TPWKY	This is Exactly Right.
Erin Welsh	"It was the end of the month and I was helping a friend paint her home. Her house was about 35 miles away from mine which is in the city of Boston. So in lieu of driving home, she opted to get me a room because I was going to be helping her the following day. Once I opened the hotel door it was hot and musty and you could tell no one had entered that room for a while. I turned on the A/C and was hit in the face with a musty mist. That smell still lingers with me today. Didn't think anything of it, ate food and went to sleep. Continued with my weekend as scheduled, basically the gym and sleep. That following Monday I felt out of it. I wasn't sick, just exhausted. I thought it was simply from going to the gym.
	I didn't have work because it was Memorial Day and wasn't due back to work until Wednesday but I stayed in bed the whole holiday and a day after. I just remember being at work tired. I thought it was from oversleeping and the best cure for that was more sleep. As the weekend rolled around I was back at my friend's house painting but I noticed I needed a break every 5-10 minutes or so, I was a bit sore and always out of breath and sweating profusely. Monday rolled around and it had been 9 days since I was at the hotel. I went to bed and when I awoke I could no longer walk straight, I was slamming into walls and couldn't see straight.
	When I awoke it was already midnight, I'd overslept again but now I'd lost all motor skills, couldn't walk at all, and my speech was slurring so Siri didn't recognize my voice. I had to crawl to use the restroom and had a hard time not knocking things over when I did. I awoke in my bed to my mom asking me about the mess in the bathroom. She immediately knew I was sick once she heard me speak. I woke up in the hospital surrounded by nurses and doctors trying to figure out why I couldn't talk or walk and why I had a fever of 106 degrees. It took about four days before they figured out it was Legionnaires'. I still had a temperature of 103, still couldn't walk, no motor skills at all, and was unable to speak. Hallucinating at this point was the most enjoyable part of the day. I know I had rooms of family and friends and by the look on their faces, I could tell they were told the severity of everything which I didn't even know.
	I was in the hospital and rehab for about 3.5 weeks. I can walk and talk again and all my motor skills have returned. I drop things a lot and I'm very forgetful at the minor tasks. I had to relearn what I did for a living and how to drive. I used to love working out but it's so dangerous now because I can't balance weights like I should and walking hurts after a while. My joints feel like they are on fire most of the day. Steps are my new arch nemesis, my knees feel like they are about to buckle and crumple whilst walking up or down them. I have dizzy spells, get tired at the drop of a dime, and lose my train of thought halfway through tasks. It has been interesting and I am glad to know I am not the only one out there dealing with these side effects and that things can get better."
TPWKY	(This Podcast Will Kill You intro theme)
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah. That sounds very horrible and terrifying.
Erin Allmann Updyke	Yeah.
Erin Welsh	So that was from a website called legionella.org under a section called Share Your Story.
Erin Allmann Updyke	I didn't realize until kind of reading through some of those firsthand accounts and researching this episode how long-lasting some of the effects of infection with Legionella can be.

Erin Welsh	Oh yeah. No it's like I think there's a lot more under the surface as per usual than we think there is at the beginning of these episodes.
Erin Allmann Updyke	Yeah.
Erin Welsh	Hi, I'm Erin Welsh.
Erin Allmann Updyke	And I'm Erin Allmann Updyke.
Erin Welsh	And this is This Podcast Will Kill You.
Erin Allmann Updyke	And today of course we're talking about Legionella, the causative agent of Legionnaires' disease.
Erin Welsh	Yeah and Pontiac fever.
Erin Allmann Updyke	And Pontiac fever.
Erin Welsh	And other things. It's gonna be an interesting... I have lots of biology questions already.
Erin Allmann Updyke	Oh gosh. I knew that was coming and I hope that I know the answers to them but you're probably not gonna like a lot of them as usual.
Erin Welsh	You mean I'm not gonna like them because it's, 'Well we don't quite know.'
Erin Allmann Updyke	Yep, yeah.
Erin Welsh	Great, great, great. (laughs)
Erin Allmann Updyke	(laughs) They're not satisfying answers.
Erin Welsh	Dang it, that's okay. We'll get there. But first should we do some podcast stuff?
Erin Allmann Updyke	We should yeah cause it's - let me check - quarantini time.
Erin Welsh	It is quarantini time. What are we drinking this week?
Erin Allmann Updyke	We're drinking Losing Your Cool.
Erin Welsh	Yup. For reasons, I think we always say this but that will become more clear as the episode goes on. Basically we're talking about air conditioning, we're talking about fevers.
Erin Allmann Updyke	You're just gonna lose your cool.
Erin Welsh	You're gonna lose your cool.
Erin Allmann Updyke	And what's in Losing Your Cool, Erin?

Erin Welsh	I think it's actually a really delicious one. So it has normal rum, pineapple rum, lime juice, apricot liqueur, and simple syrup. And we will post the full recipe for Losing Your Cool on our website thispodcastwillkillyou.com as well as on all of our social media channels like Twitter, Facebook, Instagram. And those are the places where you can also find the nonalcoholic placeborita recipe.
Erin Allmann Updyke	Exactly. Speaking of our website thispodcastwillkillyou.com, check it out if you haven't already. We have so many things there like merch and a bookshop.org affiliate account, we've got a Goodreads list, we have a Patreon, we have links to Bloodmobile, our music, we have transcripts for so many of our episodes, soon to be all of them. So definitely check out our website.
Erin Welsh	Yes, check it out. I guess like I feel like this was a really fast intro.
Erin Allmann Updyke	It was.
Erin Welsh	But I don't know what else to do here.
Erin Allmann Updyke	I'm excited about this episode so maybe let's take a quick break and then just get started.
TPWKY	(transition theme)
Erin Allmann Updyke	So Legionella is a genus of bacteria that has a whole bunch of species, way more than I realized, I think at least over 50.
Erin Welsh	Yeah. I think that's been a fairly recent development.
Erin Allmann Updyke	Yeah. And I believe that at least 30 of these bacterial species can be pathogenic to humans. And in general these are a much more interesting group of bacteria than I realized, I feel kinda bad cause I was just like oh they're another gram-negative, meh. They're much more interesting than that. They are gram-negative little rods and when they're not infecting us humans, they live in freshwater sources. But not just free-floating in water, no, no.
Erin Welsh	I'm so glad you're gonna talk about this.
Erin Allmann Updyke	Oh yeah, it's so cool! So they don't just live free-floating in the environment, they exist as pathogens of amoebae.
Erin Welsh	Uh huh.
Erin Allmann Updyke	And other protozoa.
Erin Welsh	When I was reading that cause I was reading about the evolutionary history and I came across that and I was like this is so well timed with our Naegleria fowleri episode.
Erin Allmann Updyke	Exactly.
Erin Welsh	It's wild. And also I was like oh this is definitely like I'm reading too much about Erin's biology section and I need to stop.

Erin Allmann Updyke	Yeah it's so fascinating. So I always thought of them as just a water-borne bacteria which they are but in water they can live and persist free-floating as well as in biofilms which is what makes them very difficult to deal with in pipes or water heaters, air conditioning coolers, etc. But they only multiply inside of another organism like an amoeba or another protozoa.
Erin Welsh	It's really cool. Cause that also has implications for why it infects humans or how it infects humans.
Erin Allmann Updyke	That's what I was just gonna say but I'm gonna put a pin in that. But keep that in mind cause when we talk about the sort of pathophysiology of how it gets us sick, yeah, it makes complete sense. Okay. So we have a lot of different species of Legionella but the one that's most famous and probably the most common pathogen of humans at least in the U.S. and throughout Europe is Legionella pneumophila which has a whole number of different subgroups and specific strains within those subgroups. So this is a pretty large overall group of bacteria. And so this is an environmental pathogen. And the way that people get infected with it is through contact, generally aerosol contact with water that is contaminated with Legionella and also amoeba of course. And Legionella in general grows well at warm temperatures, like 25-45 Celsius just like the amoebas that we talked about in our Naegleria fowleri episode. It's happiest around 35 Celsius which is like 95 Fahrenheit, it's pretty warm water.
Erin Welsh	Yeah.
Erin Allmann Updyke	And what's interesting is that although this is a bacterial species that's found naturally in aquatic environments across the globe, it generally doesn't reach high enough levels to get you sick in those natural environments.
Erin Welsh	So what's the infectious dose then?
Erin Allmann Updyke	Erin I knew you were gonna ask that. I have it in bold. We don't know.
Erin Welsh	(laughs) You have in bold 'we don't know'.
Erin Allmann Updyke	Well no I have in bold 'what is infectious dose'.
Erin Welsh	Oh my gosh.
Erin Allmann Updyke	Because yeah, that was my biggest question too because all these papers say it's in human-altered environments where we're artificially heating water, then you have this disproportionate growth of Legionella the bacteria in comparison to the amoebae and that's what leads to human infection. But there isn't a well established dose-response relationship or even a clear infectious dose or lethal dose. There are some papers that list numbers but those studies were in guinea pigs so we really don't know how accurate they are.
Erin Welsh	Well and it's really interesting too because as I'm sure you'll talk about, there's a wide range of host susceptible where your immune system and your age and your whatever risk factors must change a lot of the infectious dose for one person might not be an infectious dose for somebody else.
Erin Allmann Updyke	Exactly. And we'll talk a little bit more about that when we talk about the kind of range of symptoms that you see in these disorders because I think that plays a huge part in it.
Erin Welsh	Okay.

Erin Allmann Updyke	Yeah. It also makes it difficult in terms of prevention and control to do environmental monitoring because we don't know what is a safe level vs an unsafe level of Legionella in water sources.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah. Great question, Erin. But in general this is not a pathogen that's transmissible person to person. Asterisk, it has happened maybe a handful of times, at least once that I saw documented but that's very rare and in general outbreaks that happen are from a shared environmental source.
Erin Welsh	What were the circumstances of the person to person transmission?
Erin Allmann Updyke	It was a mom who was caring for someone who was very severely I'll for like over 8 hours a day in a very small room without any ventilation and she didn't have contact with that same water source that he had had contact with.
Erin Welsh	Okay, interesting.
Erin Allmann Updyke	But that was the one that I saw.
Erin Welsh	Yeah.
Erin Allmann Updyke	All right so let's talk about what happens when these bacteria get inside of our body because I think it's really fascinating. I might go into more detail than I sometimes disease on this but I think it's gonna be fun. Okay?
Erin Welsh	Let's do it.
Erin Allmann Updyke	So since these are bacteria that generally live inside of amoebae when they're in the environment, it's not surprising that once they get inside our body via inhalation into our respiratory tract, these are also intracellular bacteria like Rickettsia and chlamydia and a lot of other bacteria that live and multiply inside of our cells rather than just in our bodies. So in us what they do is these bacteria adhere to our cells. I think from what I read they can infect other cells like our respiratory cells, our epithelial cells, but primarily they infect macrophages. Macrophages are white blood cells that normally serve the function of gobbling up bacteria and then killing them. But Legionella is able to persist inside these macrophages. Here's how they do it. Normally when a macrophage gobbles up a bacteria you can imagine them taking their little... Macrophages kind of almost look like amoeba, they have like wiggly arms and they take those wiggly arms and they wrap it around a bacterium like a giant hug and then they bloop it inside of the macrophage cell. But once it gets inside the cell, it's wrapped in a little bubble of macrophage cell membrane.
Erin Welsh	Mm-hmm.
Erin Allmann Updyke	It's called the phagosome.
Erin Welsh	Oh yeah.

Erin Allmann Updyke	Yeah, you know this Erin. And now normally once that phagosome is inside the macrophage, all of these other mechanisms inside of the macrophage cell would see that bubble and be like, 'Ugh, there's another bacterium. Boop.' And they'd pop that bubble, release the bacterium, and kill it. But Legionella prevents that bubble from ever popping. So they persist inside a bubble inside a macrophage and they replicate and replicate and replicate. The reason I think this is fascinating is because that's exactly the same thing that they do inside an amoeba because amoebas eat bacteria the same way that our macrophages do.
Erin Welsh	Right. It's also very virus-like behavior.
Erin Allmann Updyke	It is, it's very viral.
Erin Welsh	Yeah.
Erin Allmann Updyke	And then inside of us they do the same thing that they do to amoeba, they kill our cells just like they would kill an amoeba. So that's how we get infected, how we get sick. What does the disease that Legionella causes actually do? Kind of like in our chickenpox episode, and we already mentioned this at the top, there are two different named diseases that are associated with infection with Legionella bacterium. But as I was reading this I was like I find it annoying that we have these two different named diseases because they're not truly, really different. They're kind of just a spectrum of symptoms which all seem possible after a Legionella infection including asymptomatic infection. There's evidence of people who become infected seroconvert, so they show evidence of infection and immunity but never have any symptoms of infection with Legionella. So some places have started just sort of naming this legionellosis as a spectrum of disease rather than Legionnaires' disease vs Pontiac fever.
Erin Welsh	Right. And I also think that probably the likelihood of someone being diagnosed with Pontiac fever is much lower than with Legionnaires' disease and like if the exposure is the same, okay I guess that leads into the question of why are there two diseases? Why are there two named diseases? I mean historically it makes sense but why did that differentiation persist for so long?
Erin Allmann Updyke	Great question and I knew that you were gonna ask this question. This is another place I have it in bold. I don't know.
Erin Welsh	We don't know.
Erin Allmann Updyke	Yeah. So my big question was is it species specific, is it different species of Legionella that are causing Pontiac fever vs Legionnaires' disease? Maybe but not really as far as I can tell from all of my research because not only so we mostly test for Legionella pneumophila serogroup 1, so like one specific group of Legionella pneumophila, that particular bacterial species has been found to cause both Legionnaires' and Pontiac fever as well as asymptomatic infections. So it can't be entirely based on serogroup and it can't be entirely based on species of bacteria because again there's a lot of different species of Legionella. So there's likely a huge amount of host factors that go into it.

	We know there are risk factors that make Legionnaires' disease a lot more likely, things like if you smoke or have any kind of chronic lung disease, an older age especially anyone over age 50 is at higher risk than people younger, and any kind of immunocompromise especially immunocompromise associated with cancers or being on cancer therapy or steroid treatment. So those things we know make it more likely that someone exposed to Legionella will develop Legionnaires' disease but like you said Erin, we also just don't know as much about Pontiac fever because it's pretty mild. So Pontiac fever is basically just a mild, flu-like illness caused by Legionella. It's fever, body aches, maybe some respiratory symptoms but it lasts for a few days and then you get better.
Erin Welsh	No pneumonia, no death.
Erin Allmann Updyke	No pneumonia, no death. Exactly.
Erin Welsh	Yeah.
Erin Allmann Updyke	Legionnaires' disease on the other hand is a pneumonia. And we've talked about pneumonia a lot actually even this season in our coccidioidomycosis episode.
Erin Welsh	That's what kept popping into my head when I was reading about this.
Erin Allmann Updyke	Yeah, definitely. So the symptoms of Legionnaires' pneumonia generally start anywhere from 2-14 days after infection, so that's the incubation period, it can be quite long. It starts very often with a fever and like you heard in the firsthand account, this fever can get quite high. Often you'll have chills which are associated with such high fevers, a cough. Unlike some of the more quote "typical" pneumonias, this cough is not often very productive so you don't have a ton of phlegm that you're bringing up but you still likely have a cough. You'll probably have some difficulty breathing and some chest pain because there's intense inflammation happening in the lungs. And if you read the kind of classic descriptions of Legionnaires' disease, it's often described as having GI involvement, so like diarrhea, nausea, vomiting. But in reality this can happen with other atypical pneumonias as well. Atypical pneumonia just means a pneumonia that doesn't fit the old school, very classic definition of pneumonia that's generally caused by Streptococcus pneumoniae or Klebsiella or something like that. So there's a whole group of atypical pneumonias of which Legionnaires' disease is one.
Erin Welsh	Right, yeah. I kept wondering what distinguishes atypical pneumonia from typical pneumonia.
Erin Allmann Updyke	Yeah, there are things like maybe the X-rays will look a little bit different than pneumonia with Strep. pneumo but there isn't any one specific X-ray finding that tells you that this is Legionnaires' vs something else.
Erin Welsh	Okay.
Erin Allmann Updyke	So it's a very nonspecific way of grouping pneumonias.
Erin Welsh	So if somebody came in with symptoms of pneumonia, some kind of pneumonia, what would make you go, 'Oh that's typical pneumonia vs atypical?' Would it be like you screen them for strep or you look at the X-ray? Is it a combination? Yeah.
Erin Allmann Updyke	It's a really good question. There's not a good answer to that because what we end up doing is just treating for all of it very often.

Erin Welsh	Okay.
Erin Allmann Updyke	Yeah so there are X-ray findings that are maybe more specific for a Strep. pneumo pneumonia vs more atypical pneumonias, like maybe the X-ray will be a little bit more diffuse and patchy vs like oh here's a pneumonia in one lobe of your lung very clearly defined. But that's not specific, right. None of the kind of ways that we use to diagnose like is your cough productive vs not productive, are you very, very, very sick vs your X-ray looks terrible but you don't look that sick. That's something that's usually associated with a quote "atypical" pneumonia is the X-ray might look really bad but the person doesn't seem that sick clinically.
Erin Welsh	Gotcha.
Erin Allmann Updyke	Also like I said GI involvement, right. Classically you would think GI involvement, maybe I'm thinking Legionella is more likely but that can happen in other pneumonias as well. So there's no one specific thing that if someone walked in you would say, 'Oh well this is most definitely this one cause' etc etc. And that's what makes pneumonia in general difficult because it's often difficult to test for direct causative agents, especially if someone doesn't have a lot of phlegm that they can cough up that you can use as something to culture.
Erin Welsh	Right.
Erin Allmann Updyke	For Legionella there is another test that you can use on urine, it's a urine antigen test that can test directly for the presence of the bacteria.
Erin Welsh	Which is very cool.
Erin Allmann Updyke	It is very cool. And so that is something that you can do to test directly for it. It's of course not a perfect test, just like any diagnostic test but it is effective so that's pretty awesome and it's a lot faster than something like culture which takes many days. Yeah so that's kind of what it would look like if somebody was infected. In general Legionnaires' disease, legionellosis with pneumonia has about 5-10% fatality rate, that's with treatment.
Erin Welsh	Is that just because of just how fast the bacteria has already caused damage before it's caught or is it like the efficacy of treatment isn't as great as for other pneumonias, like why is that?
Erin Allmann Updyke	It's actually pretty similar to the fatality rate for pneumonias in general.
Erin Welsh	Okay. It's just a bad-
Erin Allmann Updyke	It's just a bad pneumonia and I think that historically Legionnaires' disease was considered a more severe from of pneumonia. And if untreated, the mortality rate can be a lot higher than for other forms of pneumonia, it can be as high as 40-80% whereas for other pneumonias it might be less like 30% or so. But as we've gotten better at recognizing Legionnaires' disease I think people get diagnosed earlier and so we've seen that it's not always necessarily the most severe form of pneumonia, it's just that previously we were only seeing the sickest of sick people, if that makes sense.
Erin Welsh	Gotcha. Yeah, yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	Okay.

Erin Allmann Updyke	And the other thing that you would say would make this a more atypical pneumonia is that if you treat it like we would treat a typical pneumonia with something like a penicillin or cephalosporin, it wouldn't respond because those type of antibiotics that we use for more quote "typical" - and when we say typical and atypical, that doesn't mean common vs uncommon. Atypical pneumonias are still quite common.
Erin Welsh	It's very confusing, the terminology.
Erin Allmann Updyke	I don't like it.
Erin Welsh	Yeah. (laughs)
Erin Allmann Updyke	At all. But if you read about pneumonias, they use that terminology all the time, I'm not a fan. But yeah, so it doesn't respond to those, you have to use different antibiotics which is why in the U.S. and a lot of other places, if somebody comes in with pneumonia they'll often get an antibiotic that'll cover both the atypicals and the typicals, if that makes sense.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah. Because if we aren't able to test for the exact bacteria that causes it, you just wanna cover everything.
Erin Welsh	Makes sense.
Erin Allmann Updyke	Yeah. Well that's the biology pretty much.
Erin Welsh	Oh my goodness, that was so fast.
Erin Allmann Updyke	It was! Do you have any more questions?
Erin Welsh	(laughs) I guess I have more questions about exposure I think and so maybe that's for the current status situation.
Erin Allmann Updyke	Yeah, we'll probably talk about that a bit.
Erin Welsh	Yeah, I think I don't have anymore for the biology.
Erin Allmann Updyke	Even though all my answers were, 'I don't know!' We made it through. So Erin, do you know more than I do? Like where did this pathogen come from and what's up with it?
Erin Welsh	I will try to answer those right after this break.
TPWKY	(transition theme)
Erin Welsh	I like the story of Legionnaires' disease because on the surface it seems like a fairly straightforward example of a classic outbreak investigation and unraveling the mystery of a new infectious agent which is basically what I thought it was when I first started researching for this episode. And that investigation, that whole outbreak epidemiology part of it is super duper interesting. But what I find makes it even more interesting is of course the context.

Erin Allmann Updyke	Always the context.
Erin Welsh	Why did this outbreak happen when it did and what about its circumstances led to the way it played out both in terms of the epidemiological investigation as well as how it was portrayed by the media? So let's get into it by going back to 1976, Philadelphia, Pennsylvania, aka the City of Brotherly Love. This entire year everyone around the U.S. was celebrating the bicentennial of the country including more than 4000 members of the American Legion which if you didn't know, because I had to google it, is an organization of U.S. war veterans. They do a lot of lobbying on behalf of veterans and they also hold meetings or commemorative events. And one of these such events took place from July 21st to July 24th at the Bellevue Stratford Hotel in Philadelphia. This was specifically the 58th annual convention of the American Legion Department.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah. Over the course of that convention and in the weeks that followed, 221 people became I'll with a mysterious disease and 34 died.
Erin Allmann Updyke	Wow.
Erin Welsh	Which is a rate of about 15%. Most but not all of those affected were members of the American Legion, hence the name Legionnaires' disease. So what went down at this hotel?
Erin Allmann Updyke	Yeah.
Erin Welsh	The outbreak was first brought to the attention of the CDC when a local physician at the VA diagnosed several of his patients with pneumonia. But this pneumonia wasn't typical pneumonia, whatever that means. (laughs)
Erin Allmann Updyke	(laughs) It wasn't, was it?
Erin Welsh	And this one didn't seem to respond well to the normal antibiotics that he generally prescribed. And alarm bells started going off when four of his pneumonia patients died.
Erin Allmann Updyke	Oh gosh.
Erin Welsh	On the morning of August 2, David Fraser, a former EIS officer who worked as an epidemiologist at the CDC got the call that something was going down in Philadelphia and he was put in charge of a field team to find out what. Fraser and his team arrived on the scene fairly early on in the epidemic curve and while they had a lot to go on epidemiologically, that knowledge didn't help them too much in their top priority, stopping or at the very least slowing the epidemic. They knew that the linking factor among all of the people getting sick was this convention at the Bellevue Stratford Hotel and as it turned out these first few patients that the doctor at the VA sort of sounded the alarm on, that was just the tip of the iceberg. More and more cases of pneumonia began to appear in doctors' offices around the city and the death toll was mounting.
Erin Allmann Updyke	Can you remind me how long after the convention this doctor told the CDC? Like what the timeframe was?
Erin Welsh	So I think the doctor told the CDC in like August 1 or the very end of July.

Erin Allmann Updyke	Okay.
Erin Welsh	And I think the first cases were a few days in the middle of that convention which was July 21 to July 24.
Erin Allmann Updyke	Right.
Erin Welsh	And so the CDC got there at like the first week of August, so like pretty soon. And it's like the epidemic curve maybe hadn't quite peaked, it was close to peaking.
Erin Allmann Updyke	Yeah.
Erin Welsh	But yeah, more and more cases started to roll in but it is likely that given the incubation period of 2-14 days, those that were going to get sick had already been exposed.
Erin Allmann Updyke	Right.
Erin Welsh	And there there may not have been a whole lot more exposures happening.
Erin Allmann Updyke	And then that convention was over and they presumably had left the city, a lot of people.
Erin Welsh	I think a lot of them were in Pennsylvania at least.
Erin Allmann Updyke	Okay.
Erin Welsh	So yeah, even though probably a lot of the exposures had already happened, the disease was still showing up and so more and more of these cases of pneumonia began to appear in doctors' offices, death toll was mounting. And immediately the first thing that they suspected, the CDC suspected was influenza but not just any influenza, swine flu or H1N1.
Erin Allmann Updyke	Oh.
Erin Welsh	And so here comes some of the historical context. So earlier that year there had been some cases of H1N1 swine flu at Fort Dix New Jersey which got a lot of public health officials a bit concerned that this could be the start of another influenza pandemic similar to the one that happened in 1918. And these cases of influenza were worrisome for a couple of reasons. One was that although in 1976 people didn't know exactly what strain the 1918 influenza one was, studies had suggested that it was a similar isolate to the H1N1 swine flu that had popped up at Fort Dix and as we know now it is very similar.
Erin Allmann Updyke	Okay.
Erin Welsh	And another thing that was concerning was the timing. So these Fort Dix cases had happened very early in the year, like in January which is much earlier than seasonal flu tends to increase in incidence and that was another characteristic that it shared with the 1918 influenza.
Erin Allmann Updyke	Okay.

Erin Welsh	And so even though the 1976 swine flu outbreak at Fort Dix had caused only 13 hospitalizations and one death, these similarities between the 1918 influenza were striking enough to lead to Gerald Ford, who was president at the time, to call for a mass immunization program. Over the next 6 months after first appearing at Fort Dix, swine flu had caused no additional cases, no hospitalizations, no deaths, and its spread seemed unlikely. And so the momentum for its vaccination or control seemed to be slowing somewhat.
	That is until these mysterious pneumonia deaths began to happen in Philadelphia. And these deaths led people to urge congress to pass legislation indemnifying vaccine manufacturers for a swine flu vaccine which is a decision that Ford later received a lot of criticism for and in general this rapid response and some of the subsequent decisions regarding the potential 1976 swine flu epidemic that never was. They were really controversial at the time and have in retrospect been called too strong of a response for this outbreak that never was, sort of like the miscalculation of risk and being overly cautious. And I think it just serves as an example of like it's really hard to know what the right move is.
Erin Allmann Updyke	Right.
Erin Welsh	I bring it up because it's really important in understanding at least in part why there was such media frenzy around this mysterious illness in Philadelphia. You have newspaper headlines calling it the Philly killer or killer fever, ill in Philly and actually I think I made that last one up.
Erin Allmann Updyke	Everyone was just sort of primed to be paying attentions to something like this.
Erin Welsh	Yes, exactly.
Erin Allmann Updyke	Okay, that's makes sense.
Erin Welsh	I mean it's sort of like I was thinking about it in the context of today and COVID and how like if there was a convention, let's say like this summer or next summer and it was like oh these cases of atypical pneumonia and fever, people would be very concerned for good reason.
Erin Allmann Updyke	Remember that for later.
Erin Welsh	Yeah. Oh great, okay.
Erin Allmann Updyke	Oh yeah.
Erin Welsh	And the other thing is that swine flu, this H1N1, this wasn't the only potentially deadly epidemic disease that was featuring in headlines during the 1970s. Ebola, Lassa fever, Marburg virus, Campylobacter enteritis and gastritis, Lyme disease, these were all making themselves known and scaring the world along the way throughout the 1970s. And there's a quote that's often used to characterize the attitude of western medicine in the middle of the 20th century regarding infectious disease. Quote, "It's time to close the books on infectious diseases, declare the war against pestilence won, and shift national resources to such chronic problems as cancer and heart disease." So it turns out, and I found this out while trying to find this exact quote, that this is an urban legend.
Erin Allmann Updyke	I knew it. I feel like I remember looking up that quote when we first started this podcast and being like it's not real. Right?
Erin Welsh	It's not real, yeah. No. This quote was never said. Yeah, no one can find the origin.

Erin Allmann Updyke	That's so bizarre!
Erin Welsh	I know, I know. And so yes, it may be a misquote and while the war on infectious disease was never declared over, it is true that advancements in antibiotics and vaccines may have made many clinicians a bit overconfident maybe regarding their ability to handle whatever came their way.
Erin Allmann Updyke	Totally.
Erin Welsh	And even if we lacked the tools to take care of a pathogen, the number of newly diagnosed human pathogens especially those that could cause epidemics was kind of slowing to a near crawl since the heyday of early germ theory and etc.
Erin Allmann Updyke	Right.
Erin Welsh	If the first half of the 20th century was basically stick some sputum onto a slide, pop that slide under the scope, and then describe a global pathogen that had been infecting humans for millennia, then the second half of the 20th century felt to many people that there's nothing new under the sun, we've got it all. Or just like a few things. It's more of an anomaly to find a new pathogen than it is to-
Erin Allmann Updyke	Just see your typicals.
Erin Welsh	Right, than just your typical pneumonias.
Erin Allmann Updyke	Right. (laughs)
Erin Welsh	And obviously that's not our feeling now, right, not in the age of COVID-19, of Zika, of bird flu, of Sin Nombre virus. We are keenly aware, the globe right now is keenly aware that emerging infectious diseases are very much a part of life. But this was not necessarily the case in 1976. Legionnaires' disease would really become one of the first or at the very least like part of the first cohort of emerging infectious diseases which was a new concept at that time that would eventually force humans to evaluate the ways that they interact with their environment that may increase the risk of a spillover event or at the very least alter the ecology of the pathogen that could lead to an increase in human disease.
	And this trend of emerging infectious disease isn't solely one due to environmental disturbance of course, it's also due to the constant development of technology and the growth of our own knowledge base that allows us to see more detail where previously it was all sort of a blur. Like we're gonna describe new species because we described one genus in the first place or a new genus, right. So it just kind of builds and builds and builds. But let's head back to the hotel. Let's check in on what's going on there.
Erin Allmann Updyke	Yeah.

Erin Welsh	The CDC had shown up in full force and were quickly at work serving those with the mysterious pneumonia as well as other attendees of the convention that hadn't gotten sick. These surveys revealed that older age and smoking were pretty big risk factors and that men were three times as likely to get the disease as women. They checked hospital logs to determine whether it was just the Legionnaires or if other hotel guests or if anyone local had gotten sick too. And they certainly had, there were several cases of what was referred to as Broad Street pneumonia, which is the street where the hotel was on, that had popped up. Basically these were people who weren't Legionnaires or had not even necessarily gone into the hotel, some had just been on the sidewalk next to the hotel.
Erin Allmann Updyke	Oh.
Erin Welsh	So what the heck was causing this disease and even more pressing, how was it transmitted? And it would take some time for the second question to be answered, and I'll get to it, but what all of this shoe leather epidemiology did was help with the second question, at least in the form of ruling out. So food-borne transmission was ruled out, arthropod vector-borne transmission was ruled out, person to person transmission was ruled out which also kicked influenza to the curb at the same time. And it seemed most likely to Fraser and the others on this field team who were investigating the outbreak that either airborne or water contamination might be the culprit.
Erin Allmann Updyke	Oh.
Erin Welsh	But extensive sampling of the sources of water and all of the air ducts in the hotel turned up nothing. They were baffled.
Erin Allmann Updyke	Whoa.
Erin Welsh	Not long after the CDC had arrived on the scene, cases began to decline and eventually there was nothing left to do but go back to Atlanta and begin preparing the reports which they did on August 20th. Literally just 2.5 weeks of hardcore investigation, like so many people on the ground.
Erin Allmann Updyke	Right.
Erin Welsh	And even though the fieldworkers had covered a tremendous amount of ground in their investigation of the outbreak, the fact that they had come back without a causative agent and that they seemed no closer to being able to prevent a subsequent outbreak of whatever this was, it made the CDC a big target in the media reporting at the time which was already super critical of their handling of this whole swine flu situation.
Erin Allmann Updyke	Right.
Erin Welsh	And also this was in the headlines for ages. It became part of popular culture almost.
Erin Allmann Updyke	Right.
Erin Welsh	Like Bob Dylan wrote a song called Legionnaires' Disease.
Erin Allmann Updyke	Okay I know who Bob Dylan is, so that's almost a first for the two of us.
Erin Welsh	(laughs) Good first step.

Erin Allmann Updyke	But I feel like even today most people will have heard of Legionnaires' disease, like it's a thing, people have heard of it, it's a headline, etc.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	Do you wanna hear the Bob Dylan, like a couple lines?
Erin Allmann Updyke	I would love to.
Erin Welsh	Okay, okay.
Erin Welsh	"Some say it was radiation, some say there was acid on the microphone, some say a combination that turned their hearts to stone. But whatever is was, it drove them to their knees. Legionnaires' disease."
Erin Allmann Updyke	(laughs) I love it.
Erin Welsh	Yeah and it goes on, there's more. I haven't listened to the actual song so I don't know how the melody goes but it exists. But anyway I think that the song, I think the little lyrics that I shared really speaks to the fact that no one knew what was going on and that was part of the reason that it was so persistent in headlines and the news stories at the time.
Erin Allmann Updyke	Right, people love a mystery.
Erin Welsh	Exactly. And all that the CDC and the affiliated institutions could do, all they could say was what Legionnaires' disease was not. And this was such an enormous investigation even in just a short time period. Like for instance the Franklin Institute looked into the air conditioning system, the Academy of Natural Sciences examined the water supply, Drexel University used mass spectrometry to look at whether there was anything in the water, Harvard and MIT were involved in testing hair of survivors to look for an environmental toxin, University of Connecticut examined nickel poisoning which was actually a pretty popular hypothesis for a minute until it was revealed that autopsy knives which were nickel-coated was leading to the inflated appearance of contamination. Yeah. But this was a huge undertaking.
Erin Allmann Updyke	Yeah and nobody, even when they tested the air conditioning and things, they couldn't find it.
Erin Welsh	They couldn't find it.
Erin Allmann Updyke	I have a suspicion why.
Erin Welsh	Yeah. There was at the end of this, after some reports had been produced, committees of infectious disease specialists and committees of pathologists came to one conclusion regarding the Legionnaires' disease outbreak: whatever had cause it, it definitely wasn't a bacterium.
Erin Allmann Updyke	Oh gosh.
Erin Welsh	Yeah. (laughs)

Erin Allmann Updyke	I love it when those kind of conclusions happen.
Erin Welsh	I know, I know. I mean it's so easy in retrospect to be like well come on. But why were they so sure? Well I mean it wasn't showing up on any of their routine or even in their non-routine screens.
Erin Allmann Updyke	Yeah.
Erin Welsh	Microbiologists had swabbed and smeared and cultured and stained every sample they could think of on all different types of culture media but to no avail, like nothing was there. Antigen tests revealed nothing, the pneumonia itself more closely resembled that of a viral pneumonia than a bacterial pneumonia. And so they were like well it must be either some sort of virus or some strange environmental contaminant. And I should note that there were some groups that did believe it was some sort of undescribed bacterium but by and large there were committees that were like, 'No! This is not bacterial!'. And now that the outbreak appeared to be over, the window of opportunity for uncovering what caused it seemed to be narrowing, right. Of course the failure to identify the causative agent led to constant criticism of CDC researchers assigned to the task and there were still so many people assigned to the task. One of them was Dr. Joseph McDade who was a microbiologist at the CDC and he had started working there in 1975, I think just like 8 months or so before this 1976 Philadelphia outbreak.
Erin Allmann Updyke	Okay.
Erin Welsh	And he worked in the department for Rickettsial diseases.
Erin Allmann Updyke	Ooh.
Erin Welsh	He had spent the previous decade studying various Rickettsiae both in the lab and in the field, including outbreaks of typhus in Egypt and Ethiopia. And if you think back to our Rocky Mountain spotted fever episode, which is a Rickettsial disease, you may remember that Rickettsiae are notoriously difficult to cultivate and culture since they're these intracellular pathogens.
Erin Allmann Updyke	Right.
Erin Welsh	And so McDade's background working on Rickettsiae would prove to be key in finding the missing piece of the puzzle of Legionnaires' disease.
Erin Allmann Updyke	And that's just fortuitous, just lucky that McDade was there.
Erin Welsh	Or was it? Because there were so many people working on so many different angles of this.
Erin Allmann Updyke	Okay.
Erin Welsh	Like was it fortuitous? Was it serendipitous? Or was it inevitable?
Erin Allmann Updyke	Oh yeah, yeah.

Erin Welsh	So like I mentioned, all kinds of these different hypotheses were being put forth to explain the outbreak all at the same time. So you had a million different moving parts all looking at this angle and that angle and this virus and that virus and this fungus and that fungus, whatever. And one of these hypotheses was Q fever which is a mild infection caused by Coxiella burnetii which is a Rickettsia-like pathogen, so it's really small and intracellular, that can cause atypical pneumonia in people. It doesn't generally do that but it can. And McDade didn't really think that this deadly outbreak, like I said 15% mortality rate, was Q fever especially since people get Q fever through exposure to contaminated animals and inhaling dust from them. But he was like, "No of course I'm gonna rule it out.'
Erin Allmann Updyke	Right.
Erin Welsh	And so he set to work. And so like other Rickettsial pathogens, Coxiella burnetii is a bit tricky to culture and isolate. So first you need to take the blood or tissue sample, grind it up and put it in solution and then inject that into guinea pigs. And then you cull the guinea pigs and take tissue from them to put in embryonated eggs. And when McDade did this with lung tissue from people who had died of Legionnaires' disease, the guinea pigs became febrile like right away with a severe fever.
Erin Allmann Updyke	Okay.
Erin Welsh	Nothing grew in the eggs when he tried to do that part of it but when he looked at smears of guinea pig spleen that had been stained by a technique common for staining Rickettsial species, he saw rod-shaped bacteria. And he showed other researchers who kind of shrugged it off saying it was a contaminant and not in high enough numbers to be the causative agent.
Erin Allmann Updyke	Oh my gracious.
Erin Welsh	Well and around the same time the nickel hypothesis had gathered steam because it was kind of being consistently found in all the people who had died from Legionnaires' disease which makes sense cause it was on the autopsy knives. Anyway. So he didn't pursue this rod-shaped bacterium too much.
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	But a few months later the nickel theory had been debunked and McDade found himself wondering about it, just kind of like, 'Why can't I drop this idea about this rod-shaped bacterium?' He was like why was it there, why wasn't it culture in the eggs, blah blah blah. And so he went in over the Christmas break and was like, 'There's no one here so I'm gonna have the lab all to myself and I'm gonna be able to do this work without being disturbed.'
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	And so he went back and he started to look at all of the slides again that he had prepared and on one of them he saw not just a single rod-shaped bacterium but a cluster of bacteria which made him realize that this probably wasn't just a random contaminant but likely the culprit. And additional testing revealed that he was right. More than 90% of the Philadelphia patients had antibodies to this bacterium and they were also able to isolate it from additional autopsy specimens.
Erin Allmann Updyke	Ooh.

Erin Welsh	But they still didn't know exactly what it was. Like was it a Rickettsia? No, it certainly didn't look like or behave like a Rickettsial species. So maybe it was something else. Eventually through lots of trial and error, researchers were able to put together a recipe for a culture medium that met the very specific needs of this super fastidious new bacterium.
Erin Allmann Updyke	It's very picky.
Erin Welsh	Yeah, I love the word 'fastidious' for bacteria.
Erin Allmann Updyke	Yeah, that's a good one.
Erin Welsh	It's a good one. And through this they were also able to solve the mystery of its outbreak cause it turned out that this bacterium loves warm water and the warm weather in July proved a perfect time for this bacterium to be misted out by the air conditioning system into the lobby of the hotel and into the sidewalk next to it, just like this killer mist. By the time that the CDC had examined the A/C system it had been cleaned, so no traces of the bacterium had been found. Yeah.
Erin Allmann Updyke	Interesting.
Erin Welsh	And this new bacterium was given the name Legionella pneumophila as a nod to this outbreak, who was affected by it, and then the tendency of it to cause disease in the lungs, so like lung-loving. And this turned out to be a whole new genus of bacteria. But new doesn't necessarily mean new to humans, it may just mean newly described. So had the world seen Legionella pneumophila before? Absolutely.
Erin Allmann Updyke	Always, Erin.
Erin Welsh	Always. All you needed to do, it seemed, was just to look. Once Legionella pneumophila was pinpointed as the causative agent, researchers immediately began combing through past unsolved outbreaks that resembled the one in 1976 to see if it had emerged before. And it absolutely had. In 1968 for example when 95 out of 100 people who worked in a health department in Pontiac, Michigan became ill with a mild illness, no deaths. And at that time there had been extensive epidemiological investigation into the outbreak and the air conditioning units had been suspected but it again didn't yield any solid answers.
Erin Allmann Updyke	Right.
Erin Welsh	And so it was kind of just like it's a mystery. But then once Legionella pneumophila had been described, people who had Pontiac fever, like were in that outbreak, were tested for antibodies and it was shown that they were one in the same.
Erin Allmann Updyke	Interesting. Because of just the sort of epidemiological similarities even though the disease itself wasn't nearly as severe?
Erin Welsh	Exactly.
Erin Allmann Updyke	Fascinating.

Erin Welsh	Yeah. And even at the Bellevue Stratford Hotel, so the same place where this 1976 Legionnaires' disease outbreak, first outbreak happened, two years before during a meeting of the Odd Fellows Society, several people had become ill with atypical pneumonia. So it was again shown that the same bacterium had been hiding out there. And then another outbreak of unexplained pneumonia in St. Elizabeth's Hospital in Washington, DC in August of 1965, that was also linked to the bacterium. And there was a specimen from 1943 that revealed a strain of Legionella mcdadei and then another sample in 1947 turned up Legionella.
Erin Allmann Updyke	Oh wow.
Erin Welsh	And so it had definitely been around. I didn't really find anything on the evolutionary origins of it but it was clear that outbreaks or cases of the disease weren't just a thing of the past and also not just something that happened in the U.S. After the bacterium was discovered and described in December/January of 1976/1977 additional outbreaks occurred in Vermont in 1977, in England in 1985, the Netherlands in 1999, a big outbreak in Spain in 2001 involving like 700 people.
Erin Allmann Updyke	Whoa.
Erin Welsh	2005 in Canada, in Portugal in 2014, the Bronx in 2014. I mean happening all over the world and those are just the outbreaks. Like this disease also happens very sporadically just like individual cases.
Erin Allmann Updyke	Yeah, I feel like that's important to say because I think people think of it as just this outbreak pathogen but really it can cause pneumonia in anyone, anywhere, even just one case.
Erin Welsh	Yeah, absolutely. And so I am almost ready to turn it over to you, Erin. But first I wanna talk about the timing of all of this.
Erin Allmann Updyke	Yeah.
Erin Welsh	Why did this disease seem to emerge in the mid 20th century? Because I didn't say anything about Ancient Rome or Hippocrates or the Ebers Papyrus. So was it truly new to at least the 20th century? No, not at all. I mean like you said this is an environmental bacterium. It doesn't need humans to infect in order to live out its life. So it's possible that it caused cases here and there before the 20th century but there were two important developments or trends I guess that happened to lead to its emergence then. The first is simply advancements in microbiological technology and epidemiological techniques that allowed us to isolate and describe this pathogen. The second is air conditioning and water cooling towers. Outbreaks with this bacterium are often linked to the HVAC systems in various buildings, especially hospitals and prisons, as the source of exposure which historically obviously wouldn't have been an issue. Like there were passive air conditioning systems but they weren't the things that we have today. The things that we have today, those sort of developed for more widespread commercial and at home use around the middle of the 20th century.
Erin Allmann Updyke	Well there you go.
Erin Welsh	And so that's right when these outbreaks of Legionella first started to happen.
Erin Allmann Updyke	Right.

Erin Welsh	And so it all comes back to timing and context yet again. Why did it happen when it happened? Why was it discovered then and not earlier? Why was there so much media attention? How did the demographics of the victims affect the attention it got? I didn't go into it here but there has been a lot of discussion about that and the fact that these were members of the American Legion who were largely impacted and comparing and contrasting that to the early days of the AIDS crisis and how little attention that got in comparison.
Erin Allmann Updyke	Right.
Erin Welsh	All of these things play a huge role in how epidemics or outbreaks including this one play out. So Erin, as I sit here sweating because my own air conditioning unit is broken in my apartment and it's summer in Chicago-
Erin Allmann Updyke	Oh my gosh.
Erin Welsh	(laughs) So it's kind of funny to just read constantly about air conditioning, I'm like okay yeah.
Erin Allmann Updyke	You're like dripping, dripping.
Erin Welsh	Dripping.
Erin Allmann Updyke	At least I'm not breathing in Legionella!
Erin Welsh	Will you get me up to speed on where we stand with Legionella today?
Erin Allmann Updyke	I would love to right after this break for a cold glass of water.
TPWKY	(transition theme)
Erin Allmann Updyke	Since the theme of this episode is 'we don't really know' we'll continue that here in the epidemiology portion, Erin.
Erin Welsh	Cool!
Erin Allmann Updyke	We know some things. It seems as though worldwide and in the U.S. specifically, the overall risk for Legionella infections seems to be increasing or at least the overall case numbers are certainly increasing even though we have better guidelines in terms of cleaning of air conditioning systems etc on how to try to prevent Legionella contamination. So in the U.S. from the year 2000 to around 2014, the U.S. which reports case numbers a little bit differently than the rest of the world of course, the U.S. case numbers increased from about less than 1 per 100,000 people to 1.5 cases per 100,000 people per year.
Erin Welsh	This brings to mind that paper from Naegleria fowleri where it was like, 'Is this an emerging parasite?'

Erin Allmann Updyke	There's a very similar paper for Legionella. Yeah. And so these numbers include both outbreaks and those single sporadic cases like we talked about which do happen. And it also importantly includes both Legionnaires' disease and Pontiac fever. But the biggest problem is that in all the surveillance systems in the U.S., in Europe, over like 99% of cases that are reported are Legionnaires' disease. Why? Because that's the severe disease, so those are the people who are going to the doctor, going to the hospital, getting really sick, and then that disease is then reported.
Erin Welsh	Question.
Erin Allmann Updyke	Uh huh.
Erin Welsh	Has the frequency of outbreaks or the intensity or the size of outbreaks increased or is it the number of sporadic cases that have increased? Or have they increased in parallel?
Erin Allmann Updyke	Good question. It seems like both have increased.
Erin Welsh	Okay. Interesting.
Erin Allmann Updyke	Yeah. In Europe the European surveillance system in 2011 reported a prevalence of 9.7 per 1 million people, so it's a different scale. But, and here's the biggest problem, we talked about this as well with our Coccidioidomycosis episode, even when you have a surveillance system in place, when we're dealing with a pneumonia it's not super common that we're able to actually test for or identify a specific pathogen that's causing that pneumonia. So we not only don't have a good handle on the number of true Legionnaires' cases every year, we also don't have great stats on the overall mortality rates every year because we just don't know.
	In the U.S. in one paper from the CDC they suggested that the overall burden in terms of if you look at all pneumonias, about 2-9% of total community-acquired pneumonia and again that doesn't include hospital-acquired pneumonia and like you mentioned Erin, the HVAC systems in hospitals are a big place where contamination is possible and therefore this could be a hospital-acquired infection. But if we just look at community infection, 2-9% of all pneumonias might be associated with Legionella. Other papers that looked more globally suggested even up to 15% of pneumonias that required hospitalization were associated with Legionella. So if we go back in the Coccidioidomycosis episode I did a bunch of Erin math, right, where we tried to calculate how many cases might there be. So there are in the U.S. at least between 23-27 cases per 10,000 adults of community-acquired pneumonia that results in hospitalization every year. So if we think that maybe on the high end 10% of those might be caused by Legionella, that would be 2.5 cases per 10,000 adults every year which is of course a lot more than are reported.
Erin Welsh	Right.
Erin Allmann Updyke	And that would be about 52,000 cases per year in the U.S.
Erin Welsh	So a substantial number.
Erin Allmann Updyke	It's a substantial number, yeah. So for sure globally tens of thousands of people are becoming infected, potentially even hundreds of thousands but we don't exactly know how many. The good news though is that unlike with coccidioidomycosis, in many countries and in many parts of the world the sort of standard treatment for community-acquired pneumonia does include antibiotics that treat against Legionnaires'.

Erin Welsh	Right.
Erin Allmann Updyke	So that's at least a small silver lining.
Erin Welsh	And have there been any seroprevalence studies that just like look at it out of the blue?
Erin Allmann Updyke	Good question. I didn't find many.
Erin Welsh	Okay.
Erin Allmann Updyke	Yeah. And overwhelmingly that's one of the biggest areas that we still need to do research on is just getting a handle on the true epidemiological risk.
Erin Welsh	Yeah. So a question about that. What is it about certain air conditioning systems, how are they cleaned, how does it get there in the first place, and how do you protect yourself or know whether you're inhaling this killer mist?
Erin Allmann Updyke	Yeah, killer mist. Yeah it's a good question Erin and not to freak you out-
Erin Welsh	Excellent.
Erin Allmann Updyke	Yeah but the biggest thing I've seen recently is a lot of news articles talking about the risk of Legionnaires' increasing as the pandemic of COVID-19 begins to wane because... So you asked what kind of conditions lead to this growth, right?
Erin Welsh	Yeah.
Erin Allmann Updyke	Unused air conditioning units that have a little bit of water in them, those kind of stagnant water in pipes, that is beautiful biofilm territory.
Erin Welsh	Oh no, all of these office buildings.
Erin Allmann Updyke	Exactly, all the office buildings, all the hotels. All of these things that were closed or vacant during the pandemic, all of these months of these systems not being used, there's a huge potential - again not to freak people out - but for Legionnaires' to increase.
Erin Welsh	Wow.
Erin Allmann Updyke	But the good news is that people have been thinking about this. I read one article, it was just from like a news source but it was about someone whose entire job during the pandemic was running the water in hotel bathrooms and flushing all the toilets and running water through the pipes every week so that this hotel maintains good quality of water.
Erin Welsh	Okay, yeah. How many of these cases are linked to or is it really known whether it's like these industrial HVAC systems or personal at home HVAC systems?

Erin Allmann Updyke	It's a good question, I don't think that we have a good handle on it especially because we really just don't know how many cases there are per year. And I would guess especially if you're talking about a personal HVAC system that maybe only one person ever gets exposed to it and gets infected, those cases are gonna be even harder to pick up and to link to something specific.
Erin Welsh	Okay.
Erin Allmann Updyke	Right. It's the larger outbreaks that's you can then trace back to specific environmental sources. So yeah, that's Legionnaires'. There's some other pretty cool research being done, there's a lot of cool research being done especially on the kind of detailed molecular biology, I'll link to a couple of papers on that to try and understand how Legionella is able on a molecular level to survive and persist in our cells as well as on vaccine development. So we're nowhere near having a vaccine but there are people who are working on mouse models to try and develop the vaccine because it's at least theoretically possible based on how much of an immune response humans mount to it.
Erin Welsh	Okay.
Erin Allmann Updyke	Well, sources?
Erin Welsh	Man this was like a short and sweet episode, not that sweet I guess but...
Erin Allmann Updyke	Short and moderately horrific?
Erin Welsh	Yeah, absolutely. Yeah I have a bunch but I wanna shout out a few that I found super helpful. One by Weisse from 1992 called 'A Plague in Philadelphia'. Another by McDade himself from 2002 'Legionnaires' Disease 25 Years Later: Lessons Learned'. And by Winn from 1988 'Legionnaires' disease: historical perspective.'
Erin Allmann Updyke	Wow. I love that there was a historical perspective like 12 years later.
Erin Welsh	Yeah I know, right. (laughs)
Erin Allmann Updyke	I had a number of different papers. There's a really great comprehensive one from The Lancet 2016 just called 'Legionnaires' Disease', another from 1993 in Clinical Infectious Diseases called 'Legionnaires' Disease'. We'll post the links to all of our sources on our website thispodcastwillkillyou.com where you can find every single source that we used for this episode 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 the Exactly Right network of whom we're very proud to be a part.
Erin Welsh	And thank you to you, listeners. We hope you enjoyed this one. Actually we just got an email the other day being like, 'Can you do one on Legionnaires' disease?' And I was like, 'Coming your way!' (laughs)
Erin Allmann Updyke	Yeah. (laughs) You ask, we answer.
Erin Welsh	And a big special thank you also to all of our patrons, you are amazing, we love you.

Erin Allmann Updyke	So much.
Erin Welsh	Okay well until next time, wash your hands.
Erin Allmann Updyke	You filthy animals.