of human history, tetanus remained a sporadic disease except in a few instances or populations. And one of these was of course soldiers or during times of war for all the usual reasons of basically not having access to sanitation, an increase in both small and large wounds, etc. There's a famous painting, this is the picture of tetanus I mentioned, that you've probably seen depicting a soldier in a violent rigid spasm from tetanus infection. And I'm going to post this probably for the announcement release post for this episode on our social media. That was painted in 1809 by surgeon and artist Sir Charles Bell. It's titled 'Tetanus Following Gunshot Wounds'. And guess where the soldier got those gunshot wounds? During the Napoleonic wars. I mean again, Napoleon, it's just so many parallels.

Erin Allmann Updyke

Again Napoleon. Yeah.

Erin Welsh

Specifically if you're interested the battle of Corunna. I distinctly remember seeing that painting for the first time in my high school biology textbook or something and being so fascinated but also terrified by it.

Erin Allmann Updyke

Yeah.

Erin Welsh

I couldn't believe it was a real thing.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. And soldiers of course weren't the only ones that were disproportionately affected by this pathogen. In the mid 1800s, several doctors in the American South became interested in what they called trismus nascentium which would later be called neonatal tetanus. And they remarked that it was quote "no uncommon disease among infants born to enslaved people in the South". I want to take a minute to talk about neonatal tetanus in the American South before the Civil War because I think it's important for several reasons. First, it gives us an opportunity to see how much the established knowledge about a disease is so dependent on who's looking and especially whom they're looking at. Second, neonatal tetanus is I think a really clear example of how differently medicine was practiced, how medical stats were collected, and whom those stats represented between the American North and the Confederate South. And third, I think it highlights the beginning of a shift in medicine overall from so-called heroic medicine to preventative care.

Erin Allmann Updyke

I love it.

Erin Welsh

Okay. So neonatal tetanus as you described Erin and as our first hand accounts so vividly and horribly described is when the umbilical stump gets infected with the tetanus pathogen. It's tightly linked to access to sanitation and hygiene practices following delivery and it is like adult tetanus incredibly horrific and deadly. Those are not even adequate adjectives.

Erin Allmann Updyke

No.

Erin Welsh

An inhuman calamity.

Erin Allmann Updyke

Yeah.

Erin Welsh

Maybe we could we could borrow that phrase from Aretaeus. Before the US Civil War, enslavers would frequently employ doctors to monitor the health of enslaved people, not out of the goodness of their hearts of course but to protect their financial interests. These southern doctors began to notice high rates of neonatal tetanus in the infants born to enslaved people. And when I say high rates I mean very high. Some doctors estimated that up to 2/3 of the deaths among these infants were due to neonatal tetanus.

Erin Allmann Updyke

Oh man.

Erin Welsh

Yeah. Because of this neonatal tetanus was labeled by many doctors, especially those in the north, as a disease of the South or more specifically a disease of enslaved black people. But was it especially so? We don't really have any good way of knowing considering that statistics weren't widely used at the time. But it almost certainly wasn't. There may have been a few things that contributed to the high rates observed by southern doctors. For instance, there were some postnatal practices such as using cow dung or charcoal to wrap the cut umbilical cord that could have increased exposure. And some of those practices are still used today in various places and they are associated with higher rates of neonatal tetanus. But it was also probably a matter of visibility.

Neonatal tetanus was certainly present in the north but northern doctors probably didn't see it as much because unlike the southern doctors who wrote about neonatal tetanus, northern doctors didn't treat nearly as many people living in conditions that put them at risk for the infection. Mostly they would work at hospitals. And so if someone came into the hospital maybe then they would see them. But they didn't travel as widely into his varied urban and more rural centers the way that southern doctors could do. People who were living with a lack of access to sanitation, people living in poverty, etc, northern doctors weren't getting paid to treat these people unlike southern doctors. In addition southern doctors, especially those that were employed by enslavers, were much more likely to encounter cases of neonatal tetanus than their northern counterparts since it was midwives that mostly attended the birthing and postnatal care in the north.

And another big difference was that the southern doctors tended to keep more detailed records of the people they treated not because they were inherently more meticulous but again because it was more a matter of business and economics. And slavers wanted to know which diseases were contributing to the most death and disability or in their eyes lost profit. And this informed to some degree which diseases were given priority for study. Neonatal tetanus garnered a substantial amount of interest in the mid 1800s in the southern US because it contributed so highly to infant mortality among babies born to enslaved people. And several doctors started to try to understand why that was. Dr. Marion Sims, infamous so-called father of modern gynecology, I can't resist an opportunity to dis Marion Sims or at least call him out for being someone who absolutely tortured so many, an untold number of enslaved black women.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. Marion Sims was one of the doctors who tried to say I know the cause of neonatal tetanus and he thought it had to do with the formation of the skull.

Erin Allmann Updyke

What?

Erin Welsh

People were obsessed with skull shape for decades. Too long. He said if you put the baby in a crib, you should make sure there are lots of pillows around the baby and position the baby very carefully so that their skull could grow properly.

Erin Allmann Updyke

Oh dear. Oh no.

Erin Welsh

And one of his horrifying treatments involved drilling a hole in the baby's skull with an awl.

Erin Allmann Updyke

No. No. No. No.

Erin Welsh

Yeah. And there was no evidence of course to support his hypotheses and a couple of other doctors fortunately were around to pick apart his arguments. William Baldwin, a physician who graduated med school Transylvania University in Lexington, Kentucky at age 19-

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah, I mean it was the 1850s/1840s.

Erin Allmann Updyke

Yeah.

Erin Welsh

He wrote that Sims was wrong and that the disease was more common among enslaved people not because of how they laid an infant in a crib but because of living conditions and lack of access to sanitation. He didn't agree with Sims' and others claims that there was a racial disposition to disease but instead thought it was living in an environment that led to greater exposure. Which is pretty incredible to hear or more forward thinking than I anticipated considering this was the 1850s.

Erin Allmann Updyke

But I feel like that was malaria, etc.

Erin Welsh

Yeah.

Erin Allmann Updyke

People knew of this environmental...

Erin Welsh

The miasma.

Erin Allmann Updyke

Yeah, miasma.

Erin Welsh

Yeah, exactly. Yeah so I think that was definitely part of it. But I also think he might have been ahead of his time with this next quote.

Erin Allmann Updyke

Okay.

Erin Welsh: Because he suggested that it was quote: "A grain of dust or sand or other particle of foreign substance however small may be lodged in the delicate granulations of the umbilicus just after the detachment of the cord."

Erin Allmann Updyke: There you go.

Erin Welsh: So that's not wrong really.

Erin Allmann Updyke: No. No, that's exactly what it is.

Erin Welsh: I found that fascinating. And Baldwin wasn't alone. Another physician named John M. Watson from Tennessee took up the charge and further dismissed Sims in 1859 kind of harshly and directly, I appreciated it. He too believed that it was irritation of the wound and suggested that instead of Sims' barbaric skull drilling practice, people should try for simply cleaning the wound, having a more sanitary environment overall, basically practicing preventative medicine which was not in fashion at the time. Instead doctors tended to practice heroic medicine which I talked a bit about in the antibiotics episode. Essentially it was a way of practicing medicine through intervention only. Your patient came in sick and you thought okay, how can I stop this? You made your patient sweat, purge, bleed, get a fever, be freezing cold, whatever to shock their body back into balance. Medicine was about activity and treatment rather than prevention. The concept of cleanliness and sanitation as a method of disease prevention was a fairly new one in some degree. Yes, there was a miasma theory but in terms of Semmelweis and Lister, all of those sanitation-

Erin Allmann Updyke: Right.

Erin Welsh: It was starting to come around.

Erin Allmann Updyke: Yeah.

Erin Welsh: But most doctors thought that cleaning a wound, that doesn't make you a doctor. Sawing off a gangrenous limb in five seconds, that sure did. But the tide was turning from heroic medicine to preventative medicine, partially because of germ theory and also partially because of people like Lister and Semmelweis. And also partially because the emerging field of epidemiology allowed people to see wide scale patterns of disease and how interventions such as handwashing or ventilation affected the spread of disease. But the origin story of epidemiology is more complex than the classic story of John Snow and his cholera maps. One of my favorite things about this podcast is that we are wrong sometimes and we read more, we get to learn new stuff all of the time.

Erin Allmann Updyke: Every day.

Erin Welsh: Every day. And that makes us I think both look back and go, 'Oh my goodness, I didn't know that. I said that wrong, I didn't understand the context for this.'

Erin Allmann Updyke: I know.

Erin Welsh: And part of me is like I wish I could go back in time. But another part really likes to observe the fact that we are learning and growing.

Erin Allmann Updyke: Yeah.

Erin Welsh

And this is one of those instances. Epidemiology didn't come about because of John Snow and his cholera maps, of course they played a role but it's more complicated story than that. So we've talked about how tropical medicine as a field was largely created during the huge period of colonialism in the late 1800s, right, to help the imperialists to quote "conquer an area". In a similar way epidemiology developed out of colonialism, out of slavery, out of war, when doctors were incentivized to study and treat populations rather than individuals that they may not have otherwise. These circumstances provided doctors the opportunity to see disease on a scale that they hadn't before, moving through army hospitals, prison camps, ships, etc.

You and I learned the story of epidemiology and we've told the story of epidemiology as one of the early epidemiologists, of John Snow and the Broad Street pump. But you and I as well as the royal we, those who are also in the field of public health, we haven't fully or ever acknowledged the people who made up those maps, who are mentioned in those early studies of the spread of the disease simply as cases. And many of these people were disenfranchised, they had no consent or knowledge of their involvement. And this theme, this new exploration of the origins of epidemiology is the subject of next week's bonus episode as well as the topic of a new book by Dr. Jim Downs who is my expert guest for next week.

Erin Allmann Updyke

I cannot wait.

Erin Welsh

I am thrilled to be chatting with Dr. Downs who is a professor of history at Gettysburg College about his latest book called 'Maladies of Empire: How colonialism, slavery and war transformed medicine'. I am super excited for this conversation, so mark your calendars.

Erin Allmann Updyke

I can't wait.

Erin Welsh

Okay. But for now let's get back to the history of tetanus. Moving into the second half of the 1800s, tetanus was still very much present but it would soon meet its match, first in the form of antitoxin and then in the form of a vaccine. In 1884 Carle and Rattone took pus from the skin lesion of an infected human's face who later died of tetanus and injected it into a rabbit which began showing signs of tetanus confirming the presence of the pathogen in that lesion. And so the story of the microbiology of tetanus began. Later that same year a guy named Arthur Nicolaier injected soil samples into animals who also developed tetanus symptoms. He isolated a rod-shaped bacillus from these animals and hypothesized that the bacteria produced a toxin resembling strychnine in its action, which we should add to our future topics.

Erin Allmann Updyke

I think it's on our list.

Erin Welsh

Okay, good. But he didn't isolate the organism in pure culture. That would be done by Shibasaburō Kitasato in 1889 from a fatal case of a soldier in Berlin. Does his name sound familiar to you?

Erin Allmann Updyke

A little bit, yeah.

Erin Welsh

Diphtheria episode.

Erin Allmann Updyke

Diphtheria. Makes sense.

Erin Welsh

So Kitasato and Emil von Behring worked closely together on a diphtheria antitoxin. Von Behring got the first Nobel Prize in medicine in 1901 for the work that they did and Kitasato did not. Anyway with this pure culture of *Clostridium tetani*, Kitasato was able to see that it was indeed a toxin produced by the bacteria that caused some of the symptoms which spurred him on to look for other toxin-producing bacteria including the one that causes diphtheria. Kitasato and von Behring's work on producing antitoxin for tetanus and diphtheria, essentially that started the field of serum therapy.

Erin Allmann Updyke

Wow.

Erin Welsh

And this was great. Having an antitoxin was revolutionary in a number of ways but it wasn't perfect, right. You have to administer it early on for it to be effective and in the case of tetanus you had to keep the wound clean.

Erin Allmann Updyke

Yeah.

Erin Welsh

And both of those things were pretty difficult if you were a soldier at high exposure risk.

Erin Allmann Updyke

Right.

Erin Welsh

And we have some numbers to back that up too.

Erin Allmann Updyke

Oh dear.

Erin Welsh

It's not that bad. I mean it's bad to begin with and then it gets better.

Erin Allmann Updyke

Okay.

Erin Welsh

In 1808, so pre germ theory, pre tetanus antitoxin, pre vaccine, the rate of tetanus was 12.5 per 1000 in soldiers.

Erin Allmann Updyke

Okay.

Erin Welsh

And the author of this didn't say which soldiers and where.

Erin Allmann Updyke

Okay.

Erin Welsh

But in the first months of WWI that dropped to 8 per 1000 wounded. Still high.

Erin Allmann Updyke

Yeah.

Erin Welsh

And then as wound care and antitoxin delivery improved, it dropped further to 1.5 per 1000.

Erin Allmann Updyke

Okay.

Erin Welsh

And by the time the US entered the war it was down to 0.16 per 1000.

Erin Allmann Updyke

Wow, okay. Great.

Erin Welsh: That's pretty cool.

Erin Allmann Updyke: Yeah.

Erin Welsh: Interestingly, tidbit here, where you were fighting physically played a role in your tetanus risk. Fields that had been fertilized with manure over long periods of time had more tetanus and led to the misconception that horses were the reservoirs for the bacteria.

Erin Allmann Updyke: Interesting.

Erin Welsh: But really it can be carried like you said in all kinds of animals and humans like rats, chickens, cows, horses. I'm sure many, many other animals.

Erin Allmann Updyke: Yeah.

Erin Welsh: But further declines in tetanus were in the future and not just for soldiers but for everyone. The tetanus vaccine was developed in 1924 by Gaston Ramon and widespread vaccination meant a drastic drop in tetanus wherever the vaccine was available. Soldiers in WWII experienced tetanus at a rate of 0.04 per 1000.

Erin Allmann Updyke: Wow.

Erin Welsh: Yeah. And I saw a stat that no one who was vaccinated got tetanus.

Erin Allmann Updyke: Wow.

Erin Welsh: And neonatal tetanus rates also dropped as researchers realized that vaccination during pregnancy offered some protection to the newborn.

Erin Allmann Updyke: That's the most amazing and my favorite thing.

Erin Welsh: Yes, it's so important. It is so important. And these drops in tetanus continued throughout the 20th century and into the 21st but not I'm guessing as much as they should have. So yeah, this is kind of just a quick little scoot through the 20th century on my end but I'm curious to know Erin where we stand today when it comes to tetanus.

Erin Allmann Updyke: I can't wait to tell you right after this break.

TPWKY: (transition theme)

Erin Allmann Updyke: So in the US, we'll start here, from 2009-2017 only 264 cases and 19 deaths were reported from tetanus.

Erin Welsh: Wow.

Erin Allmann Updyke: I know, that's pretty major.

Erin Welsh: Yeah.

Erin Allmann Updyke

Across the globe, while the decrease in cases overall is still very impressive, unsurprisingly we still do have a ways to go. The World Health Organization estimated in 2018, which is the latest data they have as of today, that in 2018 25,000 newborns died from neonatal tetanus. 25,000 worldwide.

Erin Welsh

What?

Erin Allmann Updyke

And as depressing as that number is, that is an 88% reduction from cases in the year 2000 and a 96% reduction from cases in the 1980s.

Erin Welsh

Oh my goodness.

Erin Allmann Updyke

I know. I had no idea just how widespread tetanus was even as recently as the 1990s.

Erin Welsh

No.

Erin Allmann Updyke

For example, a paper from 2001 estimated 800,000 to 1 million deaths worldwide from tetanus every year, including over half a million from neonatal tetanus. That's a 2001 paper estimated. And another paper from 2007 which was talking about data from the 90s estimated that up to 5% of maternal mortality was due to tetanus and 14% of neonatal mortality was due to tetanus. The scale of this disease, I had no idea.

Erin Welsh

I cannot... I can't even formulate a sentence.

Erin Allmann Updyke

I know, I know. I feel very much the same. So we have come an incredibly long way. The World Health Organization, who tracks data on vaccinations as well as cases, estimated that worldwide in 2019 86% of children were covered by DTP3 which is the three doses of vaccine in the first year of life.

Erin Welsh

Okay.

Erin Allmann Updyke

So 86% of children. And I want to take a minute to emphasize here just how preventable this disease really is. Vaccination generally starts at 2 months old and it's a series of three shots initially and then a booster around kindergarten. And then boosters every 10 years or so to maintain immunity. But like you mentioned Erin, vaccination during pregnancy also confers protection against neonatal tetanus and it's been estimated vaccination during pregnancy to reduce mortality from neonatal tetanus by 94%.

Erin Welsh

That's incredible.

Erin Allmann Updyke

It's amazing. So we have the capacity to protect people from this disease. But a really important thing is that this is a continual struggle or at least it's a continual process because this is not a human-specific disease that for example, like smallpox, if you can interrupt the chain of transmission between humans for long enough, you can eliminate the disease. You can't do that with this because it's an environmental pathogen that has always, like you said Erin, and likely always will be in our environment. So it is a process of continual protection through these incredibly efficacious, incredibly safe vaccines. And as we have seen, for example in the COVID pandemic, things that drastically alter the global landscape pose really big challenges to vaccination. So you know how I said in 2019 86% of children were covered by DTP3? Well in 2020 that number had gone down to 83%.

Erin Welsh

Ugh, yeah.

Erin Allmann Updyke

So an estimated 23 million children under the age of one did not receive their basic vaccines in 2020. And the number of completely unvaccinated children globally increased by nearly 3.4 million in that year alone. So we're not done yet.

Erin Welsh

No. We're never done.

Erin Allmann Updyke

We're never. But I want to end this episode on some really high notes and also just keep bragging about the tetanus vaccine.

Erin Welsh

It's fantastic.

Erin Allmann Updyke

Yeah. And really the tetanus toxoid. So the tetanus vaccine is a toxoid vaccine. A toxoid is just an inactivated toxin, right, and the toxin is a protein. So it's easy, it's cheap to produce. And this tetanus toxoid that is easy to produce, that is cheap, that is very immunogenic to our immune system is used to make a whole bunch of other vaccines like our pneumococcal vaccines, our meningococcal vaccine, HIB, all of these vaccines are made by conjugating or combining things like sugars, polysaccharides, to the tetanus toxoid protein to induce a better protective immunity against these other diseases as well.

Erin Welsh

That is just so cool.

Erin Allmann Updyke

Isn't it beautiful? And on top of that, the other reason that tetanus toxoid makes for such a good vaccine is that it's really shelf stable. It doesn't have to be frozen or refrigerated, it's stable at room temperature for months. So it's really transportable even to remote areas that don't have access to refrigeration.

Erin Welsh

That's fantastic.

Erin Allmann Updyke

There's more Erin. Literally not 10 minutes before we were going to record I was eating dinner and I was googling because I remember a very long time ago you were like, 'Hey, did you see this news article?' about something that we were going to record. And never had it crossed my mind to google news articles about whatever we were talking about. And ever since then, and that was a long time ago, now I always, the last thing that I do before I wrap up my research is I google tetanus and I press the news button on Google.

Erin Welsh

I love it.

Erin Allmann Updyke

So I did that while I was eating dinner right before we recorded. And lo and behold this paper was published one week ago. A group out of Albert Einstein College of Medicine published a study in Science Translational Medicine that used a combination of listeria monocytogenes which is a bacteria that we'll cover eventually.

Erin Welsh

Yeah.

Erin Allmann Updyke

We haven't, right?

Erin Welsh

No.

Erin Allmann Updyke

Okay. So a combination of this bacteria and tetanus toxoid to treat pancreatic cancer.

Erin Welsh: Incredible.

Erin Allmann Updyke: I know! Essentially briefly, they injected mice that had pancreatic cancer that had also been vaccinated for tetanus before they got cancer with a listeria that had been engineered to have the tetanus toxoid protein. And for whatever fascinating reason has to do with listeria, it preferentially congregates in these cancer cells, I think because the immune system wipes it out in other places. And then the mouse's immune system has a bunch of antibodies that recognize the tetanus toxoid because they were vaccinated. And so boom, they end up attacking the cancer that has these bacteria that have this toxoid protein. What?

Erin Welsh: That's amazing. And also first of all that's fantastic news for pancreatic cancer.

Erin Allmann Updyke: I know.

Erin Welsh: But secondly I feel like that could be a model for many other types of cancer treatment.

Erin Allmann Updyke: Exactly, yeah.

Erin Welsh: So cool.

Erin Allmann Updyke: I know. These mice had their pancreatic tumors decreased in size by 80% and metastases decreased by 87% and they lived 40% longer than untreated mice.

Erin Welsh: Wow.

Erin Allmann Updyke: It's in mice but this is a big deal.

Erin Welsh: It's a big deal.

Erin Allmann Updyke: So that's a high note to end on and I will absolutely link that paper.

Erin Welsh: Cool.

Erin Allmann Updyke: Yeah. So tetanus is a horrible disease but we have a vaccine and it is awesome.

Erin Welsh: I love that.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: Anyways.

Erin Welsh: Sources?

Erin Allmann Updyke: Sources.

Erin Welsh

I have a large number of sources for this episode. I'm going to shout out three right now and put the rest on our website. One is called 'No Uncommon Disease' by sally McMillen. Another is called 'An essay on the history of lockjaw' by William Chalian. And the last one I'll shout out is called 'The population structure of Clostridium tetani deduced from its pan genome' and that is by Chapeton-Montes et al from 2019.

Erin Allmann Updyke

I had just a few papers for this episode. I really enjoyed actually a 1994 paper called 'The mechanism of action of tetanus and botulinum neurotoxins', it was pretty thorough. And then a 2019 'Botulinum and tetanus neurotoxins', kind of an update. A few other papers on the epidemiology as well as links to the World Health Organization and the CDC surveillance. And then that awesome paper that just came out in March of 2022 was titled 'Listeria delivers tetanus toxoid protein to pancreatic tumors and induces cancer cell death in mice'. So it really tells you the whole study. And we'll post the list of these sources and every source from every one of our episodes on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com).

Erin Welsh

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

Erin Allmann Updyke

Thank you to the Exactly Right network.

Erin Welsh

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Erin Allmann Updyke

Thank you so much for listening to begin with. We love it and we love you so much.

Erin Welsh

We do. And also a special shout out to our wonderful patrons. You're incredible.

Erin Allmann Updyke

Just the best.

Erin Welsh

Okay well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals!