

TPWKY

This is Exactly Right.

Erin Welsh

"As we passed along the reeking banks of the sewer, the sun shone upon a narrow slip of the water. In the bright light it appeared the color of strong green tea and positively looked as solid as black marble in the shadow. Indeed, it was more like watery mud than muddy water. And yet we were assured that this was the only water the wretched inhabitants had to drink. As we gazed in horror at it, we saw drains and sewers emptying their filthy contents into it. We saw a whole tier of doorless privies in the open road, common to men and women, built over it. We saw a little child from one of the galleries opposite lower a tin can with a rope to fill a large bucket that stood beside her. As the little thing dangled her tin cup as gently as possible into the stream, a bucket of night soil was poured down from the next gallery."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

Ew.

Erin Welsh

Ugh.

Erin Allmann Updyke

I wanna say two things.

Erin Welsh

Yes.

Erin Allmann Updyke

One, I support the use of the words 'privy' and 'night soil' both. (laughs)

Erin Welsh

(laughs) Night soil, by the way, is human feces used as compost.

Erin Allmann Updyke

Poop? (singing) Poopy, poopy, poop.

Erin Welsh

Poop.

Erin Allmann Updyke

Also that's disgusting. That's my second point.

Erin Welsh

So I'm gonna give you a little bit of context to that.

Erin Allmann Updyke

Tell me, please.

Erin Welsh

That came from an article describing the ground zero of 1849's cholera outbreak in London.

Erin Allmann Updyke

That was London?

Erin Welsh

That was London.

Erin Allmann Updyke

That's a city. And it was that... Just poop everywhere.

Erin Welsh

Yeah. Well, there are a lot of cities that continue to be very poor sanitation just due to lack of funds for public health infrastructure.

Erin Allmann Updyke

Oh my god.

Erin Welsh	Welcome to This Podcast Will Kill You.
Erin Allmann Updyke	Episode 4. Today we're talking about-
Erin Welsh	Cholera! I'm Erin.
Erin Allmann Updyke	And I'm also Erin.
Erin Welsh	And before we get into the meat of this week's episode, we want to ask you, dear listeners-
Erin Allmann Updyke	Dearest darling listeners. (laughs)
Erin Welsh	To rate, review, and subscribe.
Erin Allmann Updyke	Because we love you and we wanna know how much you love us. Just kidding. But not really. Rating, reviewing, and subscribing is how other people are able to find our podcast. So wherever you listen to your podcast, please, please, please take a moment to just, you know, click five stars or whatever.
Erin Welsh	Or, you know, anything you want. Whatever's in your heart. And also we are on all the social medias. We're on Twitter, Instagram, Facebook. So if you want to keep up-to-date on little trivia about whatever infectious diseases, you know where to find us.
Erin Allmann Updyke	See some grody photos. And also get our drink recipes.
Erin Welsh	Oh yeah, that's important. Yeah.
TPWKY	(transition theme)
Erin Welsh	Okay Erin.
Erin Allmann Updyke	Yeah.
Erin Welsh	I wanna hear about cholera now. Tell me all about it.
Erin Allmann Updyke	Let's talk about it. As it turns out, which I did not know before doing this research, cholera is really complicated. It's a complicated lil bugger.
Erin Welsh	Uh oh.
Erin Allmann Updyke	Yeah. So I'm gonna hit on the real basics of the biology of this disease and I wanna encourage y'all to read more or heck, if you research cholera and I get it wrong, give us a shout out. Let me know that we're so incorrect about things.
Erin Welsh	We are open to being corrected. Very open.
Erin Allmann Updyke	Okay, so cholera. Cholera is a disease that's caused by a bacteria called vibrio cholerae which is a facultative pathogen. So that means that in addition to causing disease in humans, it also can persist in the environment and reproduce in the environment. Usually in water, especially brackish water, so like at river mouths, near the ocean and things like that is where it persists.

Erin Welsh: Can you give me an example of an obligate pathogen?

Erin Allmann Updyke: Smallpox.

Erin Welsh: Okay so smallpox, it can exist in the environment but it can only persist if there is a human host for it infect.

Erin Allmann Updyke: Exactly. It can't reproduce without infecting a host, whereas cholera can actually reproduce in the environment. But there are also bacteria, maybe leprosy bacteria, which also can't reproduce without being in a host. It's also an obligate pathogen.

Erin Welsh: Rocky Mountain spotted fever?

Erin Allmann Updyke: Yeah definitely!

Erin Welsh: Rickettsia rickettsii.

Erin Allmann Updyke: Yeah, cool. So generally cholera is transmitted fecally orally, which means you have to ingest fecally contaminated water or food, especially shellfish which live in water. Right?

Erin Welsh: Really?

Erin Allmann Updyke: Yeah. Icky. Cause a lot of shellfish are filter feeders so they just filter all of the poop out of the water and then you eat it. Yum, you wanna get some clams after this?

Erin Welsh: So that's how you actually get infected. The infectious dose of cholera is actually really high which means that you have to ingest a whole bunch of the cholera bacteria to actually get infected. And there are a bunch of different strains of the Vibrio cholera bacteria but only two of them actually cause the vast majority of the disease. And part of the reason that the infectious dose is so high for cholera is first because it has to survive the super acidic environment of your stomach because you ingest it. Right?

I think I actually read something about how people who take antacids have higher chances of getting cholera. Did I preempt you?

Erin Allmann Updyke: No, not at all. I wasn't gonna talk about that but I definitely saw that too. So if you lower the acidity in your stomach it makes it easier for the cholera to get through that really harsh environment. Super cool.

Erin Welsh: I've also heard something about that along the same lines with stomach cancer?

Erin Allmann Updyke: Oh really? Just because there's like various bacteria that can be associated with stomach cancer?

Erin Welsh: No, well potentially that but also because acid will kill off the more bad cells basically earlier.

Erin Allmann Updyke: Oh, that's really interesting.

Erin Welsh: And so if you don't have that pressure...

Erin Allmann Updyke: Yeah! That's cool.

Erin Welsh: I mean, I don't know, this is all like me... This is what scientists shouldn't do which is just reading abstracts of things.

Erin Allmann Updyke: It happens though.

Erin Welsh: (laughs)

Erin Allmann Updyke: Okay and the other reason that there's a really high infectious dose is that after a cholera bacteria survives your stomach, it actually has to swim all the way through the rest of your GI tract and into your small intestine. So it has a little flagellum, which is a tail, so these bacteria actually look like spermies.

Erin Welsh: Ew.

Erin Allmann Updyke: (laughs) Little sperms.

Erin Welsh: I think that they make giant microbes of cholera that are really cute.

Erin Allmann Updyke: I think they do. Not probably as cute as gerardia, cause that's the cutest.

Erin Welsh: Aw.

Erin Allmann Updyke: It's so cute. It looks like a little rastafarian.

So once the little spermy bacteria get to your small intestine, they attach themselves to your intestine wall and they begin producing cholera toxin. And this is what actually makes you sick. So it's not the bacteria alone, it's the fact that the bacteria produces this toxin. And what's super crazy and cool about this toxin is that it is actually produced by a bacteriophage. A bacteriophage is pretty much a virus that infects bacteria. I don't know why we have to call bacteria viruses something different, but we do.

Erin Welsh: They look really cool also.

Erin Allmann Updyke: They are really amazing. One time in college we got henna paint and we were all painting henna and my roommate, Jocelyn, who's awesome, painted the most beautiful bacteriophage on her arm and I was like, 'That want that'.

Erin Welsh: Tattoo.

Erin Allmann Updyke: It's beautiful.

Erin Welsh: Aw that's great.

Erin Allmann Updyke: Yeah. So anyways, this bacteria phage has basically inserted part of its genome into the cholera genome and that is what's actually producing this toxin. Which is super interesting to me.

Erin Welsh: That's fascinating.

Erin Allmann Updyke: Yeah.

Erin Welsh: And also, are you going to tell me how this toxin works? Cause I need to know.

Erin Allmann Updyke: Yeah. So basically this toxin essentially prevents your body from absorbing any water and forces you to push out all of the water in your body out of your intestine. Which means you're basically pooping water.

Erin Welsh: Oh my gosh.

Erin Allmann Updyke: Yeah. I'll more about it in just a minute.

Erin Welsh: Okay.

Erin Allmann Updyke: So the incubation period - which we've talked about before as the period from when you get infected until when you show symptoms - for cholera is about 1 1/2 days.

Erin Welsh: Wow. That's very fast.

Erin Allmann Updyke: Yeah. They're super fast lil swimmers and they usually attach themselves to your small intestine within 12-72 hours of infection. So they're super quick.

And another thing that's interesting is there's kind of a range of symptoms. So some people who get infected are almost entirely asymptomatic, some people have a rather mild infection, and the ones that we'll talk about the most today have very, very severe infections. And the severity of the illness is likely based on both prior exposure, so if you got it when you were young and you get it again when you're older you're a little better off; but also on infectious dose. Since like I said previously, it actually takes quite a lot of bacteria to really get you infected.

But in the severe cases - which let's face it, that's what we're here for - basically what happens is you just start pooping your guts out.

Erin Welsh: Ooh, boy.

Erin Allmann Updyke: So really, you just poop all of your water out. Adults that have severe infections can poop out - get this - more than a liter of fluid per hour.

Erin Welsh: Oh. My. God. Are you serious?

Erin Allmann Updyke: I'm totally serious.

Erin Welsh: I have so many questions right now. How long can you live by pooping out a liter of fluid an hour?

Erin Allmann Updyke: I'm so glad you asked because I did some research. (laughs) so we have 4.5-5 liters of blood in our body, right? And that's the fluid that's the most available for you to get water out of.

Erin Welsh: Oh my gosh...

Erin Allmann Updyke So if you think about that... And then we've got another 15 liters of fluid, or maybe 10 liters of fluid, that's surrounding all of our cells. We call it 'interstitial fluid' inbetween our cells. Right? So that's 15 liters. But that's like all the fluid that you have available until your start sucking your actual cells dry.

Erin Welsh Whoa! Oh my god.

Erin Allmann Updyke Yeah.

Erin Welsh So is this where the disease got its characteristic symptom?

Erin Allmann Updyke It does.

Erin Welsh And what's that called?

Erin Allmann Updyke It's called 'rice water stool'.

Erin Welsh Why is it called that?

Erin Allmann Updyke Because the poop that you're pooping out is literally all bacteria. It's just like tons of bacteria and water and dead cells.

Erin Welsh And it looks like what? Murky, flaky...

Erin Allmann Updyke Yep. It looks like... So if you took a bag of rice and you soaked it and then you drained the rice out, that's what's left.

Erin Welsh It's the starchy... And what are we drinking right now actually? Cause we forgot to do quarantinis earlier?

Erin Allmann Updyke (laughs) You're right! You're so right about that. Tonight we're drinking Rice Water Stool.

Erin Welsh Ugh!

Erin Allmann Updyke (laughs)

Erin Welsh Can I provide a little correction? We're drinking a quarantini that we named Rice Water Stool. (laughs) It actually is composed of cholera bacteria - no, just kidding. It's composed of RumChata-

Erin Allmann Updyke About 1 1/2 oz of RumChata.

Erin Welsh Chai.

Erin Allmann Updyke 3 oz of chai concentrate or a really strong chai tea.

Erin Welsh And 1/2 oz of whiskey.

Erin Allmann Updyke Yep. Feel free to add more whiskey, it'll just look more realistic.

Erin Welsh Because it will curdle. But the most important part of this recipe is to gently warm it to body temperature.

Erin Allmann Updyke (laughs)

Erin Welsh It's actually pretty delicious.

Erin Allmann Updyke It's surprisingly good, you guys. I don't like warm drinks that are alcoholic but this is tasty.

Erin Welsh It's perfect for this time of year, so.

Erin Allmann Updyke It is! It's really good. Oh, Happy Thanksgiving!

Erin Welsh Happy Thanksgiving.

Erin Allmann Updyke Yeah. Rice Water Stool. Cheers.

Erin Welsh Cheers.

Erin Allmann Updyke With our mugs. (laughs)

So severely ill patients will have poop that is literally a trillion individual bacteria per gram of poop.

Erin Welsh Whoa! Whoa.

Erin Allmann Updyke Yeah. Whoa is right. I did that like a hundred times to make sure I was getting the number right. It's absolutely ridiculous.

Erin Welsh Which also makes sense why epidemics happen and are so easy to spread.

Erin Allmann Updyke And the other reason is because, like I said, not everyone gets this severe illness. So people who have a mild illness are still pooping out about a million bacteria per gram of poop and even patients who are completely asymptomatic can be shedding about 10-100,000 bacteria per gram of poop.

Erin Welsh That's really interesting.

Erin Allmann Updyke Yes. The biggest range, I mean obviously there's a huge range in the number of bacteria per gram of poop, but also people who are severely ill are not just shedding while they're having massive diarrhea. They're shedding for up to 1-2 weeks after symptoms have alleviated. And people who have mild illness are shedding for less time. And people who are asymptomatic tend to shed for only about a day or two.

Erin Welsh Okay.

Erin Allmann Updyke

So yeah, it's crazy. There are just tons and tons of this bacteria that are getting into the environment. And the other thing is that since this is a pathogen that can persist in the environment, the types of *Vibrio cholerae* bacteria that you're likely to find in the environment - meaning whether they are toxigenic or nontoxigenic - will largely depend on how many severely ill people you have in that environment. So it's this vicious cycle.

Once you have people who are ill in a certain area, they're shedding so much forking virus - I mean bacteria! Oh, shoot.

Erin Welsh

(laughs) Just start over.

Erin Allmann Updyke

That's embarrassing. How many times do you think I've said virus?

Erin Welsh

I don't think you have.

Erin Allmann Updyke

Okay. So once you have people who are ill in a specific area, they are shedding so forking much bacteria that if you don't have proper sanitation, for example if you're living in London in 1850-

Erin Welsh

Or many places today.

Erin Allmann Updyke

Right, if you're, say, pooping in a river and then drinking from that river downstream. Or even if you have like an outhouse or something but that hole is near a well of upstream of a river. You're just spreading that infection like wildfire. What else do you wanna know?

So treatment for cholera. The good news is cholera is a very treatable disease. So the World Health Organization basically calls for oral rehydration solution, which is just like salty, sugary water.

Erin Welsh

Gatorade.

Erin Allmann Updyke

Kind of yeah, pretty much. They have like a proprietary blend, I'm sure.

Erin Welsh

IV.

Erin Allmann Updyke

IV for severe infections. Definitely need treatment up to like 6 liters in the first day, severe cases might need more than that. So it's quite a lot of liquid that you need. Generally they don't recommend antibiotics except in super severe cases primarily because A) antibiotics are wiping out all of the good bacteria in your gut, which can make it so you're very susceptible to other potentially more serious diseases.

Erin Welsh

And cholera has kind of done that. Like if you have a severe infection of cholera, it pretty much has taken over your entire intestine anyway.

Erin Allmann Updyke

Right. Yeah. And the thing is that because this is a bacteria that can persist in the environment, antibiotic resistance is a real concern.

Erin Welsh

And it's really kind of cool that it can be treated with just rehydration therapy.

Erin Allmann Updyke

Right, yeah. It's generally like a fairly short course of disease. The severe cases without treatment, fatality rate is about 50%.



Erin Welsh: Wow.

Erin Allmann Updyke: But with treatment it can be as low as 1%, which is amazing.

Erin Welsh: What about a vaccine?

Erin Allmann Updyke: So there is an oral cholera vaccine. There are actually three different types of OCVs. And WHO does have a stockpile of these in case of severe outbreaks and emergencies, which we'll probably talk more about when we talk about what's happening with cholera today.

Erin Welsh: Right. Well that's good that there's a vaccine.

Erin Allmann Updyke: Yeah, it's great.

Erin Welsh: Do you know anything about whether it provides long-term...?

Erin Allmann Updyke: As far as I know it's not long-term but it is short-term and so that's why it's generally used in case of outbreaks. Yeah, so I mean, I feel like that's pretty much the biology of cholera. Am I right?

Erin Welsh: You better be.

Erin Allmann Updyke: I hope I am. (laughs)

Erin Welsh: (laughs)

TPWKY: (transition theme)

Erin Welsh: So can I tell you about the history then?

Erin Allmann Updyke: Oh I cannot forking wait.

Erin Welsh: Okay. It's a good one.

Erin Allmann Updyke: Good.

Erin Welsh: I mean, they're all good.

Erin Allmann Updyke: Well yeah.

Erin Welsh: But this is a good one.

Erin Allmann Updyke: I think as we are both epidemiologists, this is especially close to our heart. Am I right?

Erin Welsh: Exactly, yeah. Because you can't really talk about the history of cholera without talking about the birth of epidemiology as a field-

Erin Allmann Updyke: Yay!

Erin Welsh -the struggle for germ theory to prevail over miasmatism. I'm not saying 'my asthma'. Just FYI. It's not my asthma.

Erin Allmann Updyke (laughs)

Erin Welsh And also the role that modern sanitation practices played and continue to play in reducing disease burdens.

Erin Allmann Updyke Yeah definitely.

Erin Welsh Huge. But let's start a little more simply than that. Let's start with what we know about the origins of the bacterium itself. Since cholera doesn't leave any physical mark on the body that you remain after death, you can't really detect it in skeletal remains the way that researchers have been able to with leprosy and smallpox, as we've mentioned.

Erin Allmann Updyke Whoa. I've never thought about that! That is so interesting.

Erin Welsh Yeah. It's really cool to look at how you can trace the physical evidence of certain bacteria because this means that we have to rely more on ancient texts and writings, which may or may not refer to the same disease that we call cholera today.

Erin Allmann Updyke Oh that's so interesting!

Erin Welsh Yeah, it makes the history of cholera a little murky.

Erin Allmann Updyke Ugh, just like rice water stool?

Erin Welsh (laughs) The first mention of cholera comes from the father of western medicine himself, Hippocrates. In around 500 BC he uses the word 'cholera' to describe an intestinal illness that causes diarrhea. In fact, it's thought that the word 'cholera' itself comes from the Greek word for gutter, 'choledra'.

Erin Allmann Updyke What?! That's so cool!

Erin Welsh Yeah, yeah, yeah. So he may have chosen this word, cholera, to describe the way poop water gushes out of you if you have cholera.

Erin Allmann Updyke Oh my god!

Erin Welsh Like the way water gushes out of a gutter. (laughs)

Erin Allmann Updyke Oh wow!

Erin Welsh There are some other loose mentions of cholera prior to the 1800s. (laughs)

Erin Allmann Updyke Your puns are killing me right now. (laughs)

Erin Welsh But any that were written outside of India were probably just using the term 'cholera' to refer to any diarrheal disease.

Erin Allmann Updyke	Okay.
Erin Welsh	It would be like saying, 'Oh man I ate Taco Bell last night and I've had cholera all day today'. (laughs)
Erin Allmann Updyke	(laughs) Every time, dude. Every time.
Erin Welsh	So it wasn't until the early 1800s that the word 'cholera' was directly linked to one disease caused by one organism, the cholera bacterium.
Erin Allmann Updyke	Cool. Yeah. 1800s.
Erin Welsh	1800s.
Erin Allmann Updyke	From Hippocrates to the 1800s. That's a big jump.
Erin Welsh	It was just in the Indian subcontinent.
Erin Allmann Updyke	Interesting.
Erin Welsh	Yeah. In fact, until 1817 cholera was confined entirely to India-
Erin Allmann Updyke	Wow!
Erin Welsh	-when it would pop up occasionally and cause an epidemic, particularly during religious pilgrimages.
Erin Allmann Updyke	Huh. Wonder why?
Erin Welsh	Oh I'm about to tell you. Because during these pilgrimages there would usually be a lot of people in a very small place and so disease like cholera, which relies on high population density, can really take hold and tear through a population.
Erin Allmann Updyke	Just thousands of people shedding trillions of bacteria. And then drinking poop water.
Erin Welsh	Trillions per gram.
Erin Allmann Updyke	Yeah. Per gram. Isn't that crazy?
Erin Welsh	That's a lot of poop, it explains why it spreads so rapidly. Really, the world in 1817 was pretty perfect in terms of opportunities for cholera pandemics.
Erin Allmann Updyke	(laughs) I thought you were just gonna leave it at perfect and I was like, 'Pretty perfect, I mean, yeah'.
Erin Welsh	(laughs) Women had the right to vote everywhere...
Erin Allmann Updyke	(laughs)

Erin Welsh

Global population density was higher than it had ever been in 1917 and trade routes were really well established. So basically bringing the furthest reaches of the world to the doorstep, you know? You could go anywhere much more rapidly than you ever had before. Or ever could before. But something happened in 1817 to tip the scales from cholera epidemic to cholera pandemic. Maybe one or two cholera victims hitched a ride on a ship or a caravan heading east, who knows. And they continued to shed the cholera bacterium even if they felt okay.

Erin Allmann Updyke

Can you remind us the difference between an epidemic and pandemic for those people who maybe haven't listened to every one of our episodes?

Erin Welsh

Sure. Basically the difference between epidemic and pandemic has to do with spatial scale. So epidemic is a lot smaller, regional outbreak, and epidemiologists tend to define pandemic as being either country-wide or global, multiple countries.

Yeah. In any case cholera raged for the next 7 years in India, China, the Philippines, Mediterranean countries, etc. all of which had probably, except for India, had never seen the disease before.

Erin Allmann Updyke

Oh man. So no immunity.

Erin Welsh

No immunity, people were dying all over the place. It was really bad. So this marked the start of the first of seven cholera pandemics that historians and epidemiologists describe. And they would happen one right after the other, pretty much. In all corners of the world.

Erin Allmann Updyke

Interesting.

Erin Welsh

Yeah I'm not sure how they defined the edges.

Erin Allmann Updyke

I was trying to find that too and I couldn't.

Erin Welsh

So we're currently in the seventh pandemic right now and that started a little bit later, which we'll get into more later in the episode. The rest of the were sort of almost separated by a year or two. So how could you say...?

Erin Allmann Updyke

I wonder if it's just that if reports dropped below a certain level, then they considered that epidemic or pandemic over. And then the next one started or whatever.

Erin Welsh

Yeah. I mean, that could be it. It's not like we're epidemiologists or anything. Uh oh, we are.

Erin Allmann Updyke

(laughs) Whoops.

Erin Welsh

During the third pandemic, in walks one of the heroes of this story.

Erin Allmann Updyke

(humming Game of Thrones theme)

Erin Welsh

John Snow. No, this is not fantasy disease ecology crossover fanfiction.

Erin Allmann Updyke

Oh that'd be great though.

Erin Welsh: I mean, let's start it. This dude's name really was John Snow. But this John Snow was an English physician living in London in 1854 when a cholera epidemic broke out.

Erin Allmann Updyke: Ooh.

Erin Welsh: Allow me to set the stage for you, Erin.

Erin Allmann Updyke: Thanks.

Erin Welsh: Okay, close your eyes.

Erin Allmann Updyke: Closed.

Erin Welsh: It's 1854.

Erin Allmann Updyke: Okay I'm probably wearing like a large dress and a corset.

Erin Welsh: Uh huh, you probably smell really bad because bathing was not-

Erin Allmann Updyke: I've never showered.

Erin Welsh: Yeah, never showered. You're living in London.

Erin Allmann Updyke: (cockney accent) 'Oh, aye mate'.

Erin Welsh: Along with 2.5 million other people. Okay, let me give you a little perspective. The population of London today is 8.7 million.

Erin Allmann Updyke: Oh, okay. So just a few friends and I.

Erin Welsh: Yeah. But the city has never been bigger in terms of population density. And as a result, it's been unable to keep up with the rapid population waste output.

Erin Allmann Updyke: Oh.

Erin Welsh: Yeah. And there's no solution.

Erin Allmann Updyke: Uh oh.

Erin Welsh: The vast majority of people were just tossing out their food, their food scraps, and their dead pets or other animals into open cesspools that led to the sewer, which was often right next to a water pump.

Erin Allmann Updyke: (cockney accent) 'Oi, guvna!'

Erin Welsh: A water pump for drinking water.

Erin Allmann Updyke: (laughs)

Erin Welsh: I really appreciate that.

Erin Allmann Updyke: Thanks. I was really just trying to get in the mood.

Erin Welsh: (laughs) Also horse poop was everywhere.

Erin Allmann Updyke: Oh, god.

Erin Welsh: Yeah. The waste problem of London and other populous cities at the time was so enormous that there was an entire industry based on sorting through the stuff that got tossed out.

Erin Allmann Updyke: Wow.

Erin Welsh: Bone pickers.

Erin Allmann Updyke: I was gonna say 'pickers' so that's pretty close.

Erin Welsh: Bone pickers, yeah. Night soil men.

Erin Allmann Updyke: Ooh, just shoveling through the poop.

Erin Welsh: They would collect the poop and then use it for fertilizer.

Erin Allmann Updyke: Cool.

Erin Welsh: Sewer hunters. These were actual names.

Erin Allmann Updyke: I feel like I could be a sewer hunter.

Erin Welsh: Yeah you could be.

Erin Allmann Updyke: I feel like that's a profession that I could do.

Erin Welsh: Would you want to?

Erin Allmann Updyke: I don't know.

Erin Welsh: Well, you can be. Just kidding. (laughs) Yeah and that was just to name a few, there were many more in that same ilk.

Erin Allmann Updyke: Wow.

Erin Welsh: If you were to travel back in time to this London the first thing you would notice is the putrid, pervasive smell of rot and filth.

Erin Allmann Updyke: Ugh, god.

Erin Welsh: And this London is the London that our hero John Snow experienced everyday as he walked to patients houses.

Erin Allmann Updyke	Wow.
Erin Welsh	Like the Jon Snow of HBO (laughs) this John Snow was also quiet, methodical, and he was also really curious.
Erin Allmann Updyke	Did he have a great jawline? (laughs)
Erin Welsh	No, he didn't. (laughs) Does the Jon Snow of HBO?
Erin Allmann Updyke	Yeah!
Erin Welsh	Does he?
Erin Allmann Updyke	Oh my god, yeah.
Erin Welsh	I feel like he always has facial hair covering it.
Erin Allmann Updyke	In the early episodes he just had little wispies. He's got a good jawline.
Erin Welsh	Okay, all right. Anyway while the cholera epidemic was raging, John Snow set out to do some detective work to see if he could track the pattern of spread to see where the outbreak originated. And out he went, notebook and pen in hand, doing some - what do you call it?
Erin Allmann Updyke	(cockney accent) 'Oh cheerio, mate! Can I get a sample of your poop there, luv?' Kind of like that?
Erin Welsh	Kind of like that but also shoe-leather epidemiology. Which is actually a real term, it's what people say when they do on-the-ground epidemiology.
Erin Allmann Updyke	Boots on the ground. Yeah.
Erin Welsh	So when he went out to try and figure out what the cause of this outbreak was, what he was doing was interviewing people who had any sort of experience with cholera during that time. And what he was looking for was a common thread in all of their stories to see if he could find the cause of this horrible disease. And why was he so interested in this?
Erin Allmann Updyke	(cockney accent) 'Poop! Poop everywhere!'
Erin Welsh	Because he loved poop. (laughs) No. At the time the prevailing thought was that all disease was spread by miasma - not by germs. Which is in other words an unpleasant atmosphere. This was what scientists, physicians thought at the time caused all disease. The wind blew in the wrong way today.
Erin Allmann Updyke	(cockney accent) 'The air has all foul-' I can't do a British accent, I should stop trying.
Erin Welsh	No. Maybe, I don't know, I mean...
Erin Allmann Updyke	I should really stop it. I worked hard-

Erin Welsh: It's better than I could ever do.

Erin Allmann Updyke: I was like really trying really hard to think of something to say there and I just... I'm gonna... yeah. (laughs)

Erin Welsh: (laughs) We're losing all listeners in the U.K.

Erin Allmann Updyke: Oh dear. (cockney accent) 'Sorry luvs'. (laughs)

Erin Welsh: Yeah so basically miasmatists were people who believed that miasma was what spread disease and they thought that epidemics could be caused by the right weather conditions. Or proximity to the foul smell coming from the sewer. Miasma or miasmatic, to disease biology, is kind of like astrology to personality psychology. It has a whiff of science-

Erin Allmann Updyke: That's gonna piss a few people off. (laughs)

Erin Welsh: It has a whiff of science in its logic but it is mostly based in nonsense.

Erin Allmann Updyke: Yep.

Erin Welsh: But the logic of miasmaticism didn't quite make sense to Snow at least, who recognized that the rate of disease wasn't any higher in the people you'd expect it to be, like the people who spent so much time in the filth such as bone pickers, night soil men, etc.

Erin Allmann Updyke: Which is interesting when you think about it because they were probably getting so much poop water on their hands that it could have been that they had higher rates of disease just from being exposed. But I guess when you have exposure just across all boards then it's kind of, it washes out?

Erin Welsh: Well or they could have been exposed in low enough dosages-

Erin Allmann Updyke: That's very true, yeah.

Erin Welsh: -that they would've had increased resistance.

Erin Allmann Updyke: Yeah, that's true. Good point.

Erin Welsh: Instead though, the disease seemed to strike somewhat randomly. Entire families would be wiped out in some houses. Seriously, entire families. But others would be completely unscathed. To try to make sense of this, he mapped out the cases, which is not the first time that maps had been used to study disease, but it was one of the most remarkable.

Erin Allmann Updyke: I don't think I knew that, I thought that was like-

Erin Welsh: I thought so too.

Erin Allmann Updyke: It was like (singing) 'The John Snow and his maps!' It was like a big deal in all of our classes.

Erin Welsh: It is a big deal because of some of the techniques he used.



Erin Allmann Updyke

Ah, yeah.

Erin Welsh

But there were maps that had been used by the miasmatists at the time to show, oh, disease cases...

Erin Allmann Updyke

Oh, that's true. Like up on this hill vs down in this valley and that kind of a thing. Especially for malaria.

Erin Welsh

Right, right. And so when he looked at the math he saw a geographical component for sure, with most of the cases appearing in a certain neighborhood. But it was the anomalies that stuck out to him. A woman across town who died during the peak of the epidemic with no other cases around her. A brewery smack-dab in the area with the highest prevalence but without any cases at the brewery itself.

Erin Allmann Updyke

Ooh!

Erin Welsh

Yeah. What was going on?

Erin Allmann Updyke

What was going on?

Erin Welsh

Well during his interviews, Snow gathered info on daily habits of those afflicted with cholera including where they got their water. You see, in 1854 there was no indoor plumbing in London and people got their water from public water pumps, some of which had a better reputation than others. The pump on Broad Street was considered to be one of the higher quality pumps.

Erin Allmann Updyke

I'm just feeling so excited cause this is such a fun story.

Erin Welsh

(laughs) I know. And some people went out of their way to load up on the sweet, sweet tasting water from the Broad Street pump. Unfortunately for them. Cause that's where all the cholera came from.

Erin Allmann Updyke

(laughs)

Erin Welsh

In his interviews, Snow heard Broad Street mentioned over and over again and sure enough, when he marked the sight of the Broad Street pump on his case map, he was basically marking the epicenter of the outbreak.

Erin Allmann Updyke

(gasp)

Erin Welsh

Yeah, with cases just spilling out from there.

Erin Allmann Updyke

Ugh, it's so cool.

Erin Welsh

All told, 700 people living within 250 yards of the Broad Street pump had died.

Erin Allmann Updyke

700 people?

Erin Welsh

700 people within 250 yards.

Erin Allmann Updyke

Wow!

Erin Welsh: And on Broad Street itself, the population had literally been decimated. 90 of its nearly 900 residents died.

Erin Allmann Updyke: That's 10%!

Erin Welsh: Yeah, decimated.

Erin Allmann Updyke: Dang!

Erin Welsh: Wow, yeah. And the anomalies he noticed? Well the lone case far away from the pump was a woman whose sons brought her Broad Street water every week as it was her favorite.

Erin Allmann Updyke: Aw.

Erin Welsh: Yeah, isn't that sad?

Erin Allmann Updyke: Poor old lady and her sons just trying to be nice. (cockney accent) 'I'll bring you the best water, mama'. That was better.

Erin Welsh: That was better! Uh, I don't think Snow told them. Which is probably a kindness.

Erin Allmann Updyke: Yeah, probably.

Erin Welsh: And the workers at the brewery? They never drank water during their shift, only beer. (laughs)

Erin Allmann Updyke: Ayo! That's the moral of our story.

Erin Welsh: And so Snow took his findings to the board of governors who actually, I was shocked about this, did something about it. They ordered that the handle of the Broad Street pump be removed. Of course but the time they already removed it, it was pretty much over, the epidemic. Still, it was a victory for germ theory that marked the birth of epidemiology which is, as we've mentioned before, the study of patterns of disease in populations.

So you would think that by removing the handle of the pump they were, you know, acknowledging that maybe John Snow was right about something.

Erin Allmann Updyke: Yeah, I mean he was the king in the north, after all.

Erin Welsh: I mean, yeah.

Erin Allmann Updyke: North of London.

Erin Welsh: Bend the knee.

Erin Allmann Updyke: Bend the knee, people.

Erin Welsh: To germ theory.

Erin Allmann Updyke Oh that was good!

Erin Welsh (laughs) That was terrible.

Erin Allmann Updyke That was on the fly, I know it.

Erin Welsh Yeah it was. And they probably agreed that, yeah, cholera was transmitted by drinking contaminated water. John Snow was almost pretty much unique in his assertion that that was how it was transmitted. But, like Cersei Lannister of Season 7 Game of Thrones, they remained firm in their denial.

Erin Allmann Updyke Ugh, oh my god.

Erin Welsh Cholera was transmitted by foul air/White Walkers weren't a real threat.

Erin Allmann Updyke (laughs) Oh my god.

Erin Welsh I had to dig deep for that one.

Erin Allmann Updyke That was good.

Erin Welsh It wasn't until a couple of decades later that Snow would be vindicated. Or until next season for the other Jon Snow. We anticipate.

Erin Allmann Updyke (laughs) I just can't wait.

Erin Welsh Oh it's like two years from now.

Erin Allmann Updyke Yeah, yeah, yeah.

Erin Welsh Sadly Snow the epidemiologist would not live to witness his vindication.

Erin Allmann Updyke Oh.

Erin Welsh Yeah.

Erin Allmann Updyke Does he die of cholera?

Erin Welsh No.

Erin Allmann Updyke Too bad.

Erin Welsh He died of a stroke at the age of 45.

Erin Allmann Updyke Oh dear.

Erin Welsh When the causative agent of cholera was described in 1883, the germ theory had taken its rightful place on the Iron Throne of disease biology. (laughs)

Erin Allmann Updyke (laughs) We're never going to stop.

Erin Welsh Nope. And there were still, though, more than a few miasmatisists lingering on. And one of them, Pettenkofer, drank an entire flask of cholera bacteria to prove that it wasn't the causative agent of the disease.

Erin Allmann Updyke Did he die? Did he die?

Erin Welsh Unfortunately no. No he didn't get sick. Probably though because he had cholera as a youth and so it didn't matter really either way.

Erin Allmann Updyke He got like a mild or an asymptomatic infection probably.

Erin Welsh Right.

Erin Allmann Updyke So he might have killed somebody else by pooping into dirty water his bacteria-filled poop. Great guy.

Erin Welsh Yeah, that's a good point.

Erin Allmann Updyke What was his name? Karkarff?

Erin Welsh Pettenkofer. Either way though, germ theory had won. There's nothing that that guy could actually have done. And Pettenkofer met his death in a very Game of Thrones way.

Erin Allmann Updyke Ooh!

Erin Welsh Maybe. I don't know if it's that Game of Thrones. After realizing that his entire scientific career was based on a fallacy - cause he spent so much energy promoting miasmatisism - he killed himself.

Erin Allmann Updyke Oh now I feel really bad. That's sad.

Erin Welsh Yeah, it's really sad.

Erin Allmann Updyke On a happier note, I don't know if you were gonna mention this, but I'd just like to point out for all the fans out there that you can visit the Broad Street pump.

Erin Welsh Yes you can!

Erin Allmann Updyke There is a little monument to John Snow there and I want to go so badly. If you've been there or if you live near there can you tweet us a picture? Because it's one of my favorite things.

Erin Welsh That's would be incredible.

Erin Allmann Updyke I love it.

Erin Welsh Bucket list.

Erin Allmann Updyke Bucket list.

Erin Welsh But not poop bucket list.

Erin Allmann Updyke (laughs) Night soil bucket list?

Erin Welsh (laughs) Okay, back to cholera. Linking the spread of cholera to unclean water was a huge motivator for developing sewage systems, and in wealthier countries the disease pretty much disappeared.

Erin Allmann Updyke Wow.

Erin Welsh Yeah the 1854 epidemic in London marked one of the last real epidemics in that area.

Erin Allmann Updyke That's awesome.

Erin Welsh Yeah because they were able to isolate the reason why it was being transmitted and stop that.

Erin Allmann Updyke That's great news.

Erin Welsh Tea drinking also may have helped.

Erin Allmann Updyke What?!

Erin Welsh Boiled water. Isn't that crazy?

Erin Allmann Updyke Oh. That's really cool.

Erin Welsh Yeah!

Erin Allmann Updyke Just like beer.

Erin Welsh Just like beer.

Erin Allmann Updyke Yeah.

Erin Welsh On a sad note, the problem of waste management does not belong in the past by any means.

Erin Allmann Updyke Definitely not.

Erin Welsh There are many economically poor countries today that are still struggling with waste disposal and sanitation practices where diseases such as cholera are still very prevalent.

Erin Allmann Updyke Yeah.

Erin Welsh And in these places it's kind of like a positive feedback loop. So these countries are unable to maintain or build adequate sanitation infrastructure because of the expense and then cholera can take hold more easily, which then reduces people's ability to work which then further destabilizes the economy so cholera gets worse, and so on and so on. Yeah.

Erin Allmann Updyke

Cycles. Cycles, cycles, cycles.

Erin Welsh

So Erin, I'm guessing that you've got some stuff to tell me about where we stand with Cholera today.

Erin Allmann Updyke

I sure do.

TPWKY

(transition theme)

Erin Allmann Updyke

So as you mentioned, we're basically currently in what is considered the seventh pandemic of cholera. So all of the cholera in the world today can actually be traced back to a single origin that happened in 1961. And so my guess is that for most of our listeners, when they hear the word cholera today in 2017, they probably think Haiti.

Erin Welsh

Yeah. I do.

Erin Allmann Updyke

And it's likely because one of the most publicized outbreaks of cholera in recent history happened in Haiti in 2010. And if you haven't heard of it, or even if you have, this outbreak happened pretty directly as a result of UN Peacekeepers who came to Haiti after the devastating earthquake that happened in January of 2010. And these peacekeepers had come from Nepal, where an outbreak of cholera had been happening and they brought it with them.

Erin Welsh

Oh! Okay, I was wondering where they came from that they had cholera.

Erin Allmann Updyke

It was Nepal. Yeah. So cholera has been endemic in Nepal for a very long time, yeah, that whole region. And so the UN still hasn't technically admitted that they were responsible-

Erin Welsh

Really?

Erin Allmann Updyke

Even after epidemiological research and molecular strain typing of the cholera bacteria has pretty conclusively shown that they is where this epidemic came from. They did issue an apology in December of last year about the way that they handled Haiti after the earthquake-

Erin Welsh

That kind of sounds like, 'I'm sorry that you were hurt by what I said'.

Erin Allmann Updyke

Yeah, like they didn't directly take the blame for it.

Erin Welsh

No.

Erin Allmann Updyke

But anyways that's probably a story for a different day. (laughs) And the outbreak in Haiti, which to be clear is not over, it's still going on, cholera is still a problem today. Over 9000 people since 2010 have died and over 700,000 people, which is about 7% of the population of Haiti, have been sickened. The stat that I saw is to this day they're averaging 37 people a month dying from cholera.

Erin Welsh

Oh my god.

Erin Allmann Updyke And if you think of all of the hurricanes and everything that have been happening in the Caribbean at this time, like... Because cholera is a disease that is associated with contaminated sources of drinking water and lack of sanitation, any time that you see destabilization of infrastructure, whether that's due to natural disasters or war, man-made conflicts, you see outbreaks of diseases such as cholera.

Erin Welsh Right.

Erin Allmann Updyke Today, or in 2015 rather since that's the most recent stats that the WHO had on their website, 42 countries reported 172,000 cases of cholera that resulted in 1304 deaths in 2015. In one year.

Erin Welsh Okay.

Erin Allmann Updyke But what's really astonishing to me, especially in doing this research, is that estimates of how many cases there actually are? 2.9 million.

Erin Welsh Interesting.

Erin Allmann Updyke Yeah.

Erin Welsh And this has to do with asymptomatic cases? Or not seeking treatment?

Erin Allmann Updyke So it's probably both. Probably there are some asymptomatic cases but a lot of it has to do with a lack of surveillance and a lack of reporting in a lot of areas.

Erin Welsh Right.

Erin Allmann Updyke Also because this is a disease that can strike so rapidly, you can have people falling ill and dying in remote areas long before they have time to get to a hospital facility or anything like that. Estimates of the number of deaths that likely happen each year due to cholera are 95,000.

Erin Welsh Whoa.

Erin Allmann Updyke Yeah. And this information is from a paper that used mathematical modeling and a bunch of disease data to make these estimates. So they estimate that cholera is likely endemic in over 60 countries, not just the 42 that actually report it. And the estimates range from 1.4-4 million cases per year.

Erin Welsh Wow.

Erin Allmann Updyke And between 21,000-143,000 deaths.

Erin Welsh Whoa!

Erin Allmann Updyke Yeah, I mean, it's a really big range because there's not super great data from a lot of places.

Erin Welsh But still.

Erin Allmann Updyke But still. It's definitely a lot more than the 1000 deaths that are actually reported.

Erin Welsh: Yeah.

Erin Allmann Updyke: So in addition to estimating the number of cases of cholera, this study also looked at what the most important risk factors were. My voice cracked. (laughs) I noticed that.

Erin Welsh: (laughs) Yeah. I'll fix it in post.

Erin Allmann Updyke: Oh thanks, thanks. Appreciate it. (laughs)

Erin Allmann Updyke: But unsurprisingly the two most important risk factors - do you wanna guess what they are? The two most important risk factors for cholera in a country?

Erin Welsh: I think I'm gonna try.

Erin Allmann Updyke: Okay.

Erin Welsh: Sanitation.

Erin Allmann Updyke: Definitely.

Erin Welsh: Water infrastructure?

Erin Allmann Updyke: Exactly.

Erin Welsh: Access to clean water?

Erin Allmann Updyke: Exactly. The percentage of the population without sustainable access to improved sanitation and improved drinking water sources.

Erin Welsh: And blood type?

Erin Allmann Updyke: And not blood type. (laughs)

Erin Welsh: But there are differences in susceptibility to cholera with different blood types, right?

Erin Allmann Updyke: Weirdly yeah. What blood type you are can actually affect the likelihood that you get infected with cholera and how severe the case it once you are infected.

Erin Welsh: That's so weird!

Erin Allmann Updyke: It's super weird. So people who are blood type O, like me, like me.

Erin Welsh: Oh, I'm AB.

Erin Allmann Updyke: You're so rare! I'm so common.

Erin Welsh: (laughs)



Erin Allmann Updyke

So people with type O are less likely to get infected with cholera, which sounds great, but if they get infected they actually are much more likely to have severe symptoms.

Erin Welsh

Okay. That's a bummer.

Erin Allmann Updyke

It's a bummer, yeah. So what's cool is that in some parts of the world, for example in the Ganges River delta where cholera is endemic and has been for a very long time, you see a very, very low prevalence of people who are blood type O.

Erin Welsh

Interesting.

Erin Allmann Updyke

So one hypothesis is that this is at least in part because there is selection against this blood type because it's associated with higher risk of severe symptoms.

Erin Welsh

I've always wondered about the geographical distribution of blood types.

Erin Allmann Updyke

It's really interesting, we were just looking at maps of that. It's so weird, I had no idea there was such a range in distribution.

Erin Welsh

Yeah. It'd huge!

Erin Allmann Updyke

And so in Latin America, for example, there's a really high prevalence of blood type O. So all of like North and South America is like really high prevalence of blood type O, and so we see much more severe disease due to cholera. You have greater need for rehydration treatment and much greater rates of hospitalization.

Erin Welsh

Whoa.

Erin Allmann Updyke

Yeah, it's really interesting.

Erin Welsh

That is really fascinating.

Erin Allmann Updyke

Yeah.

Erin Welsh

So how worried do we need to be about cholera?

Erin Allmann Updyke

It's a good question.

Erin Welsh

It's a tricky one.

Erin Allmann Updyke

It's a tricky one. I would say overall the biggest thing that we can do to prevent and majorly reduce the burden of cholera is improve access to sanitation and water worldwide. And that's something that's very doable, it just honestly takes investment, you know? To make that happen.

Erin Welsh

Right. People on the ground going out and trying to help create clean water sources.

Erin Allmann Updyke

Exactly.

Erin Welsh

The Gates Foundation is big in trying to do that.

Erin Allmann Updyke	There are a lot of organizations that are doing that, that I wish I had looked up the names of all of them. So maybe what we'll do is post on our Facebook page some of the organizations that are doing really great work on both sanitation and water improvement.
Erin Welsh	Right. The Carter Center, which last episode I kept saying was the Carter Foundation, I was confusing with the Gates Foundation. It's actually the Carter Center. They also do a lot of work in terms of reducing the burden in neglected tropical diseases in countries.
Erin Allmann Updyke	Yeah. So I'd say overall, cholera definitely is still prevalent in a lot of parts of the world, it still is something that's killing people everyday. And it doesn't need to be, which is what's really sad about it, is it is treatable and it's preventable.
Erin Welsh	Could it be eradicated?
Erin Allmann Updyke	That's a really good question, it's an interesting question. I don't know to be honest. Because it can persist in the environment I think it would be really, really hard. There are some interesting therapies out there that we don't have time to get into that could make a really big dent. Because in theory if you could eliminate this bacteriophage from the cholera, then you're not gonna be having symptomatic infections. So then it just becomes another microbe in your gut.
Erin Welsh	Okay.
Erin Allmann Updyke	But because it does persist in the environment, it's a disease that would be very, very difficult to eradicate. I do think we could certainly reduce the disease burden and the mortality rate to basically zero.
Erin Welsh	Right.
Erin Allmann Updyke	Maybe that could happen in our lifetime, who knows?
Erin Welsh	Wouldn't that be wonderful.
Erin Allmann Updyke	It would be really wonderful.
TPWKY	(transition theme)
Erin Allmann Updyke	Is that it? What books did you read this week?
Erin Welsh	Okay. I've got a few. If you want a big overview of cholera itself, there's a book called 'Cholera: The Biography' by Christopher Hamlin. And if you want to learn more about the non-HBO John Snow, you should check out 'The Ghost Map' by Steven Johnson. It's a pretty thrilling book actually about the race to try to find out what was the cause of cholera, the quite frankly shocking pushback from the miasmatisists about germ theory, and also in The Ghost Map is where the quote from the beginning of this episode came from.
	A couple of other places that I looked for info was 'The Power of Plagues' by Irwin Sherman and 'The Cambridge History of Human Disease' by Kenneth Kiple. And a bonus is 'Love in the Time of Cholera' by Gabriel Garcia Marquez, which is a great fiction book.

Erin Allmann Updyke

And most of the information about the biology of cholera I got from this really interesting paper called 'Cholera transmission: the host, pathogen, and bacteriophage dynamic' by Nelson et al in Nature Reviews Microbiology. That was published in 2009. It's a really nice review paper and there's a bunch of other ones out there as well.

And most of the data about the mathematical modeling to estimate the actual burden of cholera worldwide comes from the article 'Updated burden of cholera in endemic countries' and that was in the journal PLoS Neglected Tropical Diseases. That was published in 2015 by Ali et al. So you can find that.

Erin Welsh

Before we go, I thought of the most brilliant idea.

Erin Allmann Updyke

Oh tell it to me.

Erin Welsh

Kit Harington, who plays Jon Snow in HBO's Game of Thrones, needs to play John Snow the epidemiologist in a biopic!

Erin Allmann Updyke

(laughs) That would be really funny.

Erin Welsh

I'm serious!

Erin Allmann Updyke

I mean, are you listening, Kit?

Erin Welsh

Are you listening screenwriters everywhere? Get on this.

Erin Allmann Updyke

Yeah, we gave you a plug last episode, you know, the smallpox movie. We're basically doing your jobs for you.

Erin Welsh

Yep, yep, you're welcome.

Erin Allmann Updyke

Welcome.

Erin Welsh

And speaking of more thanks and welcomes, thank you to Bloodmobile who provided the music for this and all of our episodes.

Erin Allmann Updyke

Yeah. Thanks, you're the best, Bloodmobile!

Erin Welsh

And also a big thank you to the band Cholera who let us use their song 'The Answer to Infection' as the fade out song at the end of this episode. It's awesome, you guys should totally check them out.

Erin Allmann Updyke

Just wait for it, it's so good.

Erin Welsh

Once again, rate, review, and subscribe.

Erin Allmann Updyke

Yep. We'll do it again, we'll tell you more. And thanks so much for listening! We hope you are having fun, cause we are.

Erin Welsh

Wash your hands.

Erin Allmann Updyke

Ya filthy animals!

TPWKY

('The Answer to Infection' by Cholera plays)