TPWKY	This is Exactly Right.
Erin Welsh	Number one. "The camp at Chickamauga was a perfect hell on earth. War itself would have been a paradise compared with the peace of this camp. I saw many awful sights there, men dying under the trees for the want of a glass of water. I found there men who had been sick with Typhoid fever for days and who had not received medical attendance. No one had even taken their temperature. It was awful. For 500 men in hospitals, there were only a dozen attendants. The water from the creek was simply mud and yet the boys had to bathe in it and drink it. Everything about the camp was badly managed. As for the food, there is only one way to describe it. It was rotten."
	Number two. "Someone is to blame for keeping an army of 45,000 men at a camp where all the water was unfit for a dog to drink, where there was no drainage, no proper food or medicine, and where the conditions were so unhealthy that every man of 45,000 had intestinal troubles. 3/4 of the army slept in little 'dog tents', as we called them. They were five feet long and four feet high. There were no cots. The men slept on the ground and it rained nearly all the time for six weeks. Our division hospital was arranged to hold 200 men but we had over 500 sick men in it. Each tent was arranged to hold six men but we had ten and twelve crowded in. There were not cots enough and sick men had to lie on litters on the wet ground, sometimes for a week. The sick came in 50 and 75 at a time and there no cots, no medicines, no food for them except the regular army rations issued to well men. The men detailed for nurses were the poorest soldiers in the camp, they nursed the sick eight hours in the day and then worked three hours digging sinks and trenches and cleaning up the camps."
	Number three. "In the camp of the 3rd United States Volunteer Cavalry, we found the sinks full to the top with fecal matter. Soiled paper was scattered around the sinks and the woods behind the regimental camp was strewn with fecal matter. The 2nd Kentucky Volunteer Infantry was located in the woods. Fecal matter was deposited around trees and flies swarmed over these deposits not more than 150 feet from the company mess tents. The odor in the woods just outside of the regimental lines was vile."
TPWKY	(This Podcast Will Kill You intro theme)
Erin Allmann Updyke	Ugh!
Erin Welsh	(laughs) Yeah. Yeah.
Erin Allmann Updyke	Why are they pooping in sinks?
Erin Welsh	There was nowhere else to poop! Okay-
Erin Allmann Updyke	Dig a hole? What is happening?
Erin Welsh	I mean, so, but all the holes got filled either with poop or with water and then the rainwater would make the poop rise to the surface and spread around everywhere.
Erin Allmann Updyke	Oh god. That's atrocious.
Erin Welsh	Yeah. So that was from the report of the commission appointed by the president to investigate the conduct of the war department in the war with Spain. Essentially, the Spanish-American war. It was reports from that, around 1900, is when these reports were all made. Yeah. A few different excerpts, I thought it was more fun to do a little smattering of-

Erin Allmann Updyke	Poop stories. (laughs)
Erin Welsh	(laughs) Essentially, yes. And you'll hear why I picked the Spanish-American war for the subject of today's episode later on. But first, 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 we're back with Season 4!
Erin Welsh	We are back and I'm very excited. I think we definitely needed that break.
Erin Allmann Updyke	Oh, big time.
Erin Welsh	Yeah, so we appreciate you guys for being patient and sticking with us.
Erin Allmann Updyke	Yes, thank you.
Erin Welsh	And yeah, letting us get a little bit of a time to take a breather. And yeah.
Erin Allmann Updyke	Yeah. Well and also get a bunch of fun new episodes lined up for you.
Erin Welsh	Oh, so many fun new episodes. Yeah. Yeah. Speaking of fun new episodes, what is the topic of today's episode? Maybe our break was too long, Erin.
Erin Allmann Updyke	No no, I actually love... I feel like most of the time lately our first-hands completely give it away and now it's like suspense had been building for like two whole minutes!
Erin Welsh	Yeah! Well I guess if no one clicked on the title of the episode... (laughs) Maybe there's suspense.
Erin Allmann Updyke	Yeah. It autoplayed. But today we're talking about typhoid fever.
Erin Welsh	Ugh. Typhoid fever. This one has been a long time coming.
Erin Allmann Updyke	Ooh, very long time coming.
Erin Welsh	I am super excited to cover this one because typhoid fever was sort of the episode, I feel like, that really changed our lives.
Erin Allmann Updyke	Um, yes. It changed our lives 1000% even though we have not yet covered it.
Erin Welsh	Yeah.
Erin Allmann Updyke	Because typhoid, the story of Typhoid Mary, is the story that Georgia Hardstark told when she first gave us a shout-out on My Favorite Murder. Which is like what led to our lives changing forever.

Erin Welsh	All the way back, in case you're interested in listening, all the way back in Episode 5 titled 'Proclensity'. I looked it up and I listened to it again for research for this episode. (laughs)
Erin Allmann Updyke	It's a good episode. (laughs) Yeah.
Erin Welsh	This is definitely like a full-circle moment.
Erin Allmann Updyke	We've been waiting for this episode since like 2018?
Erin Welsh	2018 yeah.
Erin Allmann Updyke	2018, yeah.
Erin Welsh	Ugh, I'm just so excited for it.
Erin Allmann Updyke	Me too.
Erin Welsh	But before we get into the actual meat for the episode, we do have some pieces of business. Starting with-
Erin Allmann Updyke	Quarantini time!
Erin Welsh	Quarantini time. Erin, what are we drinking this week?
Erin Allmann Updyke	Of course we could be drinking nothing other than a Bloody Mary.
Erin Welsh	Bloody Typhoid Mary.
Erin Allmann Updyke	Bloody Typhoid Mary. (laughs)
Erin Welsh	(laughs) Not just any Bloody Mary.
Erin Allmann Updyke	Not just any.
Erin Welsh	This one is titled differently. But yeah, other than the title it is essentially a Bloody Mary. Who doesn't love a Bloody Mary? You can pick and choose whatever pickled vegetables you wanna put in there, it's tomato juice, it's vodka, it's you know, worcestershire sauce, it's hot sauce, it's whatever you wanna put in there. Lemon juice.
Erin Allmann Updyke	It's how you like a Bloody Mary.
Erin Welsh	Yeah. And entire hamburger on a-
Erin Allmann Updyke	On a stick?
Erin Welsh	(laughs) Yeah. Anything you wanna put in there. We will post the recipe to the Bloody Typhoid Mary as well as the non-alcoholic placeborita on our website thispodcastwillkillyou.com as well as on all of our social media channels.

Erin Allmann Updyke	What other business do we have to attend to, Erin?
Erin Welsh	Well, let's see. Let's go over the usual suspects. I mean, number one, we've got merch. We've got some super cute new things that are here.
Erin Allmann Updyke	Very new things, very exciting things in fact.
Erin Welsh	The amazing artists Holly Sullivan did some new designs for us including, and you can get prints of her designs right now and stickers of Yersinia pestis, Aedes aegypti, of the Influenza virus, of giardia, 'gerardia'-
Erin Allmann Updyke	(laughs) However you like to say it.
Erin Welsh	And then there's also really cool things. Like one of my favorites is the 'Quarantini Time' t-shirt, it is so soft and I also have to admit to always wearing the hoodie around, it's like the perfect weight. And then I drink out of the pint glasses, and the socks are just too cute, I can't handle it.
Erin Allmann Updyke	We also heard you guys when you asked for face masks, since those are now pretty much a staple of everyone's wardrobe, so we have two different face masks including one that says 'Wash Your Hands, Ya Filthy Animals'.
Erin Welsh	They both do.
Erin Allmann Updyke	Oh they both do!
Erin Welsh	(laughs) They are super cute, I love them all. So yeah, go check it out, you can get to it by the thispodcastwillkillyou.com website, click on the merch tab.
Erin Allmann Updyke	Yeah.
Erin Welsh	Great. Let's see, okay more business. We can run through the rest of the usual suspects which includes hey, check it out, we've got a bookshop.org affiliate account, so if you're interested in doing any additional reading on any of the topics that we cover, we link to the books there, also through our website. And we also have a Goodreads list, so check it out too. Other people can add suggestions there so you get like a whole smattering of fiction and non-fiction disease readings, it's pretty cool.
Erin Allmann Updyke	Mm-hmm. And if you would like alcohol-free versions of these episodes, maybe you're a teacher, you wanna use these for whatever reason, maybe you just don't want to hear us talk about quarantinis, you can find those as well on our website thispodcastwillkillyou.com.
Erin Welsh	And then we have a couple new announcements. So the first is that we are going to be picking up again our Anatomy of a Pandemic series which covers the COVID-19 pandemic. So we stopped releasing episodes in May and now we are going to take some time to revisit some of these topics. You know, what have we learned so far about the virus? Everyone wants to know about the vaccine and where we stand with that. And so we are going to be putting those out as we work through these normal episodes, so don't worry the normal episodes won't be interrupted.
Erin Allmann Updyke	Yeah.

Erin Welsh	And we also still have the COVID-19 firsthand account submission form still active, so if you would like to share your story, potentially as a first-hand account in one of these episodes, please head to thispodcastwillkillyou.com and click on the COVID-19 FIRSTHAND tab at the top of the page.
Erin Allmann Updyke	Is that all the things?
Erin Welsh	(laughs) I think that's it. I'm exhausted. All right, let's circle back around tomorrow to pick up the actual episode, Erin.
Erin Allmann Updyke	(laughs) Perfect. Good idea, good idea.
Erin Welsh	But I guess, yeah, can we finally start talking about typhoid now?
Erin Allmann Updyke	Yes. I think we are ready. We'll take a quick break first.
Erin Welsh	Great.
TPWKY	(transition theme)
Erin Allmann Updyke	I think this is one of the most classic and also most specific diseases that we've done in a very long time.
Erin Welsh	You mean like it's not super complicated where it has all these different forms and this and that?
Erin Allmann Updyke	No, no, it's plenty complicated.
Erin Welsh	Oh good, okay. It is a very classic TPWKY feel, which is kinda fun.
Erin Allmann Updyke	It is.
Erin Welsh	And why we chose to do it for our 4th Season premiere.
Erin Allmann Updyke	Exactly, it's a very classic feel but then it's also... Well, I'll get into it and you'll see what I mean by specific, okay?
Erin Welsh	(laughs) Okay.
Erin Allmann Updyke	Okay. So typhoid fever, which is also called enteric fever depending on where you live, is the disease that is caused by a Gram-negative rod-shaped bacteria whose full name is - are you ready for this? I know you know this already but it's long.
Erin Welsh	I know, it's a big one. (laughs) It's a mouthful.
Erin Allmann Updyke	Salmonella enterica subspecies enterica, serovar Typhi. That's what I mean by specific.
Erin Welsh	Honestly I don't quite understand why. Why? What is a serovar?

Erin Allmann Updyke	Great, really great question. I'm so glad you asked it, Erin.
Erin Welsh	(laughs) You know I was going to.
Erin Allmann Updyke	Yes. So first of all, we're just going to call it by its shorthand name Salmonella typhi, okay. That's how you can refer to it. Now, there are something like 2500 different serovars of salmonella, Salmonella enterica, even. And at least 50 of them are pathogenic although not all of those are pathogenic to humans. So you asked what makes a serovar?
Erin Welsh	Yeah.
Erin Allmann Updyke	You can kind think of it... You know how we name influenza strains by their H and their N?
Erin Welsh	Yeah, okay.
Erin Allmann Updyke	So serovars are differentiated from each other by those specific antigens on their surface. So in the case of salmonella, it's their lipopolysaccharide, which is an O antigen, and their flagella, flagellar antigen which is an H antigen. So that's how we identify them.
Erin Welsh	Interesting.
Erin Allmann Updyke	So if you'd like to know the serovar name of Salmonella serovar Typhi, it's 0912VIHD-. (laughs)
Erin Welsh	That's an easy thing to remember, come on.
Erin Allmann Updyke	Right? Yeah. Okay, so I'm gonna start off with a sidenote. There is another serovar, a couple of other serovars actually, that are called Paratyphi. So there's Paratyphi A, B, and C. This serovar causes a very similar but generally more mild illness. And so the term 'enteric fever' usually encompasses both the diseases caused by Salmonella Typhi and Salmonella Paratyphi.
Erin Welsh	Okay.
Erin Allmann Updyke	So we're gonna try and stay as specific as possible in this episode and really just focus in on Salmonella Typhi or typhoid fever. Cool?
Erin Welsh	Gotcha.
Erin Allmann Updyke	Cool. So Salmonella Typhi is what is referred to as a host-restricted pathogen. So it primarily infects just humans and then also like chimpanzees. All right. So how is it transmitted? I know you know, and everyone that listened to the firsthand probably has a guess.
Erin Welsh	I mean, if you're playing bingo with the number of times that 'fecal' is going to be said in this episode, like you've won.
Erin Allmann Updyke	(laughs) It's a lot. Yeah. Fecal-oral, so poop in mouth, wherever poop can end up then ends up in your mouth, you can get infected. Okay? One thing that's important, and I think this is actually really interesting considering that this is a fecal-oral transmitted parasite, is that salmonella is actually really acid labile so it does not tolerate the environment of your stomach very well at all. So that means that the infectious dose is really, really high compared to a lot of other bacteria and viruses that we've talked about on this podcast.

Erin Welsh	Interesting. Like how high?
Erin Allmann Updyke	Right? At least 10,000 bacteria to cause an infection. And even at that number, the attack rate, so the percentage of people who would actually get sick, is low. Like 10-20% at that infectious dose.
Erin Welsh	Okay. How much bacteria is an infected person or a carrier shedding?
Erin Allmann Updyke	(gasp) Such a good question! I don't even know if I know the answer to that, let me scroll through my notes and see.
Erin Welsh	Like in an average poop.
Erin Allmann Updyke	In an average poop. That's a good... Erin, what a good question that I don't have the answer to in all of my notes.
Erin Welsh	Just FYI guys, we just spent a little bit of time both looking for the answer. (laughs) I mean like not that long, but you know.
Erin Allmann Updyke	More than a few minutes.
Erin Welsh	We spent more than a few minutes and we couldn't find anything and so we just think it's safe to assume that it's probably a lot considering that like there've been a lot of typhoid fever epidemics and...
Erin Allmann Updyke	It's gotta be a lot because it takes a lot to get you sick and you poop a lot when you have typhoid fever, so. And it's a salmonella bacteria which reproduce very quickly, so...
Erin Welsh	A lot.
Erin Allmann Updyke	A lot. (laughs)
Erin Welsh	Hey, if somebody can find the actual number that would be super cool.
Erin Allmann Updyke	Would love that actual number. But what I did want to say about this is that what's really interesting is that the smaller the infectious dose, the longer the incubation period. So the longer between when you first get exposed to when you start to show symptoms, which is logical but it's nice when we can see that in data. Cool?
Erin Welsh	Okay. (laughs)
Erin Allmann Updyke	So the incubation period, that time from infection to symptoms, usually is between 5-15 days but it can be quite a bit longer, like even a month or more.
Erin Welsh	Gotcha, okay.
Erin Allmann Updyke	So let's talk about the symptoms of typhoid fever, shall we?
Erin Welsh	Let's.

Erin Allmann Updyke	Okay. The classic description goes something like this: it starts with a...?
Erin Welsh	Fever.
Erin Allmann Updyke	Fever. But not just any fever because we have to get specific. This is a fever that gets progressively worse. It's called a step-ladder or a step-wise fever. So once it begins, it remains high and then progressively rises over the course of two or so weeks before it peaks and then stays pretty high, like a plateau phase.
Erin Welsh	Huh, okay. Like how high?
Erin Allmann Updyke	Good questions, not bonkers high, like we're not talking 106, but a fever is classified as 100.4F or 38C, so it'll start there just like a low-grade fever and progressively just get higher. I don't know what the maximum peak is, probably depends on the person, but we're not talking like 106/107. It's just a slowly progressive fever. And what's important is that it stays high. A lot of other diseases you might have a fever for part of the day and then part of the day your temperature will go back down. With typhoid, once your fever rises, you stay with an elevated temperature.
Erin Welsh	Okay. Okay.
Erin Allmann Updyke	Okay? And the other classic symptom that's very interesting is that - and oh my gosh, Erin, please don't ask me why this happens, okay? I'm forewarning you.
Erin Welsh	(laughs)
Erin Allmann Updyke	But classic typhoid has what's called a 'relative bradycardia'. So that means that your heart rate is slow. And normally when you have a fever, a normal physiological response would be your body going, 'Hey, I'm feeling stressed out because my temperature's high, so my heart rate is gonna increase because of that high temperature.' But with typhoid it doesn't do that, your heart rate stays low.
Erin Welsh	I am bursting with questions, how dare you censor me. (laughs) Okay, I won't ask why. I will ask are there other diseases or other times that fever occurs when this same thing happens?
Erin Allmann Updyke	There are some others, absolutely. This isn't the only thing that causes this but that's one of those classic findings.
Erin Welsh	Okay.
Erin Allmann Updyke	Okay?
Erin Welsh	Wow.
Erin Allmann Updyke	I know! Okay. All right. Now, that's the initial phase, okay? So it's like these two weeks of increasing fever. In the second week, people might start to get a faint rash on their trunk. They're these little salmon-colored spots. Pretty sure that's not why it's called salmonella though, right?
Erin Welsh	(laughs)

Erin Allmann Updyke	Okay. And then in the third week of illness, you often get abdominal pain, you can get either diarrhea or constipation which is interesting, we'll talk more about that later. Bleeding from the intestinal tract. Often you can get secondary bacteremia, so if this bacteria enters your bloodstream and starts to replicate in your bloodstream, that's what bacteremia is. And sepsis. Almost everyone will get hepatitis and a painful hepatosplenomegaly, which is a fun word we often say on this podcast, so swelling of your liver and spleen. And now this I want to put a pin in so that you remember it, cause we're gonna talk more about it, but Salmonella Typhi is also a cause of acute cholecystitis, AKA gallbladder infection.
Erin Welsh	Okay.
Erin Allmann Updyke	That's important, just remember it. Now this is not a bacteria that tends to infect your nervous system, so neurologic manifestations are pretty uncommon, it's not impossible but when you have them they look more like febrile seizures in young children, which happens with a whole bunch of other diseases. And then it is possible to have other more serious complications like myocarditis, but this is really rare, so that would be if it infects your heart. But most of the time this is a gastrointestinal tract disease. So if you don't die from overwhelming sepsis and shock, or from your intestines becoming perforated and just like exploding your gut juices everywhere-
Erin Welsh	Oh. My. God.
Erin Allmann Updyke	-then over a period of weeks to months, your symptoms begin to gradually resolve. If you do not die.
Erin Welsh	Okay. Over a period of weeks to months.
Erin Allmann Updyke	Weeks to months. This is a long-lasting infection. So the big question in my mind is what makes Salmonella Typhi so different from all the other serovars of Salmonella enterica, right? A lot of other species of salmonella, even Salmonella enterica, can infect us and maybe we get the poops from it, but Salmonella Typhi causes this really disseminated infection. It's mostly GI symptoms but the first symptoms that you see are this fever which tells us that it's infecting a lot more than just our GI tract.
Erin Welsh	Yeah.
Erin Allmann Updyke	So, why?
Erin Welsh	Yeah. (laughs)
Erin Allmann Updyke	I'll ask myself the questions that I can answer. So the difference really is because Salmonella Typhi is this host-restricted pathogen, it can very quickly invade through our gastrointestinal walls. So it is not limited, it's not causing an infection that's only in our GI tract. Exactly how this happens, we still don't fully know. But we do know that it's at least in part due to the bacteria downregulating our immune response. So here's where it gets interesting.
Erin Welsh	Okay.

Erin Allmann Updyke	In our GI tract, we have these things called 'Peyer's patches'. I feel like we've talked about them a little bit on this podcast before, but they're basically like lymph nodes in the the walls of our small intestine. So it's where our white blood cells hang out, it's like the immune center of our GI tract. Our GI tract has its own little immune system.
Erin Welsh	Oh, it's like a big deal. It's so cool.
Erin Allmann Updyke	It's a very big deal. Yeah, it's very cool. So salmonella actually invades through these Peyer patches. So this is the area of our small intestine where it makes it's way into our body. And what's very cool is it actually uses the same channels to enter through our cells that are missing in people with cystic fibrosis, those CFTR channels.
Erin Welsh	Right, right.
Erin Allmann Updyke	Cystic fibrosis transmembrane receptor, I think. (laughs) So those also, you might remember, are channels that are important in another bacterial disease. Cholera.
Erin Welsh	Yeah, yeah, I was gonna say isn't that when we talked about Peyer's patches?
Erin Allmann Updyke	It could have been. I don't actually remember, that was a long time ago.
Erin Welsh	It was a long time ago.
Erin Allmann Updyke	But, so these Peyer's patches, which is where our white blood cells hang out in our intestine, are where salmonella first invades. So that's where it basically makes it's way through the wall of our intestine, through that epithelial cell layer into our bloodstream. And it gets better. Salmonella Typhi is also facultatively intracellular. What that means is it can live inside of our cells. And guess which cells it likes to replicate inside of?
Erin Welsh	White blood cells?
Erin Allmann Updyke	A white blood cell, Erin. Our macrophages.
Erin Welsh	Oh...Hmm...
Erin Allmann Updyke	Right? So that is how it's able to very quickly establish an infection outside of our intestine. It invades and replicates within our own white blood cells and then travels literally wherever white blood cells go. And because of that it tends to cause infection. So basically, you get infected by eating this bacteria, essentially right? And then it travels through your gut into your small intestine, invades through the wall of your small intestine, makes its way into your white blood cells, travels with these white blood cells to a few specific places where white blood cells hang out - the liver, the spleen, the lymph nodes, and the gallbladder.
	Okay. And then from all of these tissues the bacteria is continually proliferating, it re-enters the bloodstream and that's when you start to actually see disease. So that's why you have this time lag, right?
Erin Welsh	Right. It's gotta make all those journeys and bulk up its numbers.

Erin Allmann Updyke	Exactly, exactly. And then eventually because it's infecting the liver and the gallbladder, from there the bacteria actually re-enters the intestine and that's when you start to see those abdominal symptoms. And so that's why those abdominal symptoms like diarrhea, abdominal pain, is even later in the course of disease. Even though you got infected from your GI tract to begin with.
Erin Welsh	Gotcha, okay.
Erin Allmann Updyke	And that's when the most serious complications and the most life-threatening complication can occur, which is intestinal perforation. And the reason that that happens, and this is so bizarre, it's thought - and again, we still don't 100% understand this - but the bacteria, once they reinfect again your intestine, cause tissue death of those Peyer's patches. So where they initially invaded, they come back in and they kill off enough cells in the wall of your intestine that they make it so that that wall is weak and then eventually can perforate. And that has a mortality of rate of like 40-80%.
Erin Welsh	Like, that's fascinating because you would think that there would be like a trigger. Like clearly they're doing something different.
Erin Allmann Updyke	Mm-hmm. They're totally doing something different, and it's quite rare. This only happens in like less than 5% of cases.
Erin Welsh	Okay. Okay.
Erin Allmann Updyke	Listen, we haven't even gotten to the most fascinating part of Salmonella Typhi. Okay?
Erin Welsh	I am very excited, let's go.
Erin Allmann Updyke	Okay. That is that so many people can become infected and maintain a chronic carrier state without ever showing symptoms of the disease.
Erin Welsh	Oh yeah.
Erin Allmann Updyke	Okay.
Erin Welsh	Oh yeah.
Erin Allmann Updyke	About 25% of people who are chronic carriers never have any symptoms of disease.
Erin Welsh	Yep.
Erin Allmann Updyke	We all know this, this is the story of Typhoid Mary, Erin's gonna tell it to us in a lot more detail. But the real question that I need to answer is how on earth could Mary and others have been spreading this infection for so long without ever even knowing they were infected?
Erin Welsh	It's... I don't know, I wanna know, tell me.
Erin Allmann Updyke	All right. So a proportion of people who get infected with Salmonella Typhi won't ever show symptoms. That's fine. About 3-5% of people overall who get infected with Salmonella Typhi go on to become chronic carriers. So where is this bacteria hanging out? Whether or not you've ever shown any symptoms. And the answer is the gallbladder, Erin!

Erin Welsh	Oh! Okay.
Erin Allmann Updyke	So in some people, and again this is also still something that we don't 100% understand, but we have a much better understanding now than in Mary's time, for example.
Erin Welsh	I mean, yeah.
Erin Allmann Updyke	So we know that Salmonella Typhi can invade the gallbladder, it can cause cholecystitis which is like an acute infection, but in some people it can essentially start to form a biofilm.
Erin Welsh	Ooh.
Erin Allmann Updyke	So it doesn't just invade the cells of the gallbladder wall, but actually forms its own biofilm. And this happens especially in people with gallstones, which as it turned out, happened to be a medium on which Salmonella Typhi can persist and grow and form a biofilm.
Erin Welsh	What is a gallstone made of?
Erin Allmann Updyke	Often cholesterol, there's a few other things that it can be but most of the time it's cholesterol.
Erin Welsh	Okay. Interesting.
Erin Allmann Updyke	Yeah. So that's kind of the main thinking, that it's gallstone-related, biofilm-related, something like that. And we know that it definitely causes chronic inflammation because chronic infection with Salmonella Typhi is pretty strongly associated with gallbladder carcinoma, so cancer. And we know that cancer and inflammation often go hand in hand.
Erin Welsh	Oh. Mm-hmm.
Erin Allmann Updyke	But it's a little bit more complicated because at least-
Erin Welsh	It's gotta be.
Erin Allmann Updyke	-in some cases, cholecystectomy, which is the surgery we do to remove the gallbladder, doesn't always resolve the carrier state.
Erin Welsh	Right.
Erin Allmann Updyke	And also not everyone who has gallstones becomes a typhoid carrier. A lot of people have gallstones. Not every person with gallstones that gets infected with Salmonella Typhi is necessarily going to become a Salmonella Typhi carrier. So we still don't fully understand the process but we at least know more. (laughs)
Erin Welsh	Is it treatable, Erin?
Erin Allmann Updyke	Oh, great question. So it is treatable. And the good news is that treatment is extremely effective.
Erin Welsh	That's great news.

Erin Allmann Updyke	Yes. It's with antibiotics. Without any treatment, typhoid has a mortality rate between 10-30%, so pretty deadly disease.
Erin Welsh	Very deadly. Like wow.
Erin Allmann Updyke	Right. With treatment, mortality rate estimates are like 1%. So still not perfect, and I would say 1% is still pretty high, but that's what the kind of global estimates are. And we'll talk a lot in the epi section but the short answer is we have a very poor understanding of the global incidents of typhoid fever.
Erin Welsh	Yeah, okay, I kinda figured that.
Erin Allmann Updyke	Yeah. Very poor understanding. The good news is that in addition to treatment, there are vaccines. There are two different vaccines that are widely available. One is a polysaccharide, so it's like a sugar that's found on the outside of the bacteria, that can be used starting in children at age two. And children are important because a lot of typhoid fever happens in children, it's really a disease of childhood in a lot of places. That one has to have boosters every two years because it doesn't have a very long-lasting immunity.
	And then there's a live-attenuated vaccine, so it's a live bacteria that they've grown in a lab to be less virulent so it doesn't cause severe illness but it still gives you protection. That one, you can't give it to kids under six, so it's only for older kids and adults and it needs boosters every five years. But we'll talk in the current events about a very exciting new vaccine that's super new. That's very exciting.
Erin Welsh	That's fun.
Erin Allmann Updyke	But we can't talk about it yet.
Erin Welsh	(laughs)
Erin Allmann Updyke	So Erin, where did this bacteria come from? What's it doing to us?
Erin Welsh	I am very excited because this is gonna be a good one. But we have to take a short break first.
Erin Allmann Updyke	Definitely.
TPWKY	(transition theme)
Erin Welsh	So I talked a little bit at the very beginning of the episode about why we are so excited to do this topic, typhoid.
Erin Allmann Updyke	Yeah.
Erin Welsh	And so not only is this the full circle moment of like oh, you know, we're finally doing the thing that like totally changed our lives forever thanks to Georgia and Karen on My Favorite Murder, but also typhoid fever is like first season TPWKY.
Erin Allmann Updyke	Totally.

Erin Welsh	It's like a big deal, it's a classic disease, it's like one of the big names.
Erin Allmann Updyke	I'm expecting like Ebers Papyrus, Ancient Rome, etc etc. pooping in holes, all of it.
Erin Welsh	(laughs) I mean we've already got the pooping in holes, so.
Erin Allmann Updyke	We started off good.
Erin Welsh	Let's just see what else we've got here. But in addition to that, as I read more about the history of typhoid and particularly Mary Mallon who gave rise to the term 'Typhoid Mary', I realized just how relevant her story is to what's going on today. And the enormous conflict between public health and civil liberties that can emerge sometimes. And finally just how important science education and science literacy is to reducing that conflict.
Erin Allmann Updyke	(gasp) I'm excited.
Erin Welsh	Yeah, okay. So let's dive in.
Erin Allmann Updyke	Let's do it.
Erin Welsh	You can probably guess that typhoid fever has been around for millennia. Yup. Evolutionarily speaking, some researchers believe that it originated in Indonesia thousands and thousands of years ago, but it would have spread pretty easily and rapidly around the world as travel became more widespread. And one interesting thing to note is that there doesn't seem to be a whole lot of genetic variation among strains geographically, with the exception of antibiotic-resistant strains, which is thought to point towards the importance of carriers in perpetuating the disease.
Erin Allmann Updyke	Ah.
Erin Welsh	If that makes sense.
Erin Allmann Updyke	Yeah!
Erin Welsh	So like there's not a whole lot of selection pressure by which hosts survive or whatever, because carriers are there.
Erin Allmann Updyke	Right, there's always carriers to just sort of keep the disease slowly moving through populations and around the world.
Erin Welsh	Yeah! Isn't that really interesting?
Erin Allmann Updyke	I never thought about being able to... Yeah. Yeah, that's pretty cool.
Erin Welsh	It's cool. (laughs) And I know that you were hoping for the Ebers Papyrus and Ancient Roman stuff, and so I can't explicitly say, 'No, it wasn't written about'. But it's a very... As a GI illness, it's one of many. People had a lot of runny poops and like died from diarrhea all the time.

Erin Allmann Updyke	They weren't writing about a step-wise fever and relative bradycardia in the Ebers Papyrus? (laughs) I'm shocked.
Erin Welsh	I don't believe that they were. I don't believe so. (laughs)
Erin Allmann Updyke	Bummer.
Erin Welsh	Yeah, so. Anyway, so it wasn't explicitly described by a lot of Ancient Greek of Roman physicians, but I mean undoubtedly it was around.
Erin Allmann Updyke	Right.
Erin Welsh	For centuries its name, typhoid, was used to describe more a set of symptoms rather than a separate disease. Typhoid actually means, it just mean 'typhus-like'.
Erin Allmann Updyke	Huh. Interesting.
Erin Welsh	Yeah, and I just want to give a little bonus factoid even though we're gonna cover typhus at some point in the future because that's another season one era TPWKY. I'm just gonna tell you the etymology of typhus now because just to say, 'Oh, it's typhus-like' and then move on seems silly.
Erin Allmann Updyke	Yeah.
Erin Welsh	Basically typhus comes from the Greek 'typhos' meaning stupor caused by fever. It's also related to smoke or mist or fog, referring to the brain fog that's associated with typhus and occasionally with typhoid.
Erin Allmann Updyke	Okay.
Erin Welsh	So because of its similarity to other GI illnesses, it's hard to pinpoint specific typhoid epidemics or estimate its impact separate from other illnesses caused by poor sanitation or clean water infrastructure. But that doesn't mean people won't try to ascribe typhoid as causes of epidemics in history.
Erin Allmann Updyke	It's my favorite thing.
Erin Welsh	For instance, Alexander the Great may have died of typhoid at the age of 32.
Erin Allmann Updyke	What?
Erin Welsh	Yeah. He was only 32.
Erin Allmann Updyke	He was only 32?!
Erin Welsh	I know.
Erin Allmann Updyke	Oof.

Erin Welsh	I know. It also could have been, I will note, poisoning, malaria, brucellosis, etc. and typhoid has also been blamed for the Plague of Athens which happened in 430 BCE during the Peloponnesian War between Athens and Sparta.
Erin Allmann Updyke	Okay.
Erin Welsh	This epidemic, the Plague of Athens, killed approximately 1/3 to 2/3 of the population of Athens including the leader, Pericles, and about 1/4 of the army, basically sealing the fate of Athens. But was it actually typhoid? Probably not. And the reason that people think it was is because there was an article reporting Salmonella enterica genetic material in ancient DNA samples of likely victims, but those findings have been highly criticized.
Erin Allmann Updyke	Okay.
Erin Welsh	Smallpox, typhus, and measles are also decent contenders with of course the possibility that it was a totally different pathogen that's no longer circulating.
Erin Allmann Updyke	Right, yeah.
Erin Welsh	But what is definitely true, again, is that typhoid was an infamous killer during wartime or times of unrest. Primarily because of poor hygiene and a lack of clean water made transmission easy, as you heard in the firsthand snippets. And add onto that a lack of knowledge about germ theory and how the disease is transmitted and you have a recipe for disaster.
Erin Allmann Updyke	Mm-hmm.
Erin Welsh	In the Jamestown colony typhoid was responsible for wiping out an estimated 6500 of 7500 colonists in the early 1600s.
Erin Allmann Updyke	What?
Erin Welsh	Oh yeah, a lot. I mean, you know, they also weren't in the best health otherwise, there was-
Erin Allmann Updyke	Right, that's the thing! I mean, yeah.
Erin Welsh	It was sort of like, what did they call it in some of these descriptions? It was like a seasoning, like you had to get there and it was like you had to go through this hazing of a disease, like the seasoning of a disease, I don't know how else to say it. But you either survived or you didn't.
Erin Allmann Updyke	Right.
Erin Welsh	Yeah.
Erin Allmann Updyke	That was like all of childhood for a long time.
Erin Welsh	For so many thousands of years.
Erin Allmann Updyke	Yep.

Erin Welsh	Yeah. Population growth in the major cities during the industrial age way outpace the infrastructure or knowledge or technology to manage the waste that was being produced. And this is reflected in the annual incidents of typhoid in Europe during this period, which was about 1 in 200 people.
Erin Allmann Updyke	Wow.
Erin Welsh	It's really high.
Erin Allmann Updyke	That's really high.
Erin Welsh	Yeah. Albert, Prince Consort of Queen Victoria, died in 1861 of probably typhoid. And President William Henry Harrison, who was the 9th and shortest serving U.S. president, died from what was likely typhoid just 31 days after taking office. He was also a terrible person.
Erin Allmann Updyke	(laughs)
Erin Welsh	He was, he was. The 12th U.S. president Zachary Tyler may also have died from typhoid and three of Louis Pasteur's five children died from typhoid fever apparently.
Erin Allmann Updyke	Aw.
Erin Welsh	Yeah. So this was an enormously feared disease. And it was one that did not respect divisions of class or wealth.
Erin Allmann Updyke	Uh-uh.
Erin Welsh	Starting in the 18th century, physicians began to observe or describe that typhoid and typhus were two different diseases. Several physicians noted the difference in fever intensity or duration or cyclicity etc. or noted lesions in the Peyer's patches of the small intestine. Confusion lingered though, especially in the diagnosis of non-fatal cases of typhoid. In 1837, two Philadelphia physicians, William Gerhard and Casper Pennock, published their observations that typhoid and typhus were distinct diseases. An epidemic of typhus in 1836 allowed them to note not only how the diseases behave differently, like typhus was more likely to cause and epidemic and much less likely to appear in sporadic cases, as well as how their pathophysiology differed. But there was still a major piece of the puzzle missing. How was typhoid fever transmitted?
Erin Allmann Updyke	Yeah.
Erin Welsh	At this time, which was the first half of the 19th century, germ theory had not yet been developed, although the concept of contagion was well established.
Erin Allmann Updyke	I feel like that's what makes it so classic TPWKY. Like getting to talk about 'nobody knew germ theory and then we learned about germ theory!' You know? That's like very classic.
Erin Welsh	(laughs) It is, it is. I feel like also, I hope people aren't sick of hearing about the era of germ theory and like...
Erin Allmann Updyke	No!

Erin Welsh	It's just such a mind-blowing... Like the revolution of awareness of the world around us is so wild to me.
Erin Allmann Updyke	It is just like you talked about in the giardia episode when van Leeuwenhoek looked through his microscope and saw the whole world in the water. It is mind-blowing and phenomenal to think about the time of that shift in mindset.
Erin Welsh	Yeah!
Erin Allmann Updyke	It is absolutely fascinating.
Erin Welsh	Good, well I'm glad you're not sick of it because I'm not sick of it either.
Erin Allmann Updyke	Definitely not. (laughs) And we make the rules around here, so...
Erin Welsh	(laughs) So yeah, people knew, maybe not about microbes but they knew about contagion and that concept. And the English physician William Bud - and I highly recommend you check out his Wikipedia page just so you can see his incredible facial hair - he discovered the link between typhoid and fecal-oral water contamination after tracing one outbreak of the disease in a village in 1847 and finding that the only link between the households was that they shared a well. And the later, like years later, after learning about John Snow's work between cholera and the Broad Street pump, he became even more convinced that contaminated water was the source of typhoid outbreaks.
Erin Allmann Updyke	I was just about to ask what time was this in relation to John Snow and cholera. I love it.
Erin Welsh	(laughs) And just like with cholera, there may have been some resistance in accepting that water, not bad air, could be the cause of so much illness and death. But if there was resistance in the face of typhoid fever transmission, it was very short-lived. As I mentioned, the massive global population growth had led to an equally massive waste problem. In London in July and August of 1858, for instance - I mean you heard the firsthand of cholera, it's pretty memorable. The poop and trash in the river Thames baking in the summer sun led to such an overwhelming foul smell that it was called the 'Great Stink'. There's an entire Wikipedia page about it and I really just... This is an episode of gross stuff, so I wanted to read this excerpt from a contemporary newspaper about the Great Stink.
Erin Allmann Updyke	Yes!
Erin Welsh	Quote: "For the first time in the history of man, the sewage of nearly three million people had been brought to seed and ferment under a burning sun in one vast open cloaca lying in their midst." (laughs) I can't-
Erin Allmann Updyke	(laughs)
Erin Welsh	I have to try that again. I can't say 'open cloaca' without laughing.
Erin Allmann Updyke	Open cloaca. Oh, dear.
Erin Welsh	In one vast open cloaca lying in their midst. The result, we all know, stench so foul we may believe had never before ascended to pollute the lower air. Never before, at least, had a stink risen to the height of a historic event.

Erin Allmann Updyke	(laughs)
Erin Welsh	Do you see why I needed to read that?
Erin Allmann Updyke	Yes, 100%. I agree with it. It was the correct decision.
Erin Welsh	Yeah, so check out the Wikipedia page.
Erin Allmann Updyke	(laughs)
Erin Welsh	Yup. What a time. Events like the Great Stink and the cholera epidemics finally forced public officials to recognize contaminated water was a public health issue. And this was only deepened with the development of germ theory. Sidenote, the Chicago River was reversed to try to control the outbreaks of typhoid and cholera.
Erin Allmann Updyke	Whoa!
Erin Welsh	Isn't that cool? Okay. So hopefully by now I have painted somewhat of a picture of the prominence or infamy of typhoid through the 1800s so that you can understand why isolating the causative agent became a top priority for so many bacteriologists.
Erin Allmann Updyke	Yeah, definitely.
Erin Welsh	And because of its prevalence and popularity in research, it's a bit tough to establish priority on who first discovered the bacterium. One likely suspect was the Polish scientist - oh boy - Tadeusz Browicz who described rod-shaped bacteria in the organs of people infected with typhoid, and he even isolated and cultured the bacteria but he never followed through by trying to determine whether those cells were responsible for the disease itself.
Erin Allmann Updyke	Got it. He never did all of the postulates.
Erin Welsh	Right. Credit is usually given to German pathologist Karl Eberth for first isolation, and this is reflected in the fact that the first name given to the bacterium was Eberthella.
Erin Allmann Updyke	Hmm. Okay.
Erin Welsh	The rest of the late 1800s and early 1900s was a busy and productive time for typhoid researchers. The development of the Widal test allowed physicians to test for the typhoid bacterium. Basically you take serum from a suspected patient and see how it reacts when exposed to a culture of the bacteria. If a precipitant forms, you've got typhoid. And then the vaccine was next. Just like with the discovery and the description of the typhoid bacterium itself, there seems to be some debate over who first created the typhoid vaccine. Many different people at least had a hand in it. Credit usually goes to Sir Almroth Wright, who was an English pathologist, and he began testing an early typhoid vaccine on army officers in the Indian medical service. Not for effectiveness against typhoid though, but rather to see whether calcium chloride prevented hemorrhaging in those injected.
Erin Allmann Updyke	What?
Erin Welsh	As like an additive or stabilizer.

Erin Allmann Updyke	So he made a whole new vaccine and was like, 'I'm not testing this vaccine, I just want to test the adjument'?
Erin Welsh	I don't get it. (laughs) But he usually gets credited for the first typhoid vaccine even if many others paved the way for him. And he followed up his first tiny test with more extensive testing, this time to actually observe the efficacy of the vaccine in protecting against disease.
Erin Allmann Updyke	Oh, what a concept. (laughs)
Erin Welsh	What a concept. But instead of exposing the participants to typhoid, which was as we know a method still occasionally practiced, like actual challenge or whatever, he tested the serum of those vaccinated to see whether typhoid bacteria would agglutinate. So kinda smart. Yeah, pretty smart. And sure enough, the serum of those vaccinated did seem to agglutinate bacteria but did that translate into actual protection in the body?
Erin Allmann Updyke	Right.
Erin Welsh	The bacteria in the precipitates were still viable after all. So they did the unethical thing and exposed one of the participants to typhoid. And fortunately he did not get it.
Erin Allmann Updyke	Whew.
Erin Welsh	The development of a typhoid vaccine completely changed war.
Erin Allmann Updyke	Ooh!
Erin Welsh	Yeah. I've talked before on the podcast about just how much death and illness during war comes from infection rather than combat, but I didn't realize just how much typhoid was often responsible for the most damage.
Erin Allmann Updyke	Yeah, I don't think I would've put that together necessarily.
Erin Welsh	Yeah. I mean and it makes sense given the conditions of living and so on and how you prepare food in a clean way, how do you poop in a clean way, how do you clean yourself in a clean way.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. During the American Civil War for instance, 80,000 of the 2 million soldiers in the Union Army, there were no good records for the Confederate Army, got typhoid. About 5%.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah. And in the Spanish-American War, which is where the firsthand accounts came from, approximately 21,000 troops were infected with typhoid and nearly 1600 died.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah.

Erin Allmann Updyke	That's a lot.
Erin Welsh	Most of the time, typhoid killed more soldiers than direct combat.
Erin Allmann Updyke	Yeah I feel like that's a theme that we often come back to. (laughs)
Erin Welsh	It is.
Erin Allmann Updyke	It's not funny, it's awful.
Erin Welsh	WWI would be the first major conflict in which typhoid did not contribute enormously to the death toll.
Erin Allmann Updyke	Because of the vaccine. Okay.
Erin Welsh	Because of the vaccine, because of the vaccine.
Erin Allmann Updyke	(laughs)
Erin Welsh	In previous wars, the attack rate of typhoid was estimated to be 1 in 5 but that dropped to 1 in 2000 by WWI due to the vaccine and improvements in sanitation practices.
Erin Allmann Updyke	Stop it! What?! That's bonkers!
Erin Welsh	I know. It's pretty clear-
Erin Allmann Updyke	That's a phenomenal... Wow!
Erin Welsh	Huge. Huge.
Erin Allmann Updyke	Wowee.
Erin Welsh	All right. Here we are in the early 1900s. We're finally here.
Erin Allmann Updyke	We're finally here!
Erin Welsh	I just want to set the stage a bit for this next part of the story of typhoid.
Erin Allmann Updyke	Yes.
Erin Welsh	So typhoid has been a commonplace but still very much feared disease for the past centuries, and while there have been some major developments in understanding its transmission and pathophysiology, both sanitation infrastructure and medical treatments lag behind so the threat remains. A doctor can diagnose a case but they can't treat it because antibiotics haven't been discovered yet. A typhoid vaccine did exist but they were new and not trusted and generally reserved for the military.
Erin Allmann Updyke	Right, yeah.

Erin Welsh	And cities began to grow at incredible rates. All that poop with nowhere to go.
Erin Allmann Updyke	Uh oh.
Erin Welsh	Enter Mary Mallon.
Erin Allmann Updyke	(gasp)
Erin Welsh	Mary Mallon immigrated to the U.S. from Ireland in 1883 at the age of 15 and began working as a cook. And she seemed to be really good at it. She seemed to be in steady employment in the New York City area with short-term contracts working for wealthy families from season to season. And that was like a normal thing for a lot of cooks. Just like contract work.
Erin Allmann Updyke	Yeah. Right.
Erin Welsh	Mary's life continued in this rhythm for 20 and some years until the events that would turn her from Mary Mallon to the infamous Typhoid Mary.
Erin Allmann Updyke	So she was like in her late 30s, like mid to late 30s. Okay.
Erin Welsh	Yes. In 1906, an outbreak of typhoid occurred among the household of the wealthy New York City banker Charles Henry Warren who was renting a summer home in Oyster Bay in New York.
Erin Allmann Updyke	Okay.
Erin Welsh	Two of his daughters, his wife, two maids, and the gardener all became sick. Isolated outbreaks like this did happen from time to time but this was still a huge cause for concern. Not just because the disease could be fatal but because an outbreak of typhoid could tarnish a home's reputation for years because it suggested that the water lines weren't clean.
Erin Allmann Updyke	Ugh. I'm scoffing my face at that.
Erin Welsh	I know, that was a very good scoff face. I wish that I had taken like a screenshot of it or something. (laughs)
Erin Allmann Updyke	(laughs)
Erin Welsh	So the owners of the house were desperate to trace where the outbreak originated.
Erin Allmann Updyke	I mean... Okay.
Erin Welsh	I mean it makes sense like you wanna know, 'Okay if we can put a stop to this, let's put a stop to this'.
Erin Allmann Updyke	Yes, of course. And it is very deadly. But the reputation thing?
Erin Welsh	Well I mean, they were like 'We need to make sure to rent our H-E-I-R BnB'. HeirBnb, get it?
Erin Allmann Updyke	HeirBnb. (laughs)

Erin Welsh	Pretty sure I stole that joke from The Good Place.
Erin Allmann Updyke	It's a good one though.
Erin Welsh	Yeah. Okay. Anyway, so these owners hired George Soper, a sanitary engineer.
Erin Allmann Updyke	Okay, cool.
Erin Welsh	His job was basically a mix of health inspection and shoe-leather epidemiology.
Erin Allmann Updyke	Awesome.
Erin Welsh	Yeah. And he went around the entire property on Oyster Bay looking to see whether the toilet waste ran into the water sources or if the local oysters from Oyster Bay were contaminated.
Erin Allmann Updyke	All right.
Erin Welsh	And he found nothing.
Erin Allmann Updyke	Okay.
Erin Welsh	But the typhoid had to come from somewhere and the source had to be unique to that household since no other cases were detected in the nearby town. Soper learned that the family had hired a new cook just before the outbreak started. That cook's name...
Erin Allmann Updyke	Was Mary.
Erin Welsh	Mary Mallon. At first it may have been hard to see how a cook could be the source of a typhoid outbreak since the bacteria would be killed during the heating process, but then it was revealed that one of Mary's most popular dishes was ice cream and fresh peaches. Boom.
Erin Allmann Updyke	How sad. Like what a great... That's such a good dessert.
Erin Welsh	I mean, we probably should have made a quarantini that was like peach and ice cream.
Erin Allmann Updyke	We totally should have!
Erin Welsh	But Bloody Typhoid Mary? When else were we gonna do that? Come on.
Erin Allmann Updyke	But also the other thing is where can you get peaches in November? In this hemisphere you cannot, so we couldn't have taken a photo.
Erin Welsh	Ugh. It would be sad peaches, for sure.
Erin Allmann Updyke	Very sad, so...
Erin Welsh	Yeah, yeah, yeah. Well, but as you can imagine, ice cream and peaches, there's not a whole lot of heat inactivation that would happen.

Erin Allmann Updyke	No, no.
Erin Welsh	And during the time that Soper was investigating the source of this outbreak, the existence of typhoid carriers had been hypothesized and observed but it was not like a super widely known concept.
Erin Allmann Updyke	Interesting.
Erin Welsh	Yeah. Nevertheless, Soper became convinced that Mary was the one to blame. But there was one major problem because Mary had already moved on. She had gotten a new job and had left no forwarding address. So Soper set to investigating her past employment to see whether she was linked to any other typhoid outbreaks. He became a bit obsessed because he essentially thought, 'Okay, if I can show that she is the cause of all of these cases then that's my career made. Boom, done.' Like it was his ticket to fame. So anyway...
Erin Allmann Updyke	Okay.
Erin Welsh	But what he found was in 7 of the 8 families that Mary had worked for over the years, there had been a typhoid outbreak during or right after her employment.
Erin Allmann Updyke	Hm. Wow.
Erin Welsh	Yeah. 7 of the 8. And Soper finally caught up to her in 1907 amidst another typhoid outbreak in the family that she was cooking for. And this one resulted in the first death definitively linked to Mary. It was the daughter of that family.
Erin Allmann Updyke	Aw.
Erin Welsh	Unfortunately, Mary did not write or talk extensively about what happened from her perspective so we have to rely on the words of contemporary sources, including George Soper. He wrote his account of events in which he - in most subsequent retellings including this one - he framed it like a detective story with Mary as the villain at the center of it.
Erin Allmann Updyke	Right.
Erin Welsh	In 1907 when Soper tracked down Mary's current place of employment and learned of the typhoid outbreak currently occurring, he essentially stormed right in, pointed a finger at her, and loudly accused her of making everyone around her sick with her unclean habits and carelessness.
Erin Allmann Updyke	Like that's how he... He just walked in out of nowhere off the street and was like, 'You're filthy and killing people with your poop hands'?
Erin Welsh	Yeah. Yeah. You're the cause, you're the reason people are dying.
Erin Allmann Updyke	Geez.
Erin Welsh	And then he was like, 'And you know what? I need a poop sample from you right now'.
Erin Allmann Updyke	(laughs) Good luck buddy.

Erin Welsh	And so Mary was like, 'Um, excuse me?' He also, after demanding this fecal sample, it's not like he was like, 'Oh this is how it might work, this is what a typhoid carrier is'.
Erin Allmann Updyke	Right!
Erin Welsh	Listen, we know that you didn't mean any harm, we're just trying to get to the root of this'.
Erin Allmann Updyke	There was no humanity is what I feel like you're saying in his response. Like there was no humanity whatsoever.
Erin Welsh	Absolutely not. And Mary was like, 'Um, excuse me? Excuse me.' And so she grabbed a carving fork, according to Soper, and charged him. So he ran away.
Erin Allmann Updyke	(laughs) He ran away.
Erin Welsh	He ran away, yeah.
Erin Allmann Updyke	Oh my gracious.
Erin Welsh	But Soper didn't give up. Instead he found out where she lived, and she was living as an unmarried woman with a disreputable boyfriend and a big dog, which Soper felt important to note, a big stinky dog. Which probably a really cute dog, but whatever.
Erin Allmann Updyke	Ugh! Yeah, I bet it was like shaggy and drooly and nice.
Erin Welsh	And so he went to where she lived and tried to get a fecal sample from her and then tried to befriend the boyfriend to try to be like, 'Let's trick Mary into giving a fecal sample'.
Erin Allmann Updyke	What?! What is this dude's damage, man?
Erin Welsh	I don't know, I don't know. And every time Mary just shut down, crossed her arms, and was like, 'Leave.'
Erin Allmann Updyke	Yeah.
Erin Welsh	She just sent him packing every single time. It makes sense right? And eventually though he got the New York City Health Department involved, including a Dr. Sara Josephine Baker who was a huge figure in infant and maternal health. And so she was sent to try to reason with Mary more calmly. Instead Mary ran away and hid for hours. But eventually her hiding place was found out and she was dragged literally kicking and screaming to the hospital where she would be forced to provide samples.
Erin Allmann Updyke	Geez.
Erin Welsh	Sure enough, she was teeming with the typhoid bacteria.
Erin Allmann Updyke	Do you have a number on that, Erin?
Erin Welsh	I'm sorry Erin, let me just google that real quick.

Erin Allmann Updyke	(laughs)
Erin Welsh	We don't 100% know but... (laughs) So she was the first carrier described.
Erin Allmann Updyke	Like known definitive carrier.
Erin Welsh	Yeah. So because she was considered a flight risk, she was held in the hospital and then moved to North Brother Island where there was a hospital that started out as a smallpox isolation building but then turned into a 'nay disease we choose' isolation building, so like tuberculosis, leprosy, etc. and Soper tried to convince Mary to have her gallbladder removed even though A) a surgery in the early 1900s was super dangerous.
Erin Allmann Updyke	Yeah. Almost certainly death.
Erin Welsh	Like no antibiotics. And B) its removal, like you said, was no guarantee that she would then be typhoid-free. But she was like, 'No, I don't want that.' And so then he was like, 'Alright, well the I'm gonna write a book about you and I'll split the profits with you if you promise to stop cooking.' And she was like, 'No'. She basically just refused to talk to him. And she remained in isolation and he fecal samples were regularly checked for the presence of the bacteria, which were found more often than not, although there were some negative days.
	In 1909, so that's 2 years and 3 months after she was first isolated, she filed a lawsuit for her release saying that her imprisonment was unlawful and stripped her of her civil liberties. And it was at this time that the term Typhoid Mary, coined in 1908 at the annual meeting of the American Medical Association, when they presented her carrier status, this term reached the general public.
	Overall the tone of the articles were very sympathetic to Mary. Her imprisonment to the general public was seen as a violation of civil rights and prejudice against a poor immigrant woman. But this case took place at a time when courts tended to rule in favor of social protections rather than individual rights.
Erin Allmann Updyke	Interesting.
Erin Welsh	For instance, just a few years before in the 1905 decision Jacobson vs. Massachusetts, the Supreme Court unanimously ruled that required smallpox vaccination did not violate individual rights. Quote:
	"The liberty secured by the Constitution does not import and absolute right in each person to be at all times and in all circumstances wholly free from restraint."
	Basically the ruling was that if by exerting your own individual rights you are impinging on the rights or health of others, then no, you cannot do that. Those are not rights. That's how it's always been.
Erin Allmann Updyke	Yeah.

Erin Welsh	And so Mary lost the suit and continued to be held in the custody of the Board of Health of the city of New York. But not for very long. The following year, in 1910, she was released on the condition that she promise not to work as a cook anymore and to report back to be tested. She agreed to the terms and then promptly disappeared. And never went back for checkups. She was rediscovered in 1915. Soper had resumed his work as a sanitary engineer and was in the process of investigating an outbreak of typhoid at Sloane Maternity Hospital-
Erin Allmann Updyke	Oh no.
Erin Welsh	-when he learned that some of the staff referred to a Typhoid Mary cook who seemed linked to the outbreak. He was like, 'This is... Are you serious? Who am I gonna find? Am I actually gonna find Typhoid Mary? Am I gonna find Mary Mallon?' And it was, but Mary Mallon had been going by a different name.
	Turned out Mary had not upheld her end of the deal and continued to seek out employment as a cook, which was likely the only profession that she had any skill or experience in. Since her 1909 case had put her name out there and gained her some notoriety, she couldn't use her real name to get employment.
Erin Allmann Updyke	Right.
Erin Welsh	And when Mary was apprehended the second time, she didn't receive the same level of public sympathy. The New York City Health Department placed her in forceful isolation again on North Brother Island in the East River where she would live out the rest of her days. Over 20 years, never admitting her or acknowledging her role as carrier. She did have a few friends on the island and apparently a little fox terrier, and she worked a bit in the bacteriology lab, but she never felt she belonged on North Brother Island and felt that her freedom had been taken away unfairly.
	She died at the age of 69 on November 11th, 1938 of pneumonia following a stroke. In total, Mary was linked to 53 cases and 3 deaths, although it's possible that the actual numbers were higher. The impact that Mary Mallon had on the world goes way beyond the people she infected.
Erin Allmann Updyke	Yep.
Erin Welsh	And I had a hard time putting all of my thoughts and feelings about Mary Mallon and Typhoid Mary into one coherent thesis, so I decided to make a list of the different themes or lessons or whatever of the story.
	The first theme was probably also the earliest and the simplest. Just medical mystery, epidemiological detective work, a whodunit. Right? Boom, done.
Erin Allmann Updyke	Yeah.
Erin Welsh	That's one story that people use. Two, the concept of a superspreader. The term Typhoid Mary was in popular use even before this pandemic, and so even before we used it as someone who unknowingly or knowingly infected a bunch of people with something.
Erin Allmann Updyke	Without seeming like they were sick or anything like that.

Erin Welsh	Exactly. Number three, discrimination and oppression. Mary belonged to a few groups that had been historically very much discriminated against here in the U.S. Mary was poor, she was an immigrant, and she was an unmarried woman who did not fit the contemporary standards of femininity. In Soper's words, quote:
	"Those who knew her best in the long years of her custody said Mary walked more like a man than a woman and that her mind had a distinctly masculine character."
	Like, okay George.
Erin Allmann Updyke	Okay buddy.
Erin Welsh	And Mary Mallon wasn't the only typhoid carrier in New York City.
Erin Allmann Updyke	Definitely not.
Erin Welsh	In the years after she was imprisoned, at least 50 additional carriers had been identified and one estimate from 1919 put New York City as having over 25,000 typhoid carriers.
Erin Allmann Updyke	What?
Erin Welsh	Some who had been identified became repeat offenders like Mary, but none of them faced a similar lifetime imprisonment.
Erin Allmann Updyke	What?!
Erin Welsh	Most of them were given alternative jobs or means for providing for their family. But Mary wasn't considered a breadwinner because she had no family.
Erin Allmann Updyke	Because she was just a single woman.
Erin Welsh	In their eyes. Maybe she was put on the island to serve as an example. But although Mary's punishment may have been so extreme because of who she was or what she represented, the unavoidable fact that I keep coming back to is that her actions, particularly her deliberate choice to keep working as a cook, directly caused the illnesses and deaths in others.
	Which brings me to theme number four and the one I think has the most relevance for today. That of the tension between individual rights and public health. Was Mary's imprisonment too harsh or biased? I mean, yes, I think we can all agree that yeah, it was. But should measures have been put into place that would have prevented her from making others sick? Yes. Of course.
Erin Allmann Updyke	Yes, without a doubt. Yes.
Erin Welsh	In any society, there is no such thing as absolute freedom. There is a limit. If by exerting your own individual rights you are impinging on the right or health of others, then that freedom is not something owed to you. This is part of the social contract, the agreement that we all make. That by living in and benefiting from a society, we have to give up some of our individual freedoms. This can be a tough balance to strike, particularly in the realm of public health. There's a quote from one of the books I read about Typhoid Mary.

Erin Allmann Updyke	But first Erin, I just want to say that you said that really beautifully. Like I absolutely loved it.
Erin Welsh	(laughs) I feel very strongly about this.
Erin Allmann Updyke	I mean I feel 100% exactly the same way, but the way that you worded that was perfect. Excellent.
Erin Welsh	Oh thank you. That makes me feel nice. (laughs) Okay, here's the quote:
	"On the one hand is the commitment to protect the public's health; on the other is the fear of arbitrary power and the loss of individual freedoms."
	That's from Judith Leavitt. Mandatory vaccinations, forced quarantines, public identification of so-called patient zeroes, and in the context of COVID-19, mask mandates. These are all areas in which there has been ample discussion of individual freedoms being trampled upon. Some of which may be justified, others definitely not. Like masks. Let's not mistake inconvenience for oppression.
Erin Allmann Updyke	Oh, snap.
Erin Welsh	Being imprisoned on an island for decades because you are an asymptomatic carrier of typhoid, yeah okay, maybe there's a touch of oppression there. Having to wear a mask to pop into the grocery store for 15 minutes? That's not oppression, period.
Erin Allmann Updyke	Not oppression. End of story, not oppression.
Erin Welsh	It's not oppression. So what can we learn from Mary Mallon's experience?
Erin Allmann Updyke	Ooh, good question.
Erin Welsh	As I was reading about the story of Mary Mallon, one thing that stuck out to me was how much pain and suffering both for Mary and for the people that she infected could have been prevented through simple communication.
Erin Allmann Updyke	Yeah.
Erin Welsh	Her doctors, the New York City Health Department, they could have taken the time to talk with her, not down to her, about the science behind typhoid fever transmission and could've explained in a non-judgmental way how she could transmit unintentionally the bacterium to those around her. And then maybe they could've given her more opportunities or training to find employment in another area. Maybe then she wouldn't have felt like she needed to lie to continue to cook.
Erin Allmann Updyke	Yeah.
Erin Welsh	We as a society have the knowledge and the platforms to communicate accurate scientific information. And when that information has the power to save peoples lives and prevent misery and suffering, leaders have a responsibility to communicate that information without their own political agenda.
Erin Allmann Updyke	And accurately.

Erin Welsh	Yep. The disinformation and mistrust in science spread by Donald Trump and other members of the Republican Party during this pandemic, and other world leaders, I should note-
Erin Allmann Updyke	Yep. A lot. Boris Johnson. 'It's fine, you know, I'm fine'.
Erin Welsh	This has already done incalculable damage. How many deaths, how much misery, how much suffering could have been prevented by communicating science rather than sowing hatred and fear? History is full of lessons like this. And you know there's that saying that's like, 'Those who cannot learn from history are doomed to repeat it'. I mean yes, that's true, but I think what might be an addendum should be, 'And those that do learn history are just doomed to watch others repeat it'.
Erin Allmann Updyke	(laughs)
Erin Welsh	We can always do better but it feels like we rarely actually do.
Erin Allmann Updyke	Well it also might be that people are taking the wrong lessons from history or learning the wrong parts of history.
Erin Welsh	That's definitely true.
Erin Allmann Updyke	Like, 'We did a great job! We isolated Mary on an island and kept her there forever!' You know what I mean? I don't know.
Erin Welsh	No, it's a much more nuanced story than that, like let's learn the nuance.
Erin Allmann Updyke	Exactly.
Erin Welsh	I feel like that's important.
Erin Allmann Updyke	Yeah, definitely.
Erin Welsh	Like yes it was unfair but yes she also killed people, so what can we do differently? That's what we should be asking ourselves. And we have the opportunity now, so like...yeah. But yeah, I've gone on way too long already so I'll just wrap up the history by saying that with improved sanitation and clean water infrastructure combined with the development of chloramphenicol in 1948, typhoid really dropped in the second half of the 20th century in most developed countries. However-
Erin Allmann Updyke	However.
Erin Welsh	It has continued to cause enormous outbreaks, with some of these outbreaks leading to over 100,000 deaths in many other parts of the world. And the emergence of drug-resistant strains might pose an additional threat. But Erin, I'm gonna let you take it from here.
Erin Allmann Updyke	Oh, great! Love to pick it up on such a happy note.
Erin Welsh	(laughs) Oh boy, I'm sorry.

Erin Allmann Updyke	Let's take a quick break before we jump in.
TPWKY	(transition theme)
Erin Allmann Updyke	So I already said this but I'll just repeat it, we do not have good data on the incidents of typhoid fever globally. There's really big ranges. One of the biggest papers that estimated typhoid disease burden was all the way back in 2004 and that estimated over 21 million cases annually, and that one also estimated overall fatality rate of about 1% which would mean over 200,000 deaths annually globally.
Erin Welsh	Oh. My.
Erin Allmann Updyke	So that was a 2004 estimate. And another paper from 2012 estimated 13.5 million cases annually. So if you look at the World Health Organization, they say somewhere between 11-21 million people becoming sick with typhoid fever every year worldwide. And they estimate between 128,000-161,000 dying every year.
Erin Welsh	Wow.
Erin Allmann Updyke	Worldwide.
Erin Welsh	Yeah.
Erin Allmann Updyke	If that's not depressing enough-
Erin Welsh	Okay, here we go.
Erin Allmann Updyke	Like I mentioned earlier, typhoid is largely a disease of children in places where it's endemic. So Pakistan is one place that I'm gonna talk a lot about because there's some very good things happening in Pakistan right now. But 63% of cases and 83% of deaths related to typhoid were among children under the age of 15, for example.
Erin Welsh	Oh my god.
Erin Allmann Updyke	Yeah. So it's really, really awful. In the U.S., just for sort of local coverage, the U.S. estimates over 5700 cases of typhoid in the U.S. every year although we only actually diagnose about 350 cases which I think is really interesting.
Erin Welsh	Huh.
Erin Allmann Updyke	So that's like part of how we have such a huge discrepancy where we only diagnose this many and then we have to estimate that that's like less than 10% of the total number of cases we think there actually are. Now like you mentioned Erin, antibiotic resistance is a massive problem for Salmonella Typhi, as it is for most bacteria that we talk about.
Erin Welsh	Oh boy.
Erin Allmann Updyke	But another time I'll talk about Pakistan, another depressing one before we get to the good news. Since 2016, Pakistan has been in the midst of an extensively drug-resistant typhoid epidemic.

Erin Welsh	Right.
Erin Allmann Updyke	Since 2016, between 2016-2019, over 10,000 people have been infected with a strain that is resistant to all but one oral antibiotic.
Erin Welsh	Oh my gosh.
Erin Allmann Updyke	And it's not just there. I mean, typhoid is a global disease. It's in, I think, basically every country. Right? Like it's across the whole globe and antibiotic resistance has been documented across the globe. So let's end with some slightly good news, shall we?
Erin Welsh	(laughs) That sounds great.
Erin Allmann Updyke	In 2017 the World Health Organization pre-qualified a new vaccine, and this is an exciting one. If you remember from our vaccines episode - which if you want to go back and listen, you can do that but I'm gonna explain it anyways so you don't have to - there's a bunch of different types of vaccines. And I mentioned that the vaccines that we already have for typhoid are a polysaccharide, which is just a sugar, or we have a live-attenuated vaccine but you can't give that to small children.
	So a better type of vaccine would be a conjugate vaccine, which is when you take a polysaccharide, which is a sugar, and you link it to a peptide or a protein, because the proteins are what actually allow for our body to make a stronger and more long-lasting immune response. So in 2017 the World Health Organization prequalified a conjugate vaccine.
Erin Welsh	(gasp) That's very exciting.
Erin Allmann Updyke	It's very exciting. Yes it is. And so it's a very promising vaccine. That was just a prequalification. Recent data from a phase 3 clinical trial that's going on in Nepal shows that it's very effective at inducing an immune response and it reduced Salmonella Typhi infection across the study period. And this study was done in children aged 9 months to 16 years. So that means this is a vaccine that will be able to be given to children. It's already being given to children. And it's effective.
Erin Welsh	That's amazing.
Erin Allmann Updyke	Yes. Now even though this is a vaccine that's still undergoing investigation, so we're still in the last phase of trials. Typhoid is such a huge problem and especially these antibiotic-resistant strains, there's been enough studies of the safety of this vaccine that starting in 2019 this vaccine has been introduced into routine immunization in some countries.
Erin Welsh	Oh wow, that's great!
Erin Allmann Updyke	Including Pakistan! This is what's ongoing right now, is that kids now are getting this vaccine. So hopefully yeah, in the next year, two years, three years, we should really see a drop in typhoid.
Erin Welsh	That's awesome.
Erin Allmann Updyke	Isn't it? It's really like... That's incredible. To finally have a vaccine that's long-lasting, that's effective, and can be given to children so that we can really protect the most vulnerable groups, that's incredible. Especially as it becomes more widely available. That's my good news, Erin!

Erin Welsh	Oh good! I loved it. (laughs)
Erin Allmann Updyke	So that's, I think, the story of typhoid.
Erin Welsh	It's a long story.
Erin Allmann Updyke	Pretty long. Not our longest.
Erin Welsh	Not our longest.
Erin Allmann Updyke	A good start to the season though, I think.
Erin Welsh	It feels good.
Erin Allmann Updyke	It feels right.
Erin Welsh	Yeah. I'm looking forward to all of the diseases that we're gonna be covering this season, we have a few fun ones lined up already including - spoilers - a crossover, so...
Erin Allmann Updyke	Oh yes, the crossover is gonna be good. I am very excited about it. So normally, last season when we did our COVID episodes, those were entirely separate, we talked a little bit about it today because you can't not, right?
Erin Welsh	Yeah. Not when you're talking about Typhoid Mary, you know.
Erin Allmann Updyke	Right. But from this point forward we will, as last season, have our COVID episodes be separate from our regular episodes so there won't be a ton of COVID talk in our normal episodes if you're like... Don't want to listen to it or whatever.
Erin Welsh	Right. Yeah.
Erin Allmann Updyke	So, but yeah. This was a very important episode, I think, to do in this climate. (laughs)
Erin Welsh	(laughs) Oh boy. Well.
Erin Allmann Updyke	Yeah.
Erin Welsh	Sources?
Erin Allmann Updyke	Sources!
Erin Welsh	Okay, I've got a few books I can shout-out so one by Adler and Mara called 'Typhoid Fever: A History'; Judith Leavitt who wrote 'Typhoid Fever: Captive to the Public's Health'; and also did you know that Anthony Bourdain wrote a book about Typhoid Mary?
Erin Allmann Updyke	Stop.
Erin Welsh	Yeah.

Erin Allmann Updyke	Anthony Bourdain like Anthony Bourdain?!
Erin Welsh	Yeah!
Erin Allmann Updyke	What?
Erin Welsh	Yeah, so I read that one too.
Erin Allmann Updyke	Oh, cause she was a cook. Oh okay.
Erin Welsh	Yeah, she was a cook. It was an interesting one. And then I will shout-out a few papers that were super helpful. So there was a couple papers by VJ Cirillo that were actually really interesting. And then also by Priscilla Wald, 'Typhoid Mary and the science of social control'. I have actually a lot of different papers for this one so just check it out on our website, I don't want to spend the next five minutes reading them. (laughs)
Erin Allmann Updyke	I had a few different papers on the kind of mechanisms of typhoid and the clinical disease. If you wanna know more about the carrier state, that paper is by Gonzalez-Escobedo et al. in Nature Reviews Microbiology; and then the papers and information about the new vaccine, all of that will be on our website thispodcastwillkillyou.com under the episodes tab where you can find the sources for this episode and every episode we've ever done. 61! This is number 61!
Erin Welsh	61. Of our normal season episodes, we've done more with COVID, but yeah. Well thank you to Bloodmobile for providing the music for this episode and all of our episodes.
Erin Allmann Updyke	Big time shout-out to Georgia Hardstark for introducing us with typhoid so many years ago.
Erin Welsh	Yes. Thank you to also everyone at the Exactly Right network who make this podcast possible.
Erin Allmann Updyke	Yep. Definitely. Big time. Thank you, thank you.
Erin Welsh	And thank you to you, listeners, for listening. It's honestly like we're honored. We can't believe people want to listen but we love it.
Erin Allmann Updyke	This is a literal dream. A literal dream that we didn't even know we had and now we can't stop dreaming it and it's the greatest.
Erin Welsh	Yeah. That's basically what it feels like. (laughs) Well, until next time, wash your hands.
Erin Allmann Updyke	You filthy animals! And literally just wear a mask.
Erin Welsh	Please wear a mask.