Legionella in Water from the Flint River

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hi, I'm Sarah Gregory, and today I'm talking with Dr. Amy Pruden in Blacksburg, Virginia. She's a professor in the Department of Civil and Environmental Engineering at Virginia Tech. We'll be discussing the situation with the bacteria *Legionella pneumophila* in the Flint, Michigan water supply.

Welcome, Dr. Pruden!

[Amy Pruden] Hi! Thanks, Sarah. Thanks for having me.

[Sarah Gregory] Let's start off with a basic. What is Legionnaires' disease?

[Amy Pruden] Legionnaires' disease, basically, it's a very strong form of pneumonia and it's caused when the bacteria that belong to the genus *Legionella* are inhaled into the lungs. And, it's a really severe form of pneumonia and unfortunately about 10% of folks that get it are fatalities.

[Sarah Gregory] So, I always like to mention when we are talking about Legionnaires' disease that the founder of the EID journal, Joseph McDade, was the one who discovered it…or discovered the…what exactly what it was. Did you know that?

[Amy Pruden] Yeah! That's a really good point, and it got me thinking many folks might not be aware when it was first discovered. It was actually after a Legionnaires' convention in 1976. They were celebrating the bicentennial, and basically there was this mysterious illness and they didn't know why people were getting sick. And, so yeah, Dr. McDade played a big role in figuring out that it was caused by these bacteria, *Legionella*, getting inhaled in folks' lungs—they thought either from the water or the HVAC system. And now we know that a lot of the legionnaires there, they had a lot of these risk factors associated with the disease…so, a lot of them were older gentlemen, many were smokers, and had other underlying health risks… and these are the kinds of things that can put people at greater risk of getting Legionnaire's disease.

[Sarah Gregory] So, was it the water supply or the HVAC?

[Amy Pruden] I think that's still subject to debate, but people inhaled the aerosols that had *Legionella*. And that's something I think we see in the Flint crisis, when you get to a very specific…like where exactly did the people inhale the water droplets with *Legionella*, it can get dicey to answer that question specifically.

[Sarah Gregory] Okay, so, on that note, did the people in Flint get it from breathing near the water or drinking? It's only respiratory, right? They couldn't have gotten it from drinking it.

[Amy Pruden] Right! That's a really important point. So, you have to get the bacteria into your lungs to get the disease and that's usually not going to happen from drinking the water unless, like, you have trouble swallowing and get the water down the wrong pipe. Really, it's about water droplets or tiny aerosols forming, and they have to contain the bacteria and make it into the lungs.

[Sarah Gregory] So, I have a really bad habit of aspirating water and food. So, I could potentially get it then from contaminated water, you're saying, if I aspirated it?

[Amy Pruden] Right, I mean if the water's contaminated and if you're not careful, that would be one way to get the bacteria into your lungs.

[Sarah Gregory] Okay, so, let's move on to the Flint tap water crisis. What exactly happened and what led up to it?

[Amy Pruden] Yeah, wow, I mean where do you even start? It's, you know, this crisis definitely shocked the nation and the world. Books have been written about it, they're being written about it…it's definitely going to go down into history as an ethical case study, like, what can terribly go wrong with our aging water infrastructure.

From a scientific standpoint, which is where I come from…so, it was in April 2014, the city switched from using water piped in from the city of Detroit and they started using water from the Flint River instead. And this is where they actually broke the law. So, they did not add what's called a *corrosion inhibitor*—it's an orthophosphate corrosion inhibitor—and because the Flint River was much saltier and more corrosive than the Detroit water, it basically made the pipes rust. So, they have this protective scale, the iron and lead pipes, but without that corrosion inhibitor and with this new water that the pipes weren't acclimated to, the scale started to flake off and you had iron and lead getting in the water. And so, especially in parts of the city with lead pipe, you had pretty high levels of lead in the tap water.

So, it was in May 2015, so, about a year after they've been using this new water supply that my colleague Marc Edwards, he got a phone call from a Flint mom who was worried that something was wrong with the water, and she even had done her homework and suspected they might not have been adding this corrosion inhibitor. And so, we sent water kits and students to help sample for lead in August 2015 and it was while our team was there that we couldn't help but wonder if there might be a Legionnaires' problem, too. We had just published a lab study showing that corrosive water was associated with higher levels of *Legionella*, and so, while we were there we went ahead and tested the water for *Legionella*, too.

[Sarah Gregory] How many people got Legionnaires' disease? And you said 10% die, so, how many with that?

[Amy Pruden] There's a few estimates out there. So, you know, we tend to underreport *Legionella*, so, not everybody has…who has pneumonia is actually tested for the disease. Doctors only tend to test people who have certain risk factors. And then, also, the test doesn't get all the different kinds of *Legionella*, but the official count that I was most familiar with was that there were about 90 cases and 12 deaths. But, I just saw a new paper that was an independent study from the Netherlands, and they looked at each individual case more closely—where they had been, whether they've been to Flint—and the number lowered a little bit to, it looks like, 86 illnesses and 10 deaths is the most precise estimate at this point.

[Sarah Gregory] So, you said it was illegal to do what they did, and sort of an ethical issue, so, why did they do it? Why did they change how they were getting their water?

[Amy Pruden] I think initially it was just good intentions. They, like many cities around the country, are struggling financially and it was expensive to keep purchasing water from Detroit. And so, they were viewing it as a alternative that was more affordable. And as for, you know, why they didn't add the orthophosphate corrosion control inhibitor, it seems, you know, the best explanation is that, basically, they forgot or they just weren't paying close attention.

[Sarah Gregory] Oh dear, okay. So, is this study about what you did to help figure out what happened in Flint? Is that what your study is about?

[Amy Pruden] Right. So, we've published a few studies, and this is part of the story. So, we basically wanted to figure out, first of all, could we get *Legionella* from the water and, basically, what types they were.

[Sarah Gregory] Alright, well on that note, tell us about your study.

[Amy Pruden] Well, so, like I mentioned, we suspected that there could be a *Legionella* problem when we first sampled in August 2015. And, at that time, we were only testing water from people's homes and we were piggybacking on the lead testing. And we actually couldn't detect any *Legionella*, so, we were relieved at that point. But, then we thought we should go back and double check some of the larger buildings in Flint, like the hospitals. The bigger buildings can be more vulnerable to growth of *Legionella* in the plumbing because there's basically a lot more of it—a lot more surface area and places that the bacteria can live.

And so, we went back in October of 2015 and sampled the hospitals and larger buildings, and then we found a lot of *Legionella*. So, it was about 100 to 1,000 times higher than the numbers we usually see in background tap water. And, so, this definitely got us concerned and it was shortly thereafter that it was publicly announced that there was a Legionnaires' disease outbreak going on. And then they switched the water back to the original Detroit supply. But the problem was that our study was only based on DNA that we extracted from the water—so, we took water samples, we extracted DNA, and we measured some genes that we know are markers for *Legionella*—but we didn't have actual cultures of the bacteria, and you really need those if you want to identify the types of *Legionella* you have and try to compare them.

And so, we went back in March 2016, and by that time the outbreak had really stopped. You know, they switched the water back to Detroit water, they'd been flushing the system. But, we figured, you know, the bacteria were there. You know, maybe they're not as high in numbers but, you know, there's still some of the same *Legionella* and that we could try to isolate them. And so, we were able to isolate *Legionella* from one of the hospitals and several other buildings, and we were able to get some *Legionella* from some of the homes. And then, we also got in touch with the Michigan Department of Health and Human Services, and they had 11 isolates from patients. And so, that gave us the chance to do whole genome sequencing, and we could compare the isolates from patients and from the water.

[Sarah Gregory] So, tell us about whole genome sequencing. How did that play into all of this?

[Amy Pruden] The whole genome sequencing is…it's basically like the commercial "23 and Me," but for bacteria. It's not as complicated for bacteria because they only have one chromosome, and so, basically what you're trying to do is sequence all the DNA in that chromosome and then you can compare it across different kinds of bacteria. And you can see how related they are, like whether they're distant cousins, are they brothers and sisters.

And then, you can see if there's genes like virulence factors—those are genes that make some strains of bacteria more aggressive. And for *Legionella*, it's really useful because there's many, many varieties of *Legionella*. So, you mentioned *Legionella pneumophila*…that's the most commonly one recovered from patients in the U.S. So, "pneumophila" basically means that it causes pneumonia, but there's a lot of other species that cause Legionnaires' disease. So, there's *Legionella longbeachae*, *Legionella anisa* that are sometimes associated with outbreaks. But there's other *Legionella* that don't cause disease at all; there's all these serogroups and sequence

types. So, in essence, it's a really useful tool to try to figure out if you're dealing with the same or similar or very different strains of *Legionella*.

[Sarah Gregory] Okay, so, based on that, what did you discover?

[Amy Pruden] Well, it was exploratory, so, we were not exactly sure what we would find. But, nonetheless, we were surprised. There were a lot of different strains of *Legionella*. So, just looking at the patients…so, we had 11 isolates, one of them died and wouldn't grow. But out of the other ten, they were all quite different. So, they were all *Legionella pneumophila* serogroup 1, but one strain was really highly similar to a strain isolated from the original Legionnaire's dis…legionnaire's convention in 1976; three strains were really similar to a strain called the "Paris strain," which is found in Paris, but also in other parts of Europe and the U.S.; and three strains were loosely affiliated with strains from lesser-known outbreaks; and then the other three we couldn't find any similar strains from other outbreaks. So, those are the ones from patients.

From the water, most of the isolates were very different than the isolates from patients. So, most were a specific serogroup called "serogroup 6." Other researchers in Flint have reported finding serogoup 6 in Flint homes, but ours was a very different serogroup 6. Many of the water isolates from homes were serogroup 1, but again, few had similarity to strains from patients. But there was an exception. There were four water isolates that were very high in DNA sequence similarity to three of the strains from patients, and those were all very similar to the Paris strain. So, all that being said, I wish I could say more, but we can't really say from these data which patient got sick where, but we can say yes, there were a lot of different types of *Legionella* in patients and in the water, and that some of these are similar to strains known to cause disease. But the Paris strain is found in a lot of places and not unique to Flint.

In a follow-up study…I mentioned that there's a group in the Netherlands who, they had a very different approach. They got information on the patients and tracked where they were when and where they were likely exposed. So, the conclusion of that paper is that the outbreak in 2014 was from probably multiple sources, so, the cooling towers, residential tap water, and hospital tap water. But in 2015, which was more in line with where our study was focused, they mainly saw that it was hospital exposure. And so, kind of consistent with the notion that 2015, you know, we couldn't find *Legionella* in homes, but we saw it a lot in hospitals. And then, also the variety of *Legionella* strains is consistent that, in general, there are probably a lot of different sources of *Legionella* causing disease.

[Sarah Gregory] You also found some anomalies with the hot and cold water pipes. Tell us about that.

[Amy Pruden] Okay. So, *Legionella* is usually thought of as growing in hot water lines because it's a warm water-loving organism. And we saw that most of the water strains that were similar to the patient strains, that were similar to the Paris strain, were collected from hot water. But we got a lot of *Legionella* isolates from cold water, too. So, about 12% of all the places we sampled, the cold water were positive for *Legionella*, and then, a little bit higher, 19%, for the hot water taps were positive for *Legionella*.

So, some of the best advice to protect against *Legionella* growing in plumbing is keep your hot water "hot" and your cold water "cold." But we would say from our monitoring that, you know, maybe it's worthwhile to also sample cold water and not just hot water.

[Sarah Gregory] So, that means that it's not new, it just wasn't expected previously, right?

[Amy Pruden] Right, I mean it's costly to do *Legionella* testing, and it's not legally required, so, there's been a lot of debate about where you should sample and test. And most of it's driven at the building management level, and how much liability they're concerned about or if there's sensitive populations, how aggressive their…their monitoring plan is and whether they want to sample both hot and cold water.

[Sarah Gregory] So, you mentioned that the water, they went back to the Detroit water at some point and that basically stopped the outbreak. But I know they also brought in bottled water at some point. How did that fit into the whole scenario?

[Amy Pruden] Yeah, I mean it's pretty remarkable when you look at the epidemiology curve—so, that's just looking at the number of illnesses with time—and as you overlay that with the changes in the water, that the cases really went down to the baseline when they switched back to the Detroit water. So, that was some good news.

And other good news is that a lot of resources were put into Flint to try to correct the problem. So, President Obama declared a federal emergency. CDC, FEMA, EPA, other relief workers came in to flush the system and get the corrosion inhibitor back in place and basically get the pipes to heal and develop a new layer of protective scale.

So, the governor put together a task force to learn from the problem and try to prevent the problem in the future. They have new "lead in water" laws; in fact, the state of Michigan has their own laws that are more stringent than the federal laws. About 500 million dollars has been invested in Flint to address the problem and replacing pipes and other initiatives. But again, bottled water is a concern that, you know, that's…I mean, for lead, it makes a lot of sense until you can show that the lead is meeting the Lead and Copper Rule standards. But for *Legionella* it's not necessarily going to help if it's not so much an issue drinking the water, because it's hard to take a shower in bottled water, you know, you're still going to need water in the home for bathing and cooking and doing laundry and what not. So, there's still going to be potential for the water to be aerosolized.

[Sarah Gregory] Oh, yes of course. There were some real challenges involved in conducting this study, I understand…problems with types of samples collected and such. I think you sort of touched on it, but do you want to elaborate a little bit more?

[Amy Pruden] Yeah, I mean, just to hopefully give some appreciation. It's definitely not easy to do a study like this. I mean, first of all, having…you know, if the mom in Flint hadn't called us and sort of alerted us to what was going on, we wouldn't have been in there to sample early on.

[Sarah Gregory] Can I stop you?

[Amy Pruden] Sure.

[Sarah Gregory] Just right there, and what does she…what was she concerned about? What happened?

[Amy Pruden] Well, her water was brown and her children were having health problems and she felt that nobody was listening because the authorities would say, "Well, yeah, you know iron gets in the water sometimes but you know, it's…that's not a health risk. And we're meeting all the federal standards, so basically, everything's fine, just don't worry about it."

[Sarah Gregory] Okay, sorry. Go ahead.

[Amy Pruden] So, you know, from a scientific standpoint, we were fortunate that we could get some samples before the city switched back to Detroit water because, you know, there's really an opportunity to learn from what happened in the Flint disaster, and hopefully prevent this kind of thing in the future.

But it's definitely a huge logistical effort, making…like getting a team on the ground and making sure the samples are collected correctly, especially when you're dealing with microbiological samples where you have to culture bacteria and everything has to be sanitary and follow the correct protocol. And then there were just issues like, you know, we were sent 11 strains from patients, we were only able to get 10 to grow, so, one must have died in shipment. And then we found out later that three of the isolates probably weren't from patients that ever went to Flint, 'cause we got those isolates because they were all sent to this regional lab in Flint during the outbreak. But you know, things were really hectic during the crisis and they were still trying to piece together who probably got exposed where, and so, the group in the Netherlands was working on that and they realized that, oh yeah, probably three of those isolates weren't really from Flint patients.

[Sarah Gregory] Oh wow!

[Amy Pruden] And, see, everything that we did was decoded to protect the patient identities. So, there was no way for us to go back and say which those other three were. So, that kind of changed the focus of the study more to, "Okay, so, people that got sick in the region during that time, what do those isolates look like and are they similar to…if our water isolates similar to those known to cause disease."

[Sarah Gregory] What does your study add to the public health community knowledge?

[Amy Pruden] So, I think in this situation, like an outbreak, you know you have to look at many lines of evidence and then step back and look at the big picture. So, you know, clearly switching the water in Flint was the cause of these outbreaks, but you know, looking exactly at who got sick where, when, why—that's much more difficult.

So, whole genome sequencing does give us a new level of resolution. So, you know, you can compare isolates and try to get a better sense of, you know, which isolate is coming from where, but to do that…you need to have isolates, right? We only had these 11, which turned into 10, which, you know, turned into seven isolates from, you know, one of the biggest outbreaks that our country's experienced. So, this really points to where we need better diagnostics. So, doctors, if they suspect somebody has Legionnaires', they'll usually just do a urine test. And the problem with that test is, well first of all, it only detects *Legionella pneumophila* serogroup 1; it doesn't detect all the other types. But you also, then, don't have an actual culture of the bacteria. So, to do that, you need to get a sample of the patient's phlegm and do that.

So, I guess part of our study shows, like, okay, you know, now we know that there were a lot of different strains of *Legionella* in the water, and that it matches up with multiple sources of the outbreak. But really, if we want to have a better picture of where Legionnaires' disease is coming from and how we might prevent it, it'd be ideal to have better diagnostics and to try to get these bacterial cultures from patients and create a library that people can compare to.

[Sarah Gregory] You mentioned that there were several studies done about all of this. Are there any more coming out?

[Amy Pruden] So, I mean, I think it's really important that we learn from Flint and what can go wrong with the municipal water supply to trigger an outbreak. That's really unusual, because the thinking is that, it's more…it's a building-level problem, and that's where the focus is. And for sure, there's things that, you know, if you're the manager of a large hospital, you've got to make sure your hot water is hot and it's disinfected, and has good hydraulic conditions and whatnot.

But, here we see that, you know, a change in the municipal water supply could also trigger an outbreak. And so, it's opening the eyes of water utilities. And there are some studies going on to look at how you might better monitor—well, first of all, monitoring's not required, so, not necessarily better—but to monitor a city's water to keep risk of *Legionella* in check. But it's important for folks to realize that the Safe Drinking Water Act that protects our drinking water, it really ignores *Legionella*. There's no monitoring required, and the protections in place, they protect great against sanitation-related pathogens, like *E. coli*, but *Legionella* is totally different from *E. coli* and those kind of organisms because it grows in the building plumbing, and that's beyond the jurisdiction of the Safe Drinking Water Act.

So, there's research I think spawning to look at what cities can do to protect their water. And I think it's really important for folks to realize that Legionnaires' disease is not just a Flint problem. So, it's across the U.S., it's across Europe, and the globe that rates are increasing. So, like over the last decade, the incidence rate went up by five times. And so, I think general research is needed, not just Flint, to help us learn better and how we can prevent the spread of disease.

[Sarah Gregory] I did a podcast—last year, I think it was, maybe the year before, but pretty sure last year—on *Legionella* in potting soil. Did you hear about that one?

[Amy Pruden] That usually is *Legionella longbeachae*; it's another species of *Legionella*. But there's a few strains that can be in potting soil, and it seems some parts of the world are especially susceptible to that and I don't know why that is. So, New Zealand, for example, and I think in Ireland, there's been some cases of potting soil associated–Legionnaires' disease.

[Sarah Gregory] Yeah, I think the study was in Australia? I don't know, seems like a radically different climate than Ireland. Is there anything else you'd like to tell us about? About the outbreak or the study or what's going on with all of this?

[Amy Pruden] Well, again, I just want to make sure folks realize that Legionnaires' disease is not just a Flint problem. And, actually there was a National Academy of Science report that just came out, and I'd encourage folks, if they're concerned about Legionnaires' disease, to take a good look at that, because there's a lot of really good advice there on things that we could do now to help prevent Legionnaires' disease.

[Sarah Gregory] Dr. Pruden, tell us about your job. What do you do, and how does it relate to the Flint water crisis and Legionnaires' disease and…what's going on with you?

[Amy Pruden] I'm a professor, which I consider to be the greatest job in the world, and I'm quite fortunate. I get to teach students and do research. I manage a lab where a lot of the Flint samples were analyzed. But it's also a big responsibility, I think. We're…we have to be servants for the public and put the opportunity that we have as a professor to use to help solve important problems.

So, we've actually got a lot of studies going on right now on *Legionella*. So, it's one thing to do a field study, like we've been talking about, and the challenge there is it's really complex and there

are a lot of factors you don't understand or can't control, and so, you're kind of looking at patterns to try to figure out what's going on. But we've got a lot of lab-scale studies going on, so, we can construct plumbing systems and just try to recreate conditions like with the water chemistry or kinds of disinfectants added and corrosion inhibitor, and look at the role of other microbes, and basically, try to find new ways that we can help prevent *Legionella* from growing in people's plumbing.

[Sarah Gregory] One last point: Is public tap water generally safe? So many people buy individual plastic water bottles, which creates a problem in itself. Is this really necessary under normal circumstances?

[Amy Pruden] I would definitely say bottled water is not the answer. I'm sure you could do a whole other webinar on plastic pollution. And, you know, at least tap water is regulated; bottled water is not. An even scarier thing I've heard is there's this trend with people that are into drinking raw water, like from a river or stream. So, definitely don't do that!

[Sarah Gregory] Oh dear…

[Amy Pruden] That's not a good idea, you can get very sick.

[Sarah Gregory] Oh yes…

[Amy Pruden] But I personally drink tap water. I'd say trust but verify, pay attention to the information provided by your water utility, things like boil-water advisories. There's certainly parts of the country that do have really old water infrastructure and lead pipes. And so, you know, pay attention and educate yourself, get your water tested. Point-of-use filters that you can get at the hardware store, a lot of those work really well to remove a lot of contaminates and it's a nice alternative to bottled water.

[Sarah Gregory] I was going to ask you about that. Those are like the one…that's what I use, the one in the refrigerator, right?

[Amy Pruden] Right. So, lead and any kind of metals and organics…they're very effective for removing those.

[Sarah Gregory] Well, thank you so much for taking this time to talk with me today Dr. Pruden.

[Amy Pruden] Absolutely! Thank you!

[Sarah Gregory] And thank you out there for joining me. You can read the November 2019 article, Comparison of Whole Genome Sequences of *Legionella pneumophila* in Tap Water and in Clinical Strains, Flint, Michigan, USA, 2016, online at cdc.gov/eid.

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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