

TPWKY

This is Exactly Right.

Erin Welsh

"I was called on to visit the Major about the middle of May. He was lying in bed and looked pale and emaciated, his eyes were sunk, his cheeks hollow, and his countenance dejected. He told me he was in violent pain which could not be palliated without taking 2 or 3 grams of opium every three or four hours. His bowels were obstinately costive and he was obliged to take some purgative medicine every day. Food was loathsome to him and he had profuse perspirations for which he was taking wine and bark. I endeavored to restore his appetite by lessening the quantity of opium and substituting the tincture of hops as much as possible. His appetite was frequently coaxed by some delicacy and the sweet oil was frequently alternated by magnesia and rhubarb. This treatment was regularly pursued until the last of June and although he suffered much pain during that time he was evidently much better and his appetite improved. The pain in his bowels was less frequent and not so violent.

July 4th. I was sent for in great haste to visit him. When I entered his room I was astonished at his altered appearance. His countenance was pale and fallen, he was sitting up in his bed, struggling for breath. His body was covered with cold and clammy sweats and he had a most anxious and desponding look. I immediately gave him large quantities of ether and laudanum. These injections brought away from his bowels large quantities of dark and hardened feces. They were repeated every day during this month with the happiest effect and it was astonishing what masses of these dark and indurated feces were evacuated during this time.

September. He is much emaciated and exhausted by want of sleep. The pain and swelling have pervaded all his extremities. Opium can no longer lull his pain and nothing but death now seems to offer him any hope of relief.

Last entry. He is affected with erysipelas and is gradually sinking into a state of insensibility. In this state he lingered until the 13th of September when he expired without a struggle."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah. That is brutal. It's horrible. So that is an account of dysentery and it is from a book titled 'Medical Sketches of the Campaigns of 1812, 13, 14' by James Mann and it was published in 1816. 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

So today we're covering dysentery.

Erin Welsh

We are.

Erin Allmann Updyke

But that firsthand account Erin, when you read it, it doesn't really sound like dysentery.

Erin Welsh: Here's my thoughts because I kind of agree but I was like you know what Erin, you don't know anything about the biology, leave that to Erin. So you know just trust the physician from 1813 that he knew what he was doing. And the other thought I had is that yeah, this could've been any sort of diarrheal pathogen. But I wonder if some of these symptoms were caused by the things he was taking like opium and lead was a really popular treatment as well, mercury... So I don't know.

Erin Allmann Updyke: Yeah, absolutely. Cause it sounds like he was having a lot of issues losing weight and a lot of pain and then was given a ton of opium which is gonna block you up really good.

Erin Welsh: Yeah.

Erin Allmann Updyke: So that's like then his bowels became compacted, is that the word they used?

Erin Welsh: What did they say? Did they say 'obstinate'? No. Yes! "Obstinately costive".

Erin Allmann Updyke: Okay, yeah. Yeah that'll do it.

Erin Welsh: But in any case it is horrific. But also I think that the vagueness of this firsthand account or the hard to pin down-ness is kind of characteristic of the topic that we're covering today.

Erin Allmann Updyke: Absolutely.

Erin Welsh: Yeah because dysentery, why do we do this to ourselves again, is not caused by one, not two, but by several pathogens and parasites. So it's gonna be an interesting ride.

Erin Allmann Updyke: Yeah. As always, as always.

Erin Welsh: As always.

Erin Allmann Updyke: And as always I believe that it's quarantini time.

Erin Welsh: It is. What are we drinking this week?

Erin Allmann Updyke: We're drinking In Flux.

Erin Welsh: So flux was one of the old-timey names for this disease, I think it actually might still be called flux in some places. Flux or the bloody flux. And so since the definition of dysentery has kind of been in flux, that's what we're going with.

Erin Allmann Updyke: So Erin, what's in In Flux?

Erin Welsh: Well I thought it would be kind of a nice callback to the firsthand account to include rhubarb, so we're gonna do a rhubarb syrup plus some gin, plus some sparkling water, strawberries, and lime juice.

Erin Allmann Updyke: Yum.

Erin Welsh: And we will post the full recipe for this quarantini as well as the nonalcoholic placeborita on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) as well as on all of our social media channels.

Erin Allmann Updyke And speaking of our website thispodcastwillkillyou.com we just keep telling you guys to go there, have you gone there yet? It's really great. We have a bookshop.org link, we have a Goodreads link, we have links to Bloodmobile, our music, we have links to our Patreon, to merch, to transcripts, to all of the sources from all of our episodes. Wow!

Erin Welsh Yeah, it's a gold mine.

Erin Allmann Updyke It really is.

Erin Welsh Yeah. Do we have any other business, Erin?

Erin Allmann Updyke I do! I have a correction I wanted to point out that somebody emailed us and I really appreciate this about one of our recent episodes was on Legionnaires' disease. And Erin you and I talked a lot about atypical vs typical pneumonia.

Erin Welsh I recall that conversation.

Erin Allmann Updyke Yeah and how like poor of a definition it is. It's still true but a listener pointed out - and I think this is important - is that today the term 'atypical' is mostly used to mean pneumonia that's caused by bacteria that don't gram stain very well rather than previously atypical used to be clinically a little different or not responding to antibiotics or maybe radiographic differences. But like we talked about in the episode, those are not good definitions to distinguish different types of pneumonia. So at least the way that we use it today is moderately better, things that don't gram stain well.

Erin Welsh Okay.

Erin Allmann Updyke But again, some things that are not considered atypical pneumonias also don't gram stain well but that's besides the point, it's still an imprecise term but it's at least a little bit better.

Erin Welsh Oh okay, so it's more about the pathogen now than it is about the symptoms or signs.

Erin Allmann Updyke Right like the clinical picture.

Erin Welsh Gotcha. Okay. Interesting.

Erin Allmann Updyke So that's something.

Erin Welsh Yeah.

Erin Allmann Updyke So thank you again. That's all I got. Should we dysentery it up?

Erin Welsh I think so. Feels like a fast intro but I'm here for it, let's do it.

Erin Allmann Updyke It does. We'll take a quick break and then we'll dive in.

TPWKY (transition theme)

Erin Allmann Updyke I'm gonna go through this a little bit out of order from my usual because like you said Erin, this isn't a very typical disease that we cover on this podcast. So first what I'm gonna do is cover kind of the symptoms of dysentery, we'll talk about what does dysentery actually mean and then I'll focus on a few of the specific causes and then Erin you can ask me a million questions and I probably won't know the answers. Cool?

Erin Welsh I am very excited.

Erin Allmann Updyke Okay so generally dysentery can be defined as bloody diarrhea. Is that cool? Can we all be cool with that definition?

Erin Welsh I mean that's it, right?

Erin Allmann Updyke Pretty much, yeah, pretty much.

Erin Welsh Okay.

Erin Allmann Updyke Diarrhea we've talked about kind of a lot on this podcast although not for a while. The World Health Organization definition is three or more loose or liquid stools in a 24 hour period but even that definition is pretty loose. (laughs) I swear the whole episode's not gonna be like this.

Erin Welsh I think it absolutely is.

Erin Allmann Updyke But it is a loose definition because everybody is different in terms of their bowel movements, right.

Erin Welsh Right.

Erin Allmann Updyke But everyone has had diarrhea at some point, so everyone know what's diarrhea feels like and what it means. So dysentery is diarrhea with blood, visible blood and often sometimes mucus just for good measure.

Erin Welsh Okay so question about the blood.

Erin Allmann Updyke Okay.

Erin Welsh Is it bright red or is it black?

Erin Allmann Updyke Good question. It could be either color so part of what you're asking gets at where is the blood coming from in your GI tract.

Erin Welsh Right.

Erin Allmann Updyke So black blood usually means that the bleeding is coming from further up in the digestive tract. So if you have bleeding in your stomach, in your small intestine, those will usually be black by the time they make it all the way to your poop. If you have bleeding in most of your colon then that bleeding is more likely to be bright red although even if you bleed like a ton from higher up it'll end up bright red. It just all depends on how long it transits.

Erin Welsh Okay, okay.

Erin Allmann Updyke

Okay. So in the case of dysentery it's probably gonna be I would say a mixture of two but more on the red spectrum than the black spectrum. And that's because as we'll see it tends to be a colitis picture and that means inflammation in the colon.

Erin Welsh

Okay.

Erin Allmann Updyke

So let's talk a little more about it. In order to have blood in your poop it means that in one way or another your gut is very unhappy of course. In the case of dysentery what it means is that you have some kind of severe inflammation going on whether it's from a bacteria, a virus, a parasite, or even in some cases no pathogens whatsoever. So you can have aseptic inflammatory bowel disease like Crohn's disease or ulcerative colitis. Okay?

Erin Welsh

Okay.

Erin Allmann Updyke

So these are autoimmune mediated conditions that cause massive inflammation of the colon that lead to bloody diarrhea aka dysentery. So any of these different things can cause dysentery. We're gonna focus today really on just the pathogenic types of dysentery and I'm gonna focus even more specifically on two major causes of dysentery. But we'll get to that in a second, let's focus on the symptoms, shall we?

Erin Welsh

Mm-hmm.

Erin Allmann Updyke

So you can imagine that if you have a very inflamed, angry gut wall that is so inflamed that it's bleeding large enough amounts of blood that it's visible in your stools, cause if you just have a little blood you won't notice it. You can imagine that this is a very painful process. So dysentery like a lot of other diarrheas are often accompanied by major abdominal cramping and because today we're focusing on infectious dysentery it's also common to have a fever which of course causes total body pain. So with dysentery you're often in terrible pain, you're pooping like crazy, you have this diarrhea, you have abdominal cramps. Often with this type of diarrhea you have a lot of urgency, you know that feeling when you have to go it's like right this instant?

Erin Welsh

Oh yeah.

Erin Allmann Updyke

And then it's gonna be explosive and it's gonna be painful. And with any type of diarrhea one of the biggest issues is how much fluid you can lose. Your large intestine's one job really, like it's one job is to absorb all of the water back from your stool so that we don't get dehydrated. And in massive diarrhea or in dysentery that mechanism is destroyed so you're just losing water through your behind. And so that's one of the major causes of death is just from dehydration.

Erin Welsh

Okay so you stated the definition of diarrhea as being three loose stools in a period of 24 hours. But for dysentery is it three? Is it nine? Is it fifteen? Is it fifty?

Erin Allmann Updyke

Yeah so there's so number on it, it's just if those three loose stools have blood and/or mucus in them, now you'd call that a dysentery rather than just a regular old diarrhea.

Erin Welsh

Okay, right.

Erin Allmann Updyke

Yeah. Great question. So yeah, dehydration is one of the biggest concerns and complications but of course it's this podcast so there are more things that can go wrong.

Erin Welsh

Of course.

Erin Allmann Updyke

With dysentery and other types of diarrhea, like non-bloody diarrhea, you also lose a ton of electrolytes. You're losing sodium, you're losing chloride, and so this can cause problems when your electrolytes then get out of whack. So you can end up with heart arrhythmias because of problems with your potassium, you can end up with neurologic problems because of the lack of sodium. And with dysentery which is different than other forms of diarrhea you're losing a lot of blood, so there's a risk of anemia especially in the cases of more chronic dysentery, like a prolonged diarrhea.

Erin Welsh

Right like the guy in our firsthand account.

Erin Allmann Updyke

Exactly. And so that's how you get, like you heard in our firsthand account, this kind of muscle wasting malnutrition and you're just sort of wasting away because you're not able to absorb anything, right.

Erin Welsh

How much blood are we talking?

Erin Allmann Updyke

It's a good question. There's no number or amount on it that would qualify something as dysentery vs not, it's really not a strict definition.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. And different sources would give you slightly different definitions I think even, so the most general would be just to say bloody diarrhea. And then of course because today we're gonna focus on infectious causes of dysentery there's always a risk of this infection spreading beyond the gut itself, so that even if it's not the dehydration or the malnutrition that ends up killing you, you could end up with a more widespread infection. So let's get into these specific bugs. There's a lot of different bugs that can cause bloody diarrhea and like I mentioned, even noninfectious things. It's possible that viruses can cause bloody diarrhea but it's not super common because in general viruses just cause regular diarrhea, not dysentery. It's possible that parasitic worms like maybe even some we've already talked about like hookworm or maybe tapeworms, these could potentially cause bloody diarrhea but most commonly there's two things that cause bloody diarrhea. There's bacteria that cause bloody diarrhea and there's an amoeba that causes dysentery.

Erin Welsh

Mm-hmm.

Erin Allmann Updyke

We've already talked about one of these bacteria that are a very common cause of dysentery and that is E. coli.

Erin Welsh

Right.

Erin Allmann Updyke

right. So some forms of E. coli are massive causes worldwide of dysentery. There are lots of other bacteria, Salmonella, we talked about typhoid already which is a form of Salmonella that can definitely cause bloody diarrhea, also Campylobacter which is another bacteria. There's two that we're gonna focus on today cause they're the leading ladies.

Erin Welsh

Well and I think also historically these two were the ones that caused classic dysentery. Typhoid had its own thing, right? Cholera had its own name.

Erin Allmann Updyke

Yes. It's its own thing.

Erin Welsh

And so if you were to find a treatise on dysentery it would probably be these guys would cause the vast majority or these leading ladies have caused the vast majority of them.

Erin Allmann Updyke

Yes. I think so too, so that's why we're focusing on them today. And that is Shigella and an amoeba, *Entamoeba histolytica*. These are the two major causes of bacillary and amoebic dysentery. All right, I'm excited about this. So let's start with amoebic dysentery and then we'll talk about shigellosis or dysentery from Shigella and then we'll just wrap up and you can ask me questions I don't know the answer to, okay?

Erin Welsh

Okay. (laughs)

Erin Allmann Updyke

Okay I found this one seminar from The Lancet in 2003 so it's a little bit old but I just really liked this quote, I never read quotes, I'm gonna read you a quote. Ready?

Erin Welsh

Ooh, yeah.

Erin Allmann Updyke

Few pathogens are more aptly named than *Entamoeba histolytica*. The tissue-lysing amoeba that causes amoebic colitis and amoebic liver abscess. Think of this protozoan parasite as a macrophage on steroids with pumped up phagocytic, proteolytic, and cytolytic capabilities invading human colonic mucosa and occasionally penetrating through to the portal circulation, reaching the liver, and causing fatal abscesses.

Erin Welsh

Whoa. I dig the voice, if you wanted a career as a movie voiceover I think you've got one. (laughs)

Erin Allmann Updyke

Thank you, thank you.

Erin Welsh

But also I loved that quote because it really aptly describes *Entamoeba histolytica* plus it does the etymology so I don't have to do it.

Erin Allmann Updyke

Right. Yeah. It's the whole thing, I really love it. Shout out Dr. Samuel Stanley, excellent work. My biology is done, right? Just kidding cause a lot of those words people are probably like, I'm sorry, let's talk about it more clearly.

Erin Welsh

Yeah, let's go over it.

Erin Allmann Updyke

So this particular amoeba, *Entamoeba histolytica*, has a simpler life cycle than the last amoeba we talked about, *Naegleria fowleri*. This amoeba exists in two forms: in the environment as a cyst and this is the form that is infectious to humans when we ingest it. After we ingest it it passes through our stomach, survives our stomach acid, travels down our small intestine, reaches our terminal ileum or our colon, so those are the two places where it excysts and becomes a trophozoite, like the amoeba-shaped version of an amoeba, and that's where it lives. It replicates by binary fission, so it just divides, and it just lives kindly in our colon, munching on bacteria which our guts are full of, we have plenty of bacteria for them to eat. And then it also eats our food and it's fine, right? Until it's not.

Erin Welsh

I was gonna say I don't think so.

Erin Allmann Updyke

Yeah it's fine until it's not because it doesn't stop there, it's not satisfied with just eating our food remnants and our commensal bacteria. Instead once it's in our guts it attaches to the epithelium of our colon, it immobilizes those cells, and then it just kills them. It just lyses them open and kills them and then it invades its way, burrows its way through our mucosa and into the submucosa of our gut wall. Why does it do this, Erin?

Erin Welsh

I was just about to ask.

Erin Allmann Updyke

I honestly want to know. From what I read it's not fully understood, like what exactly are the triggers that cause this adherence and invasion? Because the thing is only about 10-20% of people who get infected with *Entamoeba histolytica* will end up having symptoms. A lot of people are infected and entirely asymptomatic and you're not asymptomatic if it's invading your submucosa.

Erin Welsh

Right, okay. And by infected do you mean that they're shedding-

Erin Allmann Updyke

They're shedding cysts and you can find trophozoites in their poop as well. And that's how it has to complete its life cycle, right. It has to go back into its cyst form, you have to poop out those cysts so they can then travel to find another host via water or whatever. So it's a really interesting evolutionary question, what is the drive to seek out deeper spaces in our body and why do they have the capacity to do all of this damage to our tissues?

Erin Welsh

It's really interesting because do people who are symptomatically infected shed more amoebae than those who are just asymptotically chronically infected?

Erin Allmann Updyke

That's a good question. I'm not sure, I didn't see any papers specifically addressing that but it's an interesting thought because if you have diarrhea then yeah, you probably are shedding a lot more of whatever it is that you're shedding. But then if it kills you because of that then you're gonna stop shedding whereas if you're infected chronically... So maybe it's a trade-off between how long they're able to persist in someone before our immune system shuts them down vs causing massive infection but getting a lot out into the environment.

Erin Welsh

Right. Yeah. Disease is trade-offs.

Erin Allmann Updyke

Yeah. But we can talk about sort of the ramifications of what happens when they do this burrowing because spoiler alerts, it's not good.

Erin Welsh

It's horrible.

Erin Allmann Updyke

Yeah. And if you thought the bloody diarrhea part was bad, it gets a lot worse. There's a vein in our bodies called the portal vein that drains blood from your small intestine and the right side of your colon or large intestine directly to the liver. So as this amoeba which we know is in the right side of your small intestine or large intestine, as it burrows its way through the mucosa and submucosa it can end up right in these blood vessels, hop straight on that portal vein highway and take the first exit to the liver. So the liver is the number one site of what we call extraintestinal, outside of the intestine infection with *Entamoeba histolytica*. And it can be very severe because in the liver what it does is it kills off chunks of our liver cells the same way that it kills off the epithelium of our intestine. But then our liver in trying to protect itself walls off these amoeba essentially forming an abscess within the liver.



And so depending on how many amoeba you have and how large these abscesses can get, this is a common cause of death in people with *Entamoeba histolytica* who progress to liver abscess, it can be very serious. And it's not limited to just the liver, right. This amoeba can theoretically travel anywhere in our body through any blood vessel that it makes it into, so it's not uncommon to find similar kinds of abscesses in the lungs or in exceedingly rare cases in the brain.

Erin Welsh

That's horrific.

Erin Allmann Updyke

It is. But at least the brain is very, very rare, like less than 0.1% of people with liver abscesses have brain abscesses.

Erin Welsh

Oh okay.

Erin Allmann Updyke

And it's almost never that you would get a brain abscess without first having liver abscess since that's the number one site.

Erin Welsh

So can you break down what those complications are like in terms of the proportion of people who are... You know, if 10-20% of people are symptomatic, what percentage of those would have the liver manifestations and then the other abscesses develop and so on?

Erin Allmann Updyke

It's actually more common than I realized, especially if someone has the diarrhea, like is symptomatic with amoebic colitis. In those cases one source that I found said up to 75% of people that have the colitis will also then have liver abscesses.

Erin Welsh

Wow.

Erin Allmann Updyke

Yeah. So it's kind of like once this thing starts invading, it's really able to invade.

Erin Welsh

Sure.

Erin Allmann Updyke

So that's amoebic dysentery.

Erin Welsh

I have a question before we move on to *Shigella*.

Erin Allmann Updyke

Okay, what is it?

Erin Welsh

So I really wanna go back to that 10-20% of people.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so I assume there have been studies looking at the breakdown of people who are symptomatic vs asymptomatic. Are there any patterns?

Erin Allmann Updyke

So yes, there's a lot of things that are risk factors for people who will then go on to have severe disease or this colitis. Somethings are unfortunately kids tend to have worse outcomes with all kinds of dysentery, also malnutrition is a huge one. But what's interesting is that amoebic dysentery specifically really tends to be associated with very poor living conditions and with impoverishment. So how much that's also associated with things like malnutrition or maybe like a very high amoebic load because you're being repeatedly exposed. But kids tend to have poor outcomes and people who are otherwise malnourished or have other pre-existing conditions that will leave them immunosuppressed.

Erin Welsh

Right, okay. That makes sense.

Erin Allmann Updyke

Yeah.

Erin Welsh

That makes sense. Yeah I also wonder about the role of, and this probably relates also to Shigella, but the role of the gut microbiome in-

Erin Allmann Updyke

Oh Erin, we'll talk a little bit about that later cause it's really interesting, yeah.

Erin Welsh

Okay, wonderful.

Erin Allmann Updyke

Oh yeah, definitely. It's super interesting. But what's also interesting especially in looking at the kind of overall worldwide prevalence of colonization with *Entamoeba histolytica* is that not that long ago, and I don't have an exact date on it, but not that long ago it was discovered that there's another amoeba that looks identical to *Entamoeba histolytica*, it's called *Entamoeba dispar* and that colonizes people but doesn't cause any disease, it doesn't cause dysentery. And so it's thought that some at least earlier prevalence studies that were just looking for amoeba in the stool can't distinguish between these two different species and so our estimates of overall prevalence might be off in some cases.

Erin Welsh

Yeah, yeah. I have come across similar stuff.

Erin Allmann Updyke

Yeah.

Erin Welsh

But I also wonder if you find an amoeba in the bloody stool of somebody, it's likely that the bloody stool is being caused by that and not coinfection with...

Erin Allmann Updyke

Well that's the question, is it?

Erin Welsh

Okay.

Erin Allmann Updyke

Because *Entamoeba histolytica* exists both in the same areas where *Entamoeba dispar* does and under the same conditions that other forms of dysentery do. So then you have to ask the question of what does the clinical picture look like? So let's get into what bacillary dysentery looks like and then we can kind of compare and contrast what these two diseases look like to see if you can tell if they're different.

Erin Welsh

Yeah.

Erin Allmann Updyke

Because one thing I forgot to mention, this is I guess a spoiler now, is that amoebic dysentery, like the time course of disease can be really prolonged.

Erin Welsh

Right.

Erin Allmann Updyke

I didn't get a great number of the exact incubation period but the course of disease itself can be kind of insidious and last for a number of weeks. So it's not like all of a sudden you're having diarrhea and you're pooping your brains out like crazy and you have a high fever, it's not as much of that kind of a picture. So Shigella is a genus of bacteria in the family Enterobacteriaceae. There's a number of different species, at least four different species, within those species there are multiple serotypes. And these different species and serotypes cause a really wide range of disease from a mild diarrhea without any blood to very severe dysentery with a substantial case fatality rate.

Some species like *Shigella dysenteriae* are known to cause massive epidemics especially after times of upheaval or after natural disasters whereas other species like *Shigella flexneri* tend to cause more endemic illness. And then there are a couple of other species that just tend to be a little bit more mild but can still cause dysentery under the right conditions. Okay. So these are gram-negative, rod-shaped bacteria, hence the term 'bacillary' which I think we talked about in our Legionnaire's episode. They're transmitted either from fecal-oral contact or any kind of person to person contact where poop is involved from infected water or from food-borne contamination. And in general these species are super infectious because *Shigella* survives the passage through our stomach very well so as few as 10-100 individual bacteria can infect a person.

Erin Welsh

It's wild how few it takes.

Erin Allmann Updyke

Yeah, it's terrifying truly. So it has pretty much the same transmission route we already talked about for amoebic dysentery. You get *Shigella* in your mouth, it survives your stomach, it travels through your intestine, replicating the whole way that it goes until it gets to your colon or large intestine and that is where *Shigella* likes to make its home. Once it's there unsurprisingly it invades your epithelium, the lining of your gut and in so doing what it does is stimulate a massive inflammatory response from your body. And that inflammatory response just destroys the cells that line your gut wall so that the bacterium can invade even further. So at this point you have hundreds if not thousands of bacteria burrowing into your gut wall, hence massive bloody, bloody painful diarrhea.

Erin Welsh

I have a question about the blood.

Erin Allmann Updyke

Okay.

Erin Welsh

Why does this cause bloody diarrhea? Why does it cause bleeding whereas other diarrheas don't?

Erin Allmann Updyke

Yeah, great question. It's specifically that invasion of the lining of your gut wall because in doing that... Think of it as your gut wall being a wall and this bacteria is just like poking holes into it so the blood is just gonna come leaking out because of that.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. So other things that we've covered on this podcast that cause diarrhea like for example cholera, *Vibrio cholerae*, it just sort of hangs onto your epithelial cells, like it holds onto them but it doesn't invade them, it doesn't destroy them, it doesn't disrupt that lining. Whenever you get that disruption, that's when you get the blood.

Erin Welsh

Okay.

Erin Allmann Updyke

And so that's also why viruses don't tend to cause bloody diarrhea because they don't tend to invade through that gut wall.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. Some species of Shigella, especially the ones that cause more severe disease also produce a variety of toxins at least one of which we've talked about on this podcast because it's the exact same toxin that's produced by E. coli O157-H7. Yep, Shiga toxin. And this is a cytotoxic toxin so it kills cells. Great. Really great. This particular toxin is especially dangerous and what's interesting is that it seems to do this more often with E. coli that produce Shiga toxin than which Shigella that make this Shiga toxin. But it's still possible with Shigella. Once this toxin gets into your bloodstream it can kill your red blood cells and lead to anemia but then also destroy your platelets that, since we know how important platelets are for clotting, it leads to excessive bleeding. And this also then leads to kidney failure because it causes damage to the vasculature of your kidneys. This is a syndrome called hemolytic uremic syndrome and it's very bad and can be fatal.

Erin Welsh

Does the production of this toxin in some way help the bacteria to replicate more or to spread more easily? Is someone shedding more bacteria?

Erin Allmann Updyke

It's a great question. It certainly tends to cause more severe disease so in that maybe people are having more massive diarrhea and then are shedding more bacteria like we said before. But perhaps also the cytolytic effects perhaps help it invade more deeply into epithelium, I'm not sure.

Erin Welsh

Okay.

Erin Allmann Updyke

In general the sort of clinical picture of Shigella is more abrupt and I think maybe a bit more like what we think of when you think of a food-borne diarrhea type thing.

Erin Welsh

Okay.

Erin Allmann Updyke

In that it tends to happen anywhere from 1-4 days, maybe merely up to a week after infection and often one of the first signs is a fever.

Erin Welsh

It started with a fever.

Erin Allmann Updyke

It started with a fever. And then headache, feeling crappy, and then boom, this diarrhea comes on. And it's perfuse, it's bloody, it's watery, it's mucousy. For people with mild symptoms they'll probably recover within a few days but people who progress to dysentery, here's where you can have some numbers of poops, Erin. They can pass more than 20 stools in a day.

Erin Welsh

Wow.

Erin Allmann Updyke

Yeah. And while extraintestinal manifestations, so this bacteria fully leaving the intestine and causing illness elsewhere, are rare and I don't have a number on it Erin, so I don't know exactly how rare. But they are certainly possible. And in the case of Shigella they can cause things like seizures although this is mostly in kids and probably more related to fever or other metabolic derangements from electrolyte imbalance, hemolytic uremic syndrome like I already mentioned. But in very severe cases things like intestinal perforation or separation of the wall of your intestine, like the lining separates.

Erin Welsh: Oh my god.

Erin Allmann Updyke: Yeah. It's pretty severe.

Erin Welsh: So for both of these amoebic and Shigella dysenteries, if you survive either of those what are some of the lasting effects? I would imagine that lesions with amoebic dysentery are bad and then perforation would be really bad. Are there lingering effects?

Erin Allmann Updyke: Yeah, perforation's really bad, like if you don't have surgery you're just gonna die from that.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. The lesions and ulcers themselves with treatment will heal most likely because your gut actually turns over quite a lot, so it actually can really do a good job healing itself.

Erin Welsh: Okay, okay.

Erin Allmann Updyke: But what's interesting and I was gonna talk about this later in the episode but we can talk about it now since you asked.

Erin Welsh: Microbiome?

Erin Allmann Updyke: Yeah, microbiome. So there is increasing evidence that infection with, I think most of the studies have looked at Shigella specifically but with diarrhea-causing bacteria and especially dysentery-causing bacteria and potentially amoebae as well can then put you at higher risk of having IBS.

Erin Welsh: Oh, okay.

Erin Allmann Updyke: Irritable bowel syndrome. Yeah and there's some pretty good evidence, I'll link to a paper that's kind of like a meta analysis of what we know so far, like a review paper. It's really interesting cause if you progress to dysentery, that is pretty severe. Your gut is very unhappy, you're destroying a lot of what was there both in terms of the architecture of your gut and also the symbionts that you had there. So it's not surprising that you could have potentially lasting effects. But these are both treatable infections, so that's great. They're obviously different in terms of the antibiotics that you would use to treat them but the most important thing for any kind of dysentery is oral rehydration therapy. And so that's to combat the massive amount of dehydration. So that's dysentery, Erin.

Erin Welsh: It sounds horrible, yeah.

Erin Allmann Updyke: Yeah, it doesn't sound great. So Erin, I assume we've always gotten bloody diarrhea but when did we find out about it?

Erin Welsh: Yeah, yeah. It's a tough question and I will try to answer it right after this short break.

TPWKY: (transition theme)

Erin Welsh

The story of dysentery is an interesting one because it's not the story of one pathogen or one outbreak or one epidemic or one discovery, right. The main character changes constantly throughout the history of dysentery and it can be difficult I have to admit to find one common thread sort of driving this story, especially I think because if you zoom in on one time or place, on one little snippet, one photo of that history, that common thread that you're looking at, what you've zoomed in on, that branches off into a million other paths or stories that you could follow down. Like oh, I wanna learn more about how the Shiga toxin was discovered and the implications for that in terms of cell tissue culture and the Shiga toxin or Shigella. Yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

It's complicated. And you probably already gathered that from the fact that there are these many different species of microbes that can cause dysentery.

Erin Allmann Updyke

Right.

Erin Welsh

And so what I wanna do with this history section is to present a very broad picture of the history of dysentery. The flux, the runs, the trots, whatever name you wanna use and it had gathered its fair share over the years.

Erin Allmann Updyke

Oh yeah, I bet.

Erin Welsh

Where did this come from and how did we get to where we are today? And the answer to that question is, well it's kind of the same as it has been for many of the other diseases that we've covered on this podcast and if you're a repeat listener you can probably make a pretty solid guess, no pun intended.

Erin Allmann Updyke

Oh! (laughs)

Erin Welsh

Considering that these are pathogens or parasites transmitted through the fecal-oral route, it makes sense that once humans started gathering in large groups and settling in one area for at least a growing season that it became much more likely to come into contact with poop, your own or someone in your community's poop or like livestock poop. This is not new ground that I'm covering here but in researching for this episode I realized that I hadn't ever really stopped to consider what that transition from nomadic to sedentary lifestyle, what that looked like and how sanitation or sanitation technology began to catch up, like it needed a period of time to catch up after humans started to settle in one place.

Erin Allmann Updyke

Right.

Erin Welsh

Sanitation, especially latrines, it serves such a hugely important purpose in our lives. It separates us from our urine and fecal waste and it provides a place where that waste can decompose. And that's a process that also importantly helps to reduce the prevalence of pathogens. It's when sanitation breaks down or is suboptimal that we tend to see these outbreaks of intestinal pathogens and parasites including those that can cause amoebic and bacillary dysentery. I think some of us maybe carry around this image of early human settlements as being just absolutely filthy with people and animals pooping everywhere and no clean water to be found. But in reality nothing could be further from the truth. Latrines and sewers and drains and bathrooms and wells and aqueducts and cisterns and piping, these things have all existed for thousands and sometimes tens of thousands of years. The modern flushing toilet is dated to 1596 but older versions of a flush toilet have existed since at least the neolithic, maybe to around 3000 BCE in the Indus Valley.

Erin Allmann Updyke

What?

Erin Welsh

Yeah.

Erin Allmann Updyke

Flushing toilets?

Erin Welsh

Yeah! And elsewhere like in Ancient Mesopotamia or Ancient Greece there were toilets with variations in the size of the pit or the slope of the drain or the shape of the seat and so on. The longest known horizontal drain from Ancient Mesopotamia was 200 meters long.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

And that was at the moon god complex from around the 1st millennia BCE. So it's impressive, right?

Erin Allmann Updyke

Yeah, that's is impressive. Humans are more ingenious than I realized.

Erin Welsh

I think it's sort of like necessity is the mother of invention.

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

Yeah I mean think about Ancient Rome. When i picture Ancient Rome maybe cause the lead episode we did what seems like forever ago, but all the pipes and the baths and the drainage systems.

Erin Allmann Updyke

Right, yeah.

Erin Welsh

I read a fun little tidbit that there were apparently communal toilets in Ancient Rome were very common, very popular and they used to be used as social gathering spots where you could catch up on gossip and plan your next get together.

Erin Allmann Updyke

I mean that makes sense, like bathrooms still are, right?

Erin Welsh

They are!

Erin Allmann Updyke

Like you all go to the bathroom together and you chit chat and have a fun time.

Erin Welsh

Yeah, yeah. And no, I'm not gonna spend the entire history section talking about the evolution of the toilet or sewage systems although it would be kind of fun.

Erin Allmann Updyke

It would be great, yeah. It's would be a great episode.

Erin Welsh

Yeah. But I did just wanna emphasize that as soon as humans began settling in large, permanent groups, they began to devise ways to manage waste. Over time and across different geographic areas that visceral disgust that humans have for fecal waste found its way into culture. In Ancient Mesopotamia for exactly around the 1st millennia BCE there was a demon who dwelled in latrines or bathrooms who was responsible for illness, injury, or bad luck. And there were also demons in Ancient Mesopotamia associated with rubbish heaps. And then of course I'm sure you're familiar with the saying 'cleanliness is next to godliness'. These cultural perceptions of waste, they led to the development of rules and regulations regarding where you could or could not dump your chamber pot or your dead cow or goat, they influenced the frequency of bathing or hand washing, and the way that food was prepared.

When miasma became this leading theory as to the origins of disease, it wasn't far off from the truth for several pathogens or parasites. The steps that you would take to avoid miasma, this bad contaminated air, those steps would in many cases be the same ones that you would take to avoid several intestinal diseases. For instance in the 14th century CE a Spanish physician wrote a book on army health where in it he said that you should dig pits to use as latrines at the edge of army camp and to bury the dead bodies there and also that you should dip a white cloth in a possible water source before you drink it to ensure that it remained unstained.

Erin Allmann Updyke

Yeah, I mean that's good advice.

Erin Welsh

I mean it's good advice and I think it's interesting to sort of see these practices that were developed before any knowledge of germ theory.

Erin Allmann Updyke

Yeah.

Erin Welsh

But of course this isn't to say that sanitation technology or these cultural practices or community rules of dipping a white cloth into water, that these were always successful in preventing the spread of pathogens or parasites especially those transmitted through fecal waste. Cause if they were 100% successful the world would look like a very different place and this podcast might not exist which is a great name, I wrote down here 'great name for urban legends or conspiracy theory podcast'. But great things like flooding rivers or stagnant streams, droughts, population growth leading to massive refuse piles, the proximity of cesspits to places where food was being prepared, the use of human feces as fertilizer, and the lack of knowledge of how diseases were truly transmitted, all of these things led to the continued presence of many, many different pathogens and parasites that are transmitted fecal-orally. And dysentery in its various forms was certainly one of those diseases. And not just occasionally transmitted but frequently, like enough so that Hippocrates wrote about it. Of course gotta say Hippocrates.

Erin Allmann Updyke

Of course, it's in our contract.

Erin Welsh

(laughs) It gets its name from Ancient Greece. The word dysentery comes from the Greek 'dusentheria', 'dus' meaning bad and 'entera' meaning bowels. And later of course it was known to many people as the flux or the bloody flux.

Erin Allmann Updyke

Where does that come from exactly? Just cause your guts are in flux, like the movement?

Erin Welsh

Flux just means flow.

Erin Allmann Updyke

Yeah, okay. Okay. Bloody flow.

Erin Welsh

Yeah.



Erin Allmann Updyke

That makes sense.

Erin Welsh

So we know that from writings dysentery was present in many ancient Old World civilizations. But do we have physical proof or do we have any guess as to when it arose in humans or first started infecting humans? Kind of, I mean yes more to the first question than to the second.

Erin Allmann Updyke

Okay.

Erin Welsh

And so here I have to switch from talking about dysentery as a singular subject to one that is caused by different microbes.

Erin Allmann Updyke

Okay.

Erin Welsh

And like you Erin, I'm focusing on the two big ones, right. Entamoeba histolytica and I'm grouping them all into just Shigella, I don't talk about the different species. Yeah.

Erin Allmann Updyke

That's fine, I didn't either cause...

Erin Welsh

Well that's one of the multi-branching pathways I was talking about.

Erin Allmann Updyke

Exactly.

Erin Welsh

And like how different species have seemed to take over over time and they cycle in terms of their endemicity.

Erin Allmann Updyke

Yeah.

Erin Welsh

It's complicated.

Erin Allmann Updyke

And their virulence and everything. It's a mess.

Erin Welsh

Yeah. I did wanna ask about the virulence.

Erin Allmann Updyke

It's different.

Erin Welsh

Is it from different toxins? Is this weird to do this now?

Erin Allmann Updyke

It might be weird but yeah, toxins play a big role in it. But from what I read at least it's not necessarily specific to toxin. That's one part of it but it's not the whole story.

Erin Welsh

Okay, gotcha.

Erin Allmann Updyke

Yeah.

Erin Welsh

Okay, all right.

Erin Allmann Updyke

All right, anyways.

Erin Welsh: Going back. (laughs) So generally speaking if we want to know the prevalence of things like intestinal pathogens and parasites in ancient human populations we can't really use skeletal remains like the way we can for tuberculosis and syphilis for instance.

Erin Allmann Updyke: Right.

Erin Welsh: Instead we have to turn to coprolites. We love coprolites.

Erin Allmann Updyke: Coprolites! Oh lovely.

Erin Welsh: Or soil samples taken from burial areas around where the intestines would have decomposed, so like the pelvic area which I hadn't thought of that before, very interesting.

Erin Allmann Updyke: Yeah, that's very interesting.

Erin Welsh: Or we can analyze soil samples from archeological remains of these latrines or cesspools. When it comes to dysentery though we're still pretty limited cause dysentery is diarrhea.

Erin Allmann Updyke: Yeah.

Erin Welsh: And only well-formed stools can be preserved as coprolites.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah. That being said there is some paleoparasitological evidence of *Entamoeba histolytica* infection in humans. The cysts of *E. histolytica* don't preserve particularly well and only do so under very extreme conditions, like extreme cold, extreme dryness, whatever. And so a microscopic examination of soil or preserved feces isn't often successful and even if you do end up seeing an amoeba or a cyst of an amoeba under the scope, like you said you can't distinguish between *Entamoeba histolytica* and a nonpathogenic species.

Erin Allmann Updyke: Right, right.

Erin Welsh: So instead biomolecular tools like immunological tools and antigen testing are used if possible which is great because it can distinguish amongst species. But still there have been according to a book I read published in 2015, so these numbers might have changed, only five published articles describing the discovery of *Entamoeba histolytica* in ancient samples using either microscopy or immunological assays.

Erin Allmann Updyke: Okay.

Erin Welsh: The most ancient of these samples that tested positive for *E. histolytica* antigens is from Switzerland around 3400 BCE.

Erin Allmann Updyke: Wow.

Erin Welsh: Yeah. And there were a few samples that tested positive from Greece between 5000 and 2000 BCE. And there have been additional samples from various European sites in the Middle Ages that have also tested positive.

Erin Allmann Updyke

Interesting.

Erin Welsh

Yeah. The first reliable evidence for *Entamoeba histolytica* in the New World is from the 12th century CE. I couldn't find any estimates for the emergence of *Entamoeba histolytica* or how long it's been associated with humans but people do seem to think, and I think the paleoparasitological evidence points to this as well is that it probably has an Old World origin and that it seems to be possible that it evolved with humans since there are *Entamoeba* species that can infect great apes and that also the possibility of being an asymptomatic carrier or being chronically infected asymptotically, that would allow it to persist in a community even of smaller sizes so you wouldn't necessarily need the crowd disease type thing.

Erin Allmann Updyke

Yeah. It's interesting if it's something that has been with us forever, has it always caused disease at a low level? Or at what point was it able... But if there's similar ones that do cause disease in great apes then maybe it just sort of has always caused disease but just a little bit. That's interesting, Erin.

Erin Welsh

Yeah and maybe I just has the wrong search terms of something. But I would love to read more about the early evolutionary history of *Entamoeba histolytica*.

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

And then of course the other main cause of dysentery, these various *Shigella* species, again I couldn't find an exact date but their relationship with humans is also thought to be pretty darn old. So the various species of *Shigella* that caused dysentery all evolved from *E. coli* or are still *E. coli* depending on who you ask.

Erin Allmann Updyke

I remember we talked about that in our *E. coli* episode.

Erin Welsh

Yep, yep. And so I actually went back to my notes for that episode and I was like oh okay, *E. coli* has been with humans since humans were humans.

Erin Allmann Updyke

Okay.

Erin Welsh

And so I wrote here well it stands to reason then that *Shigella* might also be fairly old.

Erin Allmann Updyke

Yeah, pretty logical.

Erin Welsh

Yeah. But regardless of precisely when *Entamoeba histolytica* or the dysentery-causing *Shigella* species, when they first started infecting humans, we can be absolutely sure that once humans began to form these large settlements they weren't just building permanent homes for themselves but also for the causative agents of dysentery. And under these conditions dysentery absolutely flourished. It became a very familiar disease and also one that was very much dreaded. And part of that was something that you talked about, who was most likely to be killed by the disease: children.

Erin Allmann Updyke

Yeah.

Erin Welsh

And also armies. Not only did military campaigns and war create absolutely wonderful conditions for fecal-oral pathogens or parasites to blossom, I mean remember the typhoid episode?

Erin Allmann Updyke

Oh yeah.

Erin Welsh

These military campaigns also played a direct role in increasing the geographic distribution of those microbes including the ones that cause dysentery, right. So you're like oh we're gonna go on the Crusades and we're gonna spread dysentery throughout everywhere we go.

Erin Allmann Updyke

Yeah. Just pooping it along with you.

Erin Welsh

Pooping it along with you. Dysentery ran through the Persian armies that invaded Greece in 480 BCE. In France in 1779 there was an epidemic of dysentery likely bacillary that was exacerbated by troop movements and led to the deaths of 175,000 people, most of them children.

Erin Allmann Updyke

Oh my god.

Erin Welsh

And in the US Civil War the annual morbidity rate for dysentery for Union soldiers was 876 per 1000, so basically everyone got it, and annual mortality rates were estimated at 10 per 1000.

Erin Allmann Updyke

Wow.

Erin Welsh

And these numbers were even higher in prisoner of war camps such as the one where Union soldiers were held at Andersonville, Georgia where 16,772 cases of diarrhea and dysentery were recorded and 4529 soldiers died.

Erin Allmann Updyke

Oh my gracious.

Erin Welsh

Benjamin Moseley who was the former English Surgeon General in Jamaica, he wrote in the early 1800s, quote - cause you know I love quotes. Quote: "The dysentery or flux, being a disease so destructive to soldiers in camps and garrisons and a constant attendant on all military operations, it is a medical inquiry of the utmost importance to investigate this disease with the utmost attention in hopes of finding some method to put a stop to its devastation. It is a subject in which the welfare of mankind is deeply interested and often the glory and honor of a nation. If the cause of humanity were not alone a sufficient motive to induce to this research, we need but turn our eyes on the political field where we should behold the best concerted measures often defeated by its influence." So yeah of course it devastated soldiers and it was like we need to get this taken care of and then off the battlefield entirely it was also devastating.

Erin Allmann Updyke

Right.

Erin Welsh

There's an impressive list of famous people killed by dysentery, the Byzantine emperor Constantine IV in 685 CE, Louis IX of France in 1270, King Henry V of England in 1422, Erasmus in 1536, Sir Francis Drake in 1596, Akbar, ruler of the Mughal Empire in 1605, Nathaniel Bacon in 1676, and on and on and on. Like I skipped a ton of people because I was like this is ridiculous.

Erin Allmann Updyke

Like who didn't die of dysentery?

Erin Welsh

Yeah, who didn't die of dysentery? And I'm sure that everyone remembers dysentery from The Oregon Trail.

Erin Allmann Updyke

Yes, I remember it. You have died from dysentery.

Erin Welsh: You have died from dysentery. Yep, yep. And dysentery was truly devastating, it was a plague, it was a pestilence, a scourge. There's no word to hyperbolic I guess to describe it.

Erin Allmann Updyke: Yeah.

Erin Welsh: And so of course people were looking into it for hundreds, thousands of years even they were looking into it. Treatises upon texts upon papyri and quite honestly it didn't do much good at least until the late 1800s. For much of the human history of dysentery there was no distinguishing between the amoebic and bacillary forms of the disease and in many ways there didn't need to be. They were transmitted in the same way, the symptoms they caused were quite similar and most importantly there was no cure for either.

Erin Allmann Updyke: Right.

Erin Welsh: But there were plenty of attempts. Bleeding, naturally.

Erin Allmann Updyke: Right.

Erin Welsh: I know. It gets worse.

Erin Allmann Updyke: It's just so illogical in this case. Like that's already part of your problem here.

Erin Welsh: Oh I know, it's like bleeding to reduce the inflammation in the intestine is like how it was prescribed.

Erin Allmann Updyke: Oh my goodness.

Erin Welsh: I know.

Erin Allmann Updyke: Okay, gimme more.

Erin Welsh: Ipecac or rhubarb for some vomiting to empty the stomach.

Erin Allmann Updyke: Sure, yeah.

Erin Welsh: Something like tartar to cleanse the bowels.

Erin Allmann Updyke: What?

Erin Welsh: Yeah, so you're basically empty. And these cures as per usual did more harm than good. I think it's interesting, it is of course really difficult to resist the temptation to be like, 'What were you thinking?'

Erin Allmann Updyke: I know.

Erin Welsh: These clearly are terrible things to do. But also I just find it fascinating because a lot of the way that treatments were designed were to keep the body's humors in balance. And so it's just like but if you wanna keep your electrolytes and your water in balance, like your losing so much water, don't you think you might wanna replace it?

Erin Allmann Updyke

But did they know that?

Erin Welsh

No. I know.

Erin Allmann Updyke

They didn't know about electrolytes, Erin.

Erin Welsh

I know, I know. I know. I need to resist the temptation.

Erin Allmann Updyke

It's hard,

Erin Welsh

For this one in particular I'm like...

Erin Allmann Updyke

I know.

Erin Welsh

Just water and sugar and salt.

Erin Allmann Updyke

Right.

Erin Welsh

Okay. Yeah. And it was only in the late 1800s that dysentery was recognized to be caused by different organisms. Entamoeba histolytica was first described in 1875 by Russian scientist Fedor Lösch who isolated the amoeba from a patient and then confirmed its ability to cause disease by feeding amoeba-rich stools to a dog who developed similar lesions. Oh and there were plenty, also I should mention, of quote "human volunteer" experiments to confirm because it was heavily debated for a while whether it was the amoeba itself causing disease or if the amoeba was just something that sustained it. And this debate makes sense in the context of the late discovery that there are indistinguishable species of Entamoeba, one of which is pathogenic and the other is not. So there was a long debate being like no, it's not the amoeba that's causing disease, it's something else.

Erin Allmann Updyke

Okay.

Erin Welsh

Yeah. I don't know.

Erin Allmann Updyke

Interesting.

Erin Welsh

Yeah. And this debate continued even after the Shigella bacillus or I guess Shigella bacilli were discovered in 1898 by Japanese physician Kiyoshi Shiga which was also the first time that it was demonstrated that dysentery could have multiple causative agents. And Shiga had cultured the Shigella bacillus from a patient with dysentery during a huge epidemic in Japan, the 1897 outbreak which had a mortality rate of 25% and ended up killing over 22,000 people. Again, the majority of them children. In fact Shiga himself described dysentery as quote, "the most dreaded disease of children." And after Shiga published his findings, other researchers repeated his isolation and culture techniques and were able to confirm that this bacillus was responsible for dysentery although later work of course revealed that it wasn't this bacillus but rather these bacilli as it turned out there were multiple species responsible for causing dysentery. I'm always struck by the period of time between the late 1800s and the early 1940s or so when our knowledge of pathogenic microbes and parasites had greatly expanded but we were still largely helpless against treating them.

Erin Allmann Updyke

Yeah.

Erin Welsh

The bacterial ones anyway. Like vaccines of course were another story for many diseases. But yeah, we were largely helpless against a lot of bacterial diseases. And so despite now having at least two causative agents in hand for dysentery, the disease still raged in the military, in prisons, in psychiatric institutions, killing so many people and so many children. We've talked recently about the horrific conditions of trench warfare in WWI in regards to trench fever and dysentery was also an enormous contributor to morbidity and mortality during that war. The development of sulfonamides in time for the Second World War or at least for the end of the Second World War reduced the military mortality of dysentery enormously for that conflict down to 0.07%.

Erin Allmann Updyke

Wow.

Erin Welsh

However it was not the same situation in the concentration camps and prisoner of war camps of course during WWII where dysentery raged unchecked and was absolutely horrific. But I have a bit of side trivia here. Before antibiotics were developed, dysentery caused by Shigella was one of the first diseases successfully treated by bacteria phages in 1919.

Erin Allmann Updyke

Oh my gosh, I saw that article, Erin.

Erin Welsh

Yeah! Isn't that so interesting?

Erin Allmann Updyke

It's fascinating. I was like, what? This is from like the early 1900s?

Erin Welsh

I know, it's so cool. Shout out to Steffanie Strathdee, please check out our antibiotic resistance episode because it's really fascinating. Yeah so anyway. From the beginning of the 20th century the landscape of dysentery had greatly changed across the globe and is still changing today. An incredible amount of progress has been made on both *Entamoeba histolytica* and the dysentery-causing *Shigella* species in terms of virulence factors and plasmids and evolution and genetic diversity and all those other things. And dysentery has greatly dropped in prevalence in many places, especially with advancements in sanitation infrastructure and the application of antibiotics.

But it is still so extremely and frustratingly prevalent across the globe, causing devastating outbreaks such as the one in Guatemala in 1969 which led to an estimated 10,000 deaths and over the next four years it's estimated that there were 500,000 cases and 20,000 deaths due to dysentery in Central America. And in the late 1970s in Central Africa an epidemic of dysentery began to spread and then to remain at high numbers, high incidence. In the early 1990s civil wars and mass genocide and the construction of refugee camps led to this sustained outbreak in Rwanda with weekly dysentery attack rates in the camps estimated to be 3.8 per 100 people. And one of the most concerning things about the epidemics and the outbreaks that have happened starting in the second half of the 20th century is antibiotic resistance. *Shigella* were one of the first bacteria to show multi-drug resistance starting in the 1950s.

Erin Allmann Updyke

The 1950s? How many multiples of drugs did we even have then? That's awful.

Erin Welsh

I know, I know. It's horrible. And as far as I can tell this trend towards antibiotic resistance, maybe you'll tell me something different, but it hasn't seemed to turn around, it seems to be remaining fairly steady and on the rise.

Erin Allmann Updyke

Yeah I'm not gonna tell you anything different.

Erin Welsh: Okay. Dysentery loves a disaster, it loves a disruption whether it's a civil war or a busted sewer, an overflowing river or a drought. It thrives on that disturbance. So much of the world does not even currently have access to clean water, leaving them extremely vulnerable to dysentery and other diseases. And I can't help but now when I watch the news and I see all the horrific climate disasters that are happening, I can't help but think oh dysentery is gonna love this. So Erin, I'm hoping you'll tell me some good news about dysentery.

Erin Allmann Updyke: Let's just take a break.

Erin Welsh: Oh great.

Erin Allmann Updyke: And then we'll just talk about it.

TPWKY: (transition theme)

Erin Allmann Updyke: So like many of our episodes that get a little complicated, like we're dealing with a lot of different things, it's hard to put a number on how many people have bloody diarrhea, etc. So we're gonna do the best that we can with numbers. I think we'll get an overall picture of how bad it still is, okay? None of these estimates are super recent, most of them come from the early 2010s or so but overall looking just first at Shigella it's estimated that there's between 165-188 million cases of shigellosis, so that's Shigella-associated diarrhea or dysentery globally every year. It's estimated that includes over 60 million cases in kids under age 5.

Erin Welsh: Oh my gosh.

Erin Allmann Updyke: And this 2018 paper that I read also estimated that Shigella infections are the second leading cause of death due to diarrhea after rotavirus and cause over 164,000 deaths annually. That includes over 54,000 deaths in kids under age 5, that's just from Shigella.

Erin Welsh: Oh my gosh.

Erin Allmann Updyke: Yeah. It's pretty horrific.

Erin Welsh: Yeah.

Erin Allmann Updyke: When we look at amoebic dysentery we have I think even harder numbers, I don't have numbers on the estimates of total infection worldwide but I did find that it's estimated that 55,000 people a year die from Entamoeba histolytica infection and of course many of those are children. It's one of the top 15 causes of dysentery in developing countries for kids. And especially with amoebic dysentery there have been some studies that suggest that in endemic areas up to 40% or more of the population shows evidence of prior infection, so this is an amoeba that's really widespread even when it's not causing disease.

Erin Welsh: Quick question about that and about immunity cause I guess this'll play a role then in any discussion of vaccines.

Erin Allmann Updyke: Yeah.

Erin Welsh: Is there any immunity to either amoebic or shigellosis?



Erin Allmann Updyke

It's a good question. So off the bat we don't have vaccines for either. There's good evidence that the potential to develop a vaccine exists for Shigella. There's work being done, there's a lot of promise, there's been patents filed to develop vaccines for Shigella especially to try and develop vaccines against both Shigella and typhoid, like combining those both in one vaccine cause that would be really beneficial, those are spread in similar ways, etc. But right now nothing exists like that. But animal model studies suggest that the type of immune response that we develop could be protective. The problem is that there's a lot of different species and there's a lot of different serotypes so how much cross protection you would get from an immune response is unclear. With Entamoeba histolytica I could find even less information. So people mount an immune response but again because it can be kind of an asymptomatic infection it's not really clear are you protected from reinfection, are you chronically infected, etc. So for that one I think we're even further from the potential for a vaccine.

Erin Welsh

Okay.

Erin Allmann Updyke

It doesn't mean it's impossible but we just have to hope.

Erin Welsh

Yeah. Geez, gotcha.

Erin Allmann Updyke

So if you look at these two causes alone of dysentery, we're talking about millions of cases and hundreds of thousands deaths due to dysentery just from these two sources. And like I said before there's other bacteria that can also cause the same illnesses essentially. So obviously the biggest deal when it comes to dysentery and diarrheal diseases in general is trying to prevent them, right. And like you mentioned, Erin, getting better at prevention means access to clean water and sanitation so that people aren't coming into contact with human feces. And that's really the bottom line. The other bottom line like I mentioned way towards the beginning is addressing problems of nutrition because malnutrition is a huge risk factor for severity of disease especially for Entamoeba histolytica but also for other forms of diarrhea and dysentery. And both of those things, addressing malnutrition and addressing sanitation takes infrastructure which takes money, right.

Erin Welsh

Yeah.

Erin Allmann Updyke

So a lot of different organizations, the World Health Organization, UNICEF, so many others have a lot of lofty goals to eliminate deaths from diarrheal diseases by 2025. That's one of their goals. I don't actually know how well they're doing on that front, again it's hard to get to some data on this but if we just look at sanitation overall the World Health Organization estimates that only 45% of the global population currently have a safely managed sanitation system, like one that is going to actually be effective at preventing intestinal pathogens from spreading. So that's not great. They also estimate, the World Health Organization, and this isn't specific to dysentery so if we look a little more broadly, the World Health Organization estimates that 827,000 people die as a result of inadequate water sanitation and hygiene. And this altogether accounts for 60% of all diarrheal deaths.

Erin Welsh

Wow.

Erin Allmann Updyke

Yeah. So improving access to clean water, sanitation, can prevent literally hundreds of thousands of deaths including nearly 300,000 children under the age of 5 every year.

Erin Welsh

Oh my gosh, yeah.

Erin Allmann Updyke: Yeah. So that's kind of where research needs to focus at this point is like what are the best ways to sort of develop and implement those systems in ways that's actually going to be sustainable and make a difference.

Erin Welsh: Mm-hmm. and permanent, like not just like let's go in, build a bunch of sanitation infrastructure and then leave and not provide any funds to maintain it.

Erin Allmann Updyke: Exactly, right.

Erin Welsh: That's such a problem. Right.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: So I mean that's kind of the status of diarrhea, of sanitation, of dysentery today. I kind of already mentioned some of the interesting research that's going on in terms of how dysentery affects your overall microbiome and associations with the development of things like irritable bowel syndrome. So we kind of already jumped ahead and talked about that. And yeah, vaccines are something that's like people are doing research on it but we're not super far along from what I read. That's dysentery, Erin. It's not a super happy ending.

Erin Welsh: It's not. I don't think we should have expected one.

Erin Allmann Updyke: No, no, we never do.

Erin Welsh: Especially when it comes to diseases that predominantly affect developing countries.

Erin Allmann Updyke: Definitely.

Erin Welsh: Yeah. Well...

Erin Allmann Updyke: Sources?

Erin Welsh: Sources?

Erin Allmann Updyke: Let's do it.

Erin Welsh: Okay. I want to shout out, I have a bunch of articles but I wanna shout out one book and a couple of articles in particular. The book is titled 'Sanitation, Latrines, and Intestinal Parasites in Past Populations' and the editor is Piers Mitchell. And then there was a great paper called 'A Brief History of Shigella' by Lampel et al from 2017. And then another paper by Haycock from 2002 called 'Exterminated by the Bloody Flux'.

Erin Allmann Updyke: Ooh, that's a good title.

Erin Welsh: Yeah, that one was in the Journal for Maritime Research.

Erin Allmann Updyke: Oh cool.

Erin Welsh

Yeah.

Erin Allmann Updyke

I had a lot of papers for this one. That awesome quote that I read was from a 2003 paper titled 'Amoebiasis' in The Lancet. There was a number of other papers, I really loved 'Dysentery including amoebiasis', it was written in 1973, published in BMJ but it was a really nice overview of both Shigella and amoebic dysentery. A few others on the biology but if you'd like to read more about dysentery and irritable bowel disease, that paper is in the journal Gut published in 2004. We'll post all of these on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) under the EPISODES tab.

Erin Welsh

We will. A thank you to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Allmann Updyke

Thank you to Exactly Right network of whom we're very proud to be a part.

Erin Welsh

And thank you to you, listeners. Thanks for listening. This was a tough one so we're very appreciative that you hung in there with us.

Erin Allmann Updyke

Yeah. And a special shout out to our patrons, thank you guys so much for supporting us.

Erin Welsh

Yes, thank you. Okay this feels very appropriate so until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.