

Erin Allmann Updyke

"I decided that I was gonna have to drink the bacteria myself. I thought I would just be having no symptoms for a few years after which I would have an ulcer and then hallelujah, it'd be proven. Actually I was very shy about this experiment, I didn't tell anyone, not even my wife or Robin until afterwards. I asked my boss in gastroenterology Ian Hislop to do an endoscopy for me one day. As he put the scope down me he was saying, 'Barry, I'm not gonna ask why I'm doing this.' And from around the tubing I gritted out, 'Just take the biopsy!' So he took some biopsies from me and they were all clear, no bacteria. Then I infected myself with bacteria that I cultured from a patient who did not actually have ulcers, just indigestion and gastritis. I was able to eradicate his infection with some antibiotics so already I knew that I could if necessarily take a treatment which worked on this bug. I had some safety features built in, I thought.

I drank the bacteria and at first I was okay but instead of being perfectly well and having a silent infection, after about 5 days I started having vomiting attacks. Typically at dawn I would wake up, run to the toilet, and vomit. And it was a clear liquid as if you had drunk a pint of water and regurgitated it straight back. Not only that, there was no acid in it. I remember from my medical student days that if you have a meal where you drink so much beer that it's coming back up straightaway, it doesn't have any acid in it. I knew there was something unusual about vomiting and not having acid. And this is just one experiment on yourself and you say, am I imagining this? Until I had another biopsy I couldn't know for certain that I had the bacteria.

Finally after 10 days I had the biopsy, had another endoscopy, and the bacteria were everywhere. In the lining of my stomach there were absolute millions of the white cells that we call pus cells, polymorphs, there was no acid being produced by my stomach. I was very uncomfortable with that endoscopy, gagging and throwing up but I'd proven that the bacteria could infect a healthy person and cause gastritis. I'd proven Robin's disease."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

That's a really good one.

Erin Welsh

I love that one. The words from the man himself, Barry Marshall. So that was from an interview conducted by Dr. Norman Swan in 2008 for the Australian Academy of Science.

Erin Allmann Updyke

Sorry I didn't read it in an Australian accent. (laughs) I'm not sorry.

Erin Welsh

(laughs) I think that everyone will forgive you.

Erin Allmann Updyke

I think they'll be thankful for it.

Erin Welsh

Hi, I'm Erin Welsh.

Erin Allmann Updyke

And I'm Erin Allmann Updyke.

Erin Welsh

And this is This Podcast Will Kill You.

Erin Allmann Updyke

And today we're talking about *Helicobacter pylori*.

Erin Welsh

Wonderful little bacteria.

Erin Allmann Updyke

Just such a gem.

Erin Welsh (laughs) Okay so before we get into all of the nitty gritty of the horrible things that it can do to you, let's get into the nitty gritty of what we're drinking. What is our quarantini?

Erin Allmann Updyke Well of course it's Barry's Beaker. (laughs)

Erin Welsh (laughs) 'Barry' because Barry Marshall, one of the co-discoverers of this link between H. pylori and ulcers and gastritis etc etc.

Erin Allmann Updyke Who we just heard from in our firsthand account.

Erin Welsh Yeah. And so imagine as you're sipping this quarantini that you are Barry Marshall, taking that sip of the inoculate of H. pylori to give yourself gastritis.

Erin Allmann Updyke Yum, delicious. So yum.

Erin Welsh In the name of science.

Erin Allmann Updyke All in the name of science.

Erin Welsh That's what we cheers to today.

Erin Allmann Updyke Yes. So what are we cheersing with? What's in this drink?

Erin Welsh Oh yeah, okay. So it has got coffee because coffee definitely exacerbates-

Erin Allmann Updyke Ulcers.

Erin Welsh Ulcers. It's got alcohol in the form of rye whiskey, it's got-

Erin Allmann Updyke Chocolate liqueur and hazelnut syrup.

Erin Welsh Yes.

Erin Allmann Updyke Yum.

Erin Welsh Yeah.

Erin Allmann Updyke Supes delish.

Erin Welsh So we'll post the recipe for that quarantini and for our nonalcoholic placeborita on all of our social media pages.

Erin Allmann Updyke @TPWKY on Twitter and @thispodcastwillkillyou on Facebook and Instagram. And we'll also post it on our website thispodcastwillkillyou.com where if you haven't already you can also find our merch.

Erin Welsh Yeah, woop-woop!

Erin Allmann Updyke All right so should we just jump right into the podcast today?

Erin Welsh: Yeah I'm really excited about this one.

Erin Allmann Updyke: Me too, we're always excited though.

Erin Welsh: I know.

Erin Allmann Updyke: It's good. Okay. After this quick break.

TPWKY: (transition theme)

Erin Allmann Updyke: All right. H. pylori is a bacterium. Dun-dun-dun. Here we go. Helicobacter pylori is a gram-negative bacterium and the truth is that over 80% of people who are infected are asymptomatic.

Erin Welsh: So that's probably at least one of us.

Erin Allmann Updyke: Yeah, statistically speaking. It's highly likely. So that's interesting, I never thought about getting tested.

Erin Welsh: Have you ever had any ulcer symptoms or gastritis?

Erin Allmann Updyke: No. Well I'm having some right now but that's unrelated.

Erin Welsh: (laughs) Another burrito for breakfast?

Erin Allmann Updyke: Well you know. Okay so H. pylori is shaped a little bit like a helix which is where it gets the name Helicobacter from but it's not a spirochete like a spiraled bacteria, it's actually just a curved rod. And importantly it has flagella on it which it uses to move and it's a very highly motile bacteria and that'll become even more important as we talk about the pathophysiology of this disease. So the transmission is actually not entirely clear which I think is so interesting.

Erin Welsh: Yeah, that is really interesting.

Erin Allmann Updyke: Yeah we don't really know how people get infected. The thing is it's estimated that up to 50% of the world's population is infected with H. Pylori.

Erin Welsh: Is it vertically transmitted then? Like mother to offspring?

Erin Allmann Updyke: Great question. I haven't seen any data that suggests that it's directly vertically transmitted, most of the data that I've seen suggests that it's either fecal-oral or just through saliva.

Erin Welsh: Okay.

Erin Allmann Updyke: So it could be that mothers pass it to their offspring indirectly but not directly through what we would normally consider vertical transmission.

Erin Welsh: Okay, okay. Interesting.

Erin Allmann Updyke

But yeah it's very interesting that it's unclear how this bacteria that is so widespread is actually transmitted.

Erin Welsh

And so is it because it could be transmitted in many different ways? It's likely not just one?

Erin Allmann Updyke

I mean potentially, yeah. I really don't know.

Erin Welsh

(laughs) That's not what I was expecting.

Erin Allmann Updyke

I know, it's not what I was expecting either!

Erin Welsh

Cool.

Erin Allmann Updyke

Yeah there's not a lot of evidence that it necessarily persists in the environment but that fact that it's so widespread suggests that maybe it actually does somehow. And the other thing is that it's really easy to infect children but the people who tend to be most infected are actually adults and not necessarily children so that's pretty weird too.

Erin Welsh

So children clear the infection?

Erin Allmann Updyke

Maybe but then do they get reinfected or is it just that they actually don't get infected as children? Like if you screen a bunch of children, most of them are not going to be infected. If you screen a bunch of adults, a lot of them will be infected. But children are just as susceptible as adults and usually if you have something that's transmitted fecal-oral you might think that children would get it more frequently than adults because they're more likely to put poop in their mouths and things.

Erin Welsh

Yeah.

Erin Allmann Updyke

Anyways. We don't know exactly how it's transmitted. But we do know the kinds of symptoms that it causes. So acutely, an acute infection, shortly after you're infected you can get symptoms of acute gastritis which basically is just inflammation and irritation of the gastrointestinal tract. So maybe some abdominal pain, maybe some nausea like good old Barry tended to experience it sounds like. But often you don't get any of these symptoms. What usually happens is that the *Helicobacter* develops into a chronic infection, it basically just lives, makes a home in your stomach mucosa.

And this is impressive because your stomach is a pretty inhospitable environment, right. The pH is like 2, it's between 1.5 and 3.5 which is really, really acidic. And on top of that it's constantly moving, your stomach fills up with food and then it has to empty out and to keep all of the stuff that you eat from going back up and out your esophagus, it's always undergoing peristalsis which are these rhythmic contractions that it does in order to push the food out into your duodenum which is the first part of your small intestine. So it's not a static environment, it's a super dynamic environment. So how can this measly little bacterium survive in such difficult conditions? Do you wanna know?

Erin Welsh

I do wanna know. It's why I'm here.

Erin Allmann Updyke

It has two main mechanisms by which it's able to survive. First of all it has those flagella. So flagella are basically protein structures coming off a bacteria that they can use to swim.

Erin Welsh

Right.

Erin Allmann Updyke

So once the *Helicobacter pylori* makes it into your stomach it can resist being flushed out of your stomach with the rest of your food cause it can swim against the current.

Erin Welsh

That's a very powerful flagella. Flagellum.

Erin Allmann Updyke

I know, right?

Erin Welsh

Yeah.

Erin Allmann Updyke

Flagellum. They have like four so you can say flagella.

Erin Welsh

Okay those are some powerful flagella.

Erin Allmann Updyke

Yeah! They're really powerful. And then they can use them not just to swim against the current of peristalsis but to swim down into the mucus that lines your stomach. So for a little bit of basic stomach anatomy, because your stomach is such a harsh acidic environment your stomach cells produce a ton of mucus and that mucus lines your stomach cells in order to protect your own cells from getting eaten away and eroded by that acid. So the mucus forms this protective lining. The *Helicobacter* can use those flagellas to kind of burrow their way into that mucus layer.

Erin Welsh

Oh.

Erin Allmann Updyke

Yeah, it's pretty cool. And a lot of time they actually live in that mucus layer. But if they wanted to they could swim down through that mucus layer and actually attach directly to the epithelial cells. They have these special proteins called adhesins that adhere to the epithelial cells. And that way it's another mechanism by which they can make sure they don't get flushed out. Okay. So they're very good at A) swimming against the current down into your mucus and potentially attaching to your epithelial cells. So that's the first way that they're able to survive. The second way is that they actually can neutralize their own micro environment.

Erin Welsh

Oh cool.

Erin Allmann Updyke

Right?

Erin Welsh

Sort of like their own little pod, a bubble, the bacteria in the bubble?

Erin Allmann Updyke

Exactly. Right, exactly. So if the pH directly surrounding the bacteria is too low or too acidic they produce urease which is an enzyme that breaks down urea which is a normal waste product that's found throughout your body that when it's broken down breaks down into carbon dioxide and ammonia. And ammonia is a base. This base neutralizes the acid immediately surrounding *Helicobacter* bacteria so that they can live happily ever after in a slightly less acidic environment. Isn't that cool?

Erin Welsh

That's really cool.

Erin Allmann Updyke

So they're good swimmers, they can stick to your cells, and they change their own micro environment to be more hospitable for their growth and survival. Okay so the thing about H. pylori infection is that there are two different interrelated long term issues associated with chronic H. Pylori infection. Because again this is a bacteria that essentially makes its home in your stomach and lives there for a very, very long time. All right. These two different issues, they're related but they're also kind of opposite and it's really interesting and it seems like it's not entirely understood yet. But the issue that you end up with depends on where in your stomach these bacteria colonize. Okay?

Erin Welsh

Okay.

Erin Allmann Updyke

So if H. pylori colonizes in what's called the antrum of your stomach which is closer to the output end of your stomach-

Erin Welsh

Okay.

Erin Allmann Updyke

Then what it tends to do by mechanisms we don't fully understand is it causes hypersecretion of acid. So it actually increases your acid output. And if your stomach is making too much acid, that acid overflows out of your stomach and into your duodenum. This causes chronic irritation of your duodenum that leads to what we call gastric metaplasia. 'Gastric' means your stomach and 'metaplasia' means your cells are changing in shape and type. So it means that your intestinal cells start to look more like your stomach cells.

Erin Welsh

Ooh that's really weird.

Erin Allmann Updyke

It's really weird and it's not good. This leads to duodenal ulcers.

Erin Welsh

Okay.

Erin Allmann Updyke

Okay. So you got acid spilling out of your stomach into your duodenum causing irritation and cell changes that lead to ulceration which are basically holes that form in the layers of your small intestine.

Erin Welsh

Okay so I have a question. So you said that if the bacteria are in the output end of your stomach then stomach acid production increases but doesn't that make the environment more inhospitable? So is it your body's reaction? It's not the bacteria that are producing the acid, it's your body being like, 'Wait, you're neutralizing too much'?

Erin Allmann Updyke

That's a really great question. It's not entirely clear. It's suggested that maybe they damage certain cells that would decrease acid production so then they end up overproducing acid because those inhibitory cells are damaged, it's totally unclear. And it's about to get even weirder cause that's not the weirdest part.

Erin Welsh

Okay, good. Great.

Erin Allmann Updyke

Yeah. Okay so that's how you end up getting duodenal ulcers if you have a H. pylori infection. That's not the only thing you can end up with. If H. pylori colonizes higher up in what's called the body of your stomach, closer to the input end of your stomach-

Erin Welsh

That's like the big section, the big fleshy lump part?

Erin Allmann Updyke

Yes. Yeah.

Erin Welsh

Okay, not so tubular?

Erin Allmann Updyke

Not so tubular, exactly. If it infects there it actually decreases acid production.

Erin Welsh

Okay now I'm confused. (laughs)

Erin Allmann Updyke

(laughs) I know, right? So H. Pylori, if it infected higher up in the body of your stomach, it actually tends to lead to acid hyposecretion, less acid secretion which increases inflammation because the cells are invading in that portion of your stomach and they're directly causing inflammation. So it's not the acid itself that's causing an ulcer like it is in the duodenum, it's the bacteria itself causing ulcers in the stomach from the inflammation.

Erin Welsh

Oh interesting, okay.

Erin Allmann Updyke

And on top of that your stomach cells undergo what's called intestinal metaplasia. So now your stomach cells look less like stomach cells, more like intestine cells, they can't handle the acid that is there. So that further leads to gastric ulcers and gastric ulcers can lead to gastric cancer.

Erin Welsh

Okay, hold on a second. So let me just get this straight. Depending on where these bacteria colonize in your stomach, it can either make your stomach look more like your intestine or your small intestine look more like your stomach?

Erin Allmann Updyke

Yes!

Erin Welsh

That's bizarre. I love it.

Erin Allmann Updyke

So bizarre. It is fascinating. And it's completely different mechanisms, right. Like in one you're ending up with hypersecretion of acid, in one you're ending up with hyposecretion of acid, in both you end up with ulcers and in one you end up with cancer.

Erin Welsh

And that's the gastric.

Erin Allmann Updyke

The gastric, yeah.

Erin Welsh

Okay so can we just do terminology really quickly cause I read so many different words in front of ulcer.

Erin Allmann Updyke

Absolutely.

Erin Welsh

So there's peptic, there's duodenal, there's gastric. And is peptic just an umbrella term for stomach ulcer?

Erin Allmann Updyke

I believe so, yeah. Peptic ulcer disease is just you've got an ulcer somewhere around your stomach. A duodenal ulcer is an ulcer in your duodenum, so that's the first part of your small intestine. Those ulcers have a very, very, very low risk of ever developing cancer, you basically never get cancer in your small intestine for whatever reason, it's very rare. They can erode all the way through and then cause massive bleeding but you don't tend to get cancer in your small intestine. Gastric ulcers are an ulcer in your stomach and those do have a pretty high rate of converting into gastric cancer.

Erin Welsh: Okay. Okay, I think I've finally got the location and the umbrella terms down.

Erin Allmann Updyke: Yeah. It's a lot of words. Yeah. So that's how they cause disease. We know very little comparatively about H. pylori, less than I expected quite honestly.

Erin Welsh: Well it's a pretty recent discovery.

Erin Allmann Updyke: It's true, it's true.

Erin Welsh: Okay so if you are infected and you are showing symptoms, what are the symptoms or signs that you experience if you have peptic ulcers or gastritis or whatever else? Is there a difference between the ulcers and the symptoms?

Erin Allmann Updyke: Yeah it's a great question. So you can't tell the difference between something like gastric cancer and just peptic ulcer disease based on symptoms alone because the symptoms are actually very similar if not exactly the same.

Erin Welsh: Oh my god, great. So you could be like, 'Is this an ulcer or cancer?' WebMD might be right. (laughs)

Erin Allmann Updyke: (laughs) Don't trust WebMD on this, let me tell you. But the symptoms include things like a burning stomach pain. So people with peptic ulcer disease might often say they have acid reflux.

Erin Welsh: Okay.

Erin Allmann Updyke: Right so you might have like a burning in your sort of substernal region. You might have a feeling of fullness or a lot of bloating in your stomach. You might have nausea or vomiting especially if you're vomiting something like blood, that's suggestive of something like peptic ulcer disease. Your face looks a little horrified at the concept.

Erin Welsh: Yeah vomiting blood, no.

Erin Allmann Updyke: Yeah. And then the other things that we get really concerned about if you have these type of signs are things like unexplained weight loss because maybe you're not eating as much because you have pain when you eat. So unexplained weight loss or appetite changes and then dark stools. Because what can actually happen is that those ulcers can cause bleeding and if you're not vomiting up the blood, it'll travel through your gastrointestinal tract and by the time it comes out in the stool it doesn't look like blood anymore, it just looks like very, very dark stools.

Erin Welsh: Right.

Erin Allmann Updyke: So if you've ever had a doctor as you are your stools dark? That's what they're asking about, is there secret blood in your stools.

Erin Welsh: Did you eat beets? No. (laughs) It's a little different.

Erin Allmann Updyke: (laughs) Isn't that an episode of Portlandia where they're... 'It's beets!'

Erin Welsh: Yeah. With Jeff Goldblum. It's the best. 'Is it beets?' (laughs)

Erin Allmann Updyke

Yeah. Okay, anyways.

Erin Welsh

Yeah, anyway.

Erin Allmann Updyke

Yeah so those are the symptoms and you can't necessarily distinguish, especially those more severe symptoms of peptic ulcer disease from gastric cancer just based on symptoms. So we do what's called an endoscopy which is when they put a camera down into your stomach and they take a look at the ulcer. If they find an ulcer then they can biopsy it and then figure out what's going on.

Erin Welsh

Okay is that usually the first step is an endoscopy if you have symptoms or do they do the breath test or what?

Erin Allmann Updyke

So the urease breath test is a test to check for H. pylori infection and yes, you can absolutely do that. So if you go to a doctor with symptoms of peptic ulcer disease it's very likely that they'll do a urease breath test. The other thing you can do is treat the H. pylori. So it is treatable, it's a little difficult to treat. There's three different medications that you give. First is a proton pump inhibitor which decreases acid production. Second is two different antibiotics and you take these for quite a long time, I think it's at least a few weeks of antibiotic treatment to clear that H. pylori infection. If your symptoms go away then it was all from the H. pylori and if they don't then they'll probably do follow up treatment. So yeah, that's H. pylori infection.

Erin Welsh

How interesting.

Erin Allmann Updyke

Yeah.

Erin Welsh

Wow.

Erin Allmann Updyke

It's a fun little bug, I think.

Erin Welsh

It's definitely got a lot of tricks up its sleeve.

Erin Allmann Updyke

It's got a lot of tricks and there's so many that we don't know yet which I think is so fun and interesting.

Erin Welsh

Yeah.

Erin Allmann Updyke

So Erin, how'd we get here? Where'd this thing come from?

Erin Welsh

Ugh, I can't wait to tell you.

Erin Allmann Updyke

Good.

Erin Welsh

But first a little break.

TPWKY

(transition theme)

Erin Welsh

I feel like there's this notion of ulcers and gastritis as being this modern disease brought on by this modern stressful work environment, acidic foods, lack of sleep, etc. But guess what?

Erin Allmann Updyke

What?

Erin Welsh

It's not.

Erin Allmann Updyke

It's old?

Erin Welsh

It's really old.

Erin Allmann Updyke

We've always had ulcers?

Erin Welsh

Actually kind of. So humans and H. pylori have been together for thousands of years.

Erin Allmann Updyke

Really?

Erin Welsh

So since before humans left East Africa over 50,000-70,000 years ago.

Erin Allmann Updyke

Holy cow.

Erin Welsh

Yeah. Which explains why there's such a huge proportion of the population that's infected, it's really just been with us. So researchers can actually see the traces of different waves of human migration in the genetic diversity of these H. pylori strains.

Erin Allmann Updyke

Stop it.

Erin Welsh

Yes!

Erin Allmann Updyke

I love it when we get to talk about human migration because of disease.

Erin Welsh

I know, it's really cool. So basically as a general rule with this, the most genetically diverse H. pylori strains are associated with the oldest migrations and the source population in East Africa when humans migrated out. And then the genetic diversity decreases with each migration and then distance and so on. So yeah, isn't that cool?

Erin Allmann Updyke

Yeah, I love it.

Erin Welsh

All right so we've got this evolutionary evidence of early human and H. pylori association and we've also got ancient writings about ulcers and gastritis. So gastric symptoms have been recorded for millennia dating back of course to Hippocrates, where would we be without Hippocrates?

Erin Allmann Updyke

Nowhere. Not on an episode of This Podcast Will Kill You.

Erin Welsh

Nope. So Hippocrates described epigastric burning, like indigestion and air swallowing, both of which are symptoms of gastritis.

Erin Allmann Updyke

Is air swallowing just burping?

Erin Welsh

Air swallowing is what was written.

Erin Allmann Updyke

Weird.

Erin Welsh

Maybe it's just burping, I don't know. And around the same time as Hippocrates there's an inscription carved on a pillar at the Temple of Asclepius at Epidaurus that might be describing how to perform surgery on a gastric ulcer.

Erin Allmann Updyke

Ooh!

Erin Welsh

Quote: "A man with an ulcer in his stomach. He incubated and saw a vision. The gods seemed to order his followers to seize and hold him that he might incise his stomach. So he fled but they caught and tied him to the door knocker. Then Asclepius opened his stomach, cut out the ulcer, sewed him up again, and loosed his bonds. He went away whole but the chamber was covered with his blood."

Erin Allmann Updyke

What? What on earth?

Erin Welsh

(laughs) One star.

Erin Allmann Updyke

That's just inscribed on a pillar at a temple?

Erin Welsh

Yeah I don't-

Erin Allmann Updyke

Just the story of we're gonna do surgery on this guy against his will?

Erin Welsh

I don't know but we should add that to our TPWKY-

Erin Allmann Updyke

Take a picture of this?

Erin Welsh

Take a picture of this and also our personal vacation list.

Erin Allmann Updyke

Oh, yes! 100%.

Erin Welsh

Yeah. So we also, in addition to this pillar, we also have a mummy dating from a little bit after this around 167 BCE from the Western Han Dynasty that appears to have a peptic ulcer. We don't know if it was caused by *H. pylori* but yeah, definitely seems possible. In a mummy.

Erin Allmann Updyke

Wow!

Erin Welsh

Isn't that cool?

Erin Allmann Updyke

That's so cool that mummies are preserved so well that you can see something like that in the tissue.

Erin Welsh

I know. So about 1000 years after that we get a bit more specific when Avicenna wrote about how some of these painful or uncomfortable symptoms appear after you eat. He even went as far to suggest that the pain, heartburn, and thirst felt by some people were all caused by a gastric ulcer. Okay then in the late 1500s, so about 500 years after Avicenna described this, the first gastric ulcer was definitely described by the Italian physician Marcelo Donati. During this time anatomical descriptions from dissections of human cadavers were getting super popular and so people were starting to take note of the inflammation and ulceration of the mucosa in their cadavers. I didn't see anything about numbers through the ages in regards to the prevalence of gastric ulcers, I think that would be a really hard thing to estimate especially since it's been with humans since humans have been humans basically.

Erin Allmann Updyke

Forever, yeah.

Erin Welsh

Yeah, it was probably pretty prevalent at least. And also we can guess that it was pretty prevalent based on how many descriptions there were of it and how much people started to pay attention to it as cadaver dissection was a lot more popular. And then came the 1600s. Microscopy was developed and popularized by a couple of big names but probably the biggest name is Antonie van Leeuwenhoek.

Erin Allmann Updyke

Leeuwenhoek!

Erin Welsh

The impact of his technology and also how far it has come today really should get an episode of it's own, wouldn't that be fun?

Erin Allmann Updyke

Yeah for sure.

Erin Welsh

I would love a history of microscopy. But the important thing is that microscopes allowed people to see this whole new world which had been invisible to them up to this point. Essentially this led to the field of microbiology and molecular biology because people could finally start understanding how the pieces that made up living organisms fit together. Bacteria were described and started being blamed, rightfully so in some cases for many diseases and people started sticking everything they could find under these new lenses. And stomach tissue or stomach contents was no exception. And because bacteria live on basically every surface ever of course stomach contents looked to be chock-full of bacteria. Some of these microscope lookers became convinced that the bacteria were the cause of gastric inflammation and disease and a couple of these people had identified bacterial colonies in gastric ulcers and in the surrounding mucosa and went so far as to say that these bacteria were the cause of ulcers. So that was in 1875.

Erin Allmann Updyke

Whoa.

Erin Welsh

Yeah. They were like, 'Oh there's bacteria here, it seems to be in the lining, it seems to be associated with inflammation. This is what causes the ulcers.'

Erin Allmann Updyke

So then what happened? Why did it take us another 100+ years to figure it out?

Erin Welsh

Okay well I'll get to that. But yeah it did kind of... The link didn't necessarily become forgotten but it definitely was not as popular as some of the other leading hypotheses.

Erin Allmann Updyke

Interesting.

Erin Welsh

And so the late 1800s did see some other progress regarding bacteria and peptic ulcers and gastritis. For instance the pathologist Arnold C. Klebs who was son of Klebs for whom Klebsiella was named.

Erin Allmann Updyke

Yes!

Erin Welsh

He spotted a bacillus in the gastric glands which he noted were inflamed. And so this could be actually the first sighting of *H. pylori* infectious gastritis in humans. And then there was an Italian anatomist named Bizzozero who reported his findings of a spirochete-like organism in the stomach lining of several dogs that he studied which was probably a *Helicobacter* species. And remember those two guys who I just mentioned that first declared this link between gastric ulcers and bacterial infections. So even though mostly everyone else had dropped that concept, they were still convinced. And so by 1888 a ton of progress had been made in identifying different bacterial species and the diseases they caused just in general. So these guys started picking candidate microbes such as *Staph. aureus* and strep to see if they caused ulcers when injected into the stomach of various alb animals. And no surprise, they did! But that was sort of a problem, right, because if all of these different species could cause gastric ulcers, how do you distinguish between the types of ulcers and between whether this bacteria causes an ulcer or whether they're just general ulcer-causing bacteria?

Erin Allmann Updyke

Right.

Erin Welsh

After Letulle was able to induce ulcers in his guinea pigs, other people started to get interested and found that a whole bunch of bacterial species could lead to gastric duodenal ulcers. But there was still so much to be figured out and gastric ulcers were a tricky business because like I said, you can get ulceration with many different diseases and you can induce it with many different bacterial species. So how do you pinpoint exactly which species causes ulcers for sure rather than just these opportunistic infections?

Erin Allmann Updyke

Right. Or which does it in real life vs just if you inject it in the lab?

Erin Welsh

Exactly.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so really what became more popular in terms of why gastritis and peptic ulcers exist was that excess acid. That was it. That could be triggered by the ingestion of foods or drinks high in acidity, stress, etc. And this explanation resolved a few things that were maybe a bit more difficult to align with the because hypothesis. So often people who experienced ulcers didn't have symptoms all of the time. They had flare ups and then they would resolve after cutting back on certain foods or taking lots of antacids. And so during this time it was basically conventional wisdom that bacteria couldn't survive in the high acidity environment of the stomach, so if bacteria were found in the lesions they were from ingested food or the stomach was weakened enough to allow for these opportunistic invaders.

Erin Allmann Updyke

So it was like they were secondary, the ulcers were the primary rather than...

Erin Welsh

Yeah.

Erin Allmann Updyke

Interesting.

Erin Welsh
Yeah. And it wasn't so much that people weren't finding *H. pylori* in stomach tissue, a *Campylobacter*-like or curved rod bacteria had been reported as part of the gastric flora for decades but no one had had much luck in investigating them. In the 1950s someone named E. D. Palmer decided to take a closer look and he concluded that they were just normal commensals of the mouth. These curved rod bacteria were basically cast aside as unimportant which really held back the field probably for a few decades. All right, let's take stock of where and when we are. It's the early 1980s and the excess acid hypothesis was the prevailing one despite some reports in the late 70s of epidemic gastritis with hypochlorhydria, so low acid.

Erin Allmann Updyke
Low acid. Ooh!

Erin Welsh
(laughs) And findings of gram-negative bacteria in association with acute gastritis.

Erin Allmann Updyke
Oh my gosh, I'm getting really excited.

Erin Welsh
So the bacteria hypothesis is still hanging in there and one of its proponents is an Australian pathologist named Robin Warren who was working at the Royal Perth Hospital in Western Australia. Warren had a hunch that the gastric ulcers he had seen in patients over the years had bacterial origins. In 1981 he had written a letter to another doctor asking whether there were any gastroenterologists that wanted to work on uncovering this mystery with him. And this doctor just happened to show this letter to a young physician named Barry Marshall.

Erin Allmann Updyke
Barry!

Erin Welsh
Who had just started his gastroenterology fellowship term where he would have to come up with a research project to do.

Erin Allmann Updyke
Oh my gosh. Can you even imagine being like, 'Yeah it's my first year of fellowship and I need a project. Oh this sounds great!' And then it's *H. pylori*? Oh my gosh.

Erin Welsh
Yep. (laughs) It would be incredible. And I think it was. So from all of the different things that I read their personalities were perfectly suited to one another and to solving this problem.

Erin Allmann Updyke
That's so cute.

Erin Welsh
Because you have Robin Warren who seemed from what I read to be very methodical, very detail-oriented, very sort of like step 1, step 2, step 3. And then on the flip side of that you have this young sort of energetic, impatient guy Barry Marshall and so they balance each other out really well. And they were both, I think most importantly, iconoclastic. They wanted to fight for this hypothesis because I think a quote or something, well I'm not gonna quote actually, cause I think that for Robin Warren he was most fascinated by the fact that these bacteria were somewhere they shouldn't be.

Erin Allmann Updyke
Yeah.

Erin Welsh
And Barry Marshall wanted this opportunity to prove everyone else wrong.

Erin Allmann Updyke
Of course.

Erin Welsh
So it was just the perfect combination of things.

Erin Allmann Updyke

I love it.

Erin Welsh

Yeah. Okay. Marshall decides to join this project and neither of them had strict backgrounds in microbiology so they decided to say who cares, we're gonna try to do this anyway, we're gonna isolate and culture this Campylobacter-like bacterium that Warren had found in so many of his patients. I also wonder a bit about whether not having that microbiology or gastroenterology-specific background probably helped them a bit too, sort of not having those preconceived notions or the dogma that are so pounded into you during particularly research training.

Erin Allmann Updyke

Exactly. Right. Yeah you haven't already been sort of indoctrinated or ingrained on any one specific belief so you have this option to just explore all these different possibilities. Yeah.

Erin Welsh

Yeah. Thinking outside the box is much easier when you don't know the shape of the box that you're in.

Erin Allmann Updyke

Totally, yeah.

Erin Welsh

In any case they started their microbe hunt, not necessarily starting out saying that these bacteria caused ulcers but more, 'Hey, look what we found, it's a new bacterial species that can survive in the gut and maybe it has some links to gastritis and inflammation.' But saying you're going to isolate and culture an undescribed bacterium is quite different than actually doing it as they both learned. Culturing something new can be a bit of a tricky game. You have to figure out or know the right culture formula to use and the right settings for optimal growth. And when something is as extreme as something that can live in your stomach's acidic environment, that's a difficult place to start.

Erin Allmann Updyke

Yeah.

Erin Welsh

So after months of trying to culture isolates from gastritis patients and not getting anything, they may have started to lose a little hope. But then a fortunate accident occurred, as these things do seem to happen. It turns out that the lab tech who was responsible for culturing the isolates and checking on those cultures was throwing away the plates or broth after two days.

Erin Allmann Updyke

Oh.

Erin Welsh

This was happening at a hospital. A hospital is a busy place, it tends to be chaotic, there's a lot of other epidemics and things going through the lab so there really wasn't room for dozens of stomach bacteria culture plates to just hang around. But on a particularly busy weekend, Easter weekend in fact, the tech didn't have enough time to look at the plates after the usual two days so he left them over the weekend until Tuesday, 5 days after the biopsy. And when he went back to check on the culture, boom, colonies were present.

Erin Allmann Updyke

They were just slow!

Erin Welsh

They were just slow.

Erin Allmann Updyke

Little babes. They're like, 'Give me some time!'

Erin Welsh

Yeah. (laughs) I'm growing here! So these bacteria had probably been in all or at least the vast majority of those samples but they just needed a little bit longer to incubate. So now that Marshall and Warren could culture these bacteria, they could do so many things. They could find out what antibiotics could be used against it, try to develop an animal model of infection, try to find out what these bacteria were related to, and most importantly try to find out what these bacteria did in the stomach. So they decided to test 100 patients to see if the bacterium was present and to look for patterns of infection or any sort of disease state. And they found that all patients with duodenal ulcers had the bacterium. Not conclusive but definitely suggestive.

Marshall and Warren then started to develop a hypothesis. These bacteria cause gastritis and then gastritis leads to ulcers. People could have recurrent ulcers because their immune system would be stronger at various points or whatever but the bacteria would always be there so it never went away completely. And this also explained why earlier trials of physicians treating their gastritis patients with antibiotics saw a reduction in acid and symptoms. They tried to publish some of their findings in The Lancet in a letter and as an abstract at an annual meeting of the Gastroenterological Society of Australia but faced difficulty and rejection. Yeah. The Lancet couldn't get reviewers to agree on whether their findings were important or whether their conclusions were true and the Gastroenterological Society of Australia just flatly completely rejected their abstract. They were like, 'We received 67 submissions and we could only accept 56 this year. We're sorry we couldn't get yours.'

Erin Allmann Updyke

Was that actually the numbers?

Erin Welsh

Those were the numbers.

Erin Allmann Updyke

(laughs)

Erin Welsh

Why did they have to point out how many there were?

Erin Allmann Updyke

Why 56?

Erin Welsh

That just seems unnecessarily harsh.

Erin Allmann Updyke

Can you not just put up a couple extra boards to tack your poster on? I mean goodness.

Erin Welsh

I know, right? Seems rude. So the bacteria hypothesis seemed to fit with so much of what was known about ulcers but this concept met with a ton of resistance among doctors, many of whom would dismiss the bacteria as being opportunistic, only able to establish after the stomach was already weakened. And they would argue that if this bacteria actually caused disease the link would've been made a long time ago. It's ridiculous.

Erin Allmann Updyke

That's so silly. Yeah.

Erin Welsh

Yeah. I mean after all it had been observed in the stomach for ages so it should've been known by now. Things weren't always civil and there was a lot of rude or dismissive comments made behind Marshall and Warren's backs and many did not take them seriously as not having official microbiology or gastroenterology credentials. Then the ulcer drug business which was one of the biggest in the 1980s wasn't exactly in support of this notion, something I never thought of before reading this article. People with gastritis or ulcers were spending a little bit of money everyday on the drugs and they were often long term if not lifetime customers.

Erin Allmann Updyke

Oh yeah, yeah.

Erin Welsh

So if you could cure those conditions with a course of antibiotics, boom, the industry would be devastated.

Erin Allmann Updyke

Yeah.

Erin Welsh

So they spent a bunch of money doing research trying to prove that ulcers were not caused by bacteria.

Erin Allmann Updyke

Shocking.

Erin Welsh

Right? Even though the research was sound, Marshall and Warren had to demonstrate the cause and effect of the bacteria and ulcer, that the bacteria caused gastritis and ulcers, not that the ulcers paved the way for the bacteria. But they couldn't get the bacteria to infect any animal models so likely you heard in our firsthand account at the beginning of the episode, Barry Marshall took it upon himself to take a swig of the bacterial culture from a 66 year old non-ulcer dyspeptic man after first establishing Marshall himself had no gastric ulceration or inflammation. Within less than two weeks all of those symptoms appeared and the final confirmation came in the form of an endoscope. The infection seemed to more or less resolve on its own for Marshall but the putrid breath that's characteristic of this disease remained.

Erin Allmann Updyke

Ew.

Erin Welsh

So his wife was like, 'If you don't take antibiotics to get rid of this, you have to leave the house.' (laughs) So he took antibiotics and got rid of it.

Erin Allmann Updyke

But it worked, so.

Erin Welsh

It worked. And so Marshall, we have two actually, or at least two that I could find. So Marshall's self inoculation was followed up by another Australian guy named Morris who did the same.

Erin Allmann Updyke

Why only Australians? They're all just like Steve Irwin, they're like, 'I'm just gonna go for it!' (laughs)

Erin Welsh

(laughs) And progress has been made. But this guy, poor guy was not as fortunate as Marshall cause it took him 5 years for his gastritis to resolve even with treatment. So don't try this at home.

Erin Allmann Updyke

No, do not.

Erin Welsh

Eventually people started coming around to the idea, especially in Australia and doctors started to use antibiotics to treat patients they would have otherwise done surgery on to remove part of the stomach or the intestine.

Erin Allmann Updyke

Ugh.

Erin Welsh

Yeah. Of course they saw positive results. But other places were a lot slower to try out the treatment and that's not surprising, like I can't really fault them for that. Giving antibiotics willy nilly is not a good idea even if you have strong suspicions they might work. And so the study had to be repeated there, all over with the drugs available and ideally using a double blind trial where both those administering the drugs and those getting the drugs didn't know whether they were giving/being given treatment of placebo.

Erin Allmann Updyke

Right.

Erin Welsh

And the results were clear. Gastritis and ulcers could be healed by antibiotics. It became the guideline for treatment in many places and I can imagine it must have felt really good to have that sort of vindication even if it came with a several year delay. Barry Marshall wasn't done yet though, he helped to develop the breath test for H. Pylori.

Erin Allmann Updyke

Cool.

Erin Welsh

Yeah and that was really wonderful cause that meant that people didn't necessarily have to have endoscopies which were uncomfortable and cost a lot of money, particularly if you're in the U.S. and you have to pay for most everything.

Erin Allmann Updyke

Right. Plus you can do it a lot easier, you don't need specialized equipment, you don't need specialists, you just breathe.

Erin Welsh

Yeah, it's a really cool concept. I kinda love it.

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

In the two decades or so after their early 1980s letters in The Lancet, the world had definitely been changed by their discovery. Long term sufferers of gastritis and ulcers could find relief and the risk of developing stomach cancer could even be reduced a bit. So for their efforts, Barry Marshall and Robin Warren were awarded the Nobel Prize in Physiology or Medicine in 2005, exactly 100 years after Robert Koch was given the Nobel for his discovery of the tuberculosis bacterium.

Erin Allmann Updyke

Wow.

Erin Welsh

And I read that Robin Warren's wife, Win, predicted them getting the prize all the way back in like 1984 after their first Lancet pub was accepted.

Erin Allmann Updyke

Really?

Erin Welsh

Yeah, they went out to dinner and she was like, 'This is gonna get you the Nobel Prize'.

Erin Allmann Updyke

That's adorable on so many levels.

Erin Welsh

Yeah, isn't that?

Erin Allmann Updyke

I really love it.

Erin Welsh

(laughs) Okay. All right so with that I'll hand it off to you. Erin, tell me about the epi of Helicobacter pylori today.

Erin Allmann Updyke

Oh I can't wait to.

TPWKY

(transition theme)

Erin Allmann Updyke

Today it's estimated that right around half of the world's population is infected with H. pylori.

Erin Welsh

That's a lot of people.

Erin Allmann Updyke

That's a lot of people. So I found a recent paper that I will definitely post a link to because it has some nice maps, it's a meta analysis trying to really look at prevalence across different countries. And in developing countries the rate seems to be about 50%, in developed countries about 34%, and overall global prevalence at least according to this study was about 45%. So maybe it's going down a little bit from the numbers that we see cited most often.

Erin Welsh

Okay.

Erin Allmann Updyke

But obviously not every person infected with H. pylori is going to get gastric cancer or even peptic ulcer disease and there's a lot of research that's being done into the mechanisms of how H. pylori causes disease. And one of the big thoughts is that it's virulence of the strain of H. pylori.

Erin Welsh

Okay.

Erin Allmann Updyke

So there's a lot, like you said, there's a lot of diversity across H. pylori, there's a lot of different strains and some of them are more virulent than others, some produce more inflammation and it tends to be that those that produce more inflammation are associated with higher risks of cancer. And it also could just be individual genetics. So if you are a person who's genetically predisposed to cancer and you happen to get an H. pylori infection, then your risk of cancer might be additionally increased.

Erin Welsh

Okay.

Erin Allmann Updyke

But those are small studies in their infancy, we don't really know who is going to get cancer if they have an H. pylori infection and who isn't at this point.

Erin Welsh

Right.

Erin Allmann Updyke

So yeah. I found something really interesting in one paper that I'll link to where they talked about hookworms.

Erin Welsh

Ooh!

Erin Allmann Updyke

They talked about helminths and people are saying maybe infection with helminths, which we know can modulate the immune system, can reduce gastric inflammation and reduce the risk of cancer. So if you're coinfecting with H. pylori and helminths maybe your risk is less of getting gastric cancer.

Erin Welsh

Hold on, first of all that's bizarre.

Erin Allmann Updyke

It's bizarre.

Erin Welsh: Second of all, didn't we learn that having chronic infection with helminths creates an inflammatory state which often leads to an increased risk of cancer generally speaking?

Erin Allmann Updyke: Totally does, yeah.

Erin Welsh: So I don't understand.

Erin Allmann Updyke: There's not evidence that this is true in humans. It does seem to work in animal models.

Erin Welsh: Okay.

Erin Allmann Updyke: Who knows? It decreases your risk of gastric cancer but increases your risk of colorectal cancer? I don't know. (laughs)

Erin Welsh: (laughs) I mean you lose if you do, you lose if you don't.

Erin Allmann Updyke: Right? We never win.

Erin Welsh: Yeah.

Erin Allmann Updyke: The bacteria always win.

Erin Welsh: That's gonna be on the gravestone of humanity.

Erin Allmann Updyke: Yeah. So in terms of gastric cancer, I thought people might be interested in some gastric cancer stats since that's kind of the most serious outcome of H. pylori infection.

Erin Welsh: I'm definitely, yeah.

Erin Allmann Updyke: Depending on what source you read, gastric cancer is either the second or third leading cause of cancer death.

Erin Welsh: Really?

Erin Allmann Updyke: Yes.

Erin Welsh: Wow!

Erin Allmann Updyke: I know. I didn't realize that it was so high either. So the first is lung cancer.

Erin Welsh: Okay.

Erin Allmann Updyke: That's the number one cancer diagnosis and the leading cause of cancer death. And then the most recent stats that I saw actually had colorectal cancer causing more deaths than gastric cancer at least in this last year.

Erin Welsh: Okay. And this is globally?

Erin Allmann Updyke: This is globally, yeah, worldwide.

Erin Welsh: And what numbers are we talking about?

Erin Allmann Updyke: Great question. According to WHO there were 1.03 million new cases of gastric cancer diagnosed in 2018, 1 million new cases.

Erin Welsh: 1 million new cases in one year.

Erin Allmann Updyke: In one year. And that's estimated.

Erin Welsh: Right.

Erin Allmann Updyke: And 783,000 deaths.

Erin Welsh: Oh my goodness.

Erin Allmann Updyke: I know! It's really high. For comparison lung cancer, which is number one, 2.09 million cases, 1.76 million deaths.

Erin Welsh: Okay so similar, that's very interesting of the new cases and the death ratio is very similar with those.

Erin Allmann Updyke: Yeah. We are, despite so much, not good at treating most cancers.

Erin Welsh: Yeah, seems like we have a long way to go.

Erin Allmann Updyke: Yeah the death rates for cancers like gastric cancer and lung cancer really have not decreased over recent decades, it's very, very interesting actually.

Erin Welsh: It's alarming.

Erin Allmann Updyke: Yeah. But the overall rates of diagnosis of gastric cancer do seem to be decreasing and it's thought that this is due to a number of different things but treatment of H. pylori is really high on the list of things that we think have helped to decrease the incidence of gastric cancer. So that's pretty exciting.

Erin Welsh: That's really cool. Thanks again to Marshall and Warren.

Erin Allmann Updyke: Marsh! Marsh and War.

Erin Welsh: By the way can I put in a quick plug for the Nobel museum in Stockholm?

Erin Allmann Updyke: Yes, tell us all about it, you just visited.

Erin Welsh: I was just there! First of all Stockholm is amazing and the museums are incredible and everything about it is a wonderful place and I love it.

Erin Allmann Updyke: Number one, ABBA museum. Number two, Nobel museum. Is that right?

Erin Welsh: Yeah probably in that order. (laughs) And yeah so they have some cool little exhibits on these two, on Marshall and Warren, and they have the tube from which Marshall drank the inoculate to infect himself.

Erin Allmann Updyke: Oh my gosh, I get so excited by things like that.

Erin Welsh: Oh it was thrilling, I just stood there and I was like, 'I don't care if I'm blocking people, I need to see this.' So I took a picture.

Erin Allmann Updyke: Do you have pictures? Good.

Erin Welsh: Yeah I'll definitely post it on social media.

Erin Allmann Updyke: Excellent. Oh I can't wait. Yeah. Oh I love those kind of museums, they're so fun.

Erin Welsh: They are so fun. Okay sorry, I totally interrupted you.

Erin Allmann Updyke: No that's okay.

Erin Welsh: So what's going on with research or more preventative things for gastric cancer and peptic ulcers in general?

Erin Allmann Updyke: Yeah so there's a vaccine. What!?

Erin Welsh: That's awesome.

Erin Allmann Updyke: It's awesome. It's super exciting. It's undergone at least phase 3 clinical trials which is usually sort of the last phase before things get licensed. In China it's an oral vaccine but I know that I found earlier studies on injectable vaccines as well but I think in this case an oral vaccine makes so much sense because first of all it's a GI bacteria, so giving something orally means that the vaccine is producing immunity in the cells that are actually going to be exposed to the bacteria, so it's a great idea.

Erin Welsh: Right.

Erin Allmann Updyke: But oral vaccines are also a lot easier to administer, you don't have to have specialized medical personnel. So I love that it's an oral vaccine. And the efficacy that they found so far is about 70% effective in preventing infection with H. pylori which is super exciting.

Erin Welsh: That's fantastic.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: So I'll post a link both to the phase 3 trial paper and then there's also a really cheeky paper, I wanna read you the title of it. It's so cute. It's called 'At Last: Vaccine-Induced Protection Against Helicobacter pylori'.

Erin Welsh: At last.

Erin Allmann Updyke: At last. So I'll post both of those on our website as well so that you can read more about it. But yeah there is a vaccine which is very exciting. I'm not sure how much longer it will take to get to market. In China where you have higher prevalence of H. pylori than you do in the states and how long it'll take to get it in the states. But it's pretty huge and very exciting.

Erin Welsh: Yeah I want that vaccine.

Erin Allmann Updyke: (laughs) Just in case?

Erin Welsh: Do you feel like every time you get a vaccine like a bit more superhuman? Like a superhero?

Erin Allmann Updyke: I think we've talked about this, yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: I could totally see that.

Erin Welsh: Yeah.

Erin Allmann Updyke: Yeah. I also think this is so exciting because we are learning more and more about the associations with infectious disease and cancer.

Erin Welsh: Yes. And other chronic diseases.

Erin Allmann Updyke: Yes! And being able to produce a vaccine that literally prevents cancer, are you kidding me? That's amazing.

Erin Welsh: I know. It's incredible. And I think that the number of unexplored links keeps growing and those that are being explored also keeps growing and I think that's just going to be one of the big futures of medicine is finding these links between infectious disease and chronic disease.

Erin Allmann Updyke: Absolutely. I agree. We're biased cause we love infectious disease but it's also true.

Erin Welsh: Yeah but no, it's huge and also really important if we can lessen some of the burden of disease around the world.

Erin Allmann Updyke: Absolutely, yeah. So yeah that's H. pylori.

Erin Welsh: Wow. I really liked this one.

Erin Allmann Updyke: Me too, it was really fun to do.

Erin Welsh: I had a great time researching it and talking about it. It was fun. And learning about it.

Erin Allmann Updyke: Yeah.

Erin Welsh: Okay. All right so should we do sources?

Erin Allmann Updyke

Let's do it.

Erin Welsh

Okay. So I had a bunch of different articles that I read and I'll post all of these but two I wanna shout out. So one was called 'A Century of Helicobacter pylori' and that was by Kidd and Modlin. And also I leaned very heavily on this incredibly thorough and long interview of Barry Marshall which is what our firsthand account was extracted from. So we'll definitely post all of those and the other articles as well.

Erin Allmann Updyke

Excellent. Yeah you can find all of those on our website thispodcastwillkillyou.com under the EPISODES tab. You can find all of our sources from this episode and every episode.

Erin Welsh

What about you, any sources?

Erin Allmann Updyke

I mean I shouted out the one and I'll post links to all of them, so.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

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

Erin Allmann Updyke

And thank you all of you listeners. We love telling you about disease and we love hearing from you about your diseases and the diseases you want us to cover eventually, we have the longest list ever and it just keeps growing. And thanks, we love you.

Erin Welsh

Yeah. Thank you. Okay well with that, wash your hands.

Erin Allmann Updyke

You filthy animals!