

Erin Welsh

Hey everyone, just wanted to give you a quick content warning here that the firsthand account for this episode does include the death of a parent. So if you would like to move past that, you can skip ahead to about 11 minutes and 15 seconds in.

Denise

Hi, my name is Denise and I'm here today to talk about the story of my mom and what she went through with Listeria. As a little back story, my mom turned 80 years old in June of 2022. She was very, very vibrant. She still worked, she golfed, she was exceptionally active. Some more backstory, she had a regular routine normal colonoscopy in June that showed no ulcerations at all. This is important a little later. In August she started having some excruciating headaches after she would eat. And when she saw her doctor they diagnosed her with a condition called temporal arteritis and started her on high dose steroids and methotrexate. At the same time she had a long standing trip planned August 18th through October 9th to go up to Washington to visit some friends and escape the heat of the Palm Springs desert.

I'm a nurse, I've been a nurse for 27 years. I talked to her about the risks of continuing to go on this vacation because of the immuno suppression that the steroids were causing. And I think because of the COVID fatigue for the past several years and not seeing her friends, she wasn't really interested in putting that off. She had people to see, things to do, and golf to play. And away she went. Fast forward up until September 24th, she texted me that she had gained 2 lbs, she'd eaten a great big bowl of ice cream and was having some macaroni and cheese for dinner. On the 28th she called because she said that she had started not feeling so good. So then the next day was Thursday the 29th, she called me in the morning and said that she was feeling worse and she did go ahead and cancel her lunch date that day.

So Friday, September 30th, I received a call at 3 o'clock in the afternoon from the people she was staying with. She'd been laying on the couch all day, had not eaten any food and only taken sips of water, had a low grade temp, negative COVID tests. And because I'm down here outside of Palm Springs, I said it was a good idea to take her to urgent care. So they did take her in. The blood work came back and showed that she had some impaired kidney function borderlining on kidney failure. And she also had a really high calcium level and a low potassium level. The doctor there though thought that she was stable enough that she could just come back in the morning and get some IV fluids and repeat the labs. The morning of October 1st they went to the urgent care straightaway where she got her fluids. The doctor did advise our friends to go ahead and take her over to the emergency department.

She was checked in and triaged about 3:00 and then because of just how life in the ER is these days, she got back to a room at like 8:30 at night and the doctor saw her at 10 o'clock at night. Luckily our friends were able to stay, they rotated staying with her so that she wasn't just by herself. And at 3:30 in the morning she had a sudden mental status change where she completely went lethargic, started reaching at the air, not communicative, not able to speak. So our friend Frank grabbed the nurse, they took her temperature rectally and it was 103.4. The staff came and drew blood cultures and she was started on an IV antibiotic cocktail that they do for sepsis of unknown origin. I got on the plane to go up to Portland at like 9 o'clock in the morning on Sunday, I arrived at the hospital at 11 am. She looked like she was going to die when I walked into the room. I worked 11 years in the emergency room and I thought oh this is not good, it's not good at all.

She was not responsive to people talking to her, she was not following commands, she was pulling at things. On Monday the 3rd, the infectious disease doctor came to me about noon and said that three of the four blood culture bottles were showing bacterial growth of some sort but that the microbiology text that he knew and really trusted didn't identify anything. So he was really concerned that it was contaminant which would be really highly unusual in three out of four bottles. So they ran what they call an extended infectious disease panel. After she came back from her lumbar puncture, the infectious disease doctor comes down the hall towards me and kind of frantically gesturing at me and says you're not gonna believe this but she's actually got Listeria and it's in her bloodstream and it's also in her spinal fluid. And this is really, really bad. And it's bad not just because the mortality rate is exceptionally high but also because the antibiotics that she had been getting are not the ones that are effective at all against Listeria.

It took until 11 o'clock at night to finally get her started on the ampicillin but I was still preparing myself that my mom was going to pass. So when I came in at 6:30 Monday morning, my mom had little restraint mittens on her hands and I thought oh my god, it's gone from bad to worse. And she was shaking those little mittens at me. And I said mom, if I take these off of you, you have to leave your things alone, you can't pull on things. And she made eye contact with me and she said okay. And I thought oh my god, she's in there. This is a glimmer of hope, I think it could be okay. And over the course of the day her mental status actually improved, she was answering yes and no questions, I was able to transfer her out of bed and get her on the little bedside commode to go to the bathroom. We also discovered at that time in her MRI that they had done of her brain that it showed that she had four areas that were possibly like septic emboli from the infection.

So to see her mental status also improving like that was really amazing. They had given her a medication called or Arixtra to prevent blood clots and they also gave her an aspirin because of the potential for cardiac strain. So I was a little worried about that when they started that the day before because her platelet count was not super low but it was low enough that I was concerned about it. So Wednesday morning when she's talking and moving and she's doing great, she told me that she had just never felt so awful. And I explained to her that most people that get as sick as she is don't even wake up. And she looked at me and she said you mean I could have died? And I said yes, mom, it's that serious. You could have died. And she said well I'm not ready to die. And I said well that's great because I'm not ready to be an orphan. Everybody was so excited. Her doctors, the hospitalists and the infectious disease doctor, they were just amazed at how good she was doing.

And then at 3:30 I got her up to the commode. As soon as she went to the bathroom, I knew right away that there was blood. When somebody has a intestinal bleed and they pass stool it has a very, very distinctive smell. And I just knew that this was not good. And that was really the very beginning of the end. The doctor came back up and looked at it and he said yeah, we're going to hold off on transferring her off the floor. So they did an upper endoscopy where they looked at her stomach on the 7th and that was negative, no ulcers. So they did do the colonoscopy and that showed that her large intestine, all throughout her large intestine and up to into what they could see in her small intestine was just riddled with ulcers. On the 14th she really started bleeding quite heavily and went into shock. And before she actually went into full blown shock from this I had to call my daughter and tell her that if this scan that they had just taken her for did not show any bleeding that we could do anything about, that her grandma was most likely going to pass away. That was the hardest phone call I've ever had to make. The results of that scan came back and they finally did see that there was bleeding coming out of an artery in her small intestine.

So interventional radiology was called in and off she went for a procedure and off to ICU. That procedure we thought was good. But then in the morning it turned out that they had maybe stopped the bleeding a little too well and some of her small intestine was starting to die. So this led down the course of a bowel resection and then re-attachment which she did great, came out of that very well. By the 26th she had had 12 units of blood, two failed interventional radiology procedures, and three surgeries. Throughout this time with her in Washington when the bleeding would stop and it would start, our only goal was to get her home, to get her back to California. And trying to navigate that when you're at a hospital system that's 1100 miles from your home is exceptionally difficult. But throughout the whole time that was our single focus, get her home so that she could pass at her home when it became obvious that she was not really going to pull through this. And thankfully we were able to do that.

On the 2nd of November, I was finally able to get her on an air ambulance home to get her admitted down here at the hospital system that I work in. I was able to have hospice come out, bring the bed and all of the equipment here on the 4th. And my dear, dear friend Julie was with her at the hospital in the morning and she called me and she said she's ready. She was alert and she knew she was in the hospital and she was ready to come home. She has a beautiful view at her condo here and she was able to see that. And she passed away on the 9th.

So we don't know what the source was. We don't know what she ate or how she contracted this. It was a very long month of stops and starts where we would think the bleeding had maybe stopped and then to have it start again. When I told her that we had gotten the air ambulance, that we were going to be flying home to California, she said oh Denise, that's wonderful. And when she saw her sunset, she said it's so beautiful. And she has missed every day. And thank you for letting me share her story.

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

Thank you so much Denise, I can't imagine. And we really appreciate you being willing to share that story and we know it couldn't have been easy to do. So thank you.

Erin Allmann Updyke

Yeah, thank you. Being able to hear a story of how this disease can really affect people and their families, it's just so powerful and thank you so much for being willing to be so vulnerable and share that with us.

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

Today is a heavy duty topic. Listeria.

Erin Welsh

Yeah, more heavy duty than I realized.

Erin Allmann Updyke

It is so gnarly.

Erin Welsh

So I feel like probably many other people can relate to this when I say that until doing this episode, Listeria to me was just one of those things that pops up occasionally with like oh, Listeria detected in this food or that food and be careful if you are pregnant. But it was just sort of another foodborne pathogen, which they can be very bad but I just sort of had lumped it all in together with some of the other culprits and I had no idea.

Erin Allmann Updyke Right. I did not know the extent of it either, even having been pregnant now twice and been like I'm not allowed to eat turkey, I'm so upset about it. But that's what it was to me, right. It was just like oh, I can't eat turkey and I'm annoyed. But I also did not realize the extent of why.

Erin Welsh Yeah.

Erin Allmann Updyke Just how scary it really is. So yeah, we're going to get into it today.

Erin Welsh We really are.

Erin Allmann Updyke Yeah.

Erin Welsh But first things first, feels very strange to dive into a cocktail or quarantini time but yet here we go.

Erin Allmann Updyke That's what time it is.

Erin Welsh That's what time it is. What are we drinking this week?

Erin Allmann Updyke We're drinking The Coldest of Cuts.

Erin Welsh We toyed with a lot of different names for this. Last episode was a dairy-filled cocktail because we did vitamin D, so we couldn't do dairy again.

Erin Allmann Updyke No.

Erin Welsh Although my second favorite name was Don't You Dairy.

Erin Allmann Updyke Which is very good, by the way. I do admit.

Erin Welsh And then there was The Salami Sling or The Salami Sour or The Cold Cut Collins. But I think I like The Coldest of Cuts.

Erin Allmann Updyke I love it, I love it. Erin, what is in The Coldest of Cuts?

Erin Welsh It is a slushy or blended Arnold Palmer with some rum in there, some spiced rum.

Erin Allmann Updyke Serve it alongside a nice turkey sandwich.

Erin Welsh Yeah.

Erin Allmann Updyke Or don't. We'll post the full recipe for that quarantini as well as the non alcoholic placeborita on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) and all of our social media channels.

Erin Welsh More podcast business website stuff. We've got lots of website stuff. We have transcripts, we have all of our references, we have links to merch, to our music by Bloodmobile, to our Goodreads list, to our bookshop.org affiliate account. We've got lots of stuff. Patreon.

Erin Allmann Updyke

I'm impressed with you.

Erin Welsh

I think I should have kept my post-it, it's not here anymore. I lost it in the break.

Erin Allmann Updyke

I'm impressed that you went through a list at all quite honestly. So you win.

Erin Welsh

Yeah, yeah. Well thank you.

Erin Allmann Updyke

All right. Well with that, shall we get into this episode?

Erin Welsh

We shall.

Erin Allmann Updyke

Okay. Right after this break.

TPWKY

(transition theme)

Erin Allmann Updyke

So the genus *Listeria* includes at least 17 different species of bacteria. But the main one that we're focusing on today is *Listeria monocytogenes* because that's the main causative agent of listeriosis, which is the disease that we're talking about today. *Listeria* in general are gram positive, this is a gram positive rod-shaped, so a little bacillus or sometimes it's called a coccobacillus because it's like a short rod, I don't know. They are a facultative anaerobe which means that they can grow both with and without the presence of oxygen. Already cool little bug. They can survive even at very low temperatures like in the refrigerator or the freezer and they can continue to grow under those conditions. And they're very resistant to other extreme environmental conditions like low pH, very acidic environments, or high salt concentrations. So these are very hardy little bugs. Most of the time they're found living, free living in soil or detritus or water and they also readily form biofilms, right. So they can form this entire biofilm that's really hard to get rid of.

Erin Welsh

Erin, what other episode were we talking about biofilms in?

Erin Allmann Updyke

I honestly have no idea.

Erin Welsh

Okay.

Erin Allmann Updyke

I would have to Google through our transcripts.

Erin Welsh

Yeah, yeah, yeah.

Erin Allmann Updyke

But yes, so that's a lot already that we've already talked about when it comes to this little bacterium. And because of all of these reasons, this bacterium poses a really big risk to the food industry because they can survive despite a lot of things that are food industry does to try to decontaminate everything, right. Like refrigeration, like acidic cleaning solutions, like high salt to preserve foods, etc. And then on top of that, you have this biofilm formation which can form on food production equipment and be really difficult to get rid of.

Erin Welsh

First of all, it's really scary. Second of all, I just did a search through our transcripts.

Erin Allmann Updyke

Love it.

Erin Welsh: And Legionnaires' disease.

Erin Allmann Updyke: Yes. Okay, that does make sense because of the little biofilms in the A/C equipment. Yeah.

Erin Welsh: If any of you listeners got that without having to search our transcripts-

Erin Allmann Updyke: You are better than us.

Erin Welsh: You win.

Erin Allmann Updyke: Okay. But this bacterium gets even cooler or rather it gets even more terrifying. Because while *Listeria* is a free living environmental microbe, it also can oscillate between being one of those, something hanging out in the soil, living and replicating just fine, and then switch to being an intracellular bacterium that invades mammalian host cells and survives and replicates inside of our cells. So it's also found as a transient inhabitant of both animal and human guts. And so there's a lot of evidence that we are all probably exposed to *Listeria monocytogenes* on a relatively regular basis, it's a really common pathogen in the environment because of this.

Erin Welsh: Again, I had no idea.

Erin Allmann Updyke: I know. I know, I know, I know. So the way that we get exposed to this in general is through our food. The way that this becomes a pathogen is it's a foodborne pathogen, which means that we eat this bacterium, we ingest it on our food, and it travels through our guts. But from there it's actually quite different from most any other foodborne illness that we've talked about. Here's why. In general, and this really did surprise me, the symptoms either go incredibly severe disseminated infection that we're going to talk about in detail, or mild if any symptoms and we might never know that you had this as an illness. So let me explain. When you ingest *Listeria* on your food, let's say on your turkey or your cheese or your lettuce even-

Erin Welsh: Anything really, which just adds to the scary column.

Erin Allmann Updyke: If you have a fully competent immune system, fully competent gut lining, no major risk factors, you may or may not get exposed to enough bacteria, a high enough bacterial load to cause an infection that's limited to your gastrointestinal tract, a gastroenteritis. So that might mean that you have some diarrhea or some nausea, vomiting. If that's the case, then those symptoms would generally start within about 24 hours of exposure and last for about 1-3 days which is a really common time frame and set of symptoms for a foodborne gastroenteritis. But we have essentially no clue how often this happens or what's the likelihood that if you're exposed to contaminated food that you get this kind of infection in the absence of any other risk factors for invasive infection, which we'll get to. Because we just don't have data on it. Most of the people that are getting foodborne illness of any kind, we're never detecting what that pathogen actually is and they recover with no issues. What we worry about with *Listeria*, the disease we know of as listeriosis, is an invasive infection. And when that happens the symptoms are different entirely, which I think is one of the most interesting parts of the *Listeria* story. Because it doesn't mean that it starts with this foodborne infection. Think of it as two different diseases entirely. Does that make sense?

Erin Welsh: Yeah. So you don't have the 1-3 day GI symptoms?

Erin Allmann Updyke: Not necessarily.

Erin Welsh: Okay, tell me why.

Erin Allmann Updyke

Why? I don't know. But from what I can gather, there are three major disorders that we worry about that are all classified under this umbrella of listeriosis, three manifestations. One are maternal fetal infections and this encompasses a lot of different possibilities that we'll get into. Two, bacteremia or septicemia, so infection of this bacteria in the bloodstream. And three, neural listeriosis or a meningitis picture, infection of our central nervous system. We've talked about other foodborne illnesses before, some of which can pose a risk of invasive infection like E. coli O157, for example.

But with those what we tend to see is a GI infection, you have these diarrhea, nausea, vomiting, fever, you're feeling crappy with a GI infection, your guts are a mess and then this leads to an invasive infection. But that is often not the case when it comes to listeriosis. So while we can see this gastroenteritis, nausea, vomiting, diarrhea, maybe fever, you're feeling crappy, but the cases that we worry about are actually separate entirely and the incubation period for these is not 24 hours, it's 1-4 weeks or more.

Erin Welsh

Whoa.

Erin Allmann Updyke

Yeah. So it's separated in time entirely. And so that's why I say was there a preceding diarrhea? Maybe. Would we even remember it? Maybe not.

Erin Welsh

I see.

Erin Allmann Updyke

But most of the data that I see doesn't even mention whether or not there was a preceding gastroenteritis picture.

Erin Welsh

That makes things so difficult I imagine for intervention. Because with something like E. coli it's clearly a GI bug that's then moving into disseminated infection and more severe infection. And this is like suddenly here's this disseminated infection but there's nothing that tips you off as to what it could be beyond the usual suspects. And Listeria is not necessarily a usual suspect.

Erin Allmann Updyke

Nailed it, Erin.

Erin Welsh

1-4 weeks. So is there like a threshold response where it's like the bacteria replicate in high enough numbers that suddenly they're systemic? Because it seems very sudden.

Erin Allmann Updyke

Yeah, let's talk about it.

Erin Welsh

Okay. I'm getting very excited.

Erin Allmann Updyke

I know.

Erin Welsh

Not excited but like intense about this.

Erin Allmann Updyke

I know.

Erin Welsh

And I can dial it back.

Erin Allmann Updyke

No, I love it. I love the intensity. I was feeling honestly the exact same way and I couldn't even wrap my brain around how interesting that part of the Listeria story is.

Erin Welsh

Yeah.

Erin Allmann Updyke

So let's first talk about the three major manifestations of listeriosis, perinatal infections, bacteremia, and the CNS, the nervous system infections. We'll talk about what those look like, how they present, how somebody would show that they have this infection, and what the results tend to be. Which are, spoilers, not good. And then we'll talk about the pathophysiology that kind of unites them about this bacteria. So when it comes to perinatal or neonatal infections, overall on average they account for an estimated 10%, plus or minus, of all listeriosis cases. And again when I say listeriosis, I just mean these three invasive infections. Think of the foodborne illness as totally separate.

Erin Welsh

Oh okay.

Erin Allmann Updyke

But perinatal infections are a huge cause of morbidity and mortality, especially of neonates. So I'm going to talk about that first. So a perinatal infection means infection with *Listeria* during pregnancy. And the symptoms here tend to be very non specific. It's often what's called a flu-like illness. So fever, chills, malaise, muscle aches, you're overall feeling really crappy. Some of the papers that I read described it as sometimes being mistaken for pyelonephritis which is infection of the kidneys. So really that could just be like back pain along with a fever and evidence of an infection.

Erin Welsh

Okay.

Erin Allmann Updyke

But with infection during pregnancy, while the infection for the pregnant person is very rarely severe or life threatening, the problem is that for the fetus, infection almost inevitably, 80% of the time or more, leads to severe complications. Because this is a bacteria that's crossing over the placental barrier very easily, infecting the fetus, and can lead to early pregnancy loss or stillbirth depending on how far along you are in pregnancy. It can lead to premature labor and delivery which can have a whole host of complications arising from that prematurity. And it can also lead to both an early neonatal infection right when that baby is born, they can become infected and have signs of either sepsis or meningitis, or if infection happens around the time of delivery, it can lead to a late onset meningitis. So a few days or weeks after delivery the baby can end up super sick from listeriosis as well.

Erin Welsh

So this is another thing where we're seeing a delay between exposure and ramping up and then severe complications.

Erin Allmann Updyke

Potentially. It all just depends on the timing of the infection during pregnancy.

Erin Welsh

So okay, speaking of the timing of infection during pregnancy, are there highest risk periods and how long is someone infected with *Listeria*? And I guess that answer is probably super variable.

Erin Allmann Updyke

Yeah, it's really variable. And it's even variable in terms of the timing of infection. Infection at any point during pregnancy, 80% of the time has severe complications. What those complications are going to be will depend on the timing of pregnancy. So more likely to lead to early pregnancy loss if you're earlier in the course of pregnancy, more likely to lead to a neonatal infection if you're very close to the end, etc. But at any time point we see severe complications for the fetus.

Erin Welsh

Okay. So it's always super high risk.

Erin Allmann Updyke

It's always super high risk, yeah. Which is terrifying.



Erin Welsh

Yeah.

Erin Allmann Updyke

And again here we tend to see a delay of 1-4 weeks between exposure for the pregnant person and when they start to have these symptoms of fever, chills, that mean that they have listeriosis and now the fetus is also infected.

Erin Welsh

These symptoms are not super severe, like I'm sure that they are extremely uncomfortable and painful but they're not necessarily something that's going to look like sepsis or whatever. So how does someone get tested for listeriosis?

Erin Allmann Updyke

Yeah. That's a really good question. And it's likely when there's a complication with the pregnancy. That's when someone is more likely to seek care when something is going wrong with the pregnancy if they haven't already sought care when they had these flu-like symptoms. And I don't want to downplay how sick someone would likely feel when they have listeriosis during pregnancy. They're feeling really sick. So it's very likely that they may go in and seek care and you would see that they have signs of an infection. But it's generally not life threatening for the pregnant person.

Erin Welsh

Right. Okay.

Erin Allmann Updyke

That's the big difference.

Erin Welsh

Yeah.

Erin Allmann Updyke

It is though life threatening for adults who are not pregnant in the other cases that we'll talk about. So let's get to that, shall we? And by the way, when I'm talking about groups who are at highest risk for infection aside from during pregnancy, there are a few groups that we see that are at highest risk. Primarily it's those of older age, especially over age 65, whether or not they have any immune compromising conditions but especially if they do have things like diabetes or perhaps were on steroids for one reason or another. So older age is the primary risk factor. We also see it like with neonatal infections in the very, very young as well as in people who are immunocompromised for one reason or another, which includes poorly controlled HIV infection or progression to AIDS, which we actually see as a really big risk factor for listeriosis. So what do these other infections look like outside of pregnancy? So in the case of a bloodstream infection with Listeria, which by the way accounts for anywhere from 30%-50% of cases of Listeriosis, which is a lot.

Erin Welsh

It's a lot, yeah.

Erin Allmann Updyke

With this infection the symptoms are incredibly non specific. And when you read them they really are just the symptoms of sepsis, which we covered in detail in our sepsis episode. So it often starts with fevers, feeling overall really bad like you're just not feeling like yourself, you often have chills. And because this is a cause of sepsis, then it's going to go on to develop the same severe complications and outcomes that we see in sepsis from any other bacterial organism. That is multi organ failure and eventually death from an overwhelming bacterial load in the bloodstream. But what's interesting is that there often isn't a single presenting organ that you might suspect as the etiology of this infection. Because while you got infected through your guts several weeks prior to presenting with the symptoms of bacteremia or septicemia, you may not have ever even had gastroenteritis symptoms. So in that way it's different than when we talked about sepsis and you're trying to think of what is the source. This would probably be a case where you'd have a really hard time identifying what is the source of this infection.

Erin Welsh: Yeah.

Erin Allmann Updyke: And when it comes to bacteremia and septicemia, the mortality rate is 20%-30%. And that is even with treatment.

Erin Welsh: It's so scary. It's so awful.

Erin Allmann Updyke: It's terrifying.

Erin Welsh: Yeah.

Erin Allmann Updyke: Finally Listeria can also cause a meningitis or in some cases, a new word, a rhombencephalitis.

Erin Welsh: Okay.

Erin Allmann Updyke: Which we'll talk more about because that includes the disease known as circling disease in animals.

Erin Welsh: Oh, thank goodness. I had that written down in my notes and then it just stayed 'circling', that was all that I...

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah.

Erin Allmann Updyke: So meningitis or infection of the central nervous system accounts for, by most studies that I saw, about 30% of cases of listeriosis in adults. So if you've been adding this up as we go, perinatal infection accounts for about 10%, bacteremia about 50%, meningitis about 30%, and we're left with an extra about 10% of cases that are very, very rare and we'll talk about in a minute.

Erin Welsh: And are these mutually exclusive categories?

Erin Allmann Updyke: Great question. No, no, they're not.

Erin Welsh: Okay.

Erin Allmann Updyke: You can certainly have a bacteremia and a meningitis picture at the same time.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. Yeah, yeah, yeah. Definitely. So in adults who end up with a meningitis or a meningoencephalitis from Listeria, again the symptoms are like another meningitis from a viral cause or a bacterial cause. So what that means is fever, headache, stiff neck. If it's infecting the brain itself, you might have things like confusion or even disruption in consciousness. Usually the onset is a little bit less abrupt than some other more common causes of bacterial meningitis, like pneumococcal or meningococcal meningitis. And it's often harder to detect Listeria in for example a spinal tap because this is an intracellular bacterium, so you have to wait until cell culture results because it's not going to show up on a gram stain necessarily.

Erin Welsh

Okay.

Erin Allmann Updyke

But one thing that's also interesting and seems to happen with Listeria and I don't know the frequency because some papers were like this isn't specific to Listeria and some were like yes it is. But it's a specific and bizarre form of meningitis that infects the cerebellum, the back part of our brain. When you look at a picture of a brain, it's like the two tiny balls on the back. And this is a rhombencephalitis, you see similar signs as a typical encephalitis, fever, headache. But more often you'll also see a lot of nausea and vomiting and then signs of what we call cerebellar dysfunction, like not being able to walk in a straight line, what we call ataxia. You might see cranial nerve abnormalities because your cranial nerves that innervate the muscles and sensory system of your face and neck come out in our brainstem near the cerebellum. And so you might see various palsies or abnormalities in the function of those nerves. And this is what we see in animals, especially ruminants who get infected with Listeria. This exact same type of infection, a rhombencephalitis. And it can lead to very odd behaviors including circling, where animals walk in a unidirectional circle and they have a head and neck deviation to one side. And it's all because of this infection in the back part of the brain and the brainstem.

Erin Welsh

Okay. So many thoughts. Number one, I remember seeing a video of circling ruminants of some kind, I can't remember what it was, going around like last fall. And I think that's when we added Listeria as a topic or we were like oh for sure, what's going on here?

Erin Allmann Updyke

So here's the thing, that video, almost certainly not Listeria.

Erin Welsh

What is it?

Erin Allmann Updyke

Don't know. There was a lot of explanations that I found online and I am not a veterinarian, so I'm not going to try and delve into the nitty gritty of what those are. But the reason that it most likely was not Listeria is because first of all, you're right, I wouldn't expect that an entire herd is going to get infected in the exact same way at the exact same time with a pathogen that's an opportunistic pathogen, that's not infecting everyone equally.

Erin Welsh

Well and so that's my other question about that, because ruminants, because livestock can be infected and be totally fine and they just shed Listeria into the environment.

Erin Allmann Updyke

Just like us.

Erin Welsh

Okay. So this would be a case, this would be an individual more likely.

Erin Allmann Updyke

Exactly.

Erin Welsh

Okay. And this would be an individual that had something else going on, that was immunosuppressed in some way.

Erin Allmann Updyke

Exactly. Yes. And it wouldn't be walking in a perfect unidirectional circle with all of your friends like that video of the sheep that was going around virally. It would be a lot more of that ataxic gait, it would be a lot more like stumbling, kind of confused gait.

Erin Welsh

Okay.

Erin Allmann Updyke

Would it still be unidirectional? Likely yes because often what we see in animals is this asymmetric infection, so you're damaging one side of the brainstem more than the other and that's why you see a unilateral picture of infection.

Erin Welsh

Okay. So let's talk about why the heck it happens there. Do you have an answer?

Erin Allmann Updyke

That we don't have an answer to.

Erin Welsh

Okay, okay.

Erin Allmann Updyke

Like why that part of the brain? I don't know.

Erin Welsh

Yeah. And why one side?

Erin Allmann Updyke

Yeah, I don't know. Great question.

Erin Welsh

Okay.

Erin Allmann Updyke

So those are all of the different ways that you can get listeriosis. I did mention the remaining 10% of cases are often localized infections. So you can actually see skin infections, especially maybe among people who get exposed from livestock. Or rarely other specific organ infect like an endocarditis infection of the heart or a liver infection or infection of the wall of the abdomen. So we can also see potentially infection in specific organs but this tends to be very, very rare compared to the other manifestations of listeriosis.

Erin Welsh

Okay.

Erin Allmann Updyke

So how does this happen? Why does this happen?

Erin Welsh

Yeah. It's crossing the placenta, it's crossing blood-brain barrier. This bacterium has a lot of tricks up its sleeve.

Erin Allmann Updyke

You nailed it. I didn't realize, something that I didn't realize at all before researching for this episode is that because of these traits, *Listeria* has actually become a model organism of infection and invasion because it is so good at invading across our normal protective barriers. So in the case of a person who's immunocompromised and exposed to *Listeria*, *Listeria* can then cross three, you named them, very important structures that we usually use to keep pathogens out. First it's crossing over our intestinal epithelium, so it's no longer just limited to our guts. It has a really easy time penetrating these tight barriers. It makes its way into our lymph system and our bloodstream where it can then travel to our liver and our spleen, and in theory any organ but primarily the liver and spleen, and continue to grow and progress to infection. It can then also, like you said Erin, cross our blood-brain barrier. So it can cross through these other really tight cell to cell junctions made to keep bacteria out. And then it very easily crosses the placental barrier and is able to infect a developing fetus.

So how is it able to do this? How is it so easily able to cross these barriers? The truth is that it's largely because this bacterium has adapted to not just survive but also divide, continue replicating, and thrive within the cytosol of our cells. Both cells like our macrophages, which I talk about a lot but these are the white blood cells whose job it is to go out and find and engulf and usually neutralize bacteria. So Listeria can survive that normal neutralization process that macrophages do by actually hijacking those macrophages' machinery and breaking out of the vacuoles that we've trapped it in and replicate inside of those macrophages. But Listeria can go one step further. They can then actually escape cell to cell.

Erin Welsh

It is so wild.

Erin Allmann Updyke

It's amazing. So they're able to spread directly from one of our cells to another of our cells without having to leave the cell that they've been replicating in. Most of the time when I've talked about intracellular pathogens like viruses and other intracellular bacteria, I say they replicate and replicate and then they burst out of our cells and they travel through the bloodstream to infect another cell.

Erin Welsh

Yeah.

Erin Allmann Updyke

Listeria don't have to do that part. They can intentionally travel from cell to cell to cell without having to burst out and enter our bloodstreams or our lymphatics. And they can do this not just in our macrophages. Our macrophages and other white blood cells intentionally engulf bacteria. So bacteria have an easy time getting inside of macrophages, there's a lot of bacteria we've talked about on this podcast that can survive inside a macrophage, they've evolved to escape that one protective response. But Listeria take it one step further. They have a whole host of other receptors that allow for them to intentionally enter our other cells like our intestinal epithelium, like other cells in our spleen and our liver and throughout our body, and survive and replicate within those cells as well. It's incredible.

Erin Welsh

It's incredible. So this bacterium is slowly invading our entire body.

Erin Allmann Updyke

Yeah.

Erin Welsh

Hopping cell to cell, or sneaking cell to cell to anthropomorphize, and most of the time it's doing this silently more or less. Right?

Erin Allmann Updyke

Well that's a really good question, Erin. That question has a lot to it because the question is what percentage of the time, if I'm exposed to Listeria in my turkey sandwich, is it getting through my guts and replicating in my cells without me ever getting sick from it? Does that happen? Or does it not? Do I have a gut barrier that doesn't allow it to penetrate? And in the case that it does penetrate, does it just take those 1-4 weeks for the bacteria to replicate to a point at which our body recognizes it and now is causing a response that is illness, right? And that is that overwhelming infection that now we're really sick from. I don't know which of those two. My suspicion is that it is the latter where in people who don't have any risk factors who are not getting severely ill from this, most of the time this bacterium is not establishing an infection in our cells for a very long period of time.

Erin Welsh

Okay. And when our body recognizes it as a pathogen, which happens at a certain point later on when things are real bad, what is that response like? Because it's unusual, right?

Erin Allmann Updyke  
Yeah. So it seems like one of the biggest risk factors for infection with Listeria, for listeriosis, these invasive infections, is lack of a adequate T cell response. So it is T cells that are primarily the ones that are blocking this infection from happening and responding to this infection when it is established. And so for cases when you lack that response for one reason or another, that is when you actually see listeriosis manifest itself. And that is largely because of the way that it's an intracellular only pathogen, our T cells are much more involved in that part of our immune response, like killing infected cells vs antibody responding to bacteria that are free floating in our bloodstream.

Erin Welsh  
Okay.

Erin Allmann Updyke  
So you don't see a lot of the more antibody mediated response with Listeria.

Erin Welsh  
Which is fascinating.

Erin Allmann Updyke  
It's interesting because it's still a bacterial infection.

Erin Welsh  
Yeah, yeah. And that means presumably that is there sustained immunity to Listeria?

Erin Allmann Updyke  
Right. Probably not. I don't think we have any data on that whatsoever though.

Erin Welsh  
Yeah, yeah.

Erin Allmann Updyke  
Because mortality is really high and because it's a very rare infection still. Thank goodness. But that is most of the biology of Listeria and the disease that we know of as listeriosis.

Erin Welsh  
It's a bad one.

Erin Allmann Updyke  
It's a really bad one. It is treatable with antibiotics and in general antibiotic resistance has yet to be a huge concern in terms of the normal antibiotics that we would use to treat it. But it tends to respond better to specific antibiotics that maybe aren't used as commonly as general antibiotics if someone comes in with bacteremia or septicemia. So a lot of times we do see delays in appropriate treatment because it's a hard disease to diagnose.

Erin Welsh  
And which I would guess contributes to mortality rate?

Erin Allmann Updyke  
Absolutely contributes to mortality rate. Yes, definitely. So any other questions, Erin?

Erin Welsh  
I mean I have a lot but I'm sure I'll come up with something again at some point?

Erin Allmann Updyke  
Yeah. Well can you tell me where this bacterium came from and how long it's been making us sick and everything that we know about it and how we got here?

Erin Welsh  
Oh yeah, everything. I'll just everything.

Erin Allmann Updyke  
All of it.

Erin Welsh  
All of it. Right after this break.

TPWKY  
(transition theme)

Erin Welsh

In many ways, I think that the story of *Listeria monocytogenes* will sound maybe fairly familiar to you.

Erin Allmann Updyke

Okay.

Erin Welsh

Especially you Erin but also you listeners if you have listened to the podcast before. It involves the discovery of a new pathogenic microbe in the early 20th century. And then it's followed by the realization that hey, this pathogen is a lot more widespread than we previously thought. And then people tracing its spread not just in present day but also in the past. And it's a fascinating story of discovery and it follows this common pattern. But what I think separates the story of *Listeria* from these other ones comes down to a few things. And by the way when I say *Listeria*, I am specifically referring for the most part unless I say otherwise to *Listeria monocytogenes*.

Erin Allmann Updyke

I mean same.

Erin Welsh

Yeah. But one of these things that separates this story out from some of the others is what I found to be a surprising delay between discovery and when people realized how it was commonly transmitted, and we'll get into that. And the other is just how well we can see the drivers of pathogen movement across time and space.

Erin Allmann Updyke

Ooh okay.

Erin Welsh

And that's not just in hypothetical terms but by looking at what this bacterium's biology can tell us about the past. I love this.

Erin Allmann Updyke

Ooh okay.

Erin Welsh

We'll get into all of it. But first, let's start at the beginning. And I'm skipping right to the discovery side of things because even though you asked where did this thing come from, *Listeria* is widely distributed in the environment and it can infect a ton of different animals. And so I don't really know when or where it first emerged. There are some papers looking at the evolutionary relationships among some of the species within the *Listeria* genus and some of the non pathogenic ones compared to the pathogenic ones and looking at when did they evolve virulence and so on and so forth. But I'm not going to get into it.

Erin Allmann Updyke

Okay.

Erin Welsh

Okay. But when did we as humans first recognize it as such?

Erin Allmann Updyke

Yeah.

Erin Welsh

Well sometimes people look for a pathogen to match a known or an infamous disease, think like plague or cholera or something. Other times it's more of like a fishing expedition. You cast your net and you see what you pull up. There are some where people are just like let's collect swabs from infants' throats and see what we find or from pond water or this rabbit's foot or something.

Erin Allmann Updyke

Okay.

Erin Welsh

Yep. And sometimes it happens I think a bit more methodically, in a bit more of an expected fashion, as much as scientific discovery can be expected in any case. *Listeria monocytogenes* or *Bacterium monocytogenes* as it was first called falls into this last category. And I'll tell you how. In 1924, a researcher named Everitt George Dunne Murray happened to be looking in the blood of lab rabbits when he found something new. And I say happened to be but it was really quite intentional, as you'll hear when I read a snippet of his paper which I felt was written in a surprisingly poetic way. And I love when that happens with older papers, it was lovely. So I have a lot of quotations here from it. Hopefully not too many but I think you'll enjoy it.

Erin Allmann Updyke

I love it already.

Erin Welsh

All right. Prepare yourself, this is a long quote.

Erin Allmann Updyke

Okay.

Erin Welsh

Quote: "An important responsibility attached to the breeding of normal laboratory animals for the Department of Pathology was the routine autopsies on animals which died. This practice was rewarded by the control it exercised over the quality of the stock and by the interesting diseases it discovered. Foremost amongst these is the disease described in this paper. In May 1924, 6 cases of rather sudden death in rabbits were observed to present strikingly similar lesions, though no direct cause of the evidently acute toxic or infectious condition could be discovered in any of them. The interesting characters presented by the disease and the increasing mortality amongst our young rabbits caused us to watch carefully for any signs of illness and to investigate all cases which occurred. Although there seemed to be every reason to suppose that the disease was of a septicemic nature, all cultures from the heart's blood remained sterile. During July 1924, small gram positive bacilli were found in films of the acidic fluid in a guinea pig and in smears from the omentum of a rabbit." Side note, I don't know what an omentum is. So I didn't look it up, I forgot to.

Erin Allmann Updyke

Do you want me to tell you?

Erin Welsh

Yeah, yeah, tell me.

Erin Allmann Updyke

So it's like this kind of like fatty layer that lays over our guts. It's attached to the top of your guts and then it kind of lays over all of your intestines and it's a little cushioning there for you. It's nice. It's really nice.

Erin Welsh

Omentum. Cool. All right, back to the quote because I have just a few more lines. "But little heed was taken of these and the heart blood cultures remained sterile. In August 1924, a pure culture of a small gram positive bacillus was obtained from the heart's blood of an obviously acute case in a pregnant rabbit. These bacilli closely resembled those seen in the two animals during July and with their isolation and pure culture, our experimental work began." End quote. So basically what happened here was that they found this disease, they found some sort of condition in these rabbits, they kept culturing and culturing, and then eventually they found this gram positive bacilli.



And after that point, once they were able to culture this, they conducted a bunch of observational and experimental work which included a combination of clinical observations of the young rabbits in the lab, autopsies, tissue preparations, experimental infection, culturing the organism, things that are not just the usual but like the usual and then some. This was a packed paper full of information. It was really quite impressive. And what they found was that the infection seemed to hit the young rabbits particularly badly, causing some to die very suddenly and others to die over the course of weeks. The researchers remarked on how striking the disease was, like how distinguishable it was. Once you saw it in an animal, there was very little else that they felt it could be which I thought was really interesting because like we've talked about in the biology section, like you talked about, it's very difficult. You can't look at someone and go oh, that's Listeria for sure.

Erin Allmann Updyke

Yeah. Right.

Erin Welsh

But they evidently could do that at least in the way it manifested in rabbits. And it was this characteristic nature of the disease that was part of the reason why Murray, the lead author on the paper, thought that this must be a new pathogen not yet described. Quote: "Both the natural and experimental disease have interesting and characteristic features and their consideration has forced us to the conclusion that the causative organism either has not been described previously or has been inadequately described and so cannot be traced in the literature. In either case, we feel justified in naming it. Its salient character is the production of a large mononuclear leukocytosis. This is by far the most important and most striking character we have discovered and we name the microorganism we shall describe in this paper Bacterium monocytogenes."

Erin Allmann Updyke

I love that.

Erin Welsh

I love it. We feel... What was it? We feel justified in naming it. I love it. I mean maybe they were justified in naming it but they certainly weren't the first people to culture it, especially given its widespread prevalence in nature.

Erin Allmann Updyke

I wonder if the really high monocytes, peripheral monocytes that they were seeing were part of what they said. Once you see this, you know it can't be anything else because that is true in rabbits but it is not true in humans.

Erin Welsh

Interesting, yeah.

Erin Allmann Updyke

Yeah. That's interesting in and of itself.

Erin Welsh

Yeah. Why do different species respond differently to this? But yeah, so not only had other, there's pretty strong evidence for other people, other researchers having identified or at least isolated this bacterium before, but either they're being punished for the crime of not writing their paper in English or they didn't describe it well enough or it was classified as something else. But then also retrospective analysis of old tissue sections seemed to indicate that there were human infections at least before WWI.

Erin Allmann Updyke

Okay.

Erin Welsh

I mean all of this is just to say that like this bacterium has been around. There was no sudden rise necessarily or any sort of reason why Murray was in the right time and place for it. It was just a really well written paper. But unlike we've seen with other infectious diseases in the past, it didn't necessarily lead to this widespread recognition where everyone's like oh my gosh, I see it, it's everywhere, suddenly here's Bacterium monocytogenes. It kind of laid low for a while. It was mentioned in textbooks, it got a genus name change along the way from Bacterium or whatever it was called to Listeria. And also side note, Listeria of course is to honor Joseph Lister.

Erin Allmann Updyke

Lister!

Erin Welsh

Who features in our sepsis episode. So go check that episode out if you want to learn more about his story if you haven't already. Anyway, in the 25 years or so since Murray first cultured this bacterium, it didn't really make itself known as a pathogen of public health importance. It took a while which I find interesting. Mostly it was found in small rodents or in domestic animals like sheep, causing occasional outbreaks in those organisms. There were a handful of human cases reported in Denmark in 1929 and at the time it was thought to be related to infectious mononucleosis. But in general it was thought to be extremely rare in humans, like so rare that it didn't merit a mention in bacteriology textbooks relevant to human health at the time.

Erin Allmann Updyke

Wow.

Erin Welsh

But it did merit a note from a researcher named Burns in 1935 who warned that Listeria monocytogenes could be a cause of granulomatous septicemia in infants and fatal meningitis in adults. But this warning by Burns was either forgotten about or never heard in the first place until 1951 when H. P. R. Seeliger at the University of Bonn, who wrote the textbook on Listeria literally, and I think there's a species named after this researcher as well. When Seeliger isolated the bacteria from lesions in newborns who had infections that resembled some that had just been written about from Germany, had just been published about. And so researchers there in Germany a couple of years before had isolated the same bacteria from various tissues of 83 newborns and stillborn infants who had been diagnosed with quote unquote "granulomatous infantiseptica" which was thought to be a never before described infection.

Erin Allmann Updyke

Ooh okay.

Erin Welsh

But these researchers thought that the bacteria they had found was a kind of Corynebacterium and it was only realized that it was Listeria monocytogenes after Seeliger recognized it as such a couple of years later. So like I said, this was certainly not the first time that Listeria had infected humans and some researchers have looked back at case reports from the late 1800s and early 1900s and hypothesized that listeriosis may have previously been diagnosed or described as quote unquote "pseudo tuberculosis" or quote unquote "neonatal septicemia". And I saw a reference to a paper that I couldn't access where the author speculates that Queen Anne, who lived from 1665-1714, had repeated pregnancy losses, stillbirths, neonatal deaths, and post natal meningitis. 17 pregnancies overall with no living offspring.

Erin Allmann Updyke

Oh my.

Erin Welsh

And some people have speculated that it was due to Listeria. I don't know.

Erin Allmann Updyke

That's a lot of Listeria.

Erin Welsh

That's a lot of Listeria. So even though we know that Listeria probably infected people throughout history, there's no way to make precise estimates of past prevalence for something like listeriosis. But infections did seem to start rising in the second half of the 20th century. This could be due in part to the increase in microbiology techniques and the fact that people knew about listeriosis. But-

Erin Allmann Updyke

Or?

Erin Welsh

I think it could be the large scale changes in food production and the lag in food safety policies that had been taking place and continued to take place throughout the 20th century.

Erin Allmann Updyke

Yeah.

Erin Welsh

Okay.

Erin Allmann Updyke

Big chicken. Big chicken all over again.

Erin Welsh

Big chicken. Yeah, I mean and this goes back even further. I love talking about the Industrial Revolution and how it changed so much in terms of health and disease, the rise of cities, the growth of hospitals, the commercialization of medicine, the poor air quality, the limited diets, the mass produced foods, etc, etc. Many pathogens as we know, as we've talked about, absolutely flourished in these new settings, including Listeria. We now think of Listeria as a pathogen that is primarily associated with food. Many outbreaks have been traced to food like milk, cheese made with raw milk, deli meats, hot dogs, fruits and veggies contaminated with manure containing Listeria. But the link between Listeria and contaminated foods was only made in 1983 after an outbreak of listeriosis among pregnant people and infants with an extremely high mortality rate of 27% of the infants born alive, despite aggressive supportive care, and 47% overall.

Erin Allmann Updyke

1983?

Erin Welsh

1983. So this particular outbreak was linked to coleslaw that had been contaminated by sheep manure containing Listeria.

Erin Allmann Updyke

Gross.

Erin Welsh

So before then, before this outbreak, researchers suspected that humans got infected with Listeria from some kind of indirect transmission from animal sources, especially given its widespread prevalence in domestic and wild animals. But this was the first time that it was actually demonstrated. Epidemiologists went to the farms or went to the food production facilities where this coleslaw had been processed and they were like oh, it's in the poop.

Erin Allmann Updyke

Everything.

Erin Welsh

Yeah. And later on I'm going to pick back up on some of these foodborne outbreaks of Listeria and lessons learned and so on but first I want to head back into the Industrial Revolution where I started this whole topic. So during this time, as more and more people began to move to live and work in cities, food production had to change to accommodate these increasing population densities. There was more of a demand for mass produced foods and processed foods as the time from harvest to table grew longer and longer. And of course as we've talked about on the podcast before, food safeties or technology allowing for analysis of food and food safety, it lagged tremendously far behind these new food production practices, especially in the US where the giants in food industry who were more concerned with profit than the health of their consumers, actively discouraged any safety legislation from being passed in the US for years. Years! Decades.

Erin Allmann Updyke

0% surprised.

Erin Welsh

Even though it's not surprising, it's shocking somehow still or just appalling maybe. Milk was diluted with pond water, it was preserved with formaldehyde, and adulterated with plaster of Paris to get rid of the murky blue tint because it had been diluted with pond water and you could see horsehair worms swimming in the milk.

Erin Allmann Updyke

Oh no. No, no. Stop it. Stop it. Stop!

Erin Welsh

But the plaster of Paris made it look farm fresh and straight from the udder.

Erin Allmann Updyke

Stop it. Oh this is worse than arsenic. I feel like you talked about similar things. Yuck!

Erin Welsh

Yeah. I mean meat production, like don't even get me started. It was equally appalling if not more so. There's a reason that Upton Sinclair's 'The Jungle' caused such a stir. No food was safe to eat. Spices like cinnamon was mostly just brick dust for instance. If you want to learn more about this, stay tuned to the podcast for a bonus episode later this season where I interview Deborah Blum about her fantastic book 'The Poison Squad' which goes into the fascinating history of food safety in the US.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

Or read the book now if you don't feel like waiting for the episode.

Erin Allmann Updyke

That sounds thrilling.

Erin Welsh

Yeah. It's such a jaw dropping book.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

It's great. Yeah. Okay anyway, it's easy to see how these practices with essentially no oversight for food safety, mass processing of milk-based products and meats, longer times between production and purchase, no refrigeration, how these things would have led to a massive increase in Listeria, both in terms of prevalence as well as geographically. But this time we don't have to settle for speculation. A paper from 2021 by Moura et al traced the global spread of Listeria, particularly one clonal group, LmCC1 if anyone's interested. And this clonal group commonly causes infection in humans and is often found in cattle and dairy products. If you remember from our anthrax episode, the clonal aspect of this really helps with being able to more closely trace diversification and rates of evolution and so on.

And when these researchers looked at the genetic diversity of this group, what they found was that around the mid 19th century, Industrial Revolution time, this clonal group underwent a big period of expansion both in overall diversity as well as geographic expansion particularly in Europe. If you overlay this with what was going on in the global food trade, you would find that in 1870 the North Atlantic Meat Trade Agreement was passed which allowed for excess cattle in North America to be shipped to Europe whose cattle population had dwindled due to things like contagious bovine pleuropneumonia and foot and mouth disease. It's all about diseases.

Erin Allmann Updyke

It's always about diseases, Erin.

Erin Welsh

It is. We're not biased or anything. But this trade agreement isn't just a matter of a few head of cattle. According to this paper, it led to a 1000 fold increase in the amount of cattle moved from North America to Europe.

Erin Allmann Updyke

Wow.

Erin Welsh

And right around this time the researchers estimate is when this particular clonal group of Listeria arrived in Europe, after which it spread across the continent, helped along by railroad expansion which was currently going on both in Europe and North America. And it continued to diversify along the way. A drought in Oceania from 1895-1903 led to cattle and their Listeria being transported there. And then subsequent decades saw the continued global spread of this pathogen from North America to Asia, to Oceania, from Europe to Africa, basically all over the world. And the pattern in genetic diversity of Listeria supports this, increasing during this time of widespread cattle movement. And then this is the part I find so interesting, slowing down during the Great Depression when countries such as the US and many other countries stopped exporting cattle and other foods for a while. Because they were like we need to feed our people in this country or whatever.

Erin Allmann Updyke

Right. Oh my gosh, that's really, really cool that they had enough data to be able to see that.

Erin Welsh

Right? And then it keeps going. When trade resumed and cattle farming and food industrialization intensified around the mid 20th century, boom, you can see that. These changing practices are reflected by what's happening also with this clonal group which is so amazing.

Erin Allmann Updyke

Yeah.

Erin Welsh

And has also been seen for a few other foodborne pathogens with a zoonotic reservoir like E. coli O157:H7. So it seems pretty likely to me that the apparent rise in listeriosis around the mid 20th century may not have been just because people knew what to look for. It seems like it could be tied to the widespread global expansion of this pathogen.

Erin Allmann Updyke

Yeah. And changes in food production that just favor this pathogen's growth.

Erin Welsh

Yep. Just favor contamination.

Erin Allmann Updyke

Yeah.

Erin Welsh

Like actively promotes contamination. But I mean it certainly did help once people knew what they were looking for. It wasn't until the 1980s that another change was made that we can see in these clonal groups, which is the stabilization of the clonal population. And that happened around the mid 1980s which is after people realized that it was tied to food production and certain food practices. And so they started to institute these safety measures.

Erin Allmann Updyke

Oh my gosh, how interesting.

Erin Welsh

It is so cool. And I really hope that I interpreted this paper correctly and granted this study did look at just one clonal group and there are others that are known to cause disease in humans, but I think it's just so cool because usually on the podcast I feel like I'm talking about the spread of this or that pathogen in purely hypothetical terms.

Erin Allmann Updyke

Right.

Erin Welsh

It's likely that this period of history led to the proliferation of this pathogen because more people were going to hospitals. Or as we know, war always leads to increased infectious disease because of crowded and unsanitary conditions. It's not very often that we can actually trace the impact that certain political practices I think had on a disease that we know about so much more recently than... I don't know, I just think it's so cool.

Erin Allmann Updyke

Yeah. And to be able to track pathogen diversity like that, that's very cool.

Erin Welsh

Yeah, it's beautiful. But not only is it interesting or beautiful, it also helps us with control or prevention today. Since Listeria is not transmitted human to human and mostly comes from contaminated food sources, even if we don't necessarily always or even often know the source of the contamination, and because of the biology of this pathogen, it's clonal nature, the fact that at the local level certain genotypes dominate, we can use all this information to trace persistent sources of infection. Like whether it be from a particular herd, maybe there's a really high prevalence in a certain herd on a farm or within a certain farm or within a certain processing facility. And that's where public health officials can sort of target or put resources to eliminate the bacterium there.

And on that front we've made a lot of progress since the 1980s in large part thanks to the outbreaks of listeriosis that highlighted just how deadly it could be, sparking these public health and food safety responses. So earlier I mentioned that 1983 Listeria outbreak in Canada tied to contaminated coleslaw and that was the one that really solidified food as a source of the pathogen. But that was really only the beginning in terms of food associated outbreaks of Listeria. That same year another outbreak of listeriosis involving 49 people, primarily infants and immunosuppressed adults, and a fatality rate of 29%, was detected in Massachusetts. This time linked to milk, not raw milk but pasteurized milk which pointed towards dairy products as a source of Listeria monocytogenes, because remember the first one was coleslaw.

Erin Allmann Updyke

Right.

Erin Welsh

And so this one really put dairy on the map. And sure enough, a couple of years later soft cheese was the culprit and a large outbreak of listeriosis in California involving at least 101 human cases and 50 or more deaths.

Erin Allmann Updyke

Oh my, that's massive.

Erin Welsh

Massive. Ice cream was next on the chopping block when the bacterium was found in large quantities of a well known brand, they didn't name it in the paper. And there have been subsequent ice cream associated outbreaks as well. And one consequence of these outbreaks was that screening for Listeria, especially in cheeses and other dairy products, ramped up significantly all over the world with the finding that Listeria was so, so much more prevalent in certain types of cheeses as well as in raw meat and meat products than anyone had guessed before. And of course with this alarming news, the WHO and national public health authorities got involved and began to investigate how to best stop this bacterium from getting into the food supply and how to raise awareness among medical professionals about potential outbreaks and how to estimate or even begin to estimate the scope of this problem.

Erin Allmann Updyke

Yeah.

Erin Welsh

Research into the ecology of this pathogen revealed how widespread it was not just in livestock settings but also in the wild, found in soil or infecting wild animals. I read one paper that found *Listeria monocytogenes* in nearly half of the black bears that they sampled in parts of the eastern US.

Erin Allmann Updyke

Bears? Oh my gosh.

Erin Welsh

I know. And also have different conditions in farms, things like herd size or livestock composition, like whether you have this many sheep or this many cattle or whatever, grazing or housing practices, how all of these things could change the amplification or dispersal of the pathogen or select for certain strains that differ in their abilities to infect humans or livestock. Basically there's been a lot of information that we have uncovered and are continuing to uncover. And while outbreaks did continue to happen and continue to happen today, these improved safety measures along with this greater understanding of the ecology of this bacterium led to a pretty substantial decrease in reported listeriosis cases in the 1990s, from 11 per million population in 1988 to 4 cases per million in 1998. So that's a pretty substantial decline.

In 1999 a US wide outbreak involving 101 cases and 21 deaths linked to hot dogs stopped Listeria from dropping further down on the foodborne priority list as it kind of had been doing since like hey, the measures we're implementing are working. And this outbreak in conjunction with other sporadic outbreaks as well as individual cases has kept people searching for ways to stop this pathogen from invading the food supply chain. And I have to admit that when reading about all of these outbreaks and the subsequent response, like it's great that there seems to be a response, but it's also frustrating or I wish it could be different that it has to be a response, it has to be reactive and people have to experience these horrible things in order for change to be made or in order for people to go hey, maybe we should re-examine how often we're testing this particular machine for Listeria or what constitutes an acceptable level of Listeria or so on.

Erin Allmann Updyke

Oh Erin.

Erin Welsh

I wish that we could be proactive.

Erin Allmann Updyke

That's a whole other set of discussion, isn't it?

Erin Welsh

Well that being said, I think it is important to recognize that we have come a long way not just in food safety practices but also in our understanding of *Listeria monocytogenes*. And as you mentioned, not just as a pathogen of public health importance but also what it can tell us about things like cell signaling, surface proteins, innate immunity, and my favorite mention was patho-epigenetics.

Erin Allmann Updyke

Ooh!

Erin Welsh

But I don't want to step on your toes, Erin. So why don't you bring us up to speed on where we stand with listeriosis today and also why the heck cellular biologists are so fascinated with this bacterium.

Erin Allmann Updyke

I can't wait to. We'll take a quick break and then get into it.

TPWKY

(transition theme)

Erin Allmann Updyke

In the US annually the CDC estimates that there are 1600 cases of listeriosis. So again, that means invasive infection, not just diarrhea. 1600 cases and 260 deaths annually. And as far as I can tell that statistic does not include necessarily things like early or premature labor or other pregnancy complications that don't result in death of a neonate, that would be counted as deaths. So that's not a massive number compared to most of the pathogens that we talk about on this podcast.

Erin Welsh

Yeah.

Erin Allmann Updyke

But it's not an entirely small number either.

Erin Welsh

Right.

Erin Allmann Updyke

When we try and look globally, unsurprisingly we don't have great numbers.

Erin Welsh

What?

Erin Allmann Updyke

But the World Health Organization estimates anywhere from 0.1-10 cases per one million people per year globally. So if we Erin math that situation-

Erin Welsh

Love it.

Erin Allmann Updyke

Trademark Erin math. That is anywhere from 800-80,000 cases globally every year which is a huge range. But altogether numbers that are significantly smaller than numbers that you mentioned, Erin. And I think one thing that's really interesting about this is that I talked about the pathogenesis of this and how terrifying and how severe the disease listeriosis is when it causes this invasive infection in people who are susceptible, immunocompromised, or during pregnancy. But this is still a very rare pathogen. And despite that, like you said Erin, it's still an incredibly important part of how we make our food safety regulations. Which I think is fascinating and it really has sparked, continues to be a big point of debate. The US actually has I learned a zero tolerance policy for *Listeria monocytogenes* in industry sampling which I was shocked by.

Erin Welsh

Yeah, me too.



Erin Allmann Updyke

How often are we testing, etc? I don't know. But it does have a zero tolerance policy. Most other countries don't necessarily have a zero tolerance policy because that's really difficult to achieve. So deciding how do we balance risk of infection vs being able to feed a growing global population, it's really difficult. But I do think that it's really interesting that a pathogen that is as rare as Listeria, when you look at it compared to other foodborne illnesses causing hundreds of millions of infections, it still has a really important role to play in making this kind of policy because of how severe it is when it does happen.

Erin Welsh

Right.

Erin Allmann Updyke

And because like you mentioned Erin, we do still see a lot of outbreaks, foodborne outbreaks associated with specific types of foods. Which means that this is a pathogen that could potentially cause quite a lot more morbidity and mortality if a large outbreak were to occur. In terms of the types of foods that are highest risk, I think you mentioned a lot of them already. But you can think of them as things that are already prepared and then refrigerated and then you eat them, right. Because despite how hearty of a bacteria Listeria monocytogenes is, it can't survive the cooking process. So foods that you take home and cook, like most meats that you're cooking thoroughly, even if they have Listeria on them, if you're cooking them thoroughly then that Listeria is going to die.

But foods like a deli turkey or deli ham, any deli meats that you don't cook when you bring home, that are cooked and then processed and refrigerated and sold for immediate consumption, those if contaminated with Listeria can pose a significant risk because that Listeria can continue to replicate even if it's at very low levels in that food to begin with and then can cause infection thereafter. The same thing is true for milks that are raw or unpasteurized or cheeses that are not cured, so like soft cheeses that are made from milks that are unpasteurized. Those are some of the highest risk things that we've seen. But we see outbreaks in other things too, like one that's ongoing currently as we record in Enoki mushrooms in the US.

Erin Welsh

Yep.

Erin Allmann Updyke

Often consumed raw, those mushrooms. In 2022 in the US we saw outbreaks in deli meats and cheeses, like generically just meats and cheeses of deli counters across the country. We also saw outbreaks in some soft cheeses like bries and camamberts, and in ice cream like you mentioned. There's been outbreaks in various bagged salads, things that again are prepared and ready to eat. So those are the kinds of things that tend to be highest risk and that's why the recommendations tend to be that people who are at high risk, who are immunocompromised or pregnant, try to avoid those foods. That's hard to do.

Erin Welsh

Yeah, it's really hard. And it seems like it could also be an issue of access where it's difficult to buy food to then prepare rather than getting... Like who has the time or it's more expensive sometimes to buy food to then prepare. And so that's an interesting I think component of it.

Erin Allmann Updyke

Yeah, absolutely. Absolutely. But that's kind of where we stand with infections with listeriosis today across the globe. A lot left to be desired I feel like. But I think we're in a very interesting place where it's definitely still a pathogen of big concern especially for the food industry and it's something that still shapes how our food industry operates and makes decisions globally.

Erin Welsh

Yeah.

Erin Allmann Updyke

I do think in terms of even bigger picture future directions and research when it comes to Listeria, the most exciting thing is all of the ways in which Listeria serves as this model organism that I mentioned in the biology section. Which again, I had no idea but I will post a few really great incredibly detailed papers about the kinds of research being done on the pathogenesis of Listeria and what the implications are for what we can learn about intracellular infection in general as well as our understandings of cell to cell communication on a broad scale. Because understanding Listeria infection has implications for understanding the process of infection and dissemination and how pathogens not just evade our immune responses but also penetrate these supposedly impenetrable barriers that are meant to keep them out. But also the way that our cells actually talk and communicate with each other because Listeria hijacks a lot of these mechanisms in our own cells. So the things that we are learning from Listeria are having and I think will continue to have implications that go far beyond this one foodborne pathogen. Which just fills me with thrill.

Erin Welsh

Yeah.

Erin Allmann Updyke

So that's listeriosis, Listeria monocytogenes.

Erin Welsh

There's a lot to it.

Erin Allmann Updyke

There really is and we probably missed a lot.

Erin Welsh

We probably did. And you can check for us by taking a look through our references.

Erin Allmann Updyke

Yes.

Erin Welsh

So I have several, I have a bunch but I will shout out just a couple in particular. So the one that was tracing the spread of that one clonal group of the stereo monocytogenes by Moura et al from 2021. And then of course I want to shout out that classic discovery paper by Murray et al from 1926. And where I saw the phrase patho-epigenetics, I just want to shout out was in a paper looking at sort of this new microbiology and understanding the cellular signaling aspects of Listeria monocytogenes by Cossart and Lebreton from 2014.

Erin Allmann Updyke

I have a paper by it sounds like one of the same authors. The two papers that were very detailed on where we stand with understanding this pathogen as more than just a pathogen, one was from 2018 in Nature Reviews Microbiology called 'Listeria monocytogenes: towards a complete picture of its physiology and pathogenesis.' And the other was from Cellular Microbiology in 2020 called 'Listeria monocytogenes, a model in infection biology.' And then I had a few older papers more specific to the symptoms and what we see with disease itself, as well as the citations for the numbers of epidemiology and all of that. You can find the list of our sources for this episode and every one of our episodes on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) under the EPISODES tab.

Erin Welsh

A huge and heartfelt thank you again to Denise for sharing your story with us. We really can't thank you enough.

Erin Allmann Updyke

Yeah, really. Thank you also to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Welsh

And thank you to Lianna Squillace for the excellent audio mixing, you're the greatest.

Erin Allmann Updyke

Thank you to the Exactly Right network.

Erin Welsh

And thanks to you, listeners. We hope you liked this one. I hope you found something new.

Erin Allmann Updyke

Yeah. Something. I did.

Erin Welsh

So did I. Lots of new. Lots of new.

Erin Allmann Updyke

And as always a special thank you to our patrons. Thank you so much for your support, it really means a lot.

Erin Welsh

It does so much. Okay well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.