Erin Welsh	By the time paramedics removed Brianne Kiner from the ambulance and wheeled her into the ER at Children's Hospital, Suzanne Kiner was doing all she could to hold herself together. Brianne was writhing in pain and the diarrhea just kept coming. So did the blood. Suzanne was afraid to leave Brianne's side, it looked and sounded like her little girl was dying. Her breathing was rapid, she had deep pain in her chest, her urine output had practically disappeared. Even her mental condition was deteriorating and she was slurring her words when she tried to speak. When the hospital transferred Brianne to the ICU for round the clock observation, Suzanne wanted answers.
	The doctors informed her that Brianne's stool culture had come back and definitely showed the presence of E. coli O157:H7 and her symptoms suggested she had hemolytic uremic syndrome. Shortly after arriving in the ICU Brianne suffered a seizure and stopped breathing. Doctors scrambled to resuscitate her. They gave her Dilantin intravenously along with phenobarbital. Tubes were inserted in her chest. By the time doctors emerged to give Suzanne an update, Brianne was in a coma. Suzanne had trouble swallowing. She wanted to scream but all she could do was cry.
TPWKY	(This Podcast Will Kill You intro theme)
Erin Allmann Updyke	Whoa.
Erin Welsh	Yeah.
Erin Allmann Updyke	Did she survive?
Erin Welsh	She did.
Erin Allmann Updyke	Phew.
Erin Welsh	Yes. So that firsthand account is pieced together from a book called 'Poisoned: The true story of the deadly E. coli outbreak that changed the way Americans eat' by Jeff Benedict and it's about the outbreak of E. coli O157 that you're going to hear a lot more about in 1993. And Brianne was one of the children who was infected with E. coli and she did survive but she has had a lot of lingering problems because of this infection. 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 E. coli.
Erin Welsh	E. Coli.
Erin Allmann Updyke	Do you know I always raise my hands up when I say the disease that we're talking about and no one can see except you.
Erin Welsh	But I appreciate it.
Erin Allmann Updyke	Thank you.
Erin Welsh	So.

Erin Allmann Updyke	So.
Erin Welsh	Today's a big one.
Erin Allmann Updyke	It's massive, Erin. Oh my gosh.
Erin Welsh	I did not realize that when we were like, 'lEt's do E. Coli!'
Erin Allmann Updyke	Yeah. We'll get into it, it's so big. It's so big. It's gonna be a short episode though, don't worry.
Erin Welsh	(laughs) Well to help us through this episode I think it's time for quarantinis.
Erin Allmann Updyke	I think it's quarantini time! I have my first real quarantini in 11 months.
Erin Welsh	Yay!
Erin Allmann Updyke	Which feels quite exciting. What are we drinking today?
Erin Welsh	We are drinking The Cookie Doughn't. And in The Cookie Doughn't, it's actually quite delicious.
Erin Allmann Updyke	It is, it's really tasty.
Erin Welsh	It is dark rum and chocolate liqueur, amaretto, ice cream, ice, chocolate syrup, you blend it and then you pour it into a glass that is rimmer with chocolate and crushed cookies.
Erin Allmann Updyke	It's so tasty.
Erin Welsh	It's really good!
Erin Allmann Updyke	So good.
Erin Welsh	It's like too good, I think.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah.
Erin Allmann Updyke	We'll post the full recipe for this quarantini as well as our nonalcoholic placeborita on all of our social medias and our website so you can drink along with us.
Erin Welsh	Yes. And it's called The Cookie Doughn't for reasons that I'm sure you'll go into, Erin.
Erin Allmann Updyke	Oh yeah, we'll talk all about it.
Erin Welsh	And I'm sure that everyone here can guess.
Erin Allmann Updyke	You can guess, cookie dough doughn't.

Erin Welsh	Yeah. It works better if you read it, I think.
Erin Allmann Updyke	It does. (laughs)
Erin Welsh	(laughs) We didn't think this one through.
Erin Allmann Updyke	It's still great.
Erin Welsh	I like it. Okay so speaking of cookie dough and doughn'ts and whatever. Erin, should we just get started?
Erin Allmann Updyke	I think so. We have merch, check it out on our website, click on MERCH, etc, business. Let's do it.
Erin Welsh	All right, cool.
Erin Allmann Updyke	We'll take one quick break.
TPWKY	(transition theme)
Erin Allmann Updyke	All right, E. Coli. I wrote that maybe this is the most important bacterial species we'll ever talk about but I feel like that's overkill.
Erin Welsh	Well I feel like a lot of people might have opinions about that.
Erin Allmann Updyke	They probably would so I'm not gonna make that statement, even though I just said it.
Erin Welsh	(laughs) But it is massively important.
Erin Allmann Updyke	It is massively important. The thing about it is that E. coli is everywhere. It's everywhere and it's everything and it causes almost every type of illness that you can think of and we also use it in the lab to study every other disease pretty much. E. coli is like the lab bacteria.
Erin Welsh	Oh and not just every other disease but life itself and how life works.
Erin Allmann Updyke	Yes. Like literally, that's not an exaggeration.
Erin Welsh	Yeah, no, I'm gonna talk about it.
Erin Allmann Updyke	Oh excellent. I can't wait. Cause I'm not gonna talk about it.
Erin Welsh	Oh good.
Erin Allmann Updyke	But we will get some of the basics out of the way first and then we'll talk about the diseases that E. coli causes, cool?
Erin Welsh	Perfect.

Erin Allmann Updyke	Okay. So E. coli is a bacterium, it's a gram-negative bacterium so it's pink when we stain it on the microscope. That's what it means for the purposes of this podcast.
Erin Welsh	(laughs) That's really the important takeaway is that it's a pink bacterium.
Erin Allmann Updyke	Yes, it's a pink little bacterium if you're gonna paint it, that's what color you should choose. It's rod-shaped so it looks like a little Tic Tac, okay.
Erin Welsh	Yeah.
Erin Allmann Updyke	You have it in your mind now. For the most part in our bodies E. coli is a normal and important component of our gut microflora. It's always there and it's supposed to be there, it's part of a healthy microbiome. But this is This Podcast Will Kill You so that's not the E. coli that we're gonna talk about today.
Erin Welsh	Nope. Although we could talk a little bit about those guys.
Erin Allmann Updyke	Sure, sure. So Erin, when you think of the E. coli that makes you sick, what do you think of?
Erin Welsh	You mean like what symptoms and signs and stuff?
Erin Allmann Updyke	Yeah.
Erin Welsh	Oh I would say after reading that firsthand account I would say bloody diarrhea?
Erin Allmann Updyke	Bloody diarrhea.
Erin Welsh	And then also whatever HUS is but I was hoping you were gonna tell me about it.
Erin Allmann Updyke	Don't worry, I'm going to.
Erin Welsh	Okay.
Erin Allmann Updyke	Bloody diarrhea is the thing that probably comes to most people's minds when they think of E. coli first and that's because of just like you said, that O157 outbreak which we'll talk about, you'll talk about, etc.
Erin Welsh	Yeah.
Erin Allmann Updyke	The diarrheagenic, that's their official name, the diarrheagenic E. coli are probably the most infamous of the E. colis that cause disease.
Erin Welsh	For sure.
Erin Allmann Updyke	But they're not the only ones. So here's how I'm gonna structure this biology section cause E. coli is so big. First we're gonna talk really quickly about what makes the pathogenic E. coli strains different than all of the normal E. coli or all of the nonpathogenic E. coli that live in our gut happily.
Erin Welsh	Okay.

Erin Allmann Updyke	And then we'll talk about the non-diarrheagenic E. coli just briefly and then we'll talk poop. Cool?
Erin Welsh	Oh great. Love talking poop.
Erin Allmann Updyke	(laughs) Me too. It's one of my favorite things to talk about. Okay so the main difference between the E. coli hanging out in our guts happily right not and the E. coli that made that little girl in the firsthand account massively sick are what are called virulence factors. We've talked about these before, right?
Erin Welsh	I think so, sure.
Erin Allmann Updyke	I think so. Well if you don't remember what a virulence factor is it's basically just stuff, things.
Erin Welsh	Oh yeah, that clears it up.
Erin Allmann Updyke	Things that a bacteria or a virus or a parasite makes that helps it's to cause disease in an organism. So let me give you some examples. Sometimes virulence factors allow for a bacteria to attach to certain cells and colonize a new area in a host that they wouldn't be able to before.
Erin Welsh	Oh yeah, okay. Like little velcro strips.
Erin Allmann Updyke	Exactly, yeah. Little velcro strips. Sometimes it might be like a capsule, kind of like an armor that allows it to evade a certain part of our immune response. That could be a virulence factor. It could be an endotoxin that the bacterium produces that also allows it to evade the immune system or an exotoxin that it produces and sends out into our body and actually causes damage to other cells. Cool?
Erin Welsh	Okay.
Erin Allmann Updyke	So virulence factors are literally anything that a pathogen can make that makes it more virulent, aka makes you get sicker. Cool?
Erin Welsh	Sounds reasonable.
Erin Allmann Updyke	So these subtypes of E. coli that are called different pathotypes because they are pathogenic collectively have a couple of main virulence factors that allow them to get us sick. And those two things are different types of adhesins which allow them to adhere and colonize new areas, and toxins. Those are the two things that E. coli tends to use to be able to invade new organs in our body and make us sick in new ways. So another important thing about the virulence factors in E. coli is that a large number of them are on plasmids.
Erin Welsh	Right.
Erin Allmann Updyke	Which we've talked about before I think, right?
Erin Welsh	Oh, did we talk about it with cholera?

Erin Allmann Updyke	Maybe cause cholera definitely has plasmids. Anyways, plasmids are little round pieces of DNA that bacteria can move from one bacterium to another, they can like pass it off. And so basically this allows for E. coli to hand off virulence factors between different strains of bacteria.
Erin Welsh	Right.
Erin Allmann Updyke	Okay. That's the whole pathogenesis, that's how all of these E. coli have come to be is just little changes in their toxins or their virulence factors or their adhesins, whatever that allows them to make us sick. Okay so what kinds of ways can E. coli make us sick? So many different ways.
Erin Welsh	Yeah.
Erin Allmann Updyke	All right. The two main kinds of disease that you can get from E. coli besides diarrhea are urinary tract infections-
Erin Welsh	Oh yeah, okay.
Erin Allmann Updyke	Did you know that?
Erin Welsh	I think I did know that at one point, I don't know, it feels like a recovered memory.
Erin Allmann Updyke	Yeah. So these strains of E. coli are called UPEC. So many ridiculous acronyms with E. coli.
Erin Welsh	I know! I don't love acronyms.
Erin Allmann Updyke	UPEC is uropathogenic E. Coli.
Erin Welsh	Okay.
Erin Allmann Updyke	Okay. They're all like that, they're all like 'blah blah pathogenic E. Coli'.
Erin Welsh	So they call end in PEC?
Erin Allmann Updyke	Yeah, mostly all.
Erin Welsh	Great.
Erin Allmann Updyke	Sometimes they're like HECs. You'll see.
Erin Welsh	Heckin' E. coli.
Erin Allmann Updyke	Heckin' E. Coli. (laughs) That was funny.
Erin Welsh	(laughs) You sound surprised.
Erin Allmann Updyke	I liked it, it was good. Okay so the UPEC, the uropathogenic E. coli are strains of E. coli that are really good at attaching to our urinary tract walls, okay. So they have adhesins that allow them to do that and they are the most common cause by far of UTIs.

Erin Welsh	Huh. Yeah, okay.
Erin Allmann Updyke	Right? Like 80% of UTIs or something like that are caused by E. coli. And if you don't know what a UTI is, the symptoms generally are things like burning on urination, increased frequency meaning you have to pee way more often than normal, or urgency where you're like if I don't pee right now I'ma pee my pants.
Erin Welsh	So that sounds a lot like gonorrhea, Erin. (laughs) How are people going to distinguish between the two?
Erin Allmann Updyke	(laughs) So another thing that UPEC can cause is prostatitis.
Erin Welsh	Gonorrhea?
Erin Allmann Updyke	No but it is prostatitis and gonorrhea is another common cause of prostatitis actually. So that's if it goes up the urethra far enough to invade the prostate.
Erin Welsh	Okay.
Erin Allmann Updyke	But then these strains of E. coli can actually keep going up and then can also cause like pyelonephritis which is kidney infections as well.
Erin Welsh	Oh yikes.
Erin Allmann Updyke	Which is you can imagine more serious than only a bladder infection. Okay. So we covered three already, we've got bladder infection, kidney infection, prostate infection, all from UPEC. Then we have the MNEC. I don't know if you're supposed to say it like that but these are the meningitis-associated E. Coli.
Erin Welsh	Oh that's right.
Erin Allmann Updyke	Yeah. So this is one of the most common causes of meningitis in neonates, so tiny babies.
Erin Welsh	Okay.
Erin Allmann Updyke	It can also cause meningitis in adults but it's much less common compared to other causes.
Erin Welsh	Why?
Erin Allmann Updyke	I think that just other bacteria are better at colonizing the meninges and so you'd have to be pretty sick already or have a route of entry. So these strains of E. coli are associated mostly with meningitis following a neurosurgical procedure in adults.
Erin Welsh	Oh, okay. Okay.
Erin Allmann Updyke	Yeah. But what's really scary is that in neonates this type of E. coli infection has a fatality rate of like 15-40%.
Erin Welsh	Wow.

Erin Allmann Updyke	Yeah, it's really gnarly. And it's also an extremely common cause overall, adults and children, of bacterial sepsis. So bloodstream infections.
Erin Welsh	Okay, right.
Erin Allmann Updyke	And that can actually be from any strain of E. coli, not only the UPEC or MNEC strains, you can have any way that E. coli gets into your blood, once it gets there, it's pretty good at establishing an infection.
Erin Welsh	Yikes.
Erin Allmann Updyke	Yeah. So those are collectively - you wanna know their acronym here?
Erin Welsh	Oh gosh, does it end in HEC or PEC or...?
Erin Allmann Updyke	Yeah it does.
Erin Welsh	What is it? Okay.
Erin Allmann Updyke	They're the ExPECs. (laughs)
Erin Welsh	(laughs) I can't, I can't Erin, I can't.
Erin Allmann Updyke	Those are the extraintestinal pathogenic E. coli, those ones we just talked about.
Erin Welsh	Oh yeah.
Erin Allmann Updyke	Cool?
Erin Welsh	Easy to remember, sure. ExPEC.
Erin Allmann Updyke	ExPEC.
Erin Welsh	ExPEC, UPEC, that's all we've learned so far?
Erin Allmann Updyke	MNEC.
Erin Welsh	Oh goodness, I can't. Okay, MNEC.
Erin Allmann Updyke	Okay. Now we get into the more fun ones.
Erin Welsh	Oh yikes.
Erin Allmann Updyke	Okay the EPECs. People are gonna hate me. So now were gonna talk about the ones that actually colonize your gut in a way that is bad, the enteropathogenic E. coli, the most famous of which we've heard a little bit about already and that is that enterohemorrhagic E. coli, EHEC.
Erin Welsh	Okay so EHEC is a form of EPEC?

Erin Allmann Updyke	Yeah, bra. It totally is. Do you wanna know what gets even worse though Erin? Even I, this is too much for even me. EHEC is also called STEC or VTEC.
Erin Welsh	Why?
Erin Allmann Updyke	Let me tell you why, I'm so glad you asked.
Erin Welsh	Oh no.
Erin Allmann Updyke	The enterohemorrhagic E. coli care the strains that cause bloody diarrhea, okay. Enterohemorrhagic, like 'hemorrhage' means bleeding out and 'entero' means your gut, okay. So that like a broad umbrella terms that encompasses a number of different strains of E. coli all of which end up with symptoms like bloody diarrhea. Some of those strains produce a toxin called Shiga toxin.
Erin Welsh	Oh yeah.
Erin Allmann Updyke	ST, STEC. Shiga toxin E. coli. Some other strains produce a toxin that's really, really similar to Shiga toxin that is called Shiga-like toxin.
Erin Welsh	Oh okay.
Erin Allmann Updyke	Or verotoxin.
Erin Welsh	Sure. So those two phrases are interchangeable and yet they still give rise to two different acronyms.
Erin Allmann Updyke	Three.
Erin Welsh	Oh I'm sorry yes, three.
Erin Allmann Updyke	Yeah. VTEC, STEC, EHEC. I think it's annoying so I just go with EHEC because it's the broadest one and it encompasses all of them. Cool?
Erin Welsh	I mean I'm just rolling with it.
Erin Allmann Updyke	Yeah, all right. So let's talk about what this actually does inside of your body. This Shiga toxin or Shiga-like toxin, it's the same toxin that produced by another bacteria, Shigella, which arguably might actually just be a subspecies of E. coli.
Erin Welsh	Okay yeah, so I'm glad. Yeah. I talk a little bit about it but yeah.
Erin Allmann Updyke	Yeah basically they are so closely related it might as well be a subspecies, it's also possible that E. coli O157 should actually be a Shigella.
Erin Welsh	Some E. coli strains should be Shigella and some Shigella strains should be E. coli is what I wrote.
Erin Allmann Updyke	Yes, 100%. Yeah, anyways.

Erin Welsh	That blew my mind by the way.
Erin Allmann Updyke	Yeah, yeah. So they all produce this toxin that the bacteria can then release that causes damage directly to the mucosa of your intestine. These bacteria tend to colonize in your large intestine, in your colon. And when they release this toxin they can cause perforation of your intestine, they can cause necrosis, so they can cause your colon to actually die in places. And this is what results in the bloody stools that you see in enterohemorrhagic E. coli infections.
Erin Welsh	Question about the stools unless you're gonna cover this in the poop section.
Erin Allmann Updyke	Oh we're in the poop section, girl.
Erin Welsh	Oh great, okay, okay. I thought so, I didn't wanna get my hopes up in case we weren't. So bloody diarrhea doesn't mean red blood in your poop.
Erin Allmann Updyke	Great question. It can and in this case it probably does.
Erin Welsh	Okay.
Erin Allmann Updyke	It all depends on where you're bleeding from.
Erin Welsh	Yeah.
Erin Allmann Updyke	So the higher up you bleed in your GI tract, the more black your stool is going to look when you poop it out.
Erin Welsh	Right.
Erin Allmann Updyke	The lower down you're bleeding, the more bright red this blood is going to be.
Erin Welsh	These STEC, VTEC, etc whatever ones that actually cause the hemorrhage EHEC, cause the hemorrhage in your gut, that can produce any shade of bloody diarrhea?
Erin Allmann Updyke	Yeah, yeah cause they colonize your colon and your colon is pretty big and large.
Erin Welsh	Okay.
Erin Allmann Updyke	So if they're colonizing closer to... Oh no, Erin. Oh, my anatomy. If they're colonizing closer to the left side where the outlet is then it might be more bright red blood. If they're colonizing closer to the start of your colon it might be a darker color.
Erin Welsh	Okay. In any case, seek medical attention.
Erin Allmann Updyke	Yeah bra.
Erin Welsh	Unless you ate beets the night before.
Erin Allmann Updyke	Unless it's beets. (laughs) I feel like we've had so many good title possibilities already.

Erin Welsh	I also feel like we've mentioned beets on a couple other podcasts or a couple other episodes before.
Erin Allmann Updyke	Probably. E. coli, unless it's beets.
Erin Welsh	(laughs) It's E. coli unless it's beets.
Erin Allmann Updyke	Okay.
Erin Welsh	Beets by E. coli. (laughs)
Erin Allmann Updyke	Beets by E. Coli. Okay so that's the damage that this toxin and that this bacteria causes in your colon where it's actually colonizing. But what's really, really dangerous about these enterohemorrhagic E. coli is that the toxin can actually leave the intestine and get into your bloodstream. If that happens it can make it all the way to the kidneys where it causes inflammation in the kidneys that can end up causing kidney failure.
Erin Welsh	Yikes.
Erin Allmann Updyke	And then what it also does is it causes damage in your small blood vessels that then leads to small clots forming inside of your blood vessels, like little teensy tiny clots that when your blood then passes over these clotted chunks in your blood vessels, it shears your red blood cells.
Erin Welsh	Oh my goodness.
Erin Allmann Updyke	Right. And so this is what's called a hemolytic anemia because your red blood cells are literally bursting open because they're traveling over these tiny micro clots.
Erin Welsh	Whoa.
Erin Allmann Updyke	And those clots are formed by platelets so now all your platelets in your blood are being used up. So the three main signs that you see are renal failure, kidney failure, this hemolytic anemia, and thrombocytopenia which means your platelet count is low. And that collectively is what's known as hemolytic uremic syndrome.
Erin Welsh	Oh! Okay.
Erin Allmann Updyke	What's that fun?
Erin Welsh	Wow! So I have a question.
Erin Allmann Updyke	Okay.
Erin Welsh	How does it benefit E. coli to produce this toxin in terms of their replication or in terms of their ability to colonize new areas? Like why do some strains produce this toxin and some don't? Does it give them some sort of fitness advantage?
Erin Allmann Updyke	That's a really, really good question. I don't fully know the answer to that but what I can tell you is that a lot of these strains of E. coli, especially like O157, are naturally found in the guts of ruminants like cows and sheep.

Erin Welsh	Okay.
Erin Allmann Updyke	So I wonder if it provides a fitness advantage in those environments in some way. Right, like the guts of cows are bananas, they have five stomachs and stuff so...
Erin Welsh	I know. What if the microflora is totally different in each one of them?
Erin Allmann Updyke	Oh it probably is. Ooh!
Erin Welsh	I know but like there's probably a study out there.
Erin Allmann Updyke	But we just haven't read it.
Erin Welsh	Isn't that fascinating?
Erin Allmann Updyke	Some veterinarian's gonna be like, 'You guys, let me tell you.' Tell us, we wanna know!
Erin Welsh	This is like old hat, yeah.
Erin Allmann Updyke	That's a really good question though. Because yeah, toxins are expensive for bacteria to produce.
Erin Welsh	Right.
Erin Allmann Updyke	So presumably in some way it has to be, you would think, because these strains are so prevalent you would think that yeah, it does cause some kind of fitness advantage probably. Great question. So yeah, that is the enterohemorrhagic E. colis, the most famous of which is E. coli O157:H7.
Erin Welsh	Let's just call it O157, that's what I do for most of...
Erin Allmann Updyke	Yeah. This is what causes outbreaks very often but it also causes tons of infection across the globe and in the U.S. that isn't outbreak-associated, so we actually often never know what the source of infection is. But in general you get sick between 1 and 3 days, you'll start having this diarrhea that's often bloody within 1 to 3 days after exposure although it can be as long as 10. And about 5-10% of people that get infected with EHEC will end up getting hemolytic uremic syndrome.
Erin Welsh	Wow, I didn't know it was that high.
Erin Allmann Updyke	The thing is that number varies a lot based on age. So in kids it's potentially even higher, especially in very young children but in adults that number is quite a lot less. So on balance. Yeah. So that's the enterohemorrhagic. There's ones last kind of poop that I'd like to talk about before we're done here.
Erin Welsh	Oh, wonderful.
Erin Allmann Updyke	So there's another strain of E. coli called ETEC.

Erin Welsh	Did we not talk about ETEC already?
Erin Allmann Updyke	No, we haven't. We've had EHEC and now we have ETEC.
Erin Welsh	Extraterrestrial E. coli.
Erin Allmann Updyke	Very, very good guess. So close. Enterotoxigenic. Okay?
Erin Welsh	Okay.
Erin Allmann Updyke	So enterotoxigenic.
Erin Welsh	Yeah. It has a toxin and it's in your guts and it's somehow different than Shiga toxin.
Erin Allmann Updyke	Yes! Exactly. That's exactly right. This is another kind of toxin and specifically this type of toxin is more similar to a toxin produced by Vibrio cholerae.
Erin Welsh	Oh!
Erin Allmann Updyke	Yeah. So it's not the same toxin but it's very similar, so you can imagine that the diarrhea that you have with this type is more similar to cholera diarrhea which is what, Erin?
Erin Welsh	Rice water stool.
Erin Allmann Updyke	Exactly. So this is a watery diarrhea, not a bloody diarrhea. Okay? Is that cool?
Erin Welsh	Yes. I mean cool is maybe not the word I would choose.
Erin Allmann Updyke	I think it's pretty cool. I mean it's actually not cool because ETEC as it turns out is the cause of what's often called traveler's diarrhea.
Erin Welsh	Oh!
Erin Allmann Updyke	Yes, that's ETEC. Which what that means is that ETEC is an extremely important cause of diarrhea in children in developing countries. So second only to like rotavirus and probably up there in competition with rotavirus for the most important diarrheal disease in the developing world.
Erin Welsh	Okay.
Erin Allmann Updyke	So it's a huge cause of morbidity and mortality and it's a watery diarrhea, so it's not bloody but you're losing so much water that you then can end up dying from dehydration.
Erin Welsh	Right, okay.
Erin Allmann Updyke	There are other enteropathogenic E. colis.
Erin Welsh	This is too big of a topic.

Erin Allmann Updyke	I know, were not going to talk about them cause quite honestly we don't know as much about them and we don't have time and etc. If you want all of the nitty gritty details of all these different pathotypes there was a great Nature review from 2004 that I read that goes into way too much detail and that will be posted on our website.
Erin Welsh	Great.
Erin Allmann Updyke	So that's the biology of E. coli, Erin.
Erin Welsh	Beautiful.
Erin Allmann Updyke	Thank you, thank you. I made it myself. So tell me how the heck did it get here? Where did this thing come from and why do some strains just wanna kill us?
Erin Welsh	Ugh, great questions. First let's take a little break.
TPWKY	(transition theme)
Erin Welsh	I think that for most people the words E. coli bring to mind these images that you kind of just went over, described, this writhing gut, bloody diarrhea, just doubled over in the bathroom trying to hang on. And a smaller subset may also think of E. coli's role as a model organism in the lab.
Erin Allmann Updyke	That's what I think of if we're being honest.
Erin Welsh	Yeah. Have you worked with E. coli before in the lab?
Erin Allmann Updyke	Yes, I used it during my master's a lot and also cause we use it as a water quality indicator, so I've worked with E. coli a lot actually in the past.
Erin Welsh	Right. Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	It's a stinky colonizer.
Erin Allmann Updyke	Yeah.
Erin Welsh	Does not smell good when you create those big cultures.
Erin Allmann Updyke	Smells so bad. (laughs)
Erin Welsh	(laughs) Its really bad. But I think that those two roles, you know this super pathogenic one and also this lab model organism account for a tiny amount of the amazing diversity of E. coli.
Erin Allmann Updyke	Ooh, cool!
Erin Welsh	Because E. coli is found all over the earth.

Erin Allmann Updyke	Yeah, bra.
Erin Welsh	Inside people and animals and stuff and also outside of them.
Erin Allmann Updyke	Which is why it makes for a terrible water quality indicator.
Erin Welsh	Right, yeah. Good point.
Erin Allmann Updyke	Yes, thank you.
Erin Welsh	And also they're incredibly numerous. So Carl Zimmer estimated in his book about E. coli which was great by the way, he estimated that there are about 100 billion billion E. coli on earth which is not a number I can comprehend and I don't know if anyone can comprehend it. Please let us know. These bacteria are among the top if not the very top most studied organisms on the planet. Research on E. coli has led to Nobel Prizes, to genetic engineering, to insights into evolution and cellular biology, how genes work, and there could really be an entire podcast series on the contributions of E. coli to our understanding of how life works. So let's start at the beginning and to do that we have to go so far back, so, so far back, before humans were even humans.
Erin Allmann Updyke	Yes.
Erin Welsh	Because E. coli has been with us for as long as we've been a species and way before and probably caused occasional food-borne illnesses during that long relationship. But until microscopy and microbiology merged, it's hard to pinpoint exactly what might've caused the fatal diarrhea of this or that person and be able to conclusively saw that it was E. coli. So this history is less 'these are the pandemics of E. coli' and more, yeah. More you're about to find out. So humans first learned about the existence of E. coli when in 1885 a German pediatrician named Theodor Escherich - which did we even say...?
Erin Allmann Updyke	Oh my god no because you know what, I can't pronounce it and I didn't want another Giardia situation.
Erin Welsh	(laughs) Well okay.
Erin Allmann Updyke	Escherichia.
Erin Welsh	Escherichia, I think.
Erin Allmann Updyke	Escherichia.
Erin Welsh	Escherichia?
Erin Allmann Updyke	I have never attempted to pronounce that word in my life.
Erin Welsh	I mean I've tried to do it but it's an attempt of course. But i remember my micro professor in undergrad saying that one of his friends who is also a microbiologist gave their daughter the middle name of Escherichia because he thought it was so beautiful.
Erin Allmann Updyke	Wow. Weird.

Erin Welsh	Yeah. Anyway, okay. So anyway Theodor Escherich was looking at baby poop under the microscope and noticed a bunch of rod-shaped bacteria. And the reason he was looking at baby poop is because he had been waging a full-on war against diarrhea, believing it to be one of the biggest killers of infants under his care. And he was right.
Erin Allmann Updyke	Totally right.
Erin Welsh	Yeah.
Erin Allmann Updyke	For sure.
Erin Welsh	He was looking under the scope to try to see if he could figure out what's good bacteria and what's bad bacteria.
Erin Allmann Updyke	Wow.
Erin Welsh	Which I think, yeah, 1885, forward thinker.
Erin Allmann Updyke	Yeah.
Erin Welsh	And so he would look for bacteria in both healthy and unhealthy children and say okay, what can I find in just the unhealthy ones vs what do I find in both? And he found E. coli in both and so he didn't really consider it to be that interesting of a finding. But he published it anyway and absolutely no one took note of it.
Erin Allmann Updyke	(laughs) Shocker.
Erin Welsh	Right? And the original name which was much easier to pronounce was Bacterium coli, so common bacteria of the colon.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah. But 7 years after his death in 1918, scientists renamed it after him. Okay so just a few years after that a biochemist named Edward Tatum - I really wanna know if he's related to Channing Tatum.
Erin Allmann Updyke	Mr. Channing? Yeah.
Erin Welsh	Edward Tatum started to culture a strain of E. coli, the K12 strain if you're curious, in the lab. And this K12 strain that's so popular for lab work today was isolated from a dude who had diphtheria and was living in California in the early 1900s.
Erin Allmann Updyke	What?
Erin Welsh	Yeah, there you go.
Erin Allmann Updyke	He had diphtheria and just happened to have this strain of E. coli?
Erin Welsh	I don't really know the full story but yeah, I assume. Cause this is a harmless strain, this is a nonpathogenic strain.

Erin Allmann Updyke	Yeah, right.
Erin Welsh	So Tatum had recently gotten super interested in the very new field of genetics, cause this is the early 1900s, and he had actually worked with Thomas Hunt Morgan and George Beadle which like two of the biggest pioneers in the field. And up until this point of time genetics had mostly been studied using things like fruit flies and bread mold which were more complex in some ways than bacteria, particularly in that they had sex, like gene exchange or were known to. Tatum wanted to see whether bacteria like E. coli also followed the one gene for every enzyme rule that had been the pattern he's discovered in mold. And he chose E. coli because it has very few requirements in the lab, grows rapidly, and produces visible colonies which is useful for monitoring what exactly is going on. And he blasted E. coli with X-rays, managing to produce a few mutants.
Erin Allmann Updyke	Awesome.
Erin Welsh	Which gave this huge indication bacteria have genes because if you blast something with X-rays and then there are mutations that happen and there are differences in the because after that, then that shows that these things have changed based on how they...on their genes.
Erin Allmann Updyke	Right. Their DNA has been affected, yeah.
Erin Welsh	That was a huge finding. But did that matter that much? Did the fact the bacteria had genes matter that much if the bacteria couldn't reproduce sexually?
Erin Allmann Updyke	Yeah.
Erin Welsh	And so from these findings another guy named Joshua Lederberg who was 21 years old, just wanted to say this.
Erin Allmann Updyke	Oh my god.
Erin Welsh	Yeah, I know.
Erin Allmann Updyke	That hurts. Don't tell me that he got like the Nobel Prize. Oh my...
Erin Welsh	(laughs) He did. Okay so Joshua Lederberg decided he would look for bacteria sex. So he was just convinced that people weren't looking hard enough. And he found it. So he found E. coli mutants could exchange genes somehow and from this monumental discovery that led to basically the amount of research is...you can't count the number of findings or new laws of biology or whatever, all these discoveries. These three dudes, so Lederberg, Tatum, and Beadle were given the Nobel Prize in 1958.
Erin Allmann Updyke	And he was 21.
Erin Welsh	He was 21 not in 1958 but he was 21 when he discovered bacteria sex. Yeah.
Erin Allmann Updyke	When he did these experiments. Shoot. Well, too late for me then.
Erin Welsh	I mean, it's great. No, come on. Come on, it's never too late.

Erin Allmann Updyke	(laughs) Just kidding.
Erin Welsh	It's never too late.
Erin Allmann Updyke	No that's true, it's not.
Erin Welsh	Studying E. coli would lead to other huge advancements such as discovering that viruses had genetic material which was learned by looking at the bacteriophages of E. coli, it would also help to show conclusively that genes are made of DNA which overturned the long held hypothesis that DNA was made of proteins.
Erin Allmann Updyke	Oh.
Erin Welsh	And it even helped to reveal the structure of DNA in what apparently is known as the most beautiful experiment in biology and I'm not gonna get into the details of it but it has to do with nitrogen at different weights and lots of centrifuging. If you wanna know more, read the book 'Microcosm' by Carl Zimmer.
Erin Allmann Updyke	Okay.
Erin Welsh	It keeps going though. E. coli also helped to show how DNA was made up of codons and how these codons matched to certain amino acids. By studying E. coli scientists were learning about the rules that govern life itself and even what it means to be alive.
Erin Allmann Updyke	Yeah.
Erin Welsh	It's amazing!
Erin Allmann Updyke	Yeah, dude.
Erin Welsh	It's amazing. E. coli has thousands of genes and scientists have a pretty good idea, if not exactly the idea, of what each of those genes do. Basically you know a gene out and you see what happens. And by fiddling with these mutant varieties of E. coli, researchers also figured out that genes can be turned off and turned on, that they don't work in isolation but are rather connected like a circuit board. E. coli has been subject to the whim of so many researchers who wanted to see if it could be grown at extremely high temperatures or super low levels of food or infected with tons of viruses. And what the scientists observed over and over again was evolution at work on a timescale that no one had thought was possible, even though now it kind of maybe seems obvious.
Erin Allmann Updyke	Antibiotic resistance and all that?
Erin Welsh	Exactly, yeah.
Erin Allmann Updyke	Yeah.

Erin Welsh	E. coli was used in genetic engineering starting in the 1970s when it caused quite a stir and now no one thinks twice. But people started using it for insulin production which led to this huge industry which was fueled initially by controversy and then by demand. Doctors sometimes would give or still give, I don't know you tell me, a strain of E. coli called A034/86 to premature infants that don't have fully formed intestines because it helps them protect against nasty gut pathogens.
Erin Allmann Updyke	Ooh! I don't know if they still do that but that's genius. Cause babies gets colonized with E. coli in like minutes after birth, it's amazing.
Erin Welsh	Oh yeah. It's amazing. So this particular helpful strain or whatever, some of its genes code for things that directly fight the weapons of strains like O157.
Erin Allmann Updyke	Stop it!
Erin Welsh	Yeah!
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	This is like a total role reversal, usually you're the one that's telling me about these strain differences.
Erin Allmann Updyke	Oh I love it.
Erin Welsh	I love it. Okay, okay. Just a couple more cool bits about E. coli before the history of the pathogenic one.
Erin Allmann Updyke	The poop.
Erin Welsh	Yes. E. coli can sense each other.
Erin Allmann Updyke	Oh yeah, oh I'm so glad you're talking about this.
Erin Welsh	It's amazing. Okay so a group of researchers released E. coli labeled with a glowing protein into a maze and wanted to see how they would move and what would happen. So you could trace these individual cells, right.
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	At first everything was random but then eventually the researchers saw a pattern emerge. The bacteria were moving towards other bacteria and soon there was this giant cluster of E. coli just hanging out. Okay so it turns out - you're doing a very happy dance, I like it. (laughs)
Erin Allmann Updyke	I am.
Erin Welsh	It turns out that E. coli shoots out serine in its waste and other E. coli might use that as a sensing mechanism to find other E. coli. And once they're all together they might even change their behavior, so instead of having their normal flagellum they grow a giant one that gets tied up with other flagella, creating a rat king of E. coli.

Erin Allmann Updyke	Oh my gosh. Bacteria having behavior is one of the coolest things.
Erin Welsh	And this whole rat king whatever, tails or flagella tied?
Erin Allmann Updyke	Yeah.
Erin Welsh	Helps them move as a group across a petri dish or maybe even your intestinal wall.
Erin Allmann Updyke	Definitely your intestinal wall.
Erin Welsh	It's amazing, it's amazing.
Erin Allmann Updyke	Dude.
Erin Welsh	Okay. Even though now I think most of us think of E. coli as this deadly food-borne terror, for several decades after its description and even after its use in a lab as basically the thing that revealed all secrets of life, people weren't aware of how sick it could make you. So it wasn't until 1945 that the link between E. coli and horrific gastrointestinal disease was really conclusively made. Have you ever heard of summer diarrhea?
Erin Allmann Updyke	No. I know in what was it the polio episode we talked about closing down pools and thing but summer diarrhea? No.
Erin Welsh	Yeah. So this was a known phenomenon, something called summer diarrhea. So if you go to Google Scholar you can find reports of now analysis of what the summer diarrhea was in writings or whatever but also in reports from the early 1900s. So every summer kids and infants in industrialized countries could get super sick with diarrhea, often bad enough to kill them. So it was this very seasonal trend of diarrhea. And a British pathologist named John Bray decided to hunt for whatever pathogen might be causing this. Using antibody tests he found that while only 4% of the healthy kids responded to the E. coli antibody test, like they were positive, 95% of sick kids did. And so then he would go on to describe this strain and several more that were pathogenic to humans.
Erin Allmann Updyke	Interesting.
Erin Welsh	Okay so now here's the part that you've probably been waiting for maybe.
Erin Allmann Updyke	Yes, definitely.
Erin Welsh	I dunno, maybe you've enjoyed all of this.
Erin Allmann Updyke	I have enjoyed all of this.
Erin Welsh	Okay good. Enter O157:H7.
Erin Allmann Updyke	Dun-dun-dun.
Erin Welsh	Although we can't say for sure, O157 seems to be a pretty recent arrival, like 1975 to be exact.
Erin Allmann Updyke	Wow, that's super recent.

Erin Welsh	Yeah. No samples can be found before then.
Erin Allmann Updyke	Fascinating.
Erin Welsh	It first made headlines in early 1982 in Medford, Oregon and later that same year in Traverse City, Michigan. The source was undercooked burgers at McDonald's. And then it went quite for about 10 years until the infamous 1993 Jack in the Box outbreak.
Erin Allmann Updyke	JTB, baby.
Erin Welsh	I've never had Jack in the Box.
Erin Allmann Updyke	Do they not have it out here?
Erin Welsh	Out east? No. Or like I don't know, past the Mississippi River?
Erin Allmann Updyke	Oh interesting, yeah. JTB man.
Erin Welsh	There have been dozens of O157 outbreaks all over the world since its first appearance. And I could probably go into each one of them to talk about the source of infection and the lessons learned but I'm just gonna focus on the 1993 Jack in the Box outbreak in the western U.S. because this is probably the most famous food-borne or E. coli outbreak in the U.S.
Erin Allmann Updyke	Yeah.
Erin Welsh	It's massive.
Erin Allmann Updyke	Everyone still talks about it.
Erin Welsh	Yeah. I mean it put E. coli as a popular phrase or like as a known phrase to people, yeah.
Erin Allmann Updyke	Totally.
Erin Welsh	It resulted in landmark personal injury lawsuits, increased oversight of food production and widespread public awareness of this deadly pathogen. Which burgers used to be safe before this besides some worms. Yeah. It started around Christmas 1992 when 6 year old Lauren Rudolph was rushed to the ER in San Diego after having bloody diarrhea. After a few days of battling the illness she passed away. And in January 1993 doctors at Children's Hospital in Seattle started noticing an unusual number of kids with hemolytic uremic syndrome which is that thing you described.
Erin Allmann Updyke	Yeah.
Erin Welsh	And this set off some alarm bells because you don't really see that number of cases very often, it's pretty rare, right?
Erin Allmann Updyke	Yeah.

Erin Welsh	And so the high number of HUS cases which is the hemolytic uremic syndrome, I'm just gonna call it HUS, it pointed towards an E. coli outbreak. But those usually happen in the summer, so where could these cases be coming from? These children weren't connected to one another in any way, like at daycare or something like that, but there must have been a shared source somewhere. Epidemiologists that were assigned to the case did their thing asking parents about their lives, their movement patterns, what food they ate at home, where they ate. And eventually a likely culprit emerged: Jack in the Box, the nation's - did you know it was the nation's oldest fast food chain?
Erin Allmann Updyke	No, I did not know that.
Erin Welsh	It beat out McDonald's by like a couple of months. Anyway so Jack in the Box had recently been having this big promotion for their monster burger, "So good it's scary". Which is like in retrospect not a great tagline.
Erin Allmann Updyke	Not great. They don't make that burger anymore.
Erin Welsh	No, I don't think so. Yeah the PR campaign to get Jack in the Box to not fold as a company is pretty I think also landmark.
Erin Allmann Updyke	Yeah, that's a whole podcast in and of itself I feel like.
Erin Welsh	Oh, for sure. So the president of Jack in the Box, Bob Nugent, when notified that the company might be the source of this horrible outbreak he immediately stopped all of the restaurants in the affected areas from serving their burgers and destroyed the potentially contaminated batches of beef.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah, oh he acted as fast as he could.
Erin Allmann Updyke	Yeah, that's awesome.
Erin Welsh	And he did all this without being entirely convinced that it was the beef, that it was Jack in the Box in the first place.
Erin Allmann Updyke	But you have dead kids so it's like...
Erin Welsh	Exactly.
Erin Allmann Updyke	Yeah.
Erin Welsh	Well and a lot of the people who were at Jack in the Box I think felt awful, like were very, very troubled with what their inactions had done.
Erin Allmann Updyke	Yeah. I can't even imagine.

Erin Welsh	And so people knew at this time, people knew that undercooked chicken could be a problem in terms of salmonella but no one really had heard of outbreaks of food poisoning associated with beef, it was a new thing at that point. Or at least it seemed to be according to this book. And so even though there had been this E. coli outbreak just 10 years before the Jack in the Box, the one that was in McDonald's, it had gotten quietly buried and so McDonald's wasn't really named. And so when Washington State epidemiologist John Kobayashi told Bob Nugent, the president of Jack in the Box, that this horrible outbreak affecting all of these kids was likely tied to E. coli contaminated burgers, Nugent was like, 'What?'. So even though the contaminated beef had been stopped, it was too late for a lot of people, mostly children. By the end of the epidemic 732 people were infected with E. coli.
Erin Allmann Updyke	732 confirmed?
Erin Welsh	Confirmed.
Erin Allmann Updyke	Whoa.
Erin Welsh	All traced back to Jack in the Box restaurants in Washington, Idaho, Nevada - how do you say Nevada? I say 'Nevah-duh' and I know that's wrong so I need to say it properly!
Erin Allmann Updyke	Nev-a-da. (laughs)
Erin Welsh	Nevada and California.
Erin Allmann Updyke	Please leave that in cause it's the funniest thing I've ever heard.
Erin Welsh	A lot of people say 'Nevah-duh'.
Erin Allmann Updyke	Nevada. (laughs)
Erin Welsh	Cause I knew it was wrong as soon as it left my mouth. It's embarrassing.
Erin Allmann Updyke	Oh god.
Erin Welsh	Avoiding these restaurants wasn't enough, though. One of the four children who died during the outbreak was 17 month old Riley Detwiler and he contracted E. coli from a friend in daycare who had picked up the bacteria from a burger.
Erin Allmann Updyke	Ugh.
Erin Welsh	There were two other children who died, Celina Shribs and Michael Nole, and all of the kids who died from this outbreak were 6 years or younger.
Erin Allmann Updyke	Ugh, those babies.

Erin Welsh	Yeah, yeah. Even if you were fortunate to survive the initial infection, many people, over 100, experienced long term side effects from the infection. Obviously with so much tragedy and suffering experienced as a result of this epidemic, people wanted answers to questions like 'How did this happen?' and 'How can we make sure this doesn't happen again?' The first question, how did this happen, actually ended up being fairly easy to answer. So in 1993 the federal regulations for the temperature for cooking beef were 140 degrees Fahrenheit, 60 degrees Celsius. Okay. However - so 140 degrees, keep that in your head.
Erin Allmann Updyke	Okay.
Erin Welsh	In Washington the state law was actually 155 degrees, 68.3 degrees Celsius. This regulation which was different than the federal regulation, higher temperature, was put in place by the same epidemiologist, John Kobayashi, that I mentioned earlier. Cause he was aware of the danger that E. coli posed.
Erin Allmann Updyke	Wow, way to go.
Erin Welsh	He chose 155 degrees Fahrenheit because that was the temperature required to kill E. coli.
Erin Allmann Updyke	Whoa.
Erin Welsh	Jack in the Box in Washington was notified of this new regulation but for whatever reason didn't change their practices, they followed the federal regulation of 140 degrees. So yeah, a lot of the cases probably could've been prevented if they had followed Washington State law. But Jack in the Box argued that they weren't completely responsible for contaminated product. The screening regulations for E. coli in beef weren't what they are today, like people didn't really screen that much for them.
Erin Allmann Updyke	Then you should've had Matt come on this episode.
Erin Welsh	Oh my god you're right.
Erin Allmann Updyke	It's what he does.
Erin Welsh	It's so true.
Erin Allmann Updyke	Shout out Matt! (laughs)
Erin Welsh	And so researchers were desperately trying to figure out where the strain came from and how to prevent it from getting into the food supply and that's something that's way easier said than done because it was found in around 28% of cows and probably that number has jumped since this book was written. And so basically what happens is that during the slaughtering process, if a cow's colon is cut, that E. coli that's in the gut can then escape and basically all the meat is all blended together, like ground together, yeah, that O157 can travel through literal tons of beef.
Erin Allmann Updyke	Yeah, that's so gross.
Erin Welsh	Horrific. Proper cooking will kill the bacteria but if a few escape then there you go.
Erin Allmann Updyke	And do you know the infectious dose for E. coli is as little as 10 organisms.

Erin Welsh	10? I remember that from micro, yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	So that's how the E. coli got into the beef. But how do you make sure it doesn't happen again? That's a much trickier issue and probably because we've had several outbreaks since then, it's obviously tricky. So there are several stages of food prep that could've been improved. First it's the beef industry itself, you clean up that process. Maybe don't allow dropped carcasses to be incorporated, maybe cleaning the floor on which they are dropped, maybe following a one cow, one burger practice which isn't what happens.
Erin Allmann Updyke	I need to not think about it or I'll never eat another burger again in my life.
Erin Welsh	It's funny that you say that cause that was my exact response when I read this in Carl Zimmer's book and then the next paragraph is, 'And if you're vegetarian, don't feel so smug' or something like that.
Erin Allmann Updyke	Yeah.
Erin Welsh	Like you're not escaping it either because cows poop on crops.
Erin Allmann Updyke	Oh like most of the outbreaks, not most but a large number of the outbreaks recently have been in lettuce and spinach. No one is safe.
Erin Welsh	Yeah, or cookie dough. We called the title of our quarantini Cookie Doughn't because raw flour is how people have gotten sick from E. coli also.
Erin Allmann Updyke	Yeah.
Erin Welsh	Okay. But then there are also these restaurant quality control improvements that could be made, cooking the beef at the temperature that actually kills E. coli. So this E. coli outbreak is notable not just because of its size but because of the changes it led to in the food industry and the government oversight of it. So it really did, it was like a huge, huge deal. And a lot of people who work in food safety are today still very unsatisfied by how it's done and that's kind of a fair point considering that outbreaks continue to happen. All right so back to the whole vegetables are not necessarily safe. There was a 1997 outbreak of O157 in Japan from tainted radish sprouts that made 12,000 people sick.
Erin Allmann Updyke	Oh my what?!
Erin Welsh	Yeah, three of whom died. 12,000. September 2006 in the U.S. there was an O157 outbreak in spinach that made 205 people sick, that same year lettuce at Taco Bell made 71 people sick. You could just go on and on and on and on. Yeah. So I could go on and on and on and on about all these different outbreaks but I'm not going to. Instead Erin, I want you to tell me where do you stand today with E. coli?
Erin Allmann Updyke	I can't wait to.
TPWKY	(transition theme)
Erin Allmann Updyke	All right, E. coli today. It's everywhere.

Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah. It's still everywhere. It causes so many different diseases it's really hard to do an epidemiology section on this because where do you even begin? I don't know. Let's start where you left off with the inflammatory, bloody EHEC. Food-borne outbreaks. Just looking over the last 10ish years which is basically where you left off around 2006/2007, there have been pretty much between 1 and 4 multi-state outbreaks of EHEC, really bad bloody diarrhea E. coli every year pretty much.
Erin Welsh	Wow.
Erin Allmann Updyke	And each of these multi-state outbreaks, the multistate outbreaks are the only ones that are reported like easily accessible on the CDC website, you can go to every state health department and probably find a handful of outbreaks that were just contained to one single state. But of these multi-state outbreaks they range in size from like 18 or 20 cases on the low end to over 200 cases on the high end. And every year from each of these cases a handful of people are hospitalized and end up getting hemolytic uremic syndrome. Most years there aren't any deaths related to this but every other year or so there's a bad outbreak and there are some deaths associated with this. So to put some numbers on that from the last couple of years, so far in 2019 there have been 263 cases in 3 multi-state outbreaks associated with ground bison.
Erin Welsh	Oh.
Erin Allmann Updyke	Also flour.
Erin Welsh	Oh.
Erin Allmann Updyke	Aka cookie dough.
Erin Welsh	Ruh-roh.
Erin Allmann Updyke	Yep. And ground beef. Of these 263 cases, 50 of them were hospitalized, nobody died so far in 2019. 2018 was a little worse although 2019's not over yet, there were three outbreaks with 290 cases but 127 hospitalizations. And that's because two of those outbreaks were actually O157.
Erin Welsh	Oh!
Erin Allmann Updyke	Yeah so these are just all of the EHEC or STEC, whatever you call it, outbreaks, not all of those are O157 and it turns out that O157 is more likely to cause HUS than some of the other EHEC strains.
Erin Welsh	Just based on the amount of Shiga toxin or what?
Erin Allmann Updyke	Yeah or just the specific subtype of that Shiga toxin, right.
Erin Welsh	Okay, yeah.

Erin Allmann Updyke	Or Shiga-like toxin. It's just more likely to end up causing HUS. So the years that you have O157 outbreaks tend to be worse in terms of the number of people hospitalized and the number of deaths. But that's just the outbreaks. The vast majority of EHEC cases are actually not outbreak-associated, they're just individuals who end up getting sick and maybe end up in the hospital. So in 2016 there were over 5400 cases of EHEC reported.
Erin Welsh	Wow.
Erin Allmann Updyke	Yeah.
Erin Welsh	That's like 20 times higher than-
Erin Allmann Updyke	Than the outbreak numbers. Yeah, the vast majority of people, they aren't actually part of an outbreak which means that you never actually figure out where their infection came from.
Erin Welsh	Oh, gotcha. Yeah.
Erin Allmann Updyke	And that's another important part of it, the only time you can identify an outbreak is if you have multiple people coming to the same hospital or at least reporting to the same health district so that someone can pick up on the fact that there's a number of cases happening.
Erin Welsh	Right.
Erin Allmann Updyke	If just one person comes or even a couple people come but to different hospitals that somehow don't end up talking to each other, there's an outbreak going on perhaps but you'll never know about it, you just have a handful of cases.
Erin Welsh	Right.
Erin Allmann Updyke	Does that make sense?
Erin Welsh	That makes sense.
Erin Allmann Updyke	So yeah and then like you mentioned that happened in the 1993 outbreak, about 10-20% of cases actually end up in what's called a secondary attack where people pass on that O157 or that EHEC strain to somebody else in a daycare facility, changing diapers, nursing homes, etc. So yeah. EHEC is gnarly.
Erin Welsh	Yeah.
Erin Allmann Updyke	But again that's not the only E. coli out there.
Erin Welsh	Great. There's the one that makes you have watery diarrhea instead of bloody diarrhea.
Erin Allmann Updyke	So let's talk about that one real quickly.
Erin Welsh	Great, let's.

Erin Allmann Updyke	So ETEC is what you were mentioning, the enterotoxigenic E. coli is a hugely important cause of morbidity and mortality worldwide especially for infants and children. So there's a lot of interest in developing a vaccine for something like ETEC because we're talking millions of children every year that are affected by this and potentially dying as a result of it. There are some candidates in trials that seem promising but nothing so far as licensed. You're gonna see that for all the different things.
Erin Welsh	Okay, great.
Erin Allmann Updyke	Yeah.
Erin Welsh	Cool.
Erin Allmann Updyke	The other big type of E. coli is of course the uropathogenic E. coli, the UPECs. There's also a lot of interest in developing a vaccine for these because 80% of all UTIs are caused by E. coli and recurrent UTIs are really, really common.
Erin Welsh	Right.
Erin Allmann Updyke	So getting one UTI puts you at very high risk of getting a second UTI in a short period of time. So there's a lot of people working on vaccines for the various types of UPECs. There's not really a lot promising so far quite honestly.
Erin Welsh	Oh my god. Is there anything promising about this section?
Erin Allmann Updyke	No. It ends on the worst note possible.
Erin Welsh	Great.
Erin Allmann Updyke	Yeah, so true. But yeah it turns out that UTIs are a massive financial burden.
Erin Welsh	Oh that makes sense.
Erin Allmann Updyke	Yeah, like $3.5 billion a year in the U.S. alone is spent on UTIs.
Erin Welsh	$3.5 billion.
Erin Allmann Updyke	Yeah, dude.
Erin Welsh	Well what about other countries that don't have as outrageous healthcare situation?
Erin Allmann Updyke	Good point, good point. But still it's like 11 million doctor's visits in the U.S. every year and 2 million emergency room visits for UTIs alone.
Erin Welsh	Wow.
Erin Allmann Updyke	Yeah.
Erin Welsh	Wow, okay.

Erin Allmann Updyke	So even though it's outrageously expensive.
Erin Welsh	I think I like those numbers for understanding more than I do of money.
Erin Allmann Updyke	(laughs) That makes sense. So yeah but there is a lot of work going on on ETEC, on UPEC, and even on the EHEC, so the enterohemorrhagic E. coli. There are people trying to come up with vaccines for all of these strains but it's proving to be pretty elusive which isn't that surprising considering how ubiquitous E. coli is and how we have co-evolved with it for literally the entire time we've existed as humans.
Erin Welsh	Because yeah, also it's part of our normal microflora so you'd have to attack it from a different angle.
Erin Allmann Updyke	Right.
Erin Welsh	And if you did the Shiga-like toxin, cause we have vaccines that are based on toxins.
Erin Allmann Updyke	Yeah and that's exactly what most of these vaccines do. They're either component vaccines or they're toxoid vaccines which are inactivated forms of a toxin essentially.
Erin Welsh	Right.
Erin Allmann Updyke	And so that's exactly what people are trying to do is to target the things that make these pathotypes different than our normal microflora, we just haven't been able to come up with one so far that produces a good immune response in humans to actually be protective. If that makes sense.
Erin Welsh	Yeah, okay.
Erin Allmann Updyke	Yeah. And the other thing that's really scary is that antibiotic resistance is on the rise for E. coli in general but especially for E. coli that tend to cause sepsis, so bacteremia, blood-borne infections.
Erin Welsh	And those are most common in a hospital setting, like after surgery?
Erin Allmann Updyke	Yeah, they're very common in hospital settings, they can happen also in babies, not just the meningitis but just blood-borne infections in general. And from what I saw in a paper that I will post on our website, from 2000-2009 the rates of antibiotic resistant E. coli have risen about 300% from 200-2009.
Erin Welsh	What?
Erin Allmann Updyke	Yeah, 300% rise. It's really bad.
Erin Welsh	Whoa.
Erin Allmann Updyke	And the numbers that I saw were that E. coli sepsis, so sepsis from e, in 2001 was estimated to have caused 40,000 deaths in the U.S. but in 2014 that number may have been as high as 85,000.

Erin Welsh	What?
Erin Allmann Updyke	Yeah.
Erin Welsh	What?
Erin Allmann Updyke	E. coli is a very common cause of sepsis and sepsis has a very high mortality rate. So these are estimate numbers.
Erin Welsh	Right but that's so many people!
Erin Allmann Updyke	I know, yeah. It's really scary.
Erin Welsh	Oh my gosh.
Erin Allmann Updyke	Oh no, that's the end.
Erin Welsh	Oh, Erin!
Erin Allmann Updyke	That's literally the end of what I have. (laughs) That's where my page ends, 'may have been as high as 85,000'.
Erin Welsh	Great, okay. So goodnight everyone, sleep well.
Erin Allmann Updyke	Oh my goodness. I'm so sorry.
Erin Welsh	We're sorry. Okay so not very much good news for E. coli.
Erin Allmann Updyke	Yeah. I should've organized that to be a happier ending but I mean we could end it with the happiness that there is so much cool research going on using E. coli in a lab setting to develop other vaccines and cool stuff. That's a stretch.
Erin Welsh	And maybe things will get better somehow.
Erin Allmann Updyke	Yeah. I mean there's people working on it, there are people out there trying really hard to make these vaccines happen, etc.
Erin Welsh	Maybe looking back these will be the dark days. Well they kind of are the dark days, but...
Erin Allmann Updyke	Right now it's pretty dark days.
Erin Welsh	We're in some weird timeline. Okay.
Erin Allmann Updyke	Yeah. But yeah, that's E. coli.
Erin Welsh	This was a massive topic.
Erin Allmann Updyke	Yeah, we just barely even scratched the surface of that agar plate, let me tell ya.

Erin Welsh	Ooh I really like that.
Erin Allmann Updyke	Thank you. I just came up with it, I didn't even plan that.
Erin Welsh	She checks her notes. (laughs)
Erin Allmann Updyke	Did I say this joke? Check!
Erin Welsh	All right well I guess on these really sad notes should we discuss sources?
Erin Allmann Updyke	Yes, let's.
Erin Welsh	So I read a couple of books, one is called 'Microcosm: E. coli and the new science of life' and that's by Carl Zimmer, I loved it, really fascinating, a lot about the lab research done on E. coli and how it's provided answers to evolution. Then I also read a book about the 1993 Jack in the Box outbreak called 'Poisoned: the true story of the deadly E. coli outbreak that changed the way Americans eat' and that's by Jeff Benedict. I can't necessarily recommend this book, that's all I'll say about it.
Erin Allmann Updyke	Oh. Okay.
Erin Welsh	And then I also watched a New York Times Retro Report that was like a news study report on the 1993 outbreak and I'll also post a few more articles that I read.
Erin Allmann Updyke	Awesome. I will post all of the articles that I read which included that really intense Nature Reviews microbiology paper if you want the deets on E. coli pathotypes and then a bunch of reviews about the current status of various vaccines and things. All of these will be on thispodcastwillkillyou.com under the EPISODES tab, you can find the sources for this and all of our episodes.
Erin Welsh	Thank you to Bloodmobile for providing the music for this episode and all of our episodes.
Erin Allmann Updyke	Thank you to all of you for listening, this is the most fun to make this podcast and we really love that you love it.
Erin Welsh	Yes, thank you for allowing us to keep talking at you.
Erin Allmann Updyke	It's so fun.
Erin Welsh	And with that, please wash your hands and cook your meat.
Erin Allmann Updyke	Dear god, wash your hands you filthy animals.