AMR Nontyphoidal *Salmonella* Infections, United States

[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. Felicita Medalla. She's an epidemiologist here at CDC in Atlanta, Georgia. We'll be discussing the increase of antimicrobial-resistant nontyphoidal *Salmonella* infections in the U.S.

Welcome, Dr. Medalla.

[Felicita Medalla] Hi Sarah. Thanks for having me today.

[Sarah Gregory] We hear more and more about *Salmonella* outbreaks. How is *Salmonella* different than enterovirus?

[Felicita Medalla] There are some differences, Sarah. *Salmonella* are bacteria, and most cause a diarrheal illness. While most enteroviruses also cause diarrhea, they can also cause a mild coldlike illness. The diarrhea caused by *Salmonella* typically lasts about a week, while viral diarrhea usually lasts only a few days.

[Sarah Gregory] What's the most common way people get sick from it (*Salmonella*)?

[Felicita Medalla] Well, most people in the U.S. get infected by eating food that got contaminated with animal fecal matter such as poultry, eggs, beef, and pork. And you might be surprised that many *Salmonella* illnesses can also come from eating raw vegetables and fruits that got contaminated with animal fecal matter. *Salmonella* can also contaminate processed foods. For example, CDC is currently investigating a multistate outbreak of *Salmonella* infections linked to frozen stuffed breaded chicken products. The chicken might look cooked, but it's actually raw. People can get infected in other ways too, such as through animal contact, contaminated water, and some environmental sources.

[Sarah Gregory] Aren't some animals more particularly prone to *Salmonella*, like reptiles and poultry (backyard chickens), that kind of thing? Live chickens?

[Felicita Medalla] Yes, absolutely. We have posted our—you know, we have our outbreak branch has posted a lot of information about that. I'm glad you mentioned that. It's been a problem that, our animal contacts such as backyard animal (backyard poultry), that has been a problem. And I can sense you've done a lot of reading already on *Salmonella*.

[Sarah Gregory] So your study (and what we're talking about today) is nontyphoidal *Salmonella*. What is it and how is it different from other forms of *Salmonella*?

[Felicita Medalla] We divide the different kinds of *Salmonella*—there are many different kinds of *Salmonella* which we call serotypes—into nontyphoidal and typhoidal. Typhoidal *Salmonella* illnesses are rare and very serious. They cause typhoid fever and paratyphoid fever. And these illnesses typically occur in travelers through areas abroad with poor sanitation and hygiene. Typhoidal *Salmonella* live only in people's intestines, not in the intestines of animals.

But the vast majority of people in the U.S. with a *Salmonella* infection have illness caused by nontyphoidal *Salmonella*. These kinds of *Salmonella* most often cause a diarrheal illness. Nontyphoidal *Salmonella*, like typhoidal *Salmonella*, live in people and many animals. And I just

want to add that we often just say *Salmonella* infection and assume it's nontyphoidal *Salmonella* unless we say otherwise. As I said, most of the U.S. infections are actually caused by nontyphoidal *Salmonella*.

[Sarah Gregory] Oh I see, okay. So typhoid fever that we take shots for or take pills for to go to certain countries, that's actually a *Salmonella*?

[Felicita Medalla] Oh yes. That is a *Salmonella*, and I think a lot more of people are familiar with that. Because as I said, although it's not as common as nontyphoidal *Salmonella*, they are very serious.

[Sarah Gregory] Yes, even I had no idea that that was actually a *Salmonella*.

So you've already sort of said that nontyphoidal *Salmonella* is what we basically have here in the United States, and so that's when there's a foodborne illness outbreak. We're usually talking about nontyphoid *Salmonella*, right?

[Felicita Medalla] Yes, yes. That's what we are usually talking about. These nontyphoidal *Salmonella* are the bacteria that most often cause foodborne illness outbreaks.

[Sarah Gregory] And is it actually very common in the United States?

[Felicita Medalla] Yes. CDC estimates that nontyphoidal *Salmonella* cause about 1.3 million infections each year in the U.S., and food is the source for about a million of these infections.

[Sarah Gregory] You mentioned diarrhea, but are there other symptoms? I mean, how would you know for sure if you were sick with *Salmonella*?

[Felicita Medalla] Yes Sarah, that's a good question. As we talked about, it causes diarrhea, and the diarrhea is typically four to six days. And other symptoms are stomach cramps and fever, and the diarrhea can be bloody. The patient may also experience nausea, vomiting, or headache. So those are the other symptoms.

[Sarah Gregory] And is there a specific test for it?

[Felicita Medalla] Yes. The infection is diagnosed when a lab test detects *Salmonella* in a person's stool, body tissue, or fluids. The test could be a culture that isolates the bacteria—I think most people have heard about a culture—or a test that detects the bacteria's genetic material.

[Sarah Gregory] And if you discover that you have it, how is it treated?

[Felicita Medalla] Well, the good news is most people with nontyphoidal *Salmonella* infection recover in about a week without specific treatment. And you know, Sarah, maintaining good hydration is always very important. But people with severe nontyphoidal *Salmonella* infection might need to be hospitalized and take antibiotics. And people who are more likely to develop serious illness might also need to be treated with antibiotics to prevent the infection from spreading to their blood or other parts of the body. So, most people actually—again, most people won't need to be treated with an antibiotic, because most people will get better. But there are people who have severe infection who will need treatment and who will need to be hospitalized.

[Sarah Gregory] And is it worse for small children and the elderly, like so many viruses and bacterias?

[Felicita Medalla] Oh, yeah. And especially the elderly, as far as they are more likely to develop a serious illness.

[Sarah Gregory] And can it be fatal?

[Felicita Medalla] Oh yes, the infection can be fatal. CDC estimates that more than 400 people in the U.S. die each year from infection with nontyphoidal *Salmonella*.

[Sarah Gregory] Antimicrobial resistance is, as we know and everyone knows by now, a big cause for concern nowadays. Do you know how AMR became a problem in the first place?

[Felicita Medalla] You're right. Antimicrobial resistance is a major concern for public health. You know, antibiotics can be lifesaving (they are lifesaving), but they contribute to resistance whenever they are used. I mean, this happens because bacteria treated with antibiotics always look for ways to survive, and they can acquire resistance to antibiotics. Bacteria do this through various mechanisms, including mutations in the genes that confer resistance. Bacteria are also able to share their genetic material that carries the resistance gene, for example, with one another. So they do have many ways to do it. And bacteria that have acquired resistance are more likely to survive and thrive despite the use of antibiotics to kill or stop their growth, and that means they're more likely to spread and cause additional infections.

[Sarah Gregory] Are there certain strains that are more associated with antimicrobial-resistant nontyphoidal *Salmonella*?

[Felicita Medalla] Yes, there are strains of some serotypes that we found are more likely to be resistant than others. Giving example, two serotypes with a lot of resistant strains are some of the most common ones—Enteritidis and the one with a long name which we call I 4,[5],12:i:- (it's a long name).

[Sarah Gregory] So what specific antibiotics is *Salmonella* resistant to now?

[Felicita Medalla] Some of them can be resistant to a wide range of antibiotics. And as I said, different serotypes and strains may have different resistance patterns. Our study focused on three antibiotics commonly used to treat severe *Salmonella* infection, which are ceftriaxone, ciprofloxacin, and ampicillin.

[Sarah Gregory] And for people infected with AMR *Salmonella*, how are they treated? Are there any treatment options available for them?

[Felicita Medalla] Yes, there are treatment options. Let me start with, you know, how a doctor will treat a patient. If a patient has a severe infection, waiting for laboratory test results before initiating antibiotic treatment might not be a good idea. You know, it's better to be cautious. And in these cases, doctors can infer the likely resistance pattern using data from other people's *Salmonella* infections, and then treat based on that. After the laboratory has tested the patient's own strain for resistance, the doctor might need to change the treatment based on the strain's resistance pattern.

So treatment is actually guided by the antimicrobial resistance result, and some of them throughout this step—you know I've mentioned them (ceftriaxone and ciprofloxacin)—are antibiotics recommended to treat nontyphoidal *Salmonella* infection. Fortunately, resistance to both antibiotics (meaning combined resistance to these two) is still uncommon. Other important treatment options include ampicillin and azithromycin. Some *Salmonella* infections can be resistant to all three of the antibiotics we looked at in our study. A few what we call reserved

antibiotics are available to treat these infections. But a big public health concern is that, over time, bacteria will become resistant even to these reserved antibiotics. Because each time we find an antibiotic that works on a resistant strain, bacteria can develop resistance (as I described earlier). Then we find another antibiotic that works, and the bacteria can develop resistance to it. We are concerned that, over time, we might run out of safe and effective treatments. Although we are not currently seeing *Salmonella* infections that cannot be treated with antibiotics, some infections can only be treated with antibiotics that must be given by injection. So, it's important to stress that…to emphasize that we need to take public health action now to limit the increase in resistance.

[Sarah Gregory] And how is antimicrobial resistance tracked? Is there a specific reporting system that's used?

[Felicita Medalla] Yes. We track resistance through the National Antimicrobial Resistance Monitoring System (which we call NARMS). And NARMS is the collaboration among CDC, FDA, USDA, and state and local health departments. NARMS tracks—meaning this interagency NARMS—tracks resistance in *Salmonella* and other foodborne bacteria isolated from people, retail meat, and food animals.

To track resistant *Salmonella* that come from people, the NARMS program at CDC works with public health laboratories in 50 states and four major cities. They submit a subset—the labs submit a subset of *Salmonella* isolates that they receive from clinical laboratories to the NARMS laboratory at CDC for antimicrobial susceptibility testing. And CDC reports the annual percentage of *Salmonella* that are resistant to medically important antibiotics as part of tracking this resistant bacteria.

[Sarah Gregory] You looked at the occurrence of resistant *Salmonella* infections from 2015–2016 and compared them to 2004–2014 in U.S. data. What did you find there?

[Felicita Medalla] Right. We looked at the annual incidence of *Salmonella* infections with resistance to the three medically important antibiotics that I mentioned: ceftriaxone, ciprofloxacin, and ampicillin. So when we compared data from 2015–2016 with data from about 10 years before, we found that the annual incidence of these resistant infections increased by an estimated 40%. This translates into about 63,000 more resistant infections each year during 2015–2016.

We also found that changes in the incidence of resistance varied by *Salmonella* serotype. Two common serotypes I mentioned earlier, Enteritidis and I 4,[5],12:i:-, were responsible for about two-thirds of the increase.

[Sarah Gregory] Just a general question about any microbial resistance. Is it specific to an individual? Or is it just that that particular strain is resistant? I mean, I know some people that take antibiotics like candy. And then like myself, I haven't had one in decades. Would I be more likely not to be resistant? Or does it not really matter?

[Felicita Medalla] Well, that's a good point Sarah, because I think antimicrobial resistance is unique because it actually is an individual problem as well as a community problem. Because resistance—once resistance emerges in a bacteria, the mechanisms are already there. So, it is a problem if you get an infection and you have a resistant infection. So that's the individual component of it. But then, of course, the more we are treated with antibiotics, the more, you know, resistance can emerge. So, it is actually both. When we talk about the antimicrobial

resistance as a problem, that is a community problem, it is in fact a global problem. But then also in terms of how it impacts you as a person, your infection—the bug or the strain that's causing your infection—might be resistant. So, it is actually both. So that's a good point. That's a really good question, Sarah. I hope that helps.

[Sarah Gregory] Thank you, yes it did. So you just mentioned global, so this isn't just a problem specific to the United States—antimicrobial resistance—it's a global issue, right?

[Felicita Medalla] Yes, this is very much a global issue. And this is not just—I mean, infection in general—and this is not unique to AR. So this is very much a global issue, not just one limited to the U.S., because antimicrobial-resistant *Salmonella* infections can emerge anywhere in the world and spread to other regions and globally. In the U.S. in fact, for example, we are seeing high rates of resistant infections in returned travelers. So, it really is a problem.

[Sarah Gregory] And why do you think it's increasing, this AMR *Salmonella*?

[Felicita Medalla] Well, the use of antibiotics in people and animals can promote the emergence and spread of resistant strains. I did mention that antibiotics are lifesaving and we need them, but of course, their use can promote the emergence and spread of these strains. Nontyphoidal *Salmonella* live in the guts of animals (as I mentioned earlier), and much of the use of antibiotics is in food-producing animals. And there's some evidence that antimicrobial resistance among nontyphoidal *Salmonella* is largely a consequence of antibiotic use in food-producing animals.

[Sarah Gregory] In your opinion, what could or should be done to stop it?

[Felicita Medalla] The previous question is a good segue to this one. The most important thing we can do is to use antibiotics only when needed and as prescribed. Appropriate use of antibiotics in animals and people can help slow the development of resistance and help prevent the spread of resistant bacteria. Again, I cannot overemphasize that antibiotics are lifesaving and they are essential, and we have to use them. But the best way is to make sure that their use is appropriate so that we can slow the development of resistance.

And something else is really important, we also need to focus on prevention. By preventing *Salmonella* infections in general, we will be preventing resistant infections. And some examples: people can decrease their risk of infection by being careful to prevent cross-contamination in the kitchen from foods of animal origin and by cooking meat and poultry well. And retailers can sell meat and poultry that comes from companies that assure no or only low levels of contamination. They can sell vegetables from companies that do a good job to prevent contamination of their products with animal feces during growing, irrigation, or processing. So, I'm just giving some examples.

[Sarah Gregory] Do you (does CDC, does anyone) have data on Big Agra versus local small farm infections?

[Felicita Medalla] Yeah, I don't…I think you're asking about whether we are finding more resistant products from big versus smaller (maybe you're asking about organic). At this point, we don't really have the hard data on that. But that's a good question because, you know, if we find any in the grocery, right? I mean, you see that, but again for now the one that we are promoting is really the appropriate use of antibiotics and primary prevention of infections. I hope that answers your question.

[Sarah Gregory] Yeah, sure. So what was the biggest challenge when you were doing this study?

[Felicita Medalla] One of the main challenges in our analysis was developing an approach to combine data from two CDC surveillance systems—so we used data from two sources—in a way that would best represent the number of resistant *Salmonella* infections by state and year during the study period. I mean, the analysis actually combined data so it wasn't the typical analysis that you use only one data source. So that was one of the biggest challenges. And the way we did it, is we paired data from NARMS—remember NARMS stands for National Antimicrobial Resistance Monitoring System—with data from the Laboratory-based Enteric Disease Surveillance system, which tracks *Salmonella* isolates that state and local public health laboratories report to CDC.

[Sarah Gregory] And what do you think is the most important part of your study? How will it help public health?

[Felicita Medalla] I think the most important part of our study is the concerning trend that resistant *Salmonella* infections have been increasing in incidence. Although our study did not examine the sources of these resistant infections, previous studies have shown associations with certain exposures. I'll give some example—for example, Enteritidis infections are commonly linked to chicken and eggs. And international travel is also an important source of these infections. Another example is multidrug-resistant I 4,[5],12:i:- infections, which have been linked to the consumption of pork. So, we think our study findings will help public health professionals set targets and priorities for reducing the number of resistant infections in the U.S.

[Sarah Gregory] And in what ways can a One Health approach help with detecting and controlling AMR?

[Felicita Medalla] Sarah, I'm glad you asked a question about One Health. On the most basic level, antimicrobial resistance is tied to how we use antibiotics. A One Health approach looks at the big picture by recognizing the connection between the health of people, animals, and our shared environment. You know…we are all in this together so it's a shared environment.

This approach brings together experts in human, animal, and environmental health and related sectors to monitor and control public health threats and to learn how drug-resistant infections emerge and spread. NARMS, as I mentioned, helps with the monitoring part of this by capturing information not just from people, but also from animals and food. And this is why we have that interagency NARMS. If we focused only on human health, we might miss emerging threats coming from animals, the environment, and other sources. By promoting collaboration across sectors, we have a better chance of identifying and controlling concerning resistance before it becomes a serious threat. Antimicrobial resistance is a complex problem, and a One Health approach can help provide more comprehensive solutions.

[Sarah Gregory] Tell us about your job and how you become involved in tracking AMR? What got you interested in this specific problem?

[Felicita Medalla] I am an epidemiologist on the team that works with human data that's collected through NARMS. The NARMS program at CDC helps protect public health by tracking emerging resistant infections caused by *Salmonella* and other foodborne bacteria, and again, the ways in which resistance is spread and how resistant infections can differ from susceptible infections.

I have been interested in resistant infections for a long time. I studied medicine because I was interested in helping people stay healthy, and as I've mentioned, antimicrobial resistance is a real threat to people's health. This study was an opportunity to better understand changes in *Salmonella* and how resistance has been spreading, and it helped provide some valuable insights. The takeaway message—and I guess I've said this many times—is that responsible use of antibiotics in people and food-producing animals will help us continue to be able to use antibiotics to treat sick people.

[Sarah Gregory] As a result of the pandemic, have you made any personal life changes that you think you'll continue?

[Felicita Medalla] Well, I've been fully vaccinated, but for now I am going to try to be very cautious still. I'll continue to wear masks where required, and in certain indoor settings… it's I think already kind of a habit for us. And I may still continue to try to avoid large indoor gatherings. But of course, I try to enjoy the outdoors as much as possible in safe ways. And I'm learning to really enjoy some of the things that, sure, we used to take for granted, like eating outside and meeting up with friends and family. And I've had a couple things that I did. I've also tried to be productive and active. For example, last year I got a mini (a tiny) sewing machine to make my own masks. Because if you remember, they were very difficult to find in stores and online. And I got a small stationary bike to use daily. Neither of those got as much use as I would have hoped, but I am going to keep trying and hopefully I'll be able to...I mean, I will be able to continue that. I will try my best.

[Sarah Gregory] Okay, well good for you.

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

[Felicita Medalla] Well Sarah, thanks so much for the opportunity to talk about our work on resistant *Salmonella* infections in the U.S. Thank you, it's been a pleasure working with you.

[Sarah Gregory] And thanks for joining me out there. You can read the June 2021 article, Increased Incidence of Antimicrobial-Resistant Nontyphoidal *Salmonella* Infections, United States, 2004–2016, online at cdc.gov/eid.

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

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