Georgia Hardstark	Hi, I'm Georgia Hardstark and I co-host the podcast My Favorite Murder. And of course I had heard about Botox for years, I think everyone knew about it, knew what it was. And it didn't even cross my mind until I had a friend who got it done and we were both in our mid 30s so you're thinking like, 'Well I don't need it yet'. And then I saw her face and she looked awake I guess was the thing that really struck me. And then I was in this really cool secret Los Angeles ladies Facebook group and they all got it done. And so it normalized it for me and they were from their mid 20s to 30s to 40s, it was all ages so it didn't suddenly feel like this thing that you had to get when you were older and already having issues.
	The way I read about it was that it was preventative which I found really interesting because the less you're furrowing your brows and making those creases, the less the lines are going to stick around. And I was really nervous because I had to get past feeling vain about it which I think is a normal thought. And then I just realized there were these little things about my wrinkles that were bothering me and I think that's the main thing is like it's not for everyone and wrinkles are beautiful and not everyone is going to want to do it and I think that's totally fair. But for me it's like a simple fix that will make me just feel a little more confident which is a big huge plus for me. So it's not gonna change your face, it's not gonna change your life but yeah.
	So I went and I got it the first time right before mine and Vince's wedding, so I was like 35 or 36. And I was super nervous, I was scared it was gonna completely change my face. It's a little needle so of course it's not gonna feel good. And then they poke it in, so you wanna do a lot of little spots, you don't just do it in one spot. And I get it done in my forehead and between my eyebrows and on my smile lines. And so it's a couple different pokes, I think mine are like 12 pokes total and you can kind of - it's really gross - you can kind of hear when they're injecting it, it's like a squish in your inner ear, you can hear it. That's the only horrible part.
	Yeah it hurts cause it's a needle but I feel like with that and like tattoos, when you're excited about what you're doing it doesn't hurt as bad. And they give you a stress ball to squeeze and it's over so quickly. And it's just part of it, if you're totally afraid of needles obviously you're not gonna want to do it. And it takes like 2 weeks to start showing up so it's kinda good that it's slow and subtle, it's not this right away change. No one knew that I had gotten done, even my closest friends hadn't known. So when I finally told my best friend she was shocked and she was like, 'Now that you're saying it, I see it.' And I was like, 'I look like I'm 30 again!' And she blurted, 'You look better than that.' (laughs) And I was like okay, I like this.
TPWKY	(This Podcast Will Kill You intro theme)
Erin Welsh	Well that was one of the most exciting things to ever happen.
Erin Allmann Updyke	Absolutely thrilling, thank you so much Georgia for being a part of this and sharing your story and wealth of knowledge.
Erin Welsh	(laughs) Yes, thank you, thank you. That was thrilling.
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	Definitely made my Friday.
Erin Allmann Updyke	And much more uplifting than other firsthand accounts of the subject of today's episode.
Erin Welsh	Which is botulism!

Erin Allmann Updyke	Botulism! Well botulinum toxin really.
Erin Welsh	Sure. Clostridium botulinum, how about that?
Erin Allmann Updyke	Yeah. How about that?
Erin Welsh	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	Today we're talking-
Erin Welsh	You know what we're talking.
Erin Allmann Updyke	Botulinum.
Erin Welsh	Well we have a couple of pieces of business to get into before we start this episode which I know we say this all the time but I am so excited for this.
Erin Allmann Updyke	Yep.
Erin Welsh	It got to the point where I was telling, because I know I didn't wanna tell you the things I was learning yet but I was like texting everyone else like oh my gosh.
Erin Allmann Updyke	Oh yeah. I do the same thing. Yesterday I was like, 'Brett, did you know?' And i just started shouting Botox facts at him.
Erin Welsh	(laughs) Yeah! Well I'm glad that we finally get to let it all off our chests today.
Erin Allmann Updyke	Me too. It's gonna be a good one.
Erin Welsh	I think so. Okay so like I said though, some business. Number one is that we are going to keep doing these regularly scheduled episodes or whatever and we are going to keep them COVID-free.
Erin Allmann Updyke	This is a COVID-free zone right now.
Erin Welsh	Yeah, so we promise we won't even say it too many more times.
Erin Allmann Updyke	After this.
Erin Welsh	And so what we're doing is as you may have seen in your feed, we're gonna keep dropping those COVID-19 episodes every so often, we don't really have a particular schedule for that, it's just sort of whenever they happen.
Erin Allmann Updyke	Nope, whenever they happen.

Erin Welsh	But we also recognize that people may not want to hear about what's going on or it might be too stressful or whatever and we totally get that and so all of these normal episodes will just be normal episodes.
Erin Allmann Updyke	Normal episodes. Jinx.
Erin Welsh	Okay, all right.
Erin Allmann Updyke	All right.
Erin Welsh	Number two, we have now joined the affiliate program of this organization called bookshop.org and so what this is, it's an online bookstore website that works with independent bookstores. And so as an affiliate we have a page where you can see our lists that we have curated for what books, you know nonfiction books, fiction books, memoirs about disease and about health and stuff like that. And so if you are so interested you could go on our website under the BOOKS tab and you will find a link to bookshop.org. And also we have links in each of our episodes where we list our sources, we will provide links to those books on Bookshop if they exist there.
Erin Allmann Updyke	Cool.
Erin Welsh	Cool.
Erin Allmann Updyke	One other piece of business if you are not aware yet, we have now alcohol-free episodes available on our website if you'd like to use those for whatever reason, if you don't want to hear us talk about quarantinis you can find those on our website.
Erin Welsh	Yep.
Erin Allmann Updyke	Cool.
Erin Welsh	Speaking of quarantinis.
Erin Allmann Updyke	It's quarantini time!
Erin Welsh	It is. What are we drinking this week?
Erin Allmann Updyke	This week we're drinking Can Of Germs.
Erin Welsh	(laughs) And we have a big thank you to Bloodmobile for providing that name.
Erin Allmann Updyke	The quarantini name for this episode and all of our episodes. Just kidding. A lot of our episodes though.
Erin Welsh	Thank you Bloodmobile/Daniel, my brother.
Erin Allmann Updyke	Really that's a phenomenal drink name. Can Of Germs.
Erin Welsh	Yeah.
Erin Allmann Updyke	For botulism! My gosh, you guys.

Erin Welsh	It's incredible. What is in Can Of Germs?
Erin Allmann Updyke	It is rum, canned pineapple of course, honey also of course, we'll talk about it, and lime juice.
Erin Welsh	Yeah. It's pretty good.
Erin Allmann Updyke	It's pretty good actually, yeah. It's not bad.
Erin Welsh	Yeah. Awesome.
Erin Allmann Updyke	All right then.
Erin Welsh	Well.
Erin Allmann Updyke	Anything else or can we just get into this episode, Erin?
Erin Welsh	Let's get into the episode please.
Erin Allmann Updyke	Awesome. Right after this break.
TPWKY	(transition theme)
Erin Allmann Updyke	So when we talk about botulism, when we talk about botulinum, Botox, whatever, we're talking about a specific pathogen that I'm very excited Erin for you to tell me about where this pathogen came from cause you specifically told me not to look that up.
Erin Welsh	Oh I was very adamant, like don't read about this!
Erin Allmann Updyke	I didn't read about it at all.
Erin Welsh	All caps text. (laughs) You're not gonna talk about this, are you?
Erin Allmann Updyke	Nope, I am not. But we will talk a little bit about the bacterium itself. So this bacterium is called Clostridium botulinum. You may have heard the term Clostridium if you've ever heard of, for example, Clostridium difficile, C. diff. Yeah, a lot of people probably have. This is another Clostridium species that causes disease in humans, it causes massive very serious diarrhea, it's a pathogen of pretty big concern especially in hospitals. So Clostridium botulinum is another bacterium in the same genus.
	These Clostridium species are gram-positive which means they stain purple when you look at them under a microscope, that what we always say on this podcast. It means that they have a thick cell wall, okay. Clostridium species are rod-shaped, so they look like little Tic Tacs, okay. And very importantly they are what we call spore-forming anaerobes. That's a lot of technical terms, let's talk about what they mean. So anaerobe means that this is a bacteria that grows and lives without any oxygen. Okay, that's really important. So it can't just grow on your table out in the open or on your fingernail or in your nose or something like that, okay. I don't know why I said fingernail.

Erin Welsh	The fingernail is my favorite frame of reference. (laughs) Man, I wanna swab my fingernail now and see what's growing there.
Erin Allmann Updyke	I mean you'd probably find some weird stuff but not Clostridium species, okay. Our atmosphere of course is 21% oxygen, so how can this bacteria survive if it's surrounded by oxygen all the time?
Erin Welsh	Quick question. Did you know that off just the back of your hand that it was 21%?
Erin Allmann Updyke	Yes I did, did you not?
Erin Welsh	No.
Erin Allmann Updyke	Oh. Well now you know. Listeners, did you know? Yeah I did know, that's a trivia fact I did know in fact.
Erin Welsh	Awesome. I'm impressed.
Erin Allmann Updyke	It's important because we talk about it in medicine because when you put someone on oxygen you have to think about how much oxygen they're getting and what that is compared to what they're normally breathing in at room air.
Erin Welsh	Right.
Erin Allmann Updyke	So if they're on 21% oxygen, that's actually like room air.
Erin Welsh	Oh, awesome.
Erin Allmann Updyke	Oh how fun, look! Medicine teaches you things, who knew? Okay so how does this bacterium survive if it's surrounded by oxygen and it needs to live and grow in an environment without oxygen? The answer is that it's a spore former. I can't remember if we've talked on this podcast before about spore-forming bacteria. So let's talk about what spores are. So bacteria that are spore formers, here we're talking about specifically what are called endospores. So these are things for lack of a better word that bacteria produce that are super environmentally stable. They're basically a stripped down structure that contains the DNA of the bacteria but can persist in the environment for a really, really long time. So these are not reproductive structures. When you hear the word 'spore' you might think of a fern spore or a mushroom spore, those are like reproductive things. So bacterial endospores are not reproductive structures, they're basically just a form that the bacteria can produce in order to resist bad environmental conditions.
Erin Welsh	Yeah, just kind of like a wait and see little blueprint for the future.
Erin Allmann Updyke	Exactly, right. And so when the bacteria senses that environmental conditions might be deteriorating to the point where they're not going to be able to survive and continue to reproduce, they begin to form this endospore. And then if those environmental conditions deteriorate and the bacteria around that endospore dies and deteriorates, the endospore stays alive essentially. It doesn't do anything, it just exists until conditions are right and then it can reactivate. Okay?
Erin Welsh	Yeah.

Erin Allmann Updyke	And go on to form another living, reproducing bacteria. So these endospores are really important because they're resistant to things like UV. In the case of anaerobes, they're resistant to oxygen which could kill reproducing Clostridium botulinum. They're resistant to alcohol, to soaps, to hot, to cold, to certain levels of radiation. They're really, really hearty little packets of DNA, which can make them especially dangerous in a hospital setting if things aren't sterilized properly. And so that's part of the reason why C. diff, Clostridium difficile is really scary in hospital setting because just using alcohol-based hand sanitizer doesn't kill the spores of these bacteria.
Erin Welsh	Right. And we'll do a whole episode on C. diff in the future at some point cause it's definitely worthy of its own massive episode.
Erin Allmann Updyke	Most definitely. Oh yeah, absolutely.
Erin Welsh	And we're also gonna do another episode at some point on another Clostridium species, tetanus.
Erin Allmann Updyke	Oh yeah! Oh my gosh, I forgot that tetanus was a Clostridium.
Erin Welsh	Another spore former, another toxin producer.
Erin Allmann Updyke	Yeah. I think that's why... I went back and watched the Sketchy microbe videos for this and tetanus and botulism are kind of opposite ends of a spectrum which is really interesting. And so I remember comparing the two between them. So maybe I thought that we had done tetanus already, I don't know.
Erin Welsh	The only other spore former I can think of off the top of my head is anthrax and we haven't done that.
Erin Allmann Updyke	Yeah anthrax, we haven't done that. Yeah, we'll do that eventually too. Anyways there's more but those are the big ones.
Erin Welsh	Yeah.
Erin Allmann Updyke	Okay. But the spore isn't actually the story here, okay.
Erin Welsh	Course not.
Erin Allmann Updyke	Of course not. It's part of the story but it's not the story that we're focusing on on This Podcast Will Kill You. What we wanna talk about of course is the part of this bacteria that makes you sick. So we're here today to talk about botulism. It turns out that botulism is caused not by the bacterium itself, not by the spore itself, but by the toxin that that bacterium produces, okay.
Erin Welsh	Oh yeah.

Erin Allmann Updyke	This is called botulinum toxin. So what I wanna do first is we'll talk about that toxin itself, the mechanism of action of that toxin which will pretty clearly tell you what the symptoms that you're going to see are of poisoning from botulinum toxin. And then we'll talk about the ways that you can get exposed to this toxin cause there's a few different very distinct ways that you can be exposed to this toxin. Okay? All right. So first of all what is botulinum toxin? We've definitely talked about toxins a lot on this podcast because lots of bacteria produce different kinds of toxins, it's basically just usually proteins that a bacteria produces that have an effect, that do something for that bacterium, okay.
Erin Welsh	Right. So like cholera toxin?
Erin Allmann Updyke	Exactly, cholera toxin. We talked about Staph aureus produces a lot of different toxins that have different effects. Right. So in the case of botulinum toxin, this is a neurotoxic protein that the bacteria produces. So it has effects specifically on our peripheral nervous system and largely on our somatic nervous system. So if you remember in our episode on belladonna way back when-
Erin Welsh	Oh let's cast my mind back.
Erin Allmann Updyke	Way back when.
Erin Welsh	Way back.
Erin Allmann Updyke	We talked about there's a lot of different ways that you can divide up the nervous system, right. We have our central nervous system which is your brain and your spinal cord, you have your peripheral nervous system which is everything outside you brain and your spinal cord like where your nerves go to your muscles and your organs. You can also divide it into your somatic and your autonomic nervous system. So your somatic meaning your sensory and muscles nervous system and then your autonomic nervous system which is like your parasympathetic and sympathetic, rest and digest vs fight or flight. Remember that kind of? Okay. So in this case the effects of botulinum toxin, they act on a couple of different places. They act both on the parasympathetic nervous system but largely on the somatic peripheral nervous system. So let's first talk about what that nervous system is and how it works so that we understand how botulinum toxin interferes with that process.
Erin Welsh	Excellent.
Erin Allmann Updyke	Okay. I'm also not a neurologist or a neuroscientist so this is real basic, okay. So your brain of course is what controls all of the movements of your body. So how does your brain do that? You have nerves, your brain is connected to your spinal cord which is connected to nerves that innervate your muscles, okay, or your organs. So the way that this kind of happens is that electrical signals in your brain are transmitted along those nerves, along what are called axons of those nerves and then when they get to the end of the nerve which is called a synapse there's a gap between that nerve and for example your muscle. And so in order for that electrical signal in the nerve to transmit across that gap and have an effect on the muscle, that electrical signal has to be translated into a chemical signal. And then the chemicals can travel across that gap, that synapse between the nerve and the muscle and they can propagate that signal into the muscle. Does that make sense?
Erin Welsh	Yeah, yeah.

Erin Allmann Updyke	Cool. That's the first time I've ever explained that so that was fun. Okay. So when you're looking at the synapse, the gap between the end of your nerve and the start of your muscle, there's the presynaptic end, that's basically the nerve that came from your spinal cord and then the postsynaptic, and you can think of that as your muscle. It turns out that for your muscles especially, like your skeletal muscles, the transmitter, the chemical signal that is used to transmit that signal is called acetylcholine, okay. Acetylcholine is released at the presynaptic, so from the nerve ending, acetylcholine is released, it travels across that gap and binds to a receptor on your muscle end. And then that is what actually causes your muscle to go, 'Hey, I'm gonna contract.' And boom, it contracts. Okay?
Erin Welsh	Gotcha.
Erin Allmann Updyke	So acetylcholine is really important in that. So how does botulism work? So it turns out that botulinum toxin blocks the release of acetylcholine from that presynaptic nerve ending.
Erin Welsh	Gotcha.
Erin Allmann Updyke	So you have an electrical signal that's transmitted from your brain, it gets to the end, and botulinum toxin is there and says, 'Nope, you can't release acetylcholine.' So then your muscle goes (poof), it's got nothing.
Erin Welsh	So are there toxins or venoms or something that block from the other end, from the muscle-binding site?
Erin Allmann Updyke	We already talked about one and that was belladonna.
Erin Welsh	Oh, belladonna!
Erin Allmann Updyke	Yeah. And belladonna tends to act only on the parasympathetic receptors because there are two different types of acetylcholine receptors, there's muscarinic and nicotinic and so botulinum acts on the presynaptic end, so it blocks all acetylcholine release.
Erin Welsh	Oh my gosh!
Erin Allmann Updyke	Atropine binds to the receptor but only the muscarinic receptor, so not the ones in your skeletal muscle.
Erin Welsh	Oh my gosh, this is so thrilling.
Erin Allmann Updyke	I know, right!? I'm so glad you find it thrilling cause I do too.
Erin Welsh	This is so exciting!
Erin Allmann Updyke	Yeah.
Erin Welsh	Oh wow.

Erin Allmann Updyke	So yes, there absolutely are things that... And there's other toxins as well too, there's others venoms, there's other toxins that interfere with this acetylcholine and whether they do it. And so that question is really important because in the case of botulinum, by blocking the release of acetylcholine, you leave those acetylcholine receptors on the muscle empty which means the muscle is not getting a signal to contract which means the muscle is relaxed. So the symptoms that we see of botulinum poisoning are a flaccid paralysis rather than a contracted paralysis which we see in other toxins that have different mechanisms of action.
Erin Welsh	Like tetanus?
Erin Allmann Updyke	Like tetanus, yeah. Yeah.
Erin Welsh	That's really cool.
Erin Allmann Updyke	I know! It's very cool.
Erin Welsh	That's really cool.
Erin Allmann Updyke	I love it. I mean I don't love it, it's horrible. Okay so now that we know the action of botulinum toxin, it's acting at the neuromuscular junction, the synapse between nerve and muscle and it's blocking the release of acetylcholine which means your muscles are getting no signal which means they are relaxed and flaccid. So we pretty much know what the symptoms of botulism are, right. They're a flaccid paralysis. These symptoms are the same no matter how you get exposed to botulinum toxin.
Erin Welsh	Right.
Erin Allmann Updyke	Because this is a toxin, it's traveling throughout your bloodstream once it gets into you, no matter how it gets in, it's gonna travel through your bloodstream and it's going to act on any nerve ending that it comes in contact with, okay.
Erin Welsh	Is the flaccid paralysis just sort of generally distributed throughout your body or is it concentrated depending on your route of exposure?
Erin Allmann Updyke	Great question, Erin. So what's very interesting about botulism specifically is that it causes a descending paralysis.
Erin Welsh	Okay.
Erin Allmann Updyke	So the paralysis starts in your face, in your head, it starts with your cranial nerves. It causes bilateral, so both sides, symmetric cranial nerve palsies that then eventually travels down and will cause flaccid paralysis throughout no matter the route of entry. And we'll talk about the specific different routes of entry.
Erin Welsh	Yeah.
Erin Allmann Updyke	This is botulism, so you're exposed to enough toxin that it is distributed throughout your body and causing botulism. If you are exposed for example like in our firsthand account to a very small amount of very, very dilute toxin in a very specific place, there's not enough of that toxin to travel throughout your body and cause systemic effects.

Erin Welsh	Right, it's a dosage thing.
Erin Allmann Updyke	Exactly, yeah. And so all of the symptoms that we see with botulism, even with botulism, are dose dependent.
Erin Welsh	Right, of course.
Erin Allmann Updyke	Yeah.
Erin Welsh	Why does it start in your head?
Erin Allmann Updyke	It's such a good question and I don't know. I couldn't figure out the exact answer to this. And what's interesting though is that it does distinguish... So if you clinically see someone with a flaccid paralysis, you have as a clinician in your head a list of what you call differential diagnoses. What could be causing this? What are all the different things that could be causing the symptoms that I'm seeing, right? And there's a few different things that you have to think about, things like Guillain-Barre for example. But Guillain-Barre causes an ascending paralysis so knowing the timeline of symptoms, like where they began and how they've changed over time is really important in trying to diagnose botulism.
Erin Welsh	Gotcha.
Erin Allmann Updyke	And I think that this is also partly why for a long time it was thought that this was a central nervous system toxin because your cranial nerves are closest to your brain, right.
Erin Welsh	Yeah.
Erin Allmann Updyke	They're coming out directly from your brainstem.
Erin Welsh	Right.
Erin Allmann Updyke	But it's actually a peripherally acting toxin, it's acting at the neuromuscular junction so it's very interesting that your cranial nerves are still the first ones affected.
Erin Welsh	This is fascinating.
Erin Allmann Updyke	I know! Okay. So here are the symptoms, right. So the first signs and symptoms are things like blurred vision as the muscles that innervate your eyes become affected. Then you'll get ptosis which is a great word that means your eyelids are droopy, okay, cause your eyelid muscles are not working right. Then you'll get slurred speech as the muscles of your mouth and face get affected, then the paralysis will continue moving down your body. You can get dry mouth and throat because again that parasympathetic nervous system is also affected.So that's actually similar symptoms as to what we saw in belladonna poisoning, dry mouth, dry as a cracker or whatever. What is it?
Erin Welsh	(laughs) I don't remember what that one was.
Erin Allmann Updyke	Dry as a bone. Mad as a hatter.
Erin Welsh	I remember there was like a hare and a chicken.

Erin Allmann Updyke	Mad as a hatter, dry as a bone.
Erin Welsh	Dry as a bone.
Erin Allmann Updyke	Etc.
Erin Welsh	Yeah.
Erin Allmann Updyke	And then your voluntary muscles will start to become paralyzed, so first your neck, your shoulders, your upper arms, lower arms, upper legs, lower legs. Eventually everyone would end up with constipation as the muscles that innervate your gut are paralyzed because in order to have poop at all, your gut has to be able to contract.
Erin Welsh	Yeah.
Erin Allmann Updyke	Cause of death is usually respiratory arrest and there's two different ways that this sort of ends up happening. The muscles that control your breathing, your diaphragm and your intercostal muscles of your ribs, those become paralyzed just like everything. And you can also get airway obstruction as the muscles of your pharynx are paralyzed so your airway can kind of collapse inward and you can't... So it's kind of a combination of those two that ends up causing death in the case of botulism.
Erin Welsh	Cool. Cool, cool, cool, cool, cool, cool. That's horrifying.
Erin Allmann Updyke	It's horrifying. The rate that this progresses, so how long this all takes and how far it actually progresses, so whether it makes it all the way to your respiratory muscles or whether you just have like only facial palsy depends largely like I said on the dose of toxin exposure.
Erin Welsh	Right.
Erin Allmann Updyke	However, and this part's really important, botulinum toxin binds irreversibly, so you cannot undo any damage that has already been done. But your body does eventually regenerate those acetylcholine channels on the nerve terminal, it's just a slow process. So it's not like if you have facial palsy, you're not gonna have a paralyzed face forever but you can't undo that paralysis, you just have to wait for it to resolve.
Erin Welsh	So how long are we talking?
Erin Allmann Updyke	Generally weeks, possibly months.
Erin Welsh	Okay, a couple questions. The first is something that I read somewhere about maintaining consciousness.
Erin Allmann Updyke	Erin, this is what I have next, okay.
Erin Welsh	Really?
Erin Allmann Updyke	Okay. For you, this is just for you, Erin. Okay. Your sensory system is generally unaffected and your intellectual function is unaffected. So yes Erin, it's your greatest fear, it can leave you essentially locked in.

Erin Welsh	Cool, cool. Awesome.
Erin Allmann Updyke	Right?
Erin Welsh	Why do we keep doing these? (laughs)
Erin Allmann Updyke	Yeah because you're paralyzed. And here's what's really scary is that because the muscles, like the voluntary muscles of your face and your throat and things are paralyzed, as you begin to have respiratory distress you don't show any of the outward signs or symptoms of respiratory distress. There's no agitation, there's no restlessness, you're not gasping or thrashing or flailing because you're paralyzed.
Erin Welsh	Great.
Erin Allmann Updyke	So the way that you know that someone is in respiratory distress is because their oxygen saturation is dropping on a monitor. So if you're at home then you wouldn't...
Erin Welsh	At that point, what can be done?
Erin Allmann Updyke	So that is jumping the gun but let's talk about treatment. The good news is there is treatment for this. It absolutely can be fatal but it is also treatable, we have an antitoxin. This antitoxin neutralizes circulating toxin and prevents it from binding to the nerve terminal.
Erin Welsh	Okay.
Erin Allmann Updyke	So it doesn't do anything for the toxin that's already bound, right, we can't unbind that toxin but it can neutralize any additional toxin that's circulating. So it's really important if these signs and symptoms start to appear that you get to a hospital for treatment because then they can continue supportive care even if it gets to the point where you have respiratory distress and things like that.
Erin Welsh	Right, to get the antitoxin early is clutch.
Erin Allmann Updyke	Yes, the earlier the better is clutch is right. Okay so that's like what botulism looks like clinically, what the picture looks like. So how do you get it? How do we avoid it, right?
Erin Welsh	Yeah.
Erin Allmann Updyke	How do we not get it is what we want to know. There's three main ways and then a couple of ancillary ways as well. The first most famous I think is food poisoning, right. So if food is contaminated with Clostridium botulinum bacteria and then those bacteria live in an environment that allows for them to grow, so no oxygen, not too low of pH so not too acidic and just basically a good environment for them to start growing and reproducing, they will then produce that toxin. You get botulism when you ingest that toxin, not by ingesting the bacteria themselves.
Erin Welsh	Gotcha.
Erin Allmann Updyke	Yeah. So this is the same way that you might remember when we talked about in our Staph aureus episode, or MRSA episode, you get food poisoning from Staph aureus from the toxin, right.

Erin Welsh	Right.
Erin Allmann Updyke	This is the same thing. You get infected with a toxin. So if you have for example like canned tomatoes are a really good example cause they're actually not that acidic. So if tomatoes are canned improperly and you have a bunch of Clostridium botulinum growing in there and then producing toxin, even if you reheat those tomatoes you might kill the bacteria but that toxin is still gonna be there. So you can still get sick from it.
Erin Welsh	Okay. But you can neutralize the toxin.
Erin Allmann Updyke	You can, absolutely, yeah. If you boiled it for I don't remember how long exactly, you can definitely, yeah.
Erin Welsh	Okay.
Erin Allmann Updyke	But that's why it's so common in foods, the bacteria can die after a certain period of time but that toxin can still be in those cans of food.
Erin Welsh	Right.
Erin Allmann Updyke	So that's one way, that's the most common way, food poisoning botulism. Okay?
Erin Welsh	Yep.
Erin Allmann Updyke	Now you can get infected with the bacteria themselves or the spores which you're more likely to come in contact with in the environment, right, in a couple of different ways. The least common but less depressing is wound botulism.
Erin Welsh	Oh yeah.
Erin Allmann Updyke	Okay. So if you have a wound that gets contaminated either with Clostridium botulinum bacteria or their spores which are very common in the environment, if that wound festers it can become anoxic in that environment, the bacteria or those spores can reactivate and begin to reproduce and produce toxin. So then the bacteria are making toxin in your own body. The effects are the same as if you got botulism from food poisoning, okay, they're the same because this is toxin that had neuromuscular effects, so overall it's the same.
Erin Welsh	Right.
Erin Allmann Updyke	Now the most common and I think the most depressing form of botulism of course is infant botulism.
Erin Welsh	Right.
Erin Allmann Updyke	It's always depressing when it's babies. And this is different, even though this happens when an infant ingests, so it's technically a food poisoning, it is not the same as when an adult gets botulism.
Erin Welsh	Okay.

Erin Allmann Updyke	And that's because infant botulism happens when infants ingest the spores of Clostridium botulinum. So unlike adults, infants, especially of a certain age so it's usually like three weeks but less than one year old. They have a very naïve and naked gut flora so their guts are not able to inactivate or prevent those botulinum spores from becoming activated and colonizing their guts.
Erin Welsh	Gotcha.
Erin Allmann Updyke	So then the bacteria in the infant gut reproduce and produce toxin inside of the baby rather than the baby eating toxin directly.
Erin Welsh	Yeah. That's horrible.
Erin Allmann Updyke	And infant botulism is often called floppy baby syndrome.
Erin Welsh	Okay. That makes sense with the flaccid paralysis.
Erin Allmann Updyke	Exactly, right. It is possible however it's extremely, extremely rare for an adult to become colonized with Clostridium botulinum and then have that same syndrome as infant botulism. It's called adult intestinal toxemia. It's just very rare because we have other microflora that are much better at competing and outcompete those Clostridium species. It's similar with Clostridium difficile, like that's an opportunistic infection, right.
Erin Welsh	Right.
Erin Allmann Updyke	It's not good at taking over our gut flora.
Erin Welsh	Right. Usually it's following huge rounds of antibiotics and stuff like that.
Erin Allmann Updyke	Exactly, right. Yeah. One question is where do infants get exposed?
Erin Welsh	Honey.
Erin Allmann Updyke	Yeah, honey.
Erin Welsh	And it's just because honey is...
Erin Allmann Updyke	It just has a ton of spores. There are a lot of Clostridium botulinum very commonly found in honey and because an infant gut can't neutralize those spores, they can get infected with Clostridium botulinum and develop botulism from honey.
Erin Welsh	Yeah.
Erin Allmann Updyke	It's not the only thing in the world but it's one of the most common routes of exposure. So that's why infants under 12 months can't have honey, shouldn't have honey.
Erin Welsh	Yep.
Erin Allmann Updyke	Yeah. It's also possible to be infected through aerosolized toxin, so you could in theory inhale this. I don't know that it's ever been recorded, it would have to be intentional.

Erin Welsh	Right. I'll talk a little bit about that.
Erin Allmann Updyke	Oh great. Can't wait.
Erin Welsh	Just a little.
Erin Allmann Updyke	And then of course you can get it through injection as well, so if you injected a large amount of this toxin into your veins or muscles then it could spread through your body and cause botulism that was as well.
Erin Welsh	Cool.
Erin Allmann Updyke	So botulinum toxin is considered the most potent toxin that we know of. Are you gonna talk more about that Erin?
Erin Welsh	Well I can drop the knowledge right here if you want me to.
Erin Allmann Updyke	Let's, cause I wanna know about it.
Erin Welsh	Okay. Well all I know in terms of that is I read somewhere in one of these papers that because the amount of botulinum toxin that it takes to kill an average human is whatever amount-
Erin Allmann Updyke	Yeah, some very small amount.
Erin Welsh	Some tiny, tiny minuscule, unfathomably small amount. If you multiply that by the number of people on earth, estimates are that it takes approximately 40 grams of botulinum toxin to wipe out humanity.
Erin Allmann Updyke	That's why you wanted me to weigh out 40 grams of something?
Erin Welsh	Yeah. I texted you and I was like, 'So how many slices of bread is 40 grams? Cause I need to visualize this.' So how many slices of bread is 40 grams?
Erin Allmann Updyke	Okay. The sourdough bread that I have right now, one slice of it weighs 45 grams, okay. For another visual, a half a cup of coffee beans is 40 grams.
Erin Welsh	There you go.
Erin Allmann Updyke	So that's how much botulinum toxin it would take to kill all of the humans on the planet right now.
Erin Welsh	Yeah. And I have the paper, I'll cite the paper on our website so you can go and read it for yourself. But yeah, like 39.4 grams or something.
Erin Allmann Updyke	Whoa.
Erin Welsh	Isn't that wild?
Erin Allmann Updyke	Yeah, man. Whoa. Well that's botulism.

Erin Welsh	Oh that was it!
Erin Allmann Updyke	Yeah, that's all I got. We already talked about how you treat it.
Erin Welsh	Cool.
Erin Allmann Updyke	It's a little terrifying but we'll talk later about how innovative people have gotten with something that is so terrifying.
Erin Welsh	Yeah, I'll talk about it. It's really fascinating. This is I think one of my favorite episodes so far to have read about.
Erin Allmann Updyke	Oh great.
Erin Welsh	I don't know why.
Erin Allmann Updyke	Well then tell me about it, Erin. How did we get here? Where did this thing come from? How did it evolve? Why does it have a toxin that can kill all of humanity? Like what's up with that?
Erin Welsh	I'm so glad you asked. I will answer as well as I can after this break.
TPWKY	(transition theme)
Erin Welsh	Okay. Doesn't this remind you of one of our crossover episodes with Matt?
Erin Allmann Updyke	100% yes. Yeah, that's why I kept talking about atropine and stuff.
Erin Welsh	Exactly. Matt, we miss you.
Erin Allmann Updyke	Yeah.
Erin Welsh	We'll do another crossover soon.
Erin Allmann Updyke	Yeah, we will. He doesn't know it but...
Erin Welsh	He doesn't know it. (laughs) We can't to do another crossover soon, Matt. Okay. So just like you asked, why does this toxin exist?
Erin Allmann Updyke	Yeah.
Erin Welsh	Why does this bacterium produce this toxin? And so that's what I wanna start off by trying to answer. Basically why are you the way you are? So in our normal episodes this type of question is generally pretty easy to answer, right, because it mostly has to do with the pathogen increasing its chances of transmission or something like that, that's generally the pattern that we see.
Erin Allmann Updyke	Right.

Erin Welsh	Like for example as we mentioned earlier the toxin that the cholera bacterium produces makes you poop out a ton of Vibrio cholerae cells so it can spread to other people.
Erin Allmann Updyke	I'm so excited about this, I can't wait. Yeah, why then?
Erin Welsh	But with botulism humans seem more like unfortunate bystanders than the stars of the show, right.
Erin Allmann Updyke	Right, yeah.
Erin Welsh	So it's not spread from person to person really, so what purpose does this paralytic or fatal toxin serve? How does it actually help the bacterium? Does it even help the bacterium?
Erin Allmann Updyke	Right.
Erin Welsh	So answer that question I gotta talk a little bit about the ecology of Clostridium botulinum.
Erin Allmann Updyke	Your favorite.
Erin Welsh	My favorite. A lot of the research on botulism focuses on humans, like outbreaks at potlucks, the toxin's use in therapeutics, the physiological mechanism of the toxin itself, etc. But to these bacteria humans play a very small role.
Erin Allmann Updyke	Right.
Erin Welsh	Erin, this is jumping the gun but around how many cases of botulism do we see a year in the US?
Erin Allmann Updyke	Like 182 in 2017.
Erin Welsh	Yeah. Like very low.
Erin Allmann Updyke	Yeah.
Erin Welsh	But it's a whole other story for some other animals, especially migratory birds.
Erin Allmann Updyke	Really?
Erin Welsh	Really.
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	Botulism is one of the biggest if not the biggest disease of migratory birds, especially those that like water, like shorebirds and waterfowl, swamp birds.
Erin Allmann Updyke	What? This is literally blowing my mind.

Erin Welsh	I'm so excited that it is. A typical outbreak of avian botulism - so they happen pretty much every year it seems, like they're pretty common - might claim the lives of 50,000 birds or more. But there have been outbreaks with over a million birds dying.
Erin Allmann Updyke	What on earth?!
Erin Welsh	Yeah. And most of these outbreaks, and you didn't really talk about types but just FYI, types of toxins cause it's a whole other can of germs...
Erin Allmann Updyke	Oh my gosh. Good one, that was good.
Erin Welsh	(laughs) But these are just for reference, type C botulinum toxin.
Erin Allmann Updyke	Okay, yeah.
Erin Welsh	Okay. So the reason that we see these outbreaks occurring among these water-loving birds is that the environments where they like to hang out, they can be full of decaying organic matter which can make for a perfect setting for the growth of these anaerobic bacteria. And these anaerobic bacteria can then be easily ingested by a dabbling duck or a filter-feeding shuffler. A dabbling duck, that's an actual term.
Erin Allmann Updyke	Oh really?
Erin Welsh	Yeah!
Erin Allmann Updyke	It's not just a cute little alliteration there?
Erin Welsh	You know when they kind of like boop-boop-boop across the surface and they duck their heads in and their little butts stick out?
Erin Allmann Updyke	Yeah.
Erin Welsh	That's a dabble, they're dabbling.
Erin Allmann Updyke	Aw. You're making me like birds, Erin.
Erin Welsh	Also apologies to any bird people who are like, 'Wow you're getting all of this wrong.' (laughs) I'm doing the best I can.
Erin Allmann Updyke	We're gonna get an email from Fred and Nick.
Erin Welsh	And Maria.
Erin Allmann Updyke	And Maria.
Erin Welsh	We have a lot of bird friends.
Erin Allmann Updyke	I know. I'm sorry.

Erin Welsh	Okay. So let's say that one of these birds, one of these dabbling sucks ingests some swamp stuff containing Clostridium botulinum. The bacteria may colonize that bird's intestines or liver without any apparent effects maybe.
Erin Allmann Updyke	Okay, yeah.
Erin Welsh	And then let's say the bird dies for whatever reason. Maybe it's because of the toxin, maybe it's because it hit a powerline, maybe it's because it ate some whatever. Maybe it just dies, right.
Erin Allmann Updyke	Okay.
Erin Welsh	That decomposing bird is a great environment for Clostridium botulinum. It's warm, it's anaerobic, it's everything you could ask for if you're Clostridium botulinum.
Erin Allmann Updyke	Yeah.
Erin Welsh	Soon that carcass is teeming with C. botulinum and its toxin and it's also hosting a ton of other decomposers, for instance some invertebrate decomposer like blowfly larvae.
Erin Allmann Updyke	Yeah, yeah.
Erin Welsh	And so normally waterfowl won't directly munch on vertebrate carcasses but do you know what they will munch on?
Erin Allmann Updyke	Blowflies.
Erin Welsh	Maggots, yes. So the larvae that these blowflies laid in the carcass become loaded with botulinum toxin and invertebrates are not affected by the toxin. And so other birds eat these maggots, die from the excessive amounts of toxin, and that leads to more toxic maggots and so on.
Erin Allmann Updyke	Whoa.
Erin Welsh	And so that's how these avian botulinum outbreaks can be absolutely explosive. It's called the carcass-maggot cycle.
Erin Allmann Updyke	What? How have I never heard of this, Erin?
Erin Welsh	I know. It blew my mind.
Erin Allmann Updyke	Oh my... Cause they don't affect invertebrates! Oh my gracious.
Erin Welsh	And then of course other vertebrates might directly feed on the contaminated carcass and then die which would then create another amazing anaerobic environment for the bacterium to replicate and then that would spread the bacterium interesting he environment and provide more anaerobic... It just sort of, the cycle continues.
Erin Allmann Updyke	Oh. I'm getting chills.

Erin Welsh	I know! This is why I was so excited for this episode. Okay so I went into all of this to show a natural cycle of C. botulinum and its ecological role.
Erin Allmann Updyke	Wow.
Erin Welsh	And I did this to get at the question earlier, why are you the way you are?
Erin Allmann Updyke	Yeah.
Erin Welsh	It could be accidental but most researchers believe that by killing a vertebrate host or even increasing the probability of a host dying, it carves out a space for itself to replicate and produce more toxin.
Erin Allmann Updyke	Totally.
Erin Welsh	And so the mechanism of that, like the paralysis and blurred vision and so on, those are things that even if the toxin doesn't necessarily kill you outright, it will in the wild greatly increase your chances of becoming a carcass.
Erin Allmann Updyke	Absolutely. Of becoming a carcass. Also I think that's our title Erin, in Why Are You The Way You Are?
Erin Welsh	Why are you the way you are. (laughs) Okay.
Erin Allmann Updyke	I love it, it's fantastic. It should just be C. botulinum, no it has to be botulism, but Botulism: Why Are You The Way Your Are is so good.
Erin Welsh	I also liked No Wrinkles In Time which was a contender for our quarantini.
Erin Allmann Updyke	That's funny but this is better.
Erin Welsh	But yeah and so if you think about it, we've done so much laboratory research, not we but the world has done so much laboratory research on botulinum toxin but those are under laboratory settings.
Erin Allmann Updyke	Right.
Erin Welsh	And so the amount that it takes to kill an animal in a lab setting is much, much, much greater than what it takes to lead to death in a natural setting.
Erin Allmann Updyke	Lead to death. Yeah, yeah, yeah. Oh that makes so much sense.
Erin Welsh	Yeah. So that I think is why this toxin exists.
Erin Allmann Updyke	Episode over, that's all I need to know. That's to cool.
Erin Welsh	I know. I honestly had the time of my life.
Erin Allmann Updyke	What a fun fact!

Erin Welsh	I know, I know. I know. Yeah.
Erin Allmann Updyke	What a clever little bacterium though.
Erin Welsh	I know! I know.
Erin Allmann Updyke	I mean it's not clever but you know...
Erin Welsh	I think the whole comparative evolution... So there's so much more that goes into this ecology, like why are there multiple toxins? Why is there variation among their toxicity or potency or whatever? Why do we see these different seasonalities? What triggers these avian botulism outbreaks?
Erin Allmann Updyke	Why quite so potent?
Erin Welsh	Yeah. I mean we could spend all day talking about just this part of it.
Erin Allmann Updyke	But that's not this podcast.
Erin Welsh	Let's go back to the human side of things, I guess. Okay so C. botulinum, as you know an environmental bacterium, is probably super old. And it doesn't really seem though to have a long evolutionary history with humans because of this more incidental nature of infection or impact.
Erin Allmann Updyke	Right, yeah.
Erin Welsh	But at the same time it has not been a stranger to humans throughout history, like probably all of human history.
Erin Allmann Updyke	Okay. That makes sense.
Erin Welsh	Yeah. I mean essentially as soon as humans started to try to preserve or store food, there were cases or outbreaks of botulism.
Erin Allmann Updyke	Right.
Erin Welsh	And probably honey, honey's one of the oldest foods in the world.
Erin Allmann Updyke	Yeah.
Erin Welsh	So infant botulism.
Erin Allmann Updyke	Boom.
Erin Welsh	And so while in ancient times people may not have recognized exactly what was causing food-related paralysis or death that they may have seen, it does seem like they took note of the foods where it seemed more likely to happen.
Erin Allmann Updyke	Okay.

Erin Welsh	Like blood sausages or cured ham or fermented fish.
Erin Allmann Updyke	Interesting.
Erin Welsh	Yeah. Let me give you a couple of examples. The powder of blood sausage, dried under anaerobic conditions, appears as an ingredient in at least one recipe for a deadly potion. And Emperor Leo VI of Byzantium who ruled in the late 9th and early 10th centuries, just go with it, he outlawed blood sausages, like the production of them and whatever.
Erin Allmann Updyke	Erin, where you get your facts... I just love it.
Erin Welsh	But some researchers think that him outlawing blood sausages is tied to blood sausages being a more common source of botulism.
Erin Allmann Updyke	Okay.
Erin Welsh	And some descriptions of poisoning with atropine aka belladonna may have actually been botulism instead because they describe the consciousness and then the full flaccid paralysis, yeah.
Erin Allmann Updyke	The paralysis, right, yeah. Cause you don't get that with atropine cause it doesn't affect your skeletal muscles.
Erin Welsh	Right.
Erin Allmann Updyke	Yeah, cool.
Erin Welsh	Oh yeah. But C. botulinum really began to get the widespread recognition it deserved starting in the late 1700s. Napoleon had been waging his wars all throughout Europe and kind of devastating the land, like these wars devastated the land, there was tons of poverty, hygiene went way down particularly in Central Europe. And one of the victims of this was apparently safety standards in food production. I don't know exactly what safety standards were like for food production in the 1700s.
Erin Allmann Updyke	But they really went downhill.
Erin Welsh	Yeah. Whatever they were, it just went down from there. And so the number of fatal food poisoning cases jumped. In a region in the southwest of Germany called - apologies for the pronunciation - Württemberg, whatever. And in one outbreak in 1793, 13 people became sick and 6 died.
Erin Allmann Updyke	Wow.
Erin Welsh	And the cases had one thing in common: blood sausages. A blood sausage can be many things but it's generally a pig's stomach stuffed with meat, grease, blood, herbs, bread, cereals, sometimes the pig's innards, and it's smoked and then boiled and then eaten. If you don't boil it long enough, guess what can happen? Over the next couple of decades these reports of fatal food poisoning continued to pour in and the term 'sausage poisoning' became the en vogue term to describe them.
Erin Allmann Updyke	Okay.

Erin Welsh	In a small town in this Württemberg region a 29 year old medical officer by the name of Justinus Kerner had become very interested in this sausage poisoning situation. And he would end up making enormous strides in research on C. botulinum even before germ theory had been developed.
Erin Allmann Updyke	Cool!
Erin Welsh	This is very cool. All right, so let's go through his various discoveries. Number one, he began doing his own groundwork on sausage poisoning cases and in 1820 he published case reports of 76 patients and the first clinical description of botulism that tracks very closely with how it's described today.
Erin Allmann Updyke	Wow.
Erin Welsh	So I'm gonna read this and I want you to just - this is 1820 - and just say wow, Erin. Just react for me. (laughs)
Erin Allmann Updyke	That's my job during this section anyway.
Erin Welsh	Okay, quote: "The tear fluid disappears, the gullet becomes a dead and motionless tube, in all mucus cavities of the human machine, the secretion of the normal mucus stands still. From the biggest, the stomach, toward the tear canal and the excretory ducts of the lingual glands. No saliva is secreted, no drop of wetness is felt in the mouth, no tear is secreted anymore, no earwax appears in the auditory canal, also signs of drying out of the eustachian tube become apparent. No mucus is secreted in the nose, no more sperma is secreted, the testicles decrease, urination can only be performed by standing and with difficulty. Extreme drying out of the palms, the soles, and the eyelids occurs."
Erin Allmann Updyke	That is a great description.
Erin Welsh	Yeah. 1820.
Erin Allmann Updyke	I especially loved that he said 'the human machine'.
Erin Welsh	(laughs) The human machine.
Erin Allmann Updyke	That is my new favorite term.
Erin Welsh	Yeah it's pretty good.
Erin Allmann Updyke	Now I will say that that description could also have been belladonna cause he didn't really talk about the paralysis aspect of the skeletal muscles.
Erin Welsh	He does in other... So that was like an excerpt from this.
Erin Allmann Updyke	Yeah, yeah.
Erin Welsh	And as we'll see yeah, he did tons and tons of work.

Erin Allmann Updyke	Right.
Erin Welsh	So he did expound more upon the paralysis aspect of it.
Erin Allmann Updyke	We should use that in school to talk about the effects of the parasympathetic nervous system cause he did a really good job of going through them all. That's nice.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	Good job, Kerner.
Erin Allmann Updyke	Earwax even.
Erin Welsh	Okay, number two. That's only number one.
Erin Allmann Updyke	Okay, wow.
Erin Welsh	Number two, he didn't stop with just describing sausage poisoning, he wanted to understand what exactly was causing these symptoms and how. So he collected the sausages that he suspected were involved in the poisonings and he compared their ingredients. And the only two commonalities he found were salt which he believed to be innocent and fat. So he came to the conclusion that fat, what he called fatty acid, was the cause of this sausage poisoning.
Erin Allmann Updyke	Okay.
Erin Welsh	And so he attempted to isolate this fatty acid or sausage poison from these poisoned sausages and conduct some experiments to see if he could recreate the symptoms. And so he fed this fatty acid to birds, cats, rabbits, frogs, flies, locusts, snails, and so on.
Erin Allmann Updyke	Wow, snails even.
Erin Welsh	Yeah. And some of these experiments worked, like they developed paralysis.
Erin Allmann Updyke	Right.
Erin Welsh	And he also experimented on himself a few times and described what happened there and then his professor was like, 'Dude, what are you doing? Stop doing that, you're going to die.'
Erin Allmann Updyke	Dude, stop doing that!
Erin Welsh	Stop doing that.
Erin Allmann Updyke	Oh my god.
Erin Welsh	Yeah. All right so number three. Through these experiments he was able to closely examine the stages of paralysis and even develop some hypotheses as to just how the toxin causes these symptoms, basically deducing that it was through an interruption of the peripheral and autonomic nervous signal transmission.

Erin Allmann Updyke	What?
Erin Welsh	Isn't that amazing?
Erin Allmann Updyke	Wow that's is incredible.
Erin Welsh	This is what he wrote. Quote: "The nerve conduction is brought by the toxin into a condition in which its influence on the chemical process of life is interrupted. The capacity of nerve conduction is interrupted by the toxin in the same way as an electrical conductor by rust." Chills.
Erin Allmann Updyke	100%.
Erin Welsh	In 1820! Like this is incredible.
Erin Allmann Updyke	Wow. That is phenomenal.
Erin Welsh	You're about to be even more blown away.
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	Because number four, he went on to suggest possible ways to prevent sausage poisoning through longer boiling times, through storing the sausage in dry, anaerobic conditions, and he also suggested a way to treat it. He invented an elastic tube that some people view as the first gastric tube to make sure that his patients got enough nutrition and didn't choke to death or didn't aspirate. Yeah.
Erin Allmann Updyke	Wow.
Erin Welsh	Okay. Number five, this is the last one. He went on to propose that this toxin could be used therapeutically to calm over excited nervous systems. He suggested it could be used to cure St. Vitus' dance, remember from dancing plague episodes?
Erin Allmann Updyke	Yeah!
Erin Welsh	And also some other things which are a little less grounded in mechanism.
Erin Allmann Updyke	Reality?
Erin Welsh	Excess sweat, rabies, plague, yellow fever. Again it was pre-germ theory days so we can give him a break on that. But it's amazing that he would recommend therapeutic applications like 150 years before they were put into practice.
Erin Allmann Updyke	Phenomenal.
Erin Welsh	Amazing. Okay so to recap real quick. Number one, the first clinical description. Number two, isolation of the toxin. Number three, explanation of the mechanism of the toxin. And also number two, it's a little hand-wavy but he was able to actually...whatever.

Erin Allmann Updyke	He tried.
Erin Welsh	He tried. Number three, explanation of the mechanism of the toxin. Number four, prevention and treatment methods. And number five, suggestions for therapeutic use. Incredible.
Erin Allmann Updyke	Human ingenuity right there.
Erin Welsh	Human ingenuity.
Erin Allmann Updyke	That is the kind of human Doctor Who is like all about.
Erin Welsh	Yeah, yeah. No, exactly.
Erin Allmann Updyke	Anyways, wow.
Erin Welsh	Yep.
Erin Allmann Updyke	Wow!
Erin Welsh	His work on sausage poisoning earned him a bit of notoriety as the leading expert and he was known as Wurst Kerner, sausage Kerner. Also he was apparently a very accomplished poet especially in his later years. You can read his poetry online.
Erin Allmann Updyke	Very cute.
Erin Welsh	Okay so I've gotten this far in the history of botulinum toxin, C. botulinum, botulism, whatever, and I have yet to talk about etymology.
Erin Allmann Updyke	Ooh, Erin.
Erin Welsh	Botulism, like the term botulism, it got its official name in 1870 and its scientific name for C. botulinum in 1897 and I'll tell that story ina second about that.
Erin Allmann Updyke	Okay.
Erin Welsh	But first, Clostridium botulinum. Originally it was called Bacillus botulinum, 'bacillus' just basically as you said meaning rod-shaped. But it was later renamed Clostridium from the Greek 'klōstēr' meaning spindle because the colonies of bacteria in this genus apparently resemble spindles.
Erin Allmann Updyke	Okay.
Erin Welsh	And botulinum from the Latin word 'botulus' meaning sausage.
Erin Allmann Updyke	Stop it! Sausage!
Erin Welsh	Sausage.
Erin Allmann Updyke	Not what I was expecting but after that story, not surprised.

Erin Welsh	Spindle sausage.
Erin Allmann Updyke	Spindle sausage!
Erin Welsh	Isn't that incredible?
Erin Allmann Updyke	That is hilarious. Sausage. Wow.
Erin Welsh	Yeah. (laughs) So by the late 1800s, botulism and its association with sausages was well known throughout Europe but it would take a funeral with pickled ham, nearly three dozen people falling ill, and three dead for it to be recognized as being caused by bacteria.
Erin Allmann Updyke	Ooh.
Erin Welsh	In December of 1895 in a small town in Belgium, around 34 musicians in the local brass band gathered to play at the funeral of 87 year old Antoine Creteur, a town elder. After the funeral was over they were given dinner at the local inn and this dinner consisted of among other things smoked or pickled ham. Unfortunately it hadn't been preserved or cured properly and within a few days the entire band began showing signs of botulism, the entire band.
Erin Allmann Updyke	Uh oh. All 34 members?
Erin Welsh	All 34. Three ended up dying.
Erin Allmann Updyke	Oh dear.
Erin Welsh	A microbiologist named Emile Pierre van Ermengem, he was professor at the University of Ghent at the time but he had previously worked with Robert Koch and he had caught wind of the outbreak. He examined the ham and tissues from those who had died and went about looking for microbes. And he found them and called them Bacillus botulinum. It would take nearly another 30 years for the toxin itself to be discovered and isolated but during that time people grew to realize that this was certainly not just a disease of sausages or ham or fish. It could also come from white beans and one of the first canning outbreaks, olives. Or basically anything. Cases of botulism continued to rise as the technology to can or preserve food continued to develop into the 20th century. And both commercial and home canning or food preservation carried risks of botulism. And it took many, many outbreaks, both from mass produced cans and home canned foods for people to gain an understanding of the techniques you had to use to properly prevent botulism from happening or the toxin from developing.
Erin Allmann Updyke	Right.
Erin Welsh	And because treatment for a good portion of this history was not an option, like we didn't have the antitoxin until relatively recently I think, the past few decades.
Erin Allmann Updyke	Yeah. It would just be supportive care in that case then, yeah.

Erin Welsh	Okay. So in 1820 at the University of California, a researcher named Dr. Herman Sommer was finally able to isolate a botulinum toxin, type A if you're interested. Makes sense that it was A cause it was the first one. And additional research showed it to be the most toxin substance known to humans as we discussed earlier. So why do you think this research was being conducted? Why were people interested in botulism?
Erin Allmann Updyke	Oh I don't know, maybe like biowarfare or something like that?
Erin Welsh	There you go. Ding-ding-ding-ding.
Erin Allmann Updyke	Oh dear.
Erin Welsh	Yeah. So it was probably a good thing that the toxin was isolated a couple years after WWI ended.
Erin Allmann Updyke	Oh dear.
Erin Welsh	But guess what was just around the corner? WWII. Not that WWII was exactly looming on the horizon in 1920 but you know, kind of. Whatever.
Erin Allmann Updyke	Right, yeah.
Erin Welsh	There was always a reason to be able to produce a bioweapon, right. So the US Army Biological Warfare Laboratories at Fort Detrick in Maryland had a special interest in developing botulism or botulinum toxin as a weapon to use in the war during WWII. And supposedly they had even developed a plan to try that out that involved having people assassinate high ranking officers in the Japanese army by dropping a gelatin capsule containing botulinum toxin into their food or drink.
Erin Allmann Updyke	Whoa.
Erin Welsh	The plan was abandoned when the capsules were tried out on donkeys and had no effect.
Erin Allmann Updyke	So they didn't make a good enough capsule or something?
Erin Welsh	Well so one of the hypotheses is that donkeys are immune to botulinum toxin but that seems to be really debated. And so it still seems unclear.
Erin Allmann Updyke	Interesting.
Erin Welsh	Yeah. In any case, botulinum toxin was abandoned as a bioweapon for a lot of the same reasons that ricin was abandoned, if you remember in that episode. It doesn't spread person to person, the dosage is hard to control, it's easily inactivated, and it now can be treated. So in terms of a bioweapon, it's not great.
Erin Allmann Updyke	It's not super fast acting. It don't know if that's a good thing or a bad thing in terms of bioweapons, I've never...
Erin Welsh	I don't know what the objective is. To terrorize people?

Erin Allmann Updyke	Right, then it's not that great.
Erin Welsh	Yeah. And now Fort Detrick is now all about biodefense rather than offense. So anyway, it was abandoned. Okay. So in keeping with the theme of poisons that we usually use for those crossover episodes that we do-
Erin Allmann Updyke	Right, yeah.
Erin Welsh	I think it's time to chat about the other side of the coin or can.
Erin Allmann Updyke	Yes! (laughs) The other side of the can.
Erin Welsh	The other side of the can.
Erin Allmann Updyke	Okay, tell me about it.
Erin Welsh	Okay. Botulinum toxin in therapeutics. So Kerner suggested it in 1820.
Erin Allmann Updyke	Way ahead of the game.
Erin Welsh	Way ahead of the game. But it wasn't until the 1960s or 1970s that it was developed for treatment purposes.
Erin Allmann Updyke	Cool.
Erin Welsh	The first pilot study of type A botulinum toxin to treat strabismus in humans, basically cross-eyed-ness.
Erin Allmann Updyke	Yeah, misalignment of your eyes.
Erin Welsh	There we go. This first study was done in 1978 and was shown to be effective. The FDA approved its use a year later.
Erin Allmann Updyke	Cool.
Erin Welsh	And that really opened the door for doctors to use it to treat all kinds of involuntary muscle contractions.
Erin Allmann Updyke	Yeah.
Erin Welsh	And Erin, I'm sure you're gonna talk more about what those treatments are in the next section.
Erin Allmann Updyke	Yep, absolutely.
Erin Welsh	But before we get to that we have one more little piece of business to cover. The Botox business to be precise.
Erin Allmann Updyke	Okay. Yes!

Erin Welsh	How did this begin? So let's head to 1987.
Erin Allmann Updyke	Okay.
Erin Welsh	Botulinum toxin had been used for these various things about 10 years at that point and an ophthalmologist named Dr. Jean Carruthers had been shooting botulinum toxin into her patients to treat abnormal, involuntary blinking. Do you know what the technical term is for that?
Erin Allmann Updyke	God I feel like I should.
Erin Welsh	Starts with a 'B', ends in 'spasm'.
Erin Allmann Updyke	Oh, blepharospasm or something.
Erin Welsh	Yeah, blepharospasm. It's a very awkward-sounding word.
Erin Allmann Updyke	It really is, yeah.
Erin Welsh	So she noticed that when she did this, when she injected this botulinum toxin into her patients near their eyes, their frown lines disappeared, some of the wrinkles around their eyes disappeared. So she went home and mentioned it to her husband who happened to be a dermatologist. And they were like, 'Holy cow, we just stumbled upon what might be the most revolutionary cosmetic procedure yet.'
Erin Allmann Updyke	Yep.
Erin Welsh	And they worked on it for about 10 years before publishing their first report in 1996. And since then it has become perhaps, and you'll maybe talk more about this, perhaps the most widespread and profitable cosmetic treatment.
Erin Allmann Updyke	By far, absolutely.
Erin Welsh	So that's kind of where my story ends. From sausage poisoning to wrinkle reducing, the glorious story of Clostridium botulinum.
Erin Allmann Updyke	Wow! That is so fun, Erin.
Erin Welsh	Isn't that fun?
Erin Allmann Updyke	Yes!
Erin Welsh	Migratory birds, blood sausages.
Erin Allmann Updyke	What an interesting story. My goodness.
Erin Welsh	It's like one of my favorites. It just feels...I don't know. It's very satisfying, the whole story.
Erin Allmann Updyke	I agree, it is satisfying. It is so fun, my goodness.

Erin Welsh	And there's a lot too... I didn't mention sort of the food outbreaks that have happened throughout the 20th century cause there have been a lot but I didn't go into detail on those. But I will say there have been many.
Erin Allmann Updyke	Yeah. So let's talk about where we stand with botulism and Clostridium botulinum today.
Erin Welsh	Let's take a quick break.
TPWKY	(transition theme)
Erin Allmann Updyke	So let's talk first just about kind of the depressing botulism part of it, get that out of the way so we can end on happy notes. Okay?
Erin Welsh	Yeah.
Erin Allmann Updyke	Okay. So in 2017 in the United States, like I mentioned already when you asked, there were 182 laboratory-confirmed cases of botulism reported to the CDC. Botulism is a reportable illness because it is very rare and serious. Most of those, the vast majority and this has been true at least since the 80s, the vast majority of botulism cases are infant botulism. So like 70-80% of all cases of botulism in the US are infant botulism. About 10% are foodborne or at least in 2017 they were, and about 10% were wound botulism.
Erin Welsh	Okay.
Erin Allmann Updyke	There were at least in 2017 three classified as other, so two of them were iatrogenic, so they somehow got infected through hospital procedures or something like that. And then one was suspected adult intestinal colonization which I mentioned can happen but is of course exceedingly rare. Cool?
Erin Welsh	Yes.
Erin Allmann Updyke	And so I don't really have a lot of details on 'these are the foods that are most common to cause botulism' because I just don't really find it that interesting. In theory almost any canned food, if it doesn't have enough acid in it, can be a medium for Clostridium botulinum to grow and therefore could put you at risk.
Erin Welsh	Right. It's like there's a decent temperature range and a decent pH range where this bacterium can reproduce under anaerobic conditions.
Erin Allmann Updyke	Yeah. And you can google that and then if you're gonna can food, just do it properly, that's fine. No big deal. But anyways it is still possible, it absolutely still happens, but the vast majority of cases are infant botulism and most of those are from honey. So yeah. Okay, so let's talk about the more interesting and kind of fun, cool aspects of botulinum toxin and that is all the different ways that we use it currently. Okay. Botulinum toxin is used medically to treat a lot of different dystonias which is what you mentioned, Erin. A dystonia is inappropriate muscle contractions. And these can be really, really painful.

	So one of the most common uses for botulism is to treat cervical dystonia which is a contraction of your neck muscles that can be really, really painful. It's also used to treat laryngeal dystonia, so contraction of your larynx that's inappropriate. It has been used to treat tremors, certain types of tremors. It's often used in the treatment of cerebral palsy which is you have a lot of inappropriate contraction in cerebral palsy. Interestingly it's more recently been used to treat headaches, both migraine headaches and chronic contraction-like muscle-type headaches.
Erin Welsh	I saw that. How does that work?
Erin Allmann Updyke	It's such a good question, we don't really know. Because from what I understand there have been a number of studies although not a ton but a number of studies like placebo-controlled studies that show that injection of Botox in your paravertebrals, like near our cervical vertebrae is more effective than placebo in treating chronic headaches. But when they have tested whether your muscles, like whether you can still have pain conduction, that is intact and it's the same as placebo. So they don't actually understand what the mechanism is that is relieving these headaches. But we also don't really understand what causes a lot of headaches.
Erin Welsh	That's what I was gonna say, we don't really know about headaches and migraines. That's very interesting.
Erin Allmann Updyke	Especially migraines.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah. It's very interesting.
Erin Welsh	And they just discovered this by accident?
Erin Allmann Updyke	No I think it was because a lot of treatments for migraines have to do with vascular dilation and things like that and you can achieve that type of dilation by relaxing the muscles around the blood vessels as well. So I don't know if that was the thought process behind it but also it's not just migraine headaches, it's other tension headaches as well.
Erin Welsh	Right.
Erin Allmann Updyke	Maybe that has to do with muscle tension.
Erin Welsh	Right, right. That's so interesting.
Erin Allmann Updyke	Also going still in your head and neck area, TMJ has been treated with Botox.
Erin Welsh	Oh.
Erin Allmann Updyke	I know, I was like can I get some of that? Anyways. You mentioned that it was suggested to be treated for excessive sweating, that is actually a use of Botox today.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah. So hyperhidrosis which is excessive sweat, you can treat that with Botox.

Erin Welsh	Kerner got one thing right.
Erin Allmann Updyke	He sure did. I have to tell you, this is really fun. I have injected Botox into someone.
Erin Welsh	Ooh!
Erin Allmann Updyke	Me, personally. I have injected Botox into the detrusor muscle of the bladder during my OB/GYN rotation.
Erin Welsh	Oh that's exciting.
Erin Allmann Updyke	So this is a treatment for overactive bladder.
Erin Welsh	Oh, that makes sense.
Erin Allmann Updyke	Yeah, you relax that muscle. I wanna say that the physician that was doing the surgery actually stuck the needle in and was guiding the camera, I literally just pushed the plunger. So I was very well supervised in doing this. So yeah, there are a lot of different ways, Botox is one of the trade names I guess for botulinum toxin.
Erin Welsh	It's registered or copyrighted or trademarked or whatever.
Erin Allmann Updyke	Yeah, there's a whole bunch of different forms of it. So in addition to Botox which was the first one, there's one called Dysport, that's actually a type B toxin where Botox is type A. There's Myobloc, there's Neurobloc, there's a brand in China called Hengli, there's a lot of different types but Botox was the first that was commercially available botulinum toxin.
Erin Welsh	Right.
Erin Allmann Updyke	Okay. So then let's talk about Botox. Cause when you hear Botox you think of...?
Erin Welsh	Face injections for wrinkle reducing.
Erin Allmann Updyke	Yes, you think of face injections, wrinkle reducing Botox. And this is absolutely without a doubt not only the most common use of Botox or of botulinum toxin but also the most common cosmetic procedure by far. So according to the 2018 plastic surgery statistics report put out by the American Society of Plastic Surgeons, there were in 2018 over 7 million Botox procedures.
Erin Welsh	Wow.
Erin Allmann Updyke	Isn't that-
Erin Welsh	Amazing, yeah.
Erin Allmann Updyke	It's a lot.
Erin Welsh	That's a lot, that's a lot of procedures.

Erin Allmann Updyke	It is by far the most common minimally invasive cosmetic procedure. And this has grown a ton. So it was licensed by the FDA for cosmetic use in 2002 and it's increased in popularity and demand over 750% in the ensuing years.
Erin Welsh	Oh my god.
Erin Allmann Updyke	Yeah. So it's just on the rise because at first when I was looking up statistics on how many people get Botox or how many Botox procedures - cause this is not people who get Botox, this is Botox procedures - in 2014 it was like 6 million that they estimated. So now we can see in 2018 it was over 7 million, close to 8 million actually.
Erin Welsh	Gotcha, gotcha.
Erin Allmann Updyke	7.5 million. So yeah, it's really, really increasing which is fascinating. So I wanna talk about a few things having to do with Botox.
Erin Welsh	Okay.
Erin Allmann Updyke	So the reason that Botox works to reduce your wrinkles is because you inject a very small, very, very, very small, very dilute amount directly into the muscles and that toxin is going to affect the neuromuscular junction, it's going to block the release of acetylcholine and it's going to cause those muscles that are innervated by those nerves to relax. Okay? And if you have relaxed muscles then you're not gonna have the appearance of wrinkles because those are caused by muscles contracting in different ways, okay. However even though botulinum toxin binds irreversibly to those nerve terminals, eventually your body regenerates the ability to release acetylcholine. So eventually you're going to have movement of those muscles again when your body is able to kind of work around the fact that those have been blocked by botulinum toxin. Does that make sense?
Erin Welsh	Yeah.
Erin Allmann Updyke	So the effects of Botox or botulinum toxin don't last forever which is why you have to reup your Botox every however many months and it depends how much you inject and also just person to person variation how often that is going to be. The other thing I wanna say is that because... So this is obviously a very, very, very potent toxin, this is drug that is highly regulated. I found at least one paper that I don't think was legit that was like, 'Someone collapsed and died in a beauty salon after Botox injection'. And I just wanna say that even if someone were to die from getting too much Botox because in theory that is of course possible because this is a very deadly toxin-
Erin Welsh	Getting too much Botox as in too much botulinum toxin, not the treatment.
Erin Allmann Updyke	Right, yes. Yeah, yeah, yeah, exactly. Like inappropriate use of botulinum toxin injection. Not just like you went a little heavy or whatever. You wouldn't die right away, right.
Erin Welsh	Oh right.
Erin Allmann Updyke	That's not how botulinum toxin works. You wouldn't just collapse and die.
Erin Welsh	Yeah.

Erin Allmann Updyke	Even the effects of Botox take time to work. It's not something that happens automatically, this isn't a toxin that just blocks all of your nerve signals and kills you right away or anything like that, that's not the mechanism of how you would die from botulinum toxin to begin with. So if you ever see something like that, that's not real, that's not how it works. And I found it on a cursory search so I feel like I need to put that out there. But it's very interesting, I think it's very fascinating that we have so many uses for something that is so deadly. It's so cool.
Erin Welsh	It's so cool. I think it's amazing. I mean it's just more of those, I don't know, being very innovative and open-minded in terms of what can we do.
Erin Allmann Updyke	Yeah.
Erin Welsh	And also testing it out in very regulated ways and sort of letting it build upon what we see.
Erin Allmann Updyke	Yeah, absolutely.
Erin Welsh	Amazing, amazing.
Erin Allmann Updyke	Yeah!
Erin Welsh	I feel like this topic is so much bigger than I thought it was going to be starting out.
Erin Allmann Updyke	Yeah and it's so much more fun. I mean botulism poisoning is really depressing.
Erin Welsh	Of course.
Erin Allmann Updyke	But the overall story of Clostridium botulinum and of botulinum toxin is fascinating and fun.
Erin Welsh	It's so interesting. It's just so interesting.
Erin Allmann Updyke	Yes. Yeah.
Erin Welsh	I love it.
Erin Allmann Updyke	Cool.
Erin Welsh	Okay. Well, sources?
Erin Allmann Updyke	Sources.
Erin Welsh	I have a bunch but I wanna highlight a few that I really enjoyed or relied heavily on. The first is a chapter called Avian Botulism in a book titled 'Infectious Diseases of Wild Birds'.
Erin Allmann Updyke	Okay.

Erin Welsh	And the other one, someone named Erbguth wrote many, many papers on the history of botulism. And so there are several of those, one that I'll call out in particular was from 2008. And then another paper about sort of the why of botulism is by Mansfield and Doxey from 2018 and it's titled 'Genomic insights into the evolution and ecology of botulinum neurotoxins'. And then finally Montecucco and Rasotto from 2015 titled 'On botulinum neurotoxin variability'.
Erin Allmann Updyke	Awesome. I have a couple really in depth papers on the toxin of Clostridium botulinum especially if you wanna know more about all the different types cause there are a lot of different types of this toxin. Those are old papers but they're still valid. There's a nice Clinical Infectious Diseases paper just title 'Botulism' that I used if you wanna know kind of about the disease syndrome of botulism. And then a few other papers that I'll put up about kind of botulinum toxin use in clinical scenarios. So yeah.
Erin Welsh	Cool.
Erin Allmann Updyke	All right. Is that it?
Erin Welsh	I think that's it.
Erin Allmann Updyke	So wow, cool. Thank you to Bloodmobile for providing our quarantini title and the music for this episode and all of our episodes.
Erin Welsh	(laughs) And thank you to you, listeners, for listening. And also we want to especially thank everyone who keeps jumping on the quarantini posts and stuff and saying, 'TPWKY did it first!' We love you.
Erin Allmann Updyke	We really do. I get a warm feeling in my heart every time I see those.
Erin Welsh	Me too. Also it came to our attention that apparently we didn't really do it first, that it was on an episode of Scrubs but I genuinely haven't watched that show.
Erin Allmann Updyke	No. And you definitely, we thought that you came up with it. So in our hearts we tried.
Erin Welsh	Yeah. I think it just goes to show that there's nothing new ever invented ever.
Erin Allmann Updyke	Ever.
Erin Welsh	That's fine by us.
Erin Allmann Updyke	Except Botox that first time. Except Wurst, what was his name?
Erin Welsh	Wurst Kerner.
Erin Allmann Updyke	Wurst Kerner, he did it first.
Erin Welsh	(laughs) The sausage king! The sausage Kerner king.
Erin Allmann Updyke	The sausage king.

Erin Welsh	Okay well, good lord. With that, wash your hands.
Erin Allmann Updyke	You filthy animals!