

# Legionnaires' Disease in Healthcare Settings—Europe

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

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Julien Beauté, a medical epidemiologist at the European Centre for Disease Prevention and Control in Sweden. We'll be discussing cases of Legionnaires' disease in healthcare settings in Europe during 2008–2017.

Welcome, Dr. Beauté.

[Julien Beauté] Thank you. Hello, Sarah.

[Sarah Gregory] Hello! So, tell us what Legionnaires' disease is?

[Julien Beauté] So, Legionnaires' disease is a severe pneumonia which is caused by a...a bacteria named *Legionella*, which infects a person mostly by inhalation. So, people breathe and get the...the bug into their lungs. And this bacteria can be found in water environments pretty much everywhere. So, we say this bacteria is ubiquitous. You can find it in water main systems in houses, in any building, but also in ponds, lakes, any freshwater environment.

[Sarah Gregory] Ok. So, what are the symptoms? It can be fatal, right?

[Julien Beauté] So, as I said, it's a mostly....a very severe pneumonia. So, the symptoms would be shortness of breath—it can be very severe, so it can also lead to multisystem failure and many of the patients will end up, well, in hospital but also in intensive care units. So it's indeed, very severe. You have high fever and it can lead to, you know, renal failure and other system failure. Now, there is a milder form of the disease which is called Pontiac fever, but it is not part of this analysis. So, the same bug can also lead to a milder form of disease, which is a bit like influenza-like disease. Regardless of the healthcare setting, it's said that about 10% of the person will die. So it's very high.

[Sarah Gregory] Ok. So, is there a treatment for it?

[Julien Beauté] There is indeed a treatment, which is...consists of antibiotics. And if treated timely, people actually have a very good outcome.

[Sarah Gregory] What would be considered timely?

[Julien Beauté] So, that is a difficult question, but the sooner the better. It also depends on your condition. Younger people will have probably more time until treatment, but it is better that within 48 hours you get appropriate treatment to...to have a good chance of a good outcome. And so far, maybe just to add, contrary to other pathogens there is virtually no resistance to drugs. So, if you treat with the appropriate antibiotics, you will cure Legionnaires' disease.

[Sarah Gregory] Oh, some good news then. Is it easy to diagnose?

[Julien Beauté] Yes and no. Yes, because we have different laboratory methods to assert in those cases and they work pretty well. Now, it may be difficult to sample the patients. Usually we need sputum, but if you are very severe it may be...or old, or if you have difficulty to spit, it may be difficult to collect a good sputum for...to do the test.

[Sarah Gregory] So, that would make getting timely antibiotics more problematic if it's more difficult to diagnose.

[Julien Beauté] Exactly, exactly. And also, you need to think about it because there is no way clinically to distinguish Legionnaires' disease from another pneumonia caused by another pathogen. So, if you don't think about it, you won't ask the specific test and then you may miss the diagnostic and may...and also lose some precious time to give the appropriate antibiotics. Because although those antibiotics are very common and easy to find, they are not the first-line treatment for pneumonia, which are more penicillin.

[Sarah Gregory] Ahh, I see, ok. Well, an interesting side note, is that the founder of the EID journal, Dr. Joseph McDade, was the person who discovered the cause of what became known as Legionnaires' disease. It was at the end of 1976, following the outbreak of a mysterious disease at a convention in Philadelphia. I assume you already know this, but I'm telling the listeners.

[Julien Beauté] Yes, that is true and is also why Legionnaires' disease is called Legionnaires' disease because this convention was held by The American Legion. So, most of the cases there were veterans from this organization attending this conference in this hotel in Philadelphia.

[Sarah Gregory] Ah, that's interesting. I know that it can get into plumbing and water misters and I even did a podcast a while back about it in potting soil. Are these the same kind or are there different strains of Legionnaires'?

[Julien Beauté] So, there are many different strains of *Legionella*. The most frequent causative pathogen for the human disease is *Legionella pneumophila*, and especially its serogroup I. Now, for potting soil, it's interesting because there is one very specific strain which is called *Legionella longbeachae*, which can also cause Legionnaires' disease but is very specific to this setting. And it's also very specific to some geographical location, mostly in...for some reason, in the British islands, especially Scotland if I remember correctly. But also New Zealand is also a hotspot for this infection caused by potting soil. But you can also find this strain in other part of the world—other European countries, I'm pretty sure, also in the U.S.

[Sarah Gregory] Your study is about Legionnaires' in healthcare settings specifically. Why did you do this study?

[Julien Beauté] So, historically—and also linked to the discovery of the *Legionella*—there was a lot of focus on travel-associated Legionnaires' disease also because there is some immediate public health action, which is possible. So, if you have a few cases (a cluster of cases) associated with some hotel or another accommodation setting, you may actually take some action. You will investigate the pipes, you will try to match the environmental specimens with the clinical ones, and you will, well, clearly try to treat both the cases and the hotel, so to speak. Now, the vast majority of cases are sporadic and for those cases it's very difficult and it would be very time-consuming to do a full investigation. So, there is less attention for those. And the last part of those cases associated to healthcare settings, I was interested because some...somehow those cases have been overlooked, in my view, and although healthcare settings, just like hotels, are the perfect location. You have many people attending those places, you have most of the time quite complex pipeworks, and also people admitted to hospitals tend to be more fragile and hence, more susceptible to...to *Legionella*. So, for all those reasons I thought that to look back at surveillance data and especially looking more specifically at healthcare settings would be...would be of interest.

[Sarah Gregory] And when you say healthcare settings, do you mean hospitals or nursing homes or both? Or something else?

[Julien Beauté] So, I mean both. So, for the purpose of this study we included any type of healthcare setting, so that includes long-term care homes with some level of care, hospitals of various levels from general wards all the way to intensive care units.

[Sarah Gregory] Ok. So, is it...you said that it was like a perfect storm to get Legionnaires' because of the way they're structured, the whole infrastructure of healthcare settings. So, is it very common in hospitals or other healthcare settings?

[Julien Beauté] In general, Legionnaires' disease is not very common to start with. Now, in terms of healthcare-associated infections, it is...you have basically an estimate that says out of 20 patients, 1 could potentially get some healthcare-associated infection. So, I think it's a lot. Of course, there is a lot of heterogeneity depending on the type of ward, how...the type of investigation, and so on. Now, out of those healthcare-associated infections, we could say that roughly 20% would be pneumonia, 20% would be more urinary tract infections, and 20% would be surgical site infections. And out of those 20% that have pneumonia, <5% would be Legionnaires' disease. So, pneumonia...rather frequent in terms of healthcare infections and about....yeah, 3-4% will be caused by *Legionella*. So, it is not super common. But again, associated with a very high mortality.

[Sarah Gregory] Right. And those sound like low numbers, but when you multiply it out by all the number of people in these settings, it doesn't end up that few people, probably.

[Julien Beauté] It is. But just also to the fact that we are talking about people admitted to hospital for another reason. So theoretically, you are not expecting to get an additional infection when you are being treated for something else. So, it's just additional burden.

[Sarah Gregory] Yes. So, that's something that CDC works very hard to try to overcome. But it's a serious issue. So, the pathogen that causes Legionnaires' flourishes in water systems, especially ones that are large and dark. How does it end up actually infecting hospital patients?

[Julien Beauté] As I said at the very beginning, you can find *Legionella* virtually everywhere. So, if you were to sample the pipes in the building you are standing now or the one I'm standing in, you would find some *Legionella*. So, of course it will also matter of the quantity. So, there are some threshold that are...under which it is acceptable to have some *Legionella*. But beyond those...those threshold, it may be problematic. This risk increases with long pipe systems and especially if you have dead-end, complex and...pipe lengths that are not flushed on a regular basis.

Why hospitals? Well, hospitals are large buildings most of the time, so it's more challenging to maintain properly the...the water system. So you...and you also have potentially some cooling system—so, cooling towers or air conditioning. And those are also of high risk of being contaminated by *Legionella*. So, yes. I mean, we...it is impossible to stay entirely clear of *Legionella*. So...but regular checks control help reduce the risk. That's why hospitals usually pay a lot of attention to detection of *Legionella* in their pipes.

[Sarah Gregory] So, if cooling systems and plumbing and stuff...so what happens is when the water...it sort of mists into the air, then, with the pathogen. I'm just trying to make the connection between in the plumbing and into your lungs.

[Julien Beauté] So, yes. Now, there are different ways of getting infected, unfortunately. Especially in hospitals, it can go from shared fountains in the main lobby, it can be just by taking

your shower, it can be because you have some invasive procedure, maybe there are some...you know, there are some procedures that are associated with aerosols. So, all those different roots are possible transmission modes.

[Sarah Gregory] I see. Well, would you give us a brief summary of your study? How you went about it and that sort of thing?

[Julien Beauté] So, as for all the diseases that are under surveillance at the European level, we collect data for most of them annually. But for some diseases, you may have some higher frequency. That's the case, by the way for travel-associated Legionnaires' disease where we do have some almost real-time surveillance system. But for the purpose of this analysis, I used the data that is...are collected annually. All this surveillance is based on the European Legionnaires' disease Surveillance Network. So, in the various member states we do have epidemiologists and microbiologists working together to collect all this data which are then sent to the European CDC. As part of the ECDC mandates is the surveillance...the analysis of the surveillance data. So, I used...well, quite a large data set from 2007. For Legionnaires' disease, I...for the purpose of this analysis, I excluded all the travel-associated cases because they are associated to accommodations that are very specific. So...and my purpose was to compare the healthcare-associated ones with the locally acquired ones. So, I selected countries reporting these data and then carried out...carried out a rather simple analysis at the end of the day. There is no...I mean, I think it's readable for a large audience. There is no fancy statistical analysis there. So, pretty straightforward but yet, because we have such a large dataset, we still able to find some quite interesting results on the epidemiology of healthcare-associated Legionnaires' disease.

[Sarah Gregory] So, your study was done in Europe from 2008–2017. Did this include all of Europe? I imagine that different countries have different trends, right?

[Julien Beauté] Yes, absolutely. So, this is a challenge we face for all diseases, not just Legionnaires' disease. There are different countries, meaning different surveillance systems, different lab capacities, different health-seeking...healthcare-seeking behaviors (especially for mild diseases), so it is challenging to include all this...all this data. Now, for the purpose of this analysis we have 30 countries. So, it's the EU plus...well, the UK, which was still until the end of the year part of the EU. We also have the European Economic Area countries. So, it's Iceland and Norway, and Liechtenstein on top of the...of the rest of the EU. And as you said, yes, they do have different trends. But we think that for the purpose of this work, it doesn't really matter because we...although the risk for one even country compared to another would be different, maybe the exposure is different. We don't think that the characteristics of healthcare-associated Legionnaires' disease would differ from one country to another.

[Sarah Gregory] Well, did some of the countries report their data differently than others that added to this challenge?

[Julien Beauté] We do have ways to try to harmonize the data. So, for instance, we do have...well, I mentioned the networks. We have regular meetings...used to be a phase 1 annual meeting where we would meet face to face. During COVID times, it is no longer possible, but we still can meet virtually to discuss the common reporting protocols—we have a common case definition. So, all the metadata, the way we report information is the same for all countries. Now, this will not solve all the differences—the ones I mentioned earlier on—because countries are not all the same. But I think in the U.S., you may also face some similar challenges when pulling data from various states to some extent, because there are differences in terms of...yeah,

hospitals, healthcare systems, and even coverage. When it comes to Legionnaires' disease, I think those differences are even more pronounced when you look at milder conditions. When it comes to Legionnaires' disease, because most of these cases will end up in hospitals, you less likely to have those biases related to behaviors. Now, lab capacity may be a big challenge because within/across European countries, some countries are wealthier with more advanced lab capacities and others maybe don't have access to all the latest technology.

Now, they also...once the data has been collected, there are ways to try to manage heterogeneity when analyzing data from different surveillance systems. So, some of the techniques are the same you use for meta-analysis, for instance, and other may be very simple, just adjusting for some of the variables by excluding some countries if the completeness is not good enough, for instance. So, there are ways to deal with such heterogeneity even when doing your data cleaning or your analysis itself.

[Sarah Gregory] I understand that you pooled all the data then. But did some countries have more of it than others? And why would this be?

[Julien Beauté] Yes. In absolute numbers, there is a handful of countries that accounted for most cases reported, namely Italy, France, and Spain. But those countries are also the ones reporting most Legionnaires' disease cases, regardless of the setting of infection. There are different reasons for that; those are populous countries—I mean, everything is relative, but within Europe—and also we know that *Legionella* thrives in warm and humid weather. So...well, at least some region of those countries are very suitable for...for *Legionella*. When it comes to healthcare-associated cases, it's likely different because it's interesting to see that the proportion of cases that were reported as healthcare-associated was higher in countries that report relatively fewer cases of Legionnaires' disease, meaning that their notification rates—when you use their population as denominator—are lower than the average. So, it's...one would assume...I mean, it's a classical observation in surveillance that you tend to capture the severe end of the disease more easily. But when it comes to Legionnaires' disease, it may be only partly true because all cases are quite severe. Now, it may well be that in some hospitals (tertiary hospital), lab capacities are better than compared to the rest of the country or other hospitals. So, that's why you only have maybe in those countries the most advanced laws that are also those better equipped that were able to capture those healthcare-associated cases. But I don't have, like, a definite answer on...on that one.

[Sarah Gregory] Your study distinguishes between cases that were acquired at hospitals versus other healthcare settings. Why did you make this distinction?

[Julien Beauté] Well, because we assumed that we were dealing with two populations that possibly could be different. People that are admitted to hospitals are more likely to have acute conditions and possibly would be slightly younger. In other healthcare settings, you would...you will have care homes where the population may be probably older, with or without acute conditions, but not acute enough to be in an acute hospital. But also the length of stay, you would assume that people admitted to hospital would stay for shorter periods while people (in care homes, for instance) would stay for weeks, months, or even longer. So, for all those reasons, we thought it would probably be of interest to distinguish between those two slightly different settings.

[Sarah Gregory] I see. So, ultimately what were your conclusions from your study?

[Julien Beauté] Our first conclusion was...was, first of all, we...there is a lot of description there because it was interesting to see the differences in terms of strains involved—we already mentioned that in an earlier question. We then looked at predictive factors for being reported as healthcare-associated, and the driving one was age, which was hardly surprising. But more surprisingly, we found that females were more likely to be reported as healthcare-associated, which was, for me, quite a...quite a surprise. And then we looked at predictive factors for data outcome. And then again age—increasing age, above 60 years of age—was associated with increased mortality. But also a very young age...so, although... we only have a few cases aged below 20 years, the mortality was higher for...for this population, probably associated with some underlying condition or immunodeficiency.

[Sarah Gregory] So, men have a higher risk for Legionnaires' disease, apparently. But if a woman gets it, it's more likely to have come from a healthcare setting and be worse? Is that right? And why is this?

[Julien Beauté] Let me rephrase that. So, men have a higher risk of both healthcare-associated and community-acquired Legionnaires' disease. Now, if a woman is reported with Legionnaires' disease, she's more likely compared to men to be reported as healthcare-associated. Why is that? It's...as I said, it was quite a surprise. I think the most likely explanation is the other way around, that women are less likely to be community-acquired because—and that's a maybe because I can't prove it—some community-acquired infections are associated with very specific occupations. There are reports suggesting that plumbing activities or other occupations may be associated with a higher risk, and I would assume that maybe some women at least are less likely to engage in those activities.

Another possible explanation is that for community-acquired cases, some risk factors (smoking, for instance) could be, but it's...it's a really...will remain to be proven because we know that women unfortunately tend to...to smoke as...as much as men these days. So, that would maybe level off this...this effect. So, to...to recap, I would say that it's likely that the risk when you are admitted to hospital is not significantly higher for women. Now, because of this high risk of men especially in the community setting, you see the difference of women more likely to be reported as healthcare-associated compared to men.

[Sarah Gregory] As we said, most cases of Legionnaire's disease are caused by the bacteria, *Legionella pneumophila*. However, this bacteria seems to have been less common in cases that were acquired in healthcare settings. Why would this be? And could this discrepancy impact diagnosis or treatment?

[Julien Beauté] So, let me be just specify something here. It's *Legionella pneumophila* serogroup 1. So, this strain was indeed less common in cases acquired in...at a healthcare setting. Why would that be? Well, two reasons. One, which is the most likely one, is that some strains with somehow a lesser virulence are more likely to be...to cause disease in a more fragile person, and hence people are admitted to the hospital. Now, it may also be that because the laboratory methods used to ascertain the disease in hospitals are more likely to detect those strains which are less common. So, it leads to the last part of your question. Yes, this may have an impact on diagnosis because if you do not ascertain Legionnaires' disease by culture or PCR, you are likely to miss *Legionella pneumophila* nonserogroup 1 or other strains—non-*Legionella*, non-*pneumophila*. It is of...quite importance because the vast majority of cases are diagnosed by urinary antigen tests, and we know that this test is not good at detecting these other

strains. Could these have an impact on treatment? Potentially, yes, if you have a...a negative treatment for *Legionella* and you do not prescribe the right...the appropriate antibiotics, then you will miss...you may lose some precious time.

Now, the protocols...if the first-line antibiotic does not work within a certain...I mean, I think it's 24 hours but this needs to be double-checked, then you would switch to other antibiotics or add another one (macrolides, for instance) and that would cover *Legionella*. So, you would maybe miss the real diagnostics, but you would still be able to treat the disease, hopefully, if you follow the other guidelines.

[Sarah Gregory] So in the end, where a patient got sick, whether that was in the community, a hospital, or a nursing home or wherever, it made a big difference. Do you have anything more to say about that?

[Julien Beauté] Yes. So, yes, in our analysis one of the main drivers for fatal outcome is actually the setting. So yes, if you are in a hospital or another healthcare setting, you are more likely to...to die. Now unfortunately, there is one key variable which is not collected in the routine surveillance, which is the underlying condition. And it's very likely that even if you adjust for age, you're still missing that information. So, it's probably the main explanation for that.

[Sarah Gregory] How did the patients fare in this study? Were you able to tell how many got better versus how many didn't (died)?

[Julien Beauté] So, yes. Unfortunately, about 30% of the people that got healthcare-associated Legionnaires' disease died in this study. Now, this information about the outcome was missing for approximately 20% of the cases. For...I mean, the surveillance data are not very good at collecting information on follow-up. We hope that most of these people got better, but we don't know for sure because we know that Legionnaires' disease may be associated to long-term sequelae, so maybe the lung functions are not back to normal, for instance. But we were not able to capture...capture this...this information. So, some got better but many did not, unfortunately.

[Sarah Gregory] That's a pretty high percentage, sadly. Other than that women seem to be more susceptible to serious outcomes, did any other finding surprise you?

[Julien Beauté] Maybe surprising would be a big word, but I was happy to see...happy, I don't know if it's the appropriate word, but to see the severity of healthcare-associated Legionnaires' disease compared to the community-acquired ones was different. I mean, there is I think a different explanation for that, that healthcare-associated cases are less likely to be impacted by the weather. So, you can still have some warm water in pipes running year-round, whereas community-acquired cases are clearly more likely to be reported during the...the warmer season. So I think that's an important finding, but maybe not as surprising for, in my opinion, than the gender finding.

[Sarah Gregory] So, what do you consider the most important public health aspect of your study?

[Julien Beauté] Well, I mean we've discussed at length the...the case fatality, which is very high, especially in the healthcare setting. Now, healthcare-associated infections (and especially Legionnaires' disease) is preventable. So, the public health message for me would be first to, you know, to have some protocols for maintaining, testing the water systems in those...in those buildings, and the second would be to investigate. So, if there are cases of Legionnaires' disease and you suspect that they've been acquired within a healthcare setting, you should investigate.

You should try to really understand what was the source of the infection because you will prevent more cases in this highly susceptible population.

[Sarah Gregory] Are there any proactive ways that these results can be used for public health?

[Julien Beauté] So, yes. On top of what I just mentioned, I can extend maybe a bit further. So, you could...environmental investigations are very important, do PCR and culture as much as...as possible. Another way also would be to do some retrospective analysis. So if you identify one case, you may also want to look back at pneumonia in the...that were diagnosed in the same hospitals and see whether you can access some specimen and try to test for Legionnaires' disease if...if it was not done at the time. That would be also some important information.

[Sarah Gregory] You mentioned early on in one of your answers about Legionnaires' being in pipes that aren't used regularly, and we've been hearing in the news with a lot of these school shutdowns and things that they're finding Legionnaires' when they reopen the schools. Can the same thing happen in my house if I don't use the plumbing for a while? Like I have a back bathroom or something that I don't use much, if I go in there am I potentially going to spew out a bunch of Legionnaires' if I haven't turned it on...a tap on in a month or so?

[Julien Beauté] So, yes. Yes, especially if you have some very long pipework and complex ones, so I would invite you to flush your system. But maybe if you did not use your bathroom for a long period of time, you may just run the water for some time with hot water to make sure you don't just go and take the first shower with the...after a month of the system being not used.

[Sarah Gregory] That's really important advice because I don't think that that would have occurred to most people, ever. It certainly didn't occur to me before. Glad to know that, a little worrisome.

[Julien Beauté] I don't want to scare people. The risk remains low, but especially if you are a man, if you are getting older, and maybe if you have some preconditions, then you should be careful. Especially if you have, like, a summer house maybe which is not used for most of the year. Yes, maybe you want to flush the system before taking the first shower.

[Sarah Gregory] Ok, alright. Can people—other than flushing their plumbing—can people do anything personally to protect themselves from Legionnaires'?

[Julien Beauté] So unfortunately, not really. Meaning that you...as I said, the...the bacteria is everywhere, so it's difficult not to breathe, basically, especially when you have some humid weather. Now, you may want to act on risk factors. We know that smoking, for instance, is a...if you do, quit. I mean, it's not just good for Legionnaires' disease but for many other conditions. You...if you have a condition which is likely to be associated with immunodeficiency, for instance diabetes, you want to make sure you take your treatment and you are at a good equilibrium. And then of course there are factors on which it is difficult to act (age and sex); we can't treat that, so this will remain. So, there are ways. It won't be perfect, but yes, you...we should try to act on those risk factors as much as we can.

[Sarah Gregory] You work at the European Centre for Disease Prevention and Control. That's not associated with the U.S. one, is it?

[Julien Beauté] No, although we have very good contact with the U.S. CDC. But it's a completely different organization, yes.

[Sarah Gregory] I see. So, tell us about your job and what you like most about it.



[Julien Beauté] So, I am a medical doctor specializing in epidemiology. What I like the most I think is just the diversity of infectious disease epidemiology. I mean, you potentially...well, depending on your interests, you can cover very different aspects, from the environment (Legionnaires' disease is a good example for that), transmission, vectors, but also socioeconomical factors for more chronic infectious disease such as TB or HIV, vaccines. And everything of course is linked to healthcare systems, funding outbreak investigations...I mean, you...you really cover various aspects of epidemiology. So, I think it is both challenging but also very interesting.

[Sarah Gregory] You live in Sweden. What are you doing to relax in these somewhat complicated times?

[Julien Beauté] So...well, I mean we...the European CDC is based in Stockholm, which is the capital of Sweden. It is a middle-sized city, about a million inhabitants, so it's still a capital. So you have cultural activities...it's a quite...quite vibrant city. But the setting is really interesting because the city is between a very large lake (Lake Malaren) which is about 100 miles long. And on the eastern side of the city, we have the Baltic Sea with a very large archipelago—they say there is roughly 10,000 islands. So, basically from downtown Stockholm you can just hop on the boat and go to one remote island, which most of them are inhabited. So, you...so that's what I like to do to relax, just go to the archipelago. Of course, now the weather is getting a bit cold, but during most of the summer you can swim, if you like sailing...so that's...that's really nice.

During wintertime, if you're lucky and you have a real winter, you could do some ice skating on lakes or even on the sea if it's really cold, cross-country skiing. So yeah, there is a bit for everyone and for every season. It's a very pleasant town.

[Sarah Gregory] It sounds wonderful. I especially like the archipelago idea. If I ever get there, I'm doing that.

Thank you for taking time to talk with me today, Dr. Beauté.

[Julien Beauté] Thanks to you, Sarah. It was a pleasure.

[Sarah Gregory] And thanks for joining me out there. You can read the October 2020 article, Healthcare-Associated Legionnaires' Disease, Europe, 2008–2017, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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