Two Ways of Tracking *C. diff* in Switzerland

[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 Sarah Tschudin-Sutter, a professor of infectious disease epidemiology at the University Hospital – Basel in Switzerland. We'll be discussing two different surveillance measures that can be used to detect *C. difficile*.

Welcome, Dr. Tschudin-Sutter.

[Sarah Tschudin-Sutter] Hello, welcome.

[Sarah Gregory] Remind us, what is *C. difficile*?

[Sarah Tschudin-Sutter] So, *C. difficile* is an anaerobic, gram-positive rod. And it can produce toxins and can cause colitis. It's actually one of the most common causes of hospital-acquired diarrhea and one of the most common causes of hospital-acquired infection overall.

[Sarah Gregory] You mentioned diarrhea, so is that the only symptom or are there others?

[Sarah Tschudin-Sutter] So, diarrhea is the most typical symptom. And then there can also be abdominal pain, maybe accompanied by fever, and result in dehydration. Some patients may even present with more severe symptoms such as septic shock or signs of severe colitis.

[Sarah Gregory] Do we know how many people die of it…annually?

[Sarah Tschudin-Sutter] So, there are some estimates regarding deaths, especially in the United States. I don't know those figures off by heart, but it's definitely a substantial number. Unfortunately there are very poor estimates regarding the burden of disease in Switzerland.

[Sarah Gregory] How do people catch this infection?

[Sarah Tschudin-Sutter] So, traditionally, *C. difficile* has been considered a hospital-acquired infection—so, a pathogen which is acquired during a hospitalization. But more recently, community acquisition has been commonly reported. And in the community, acquisition may occur by contact with infected patients or people who just may be colonized with *C. difficile*. And some recent evidence even points to the food chain of being a potential source.

[Sarah Gregory] Is it treatable?

[Sarah Tschudin-Sutter] Yes. So, *C. difficile* infection fortunately is treatable with specific antibiotics. And most guidelines currently recommend either vancomycin or fidaxomicin to be administered.

[Sarah Gregory] Just curious, I'm allergic personally to almost all antibiotics, are there…and the mycins, particularly. Would there be anything for me if I caught it?

[Sarah Tschudin-Sutter] So, if you were allergic to…to vancomycin, you could for example be treated with fidaxomicin. That's another class of antimicrobials, so there should not be a cross-allergic reaction to this substance. And then, of course, there is also the treatment consisting of metronidazole. Which again, would be another class of drugs—probably less effective than vancomycin or fidaxomicin—but that would also be an option for someone with an allergy.

[Sarah Gregory] Oh, that's good to know. You mentioned that *C. difficile* is usually found—or was traditionally usually found—among hospital patients. Are these bacteria in hospitals everywhere around the world? Or just geographically in certain places?

[Sarah Tschudin-Sutter] Well, probably. And it's most likely that from some places in the world, we just don't have enough data to really be able to answer your question. So in the early 2000s, *C. difficile* outbreaks were primarily reported in the U.S. and in Canada, then also in many European countries including Switzerland. And some more recent data is emerging from Southeast Asia, Australia, South America…most parts of the world that *C. difficile* is also around in those hospitals.

[Sarah Gregory] So your study was about *C. difficile* in Switzerland in 2015. Is it a big problem there?

[Sarah Tschudin-Sutter] So we actually don't know, and this is the reason why we performed this study. And the burden of *C. difficile* is largely unknown in Switzerland and there has just been very few studies—single-center studies—looking into the burden of *C. difficile* infection in Switzerland. And those are…were also performed some years ago. As CDI burden has increased throughout Europe during the last years, we also hypothesized that…that *C. difficile* must have increased in Switzerland, too, over the last years.

[Sarah Gregory] Should people be concerned about this infection when they go to a hospital or in contact with someone who works in a hospital?

[Sarah Tschudin-Sutter] Well, yeah. I mean, it's definitely an infection which is concerning, especially given also that it's been increasing in most parts of the world over the last years. And on the other side, it has to be said that many hospitals have introduced infection prevention and control measures to…to reduce rates of *C. difficile* infection in hospitals. And, as mentioned before, quite a substantial amount of *C. difficile* is probably acquired in the community rather than in the hospital. So, patients may be colonized with *C. difficile* when they enter a hospital rather than acquiring *C. difficile* within the hospital.

[Sarah Gregory] Ah, okay. That's a new twist. So, your study specifically was about two different ways that countries can test for and monitor this disease. One of them was surveillance. What is surveillance and why is it important?

[Sarah Tschudin-Sutter] So, surveillance is about capturing the burden of a specific disease, in this case, *C. difficile*. It's important to be able to compare rates within specific institutions or between institutions, or even between countries. And over time, surveillance provides the actual basis to evaluate the effectiveness of targeted prevention and control measures.

[Sarah Gregory] So as I said, there are different ways to test for *C. difficile* infections. Does it really matter which test you use, as long as the results are accurate?

[Sarah Tschudin-Sutter] Well, for surveillance purposes, it definitely matters because some tests' strategies may be more sensitive than others. So, to compare rates over time or between institutions or between countries, it's important to use a similar diagnostic approach. Otherwise, the rates won't…won't be comparable.

[Sarah Gregory] Okay. So your study investigated two testing methods: enzyme-linked immunoassay, called EIA, and PCR. Would you explain what the difference is between these two tests?

[Sarah Tschudin-Sutter] So the enzyme-linked immunoassay for detection of *C. difficile* detects GDH (glutamate dehydrogenase). This is an enzyme which is highly specific to *C. difficile*. If GDH is detected, then a second step is required for detection of toxin-producing *C. difficile*. So,

there's a second enzyme-linked immunoassay, which follows the first step, which then detects toxins A and B. And then on the other side, PCR detects the gene which is encoding for mainly the toxin B. And this was also the diagnostic approach which was evaluated in our study—so, a PCR to detect the gene encoding for toxin B. So, PCR as a nucleic acid amplification test is more sensitive to detect *C. difficile* as compared to the enzyme-linked immunoassay-based approach.

[Sarah Gregory] You mentioned the reason, or one of the reasons, you did this study was to get some real data on the burden in Switzerland. Do you have more to tell us about that? Why you did your study?

[Sarah Tschudin-Sutter] Yes. So, that was exactly the reason why it was performed. So actually, a nationwide study on the burden of *C. difficile* has…has to date not been performed in Switzerland. So, the only figures regarding *C. difficile*'s burden were a couple of incidence studies performed at individual centers. But no nationwide data had been collected so far for Switzerland.

[Sarah Gregory] Well, why don't you tell us about your study, then—how you went about it, that sort of thing.

[Sarah Tschudin-Sutter] Yes. I've mentioned this was a nationwide prevalence study. It was performed in two days in 2015, and we asked all laboratories who were serving 76 Swiss hospitals to collect all liquid stool samples, which they received the standard of care on both of the study days. And they sent us those stool samples, and we analyzed them independently of any requests by the submitting clinician for the presence of toxigenic *C. difficile* using both the diagnostic approaches we discussed previously. So, either to detect *C. difficile* by enzyme-linked immunoassay for detection of GDH and toxins A and B, and in addition we also performed PCR for detection of the gene encoding for toxin B. So we performed both diagnostic test strategies on all samples in…in parallel.

[Sarah Gregory] And what did you find? Was one test more accurate than the other?

[Sarah Tschudin-Sutter] So, what we found was that the rates were higher when taking the results obtained by the PCR into account as compared to the results as determined by the enzyme-linked immunoassay diagnostic approach. One can't necessarily say that one test is more accurate than the other—the finding just confirms that the PCR-based approach is more sensitive as compared to the enzyme immunoassay-based approach for detection of *C. difficile*. This may, however, also result in more patients being detected as carrying *C. difficile* who may be colonized rather than infected. But I think what the results clearly show is that it's very important to use the same algorithm, and that's only then results can be compared between different institutions and countries.

[Sarah Gregory] How would you like these findings to be used? Should they help a doctor choose which test to use, or are they more helpful for policy decisions?

[Sarah Tschudin-Sutter] So, I think these findings are…are more helpful for policy decisions than for an individual physician or…or doctor. So in order to have comparable results, the study just shows that it's really important that the same testing strategies are applied. Otherwise, the findings will not be comparable.

[Sarah Gregory] You also looked at different types of *C. difficile* bacteria. What did you find there?

[Sarah Tschudin-Sutter] So, what we looked into were different ribotypes of *C. difficile* circulating in Switzerland. So, all the strains we identified during this study were analyzed by PCR ribotyping. And what we found was that we had a large diversity of different ribotypes currently circulating in Switzerland, and this may point to multiple sources of *C. difficile* within the Swiss population rather than to just the presence of one common outbreak strain. It's also quite noteworthy that the hypervirulent PCR ribotype O27, which is actually quite common in Europe and also in the United States, was not discovered during this study in Switzerland. We did, however, find another hypervirulent PCR ribotype, ribotype O78, in Switzerland. And this ribotype has actually been (again) linked to some food sources.

[Sarah Gregory] You mentioned food. That's a new one for me. I had never heard that before. That seems very concerning, I mean we have so many outbreaks now, *Salmonella* in food sources and *E. coli* right here in the United States, right now we have *E. coli* in peaches and onions. Do you have any more information on these food sources other than that seems to be a culprit?

[Sarah Tschudin-Sutter] Well, I should note that in our study, it was not designed to be able to establish a relationship with a food source. But what is known from the literature is some data showing that, for example, this ribotype O78 is present in, for example, in pigs and also in quite a variety of other domestic animals. So for example, in the Netherlands it has been shown that for some populations living very near to animal farming, there may be a higher incidence of *C. difficile* infection. And…and this has been linked to…to these food sources.

[Sarah Gregory] I see, okay. Well, in your opinion, what's the most important public health takeaway from your study?

[Sarah Tschudin-Sutter] So, I think the most important takeaway is that we really need unified diagnostic approaches to be able to compare rates of specific infections across institutions and countries and…and to then to ultimately be able to draw conclusions regarding the local and global epidemiology of this specific infection.

[Sarah Gregory] Are there ways that people can protect themselves?

[Sarah Tschudin-Sutter] Well, the most important risk factor for *C. difficile* infection is exposure to antibiotics. So, prudent use of antibiotics is probably the most important prevention measure for *C. difficile* infection.

[Sarah Gregory] Use of antibiotics? I'm sorry, I'm not quite clear on what you just said.

[Sarah Tschudin-Sutter] Sorry. Yeah, no…So, prudent use of antibiotics I believe is the most prevention measure for *C. diffic*ile infection, and so, to really only administer antibiotics when they are really needed. And so, for example, be very restrictive with antibiotics if there is not a clearly established bacterial infection. And then also to…to streamline antibiotics and to use antibiotics with a spectrum as narrow as possible, rather than to administer broad-spectrum antibiotics.

[Sarah Gregory] Ah, okay. That's, that's….I understand that, okay. So, tell us about your job, where you work and what you enjoy most about it.

[Sarah Tschudin-Sutter] So, I work as an infectious disease specialist at the University Hospital – Basel in Switzerland. I guess I really enjoy all aspects of this work. I have a special research

interest in epidemiology and transmission of important hospital-acquired infections and also in respective prevention measures.

[Sarah Gregory] So, Switzerland is a very beautiful country. What do you do for fun and relaxation, especially right now in these troubled COVID times?

[Sarah Tschudin-Sutter] Well yeah, as you say, unfortunately due to the challenging COVID situation, it's…there hasn't been that much time for…for fun and relaxation recently. But, yeah, I would definitely agree with you that Switzerland is a truly beautiful country, and probably also the COVID situation has…has led many people to explore their immediate surroundings in more detail rather than travel further abroad. So…so this is something I've been trying to do whenever possible.

[Sarah Gregory] Well, thank you so much for taking the time to talk with me today, Dr. Tschudin-Sutter.

[Sarah Tschudin-Sutter] Well, thank you very much for your interest in this study.

[Sarah Gregory] And thanks for joining me out there. You can read the October 2020 article, Multicenter Prevalence Study Comparing Molecular Toxin Assays for *C. difficile* Surveillance, Switzerland, online at cdc.gov/eid.

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

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.