A Decade of *E. coli* Outbreaks in Leafy Greens in the U.S. and Canada

[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 Katherine Marshall, an epidemiologist at CDC. We'll be discussing *E. coli* outbreaks in leafy greens in the United States and Canada from 2009 to 2018.

Welcome, Katherine.

[Katherine Marshall] Hi, thanks! Glad to be here.

[Sarah Gregory] So, what is Shiga toxin *E. coli*? Don't people already have some sort of *E. coli* in their intestines?

[Katherine Marshall] They do. *E. coli* bacteria, they actually normally live in the intestines of people and…and also animals. So, some people might be surprised to know that most *E. coli* are harmless, and they're actually an important part of a healthy gut. But, Shiga toxin-producing *E. coli*, or STEC, is not harmless, at least for humans. So, STECs are a type of *E. coli* that produce a toxin called the Shiga toxin, which was named after a Japanese scientist who discovered it. And STEC was first identified as a cause of outbreaks in 1982 when it caused a large outbreak linked to beef. So, there are two main groups of STECs. There's first O157 and then all of the other STECs are lumped together in a group called non-O157. They both cause a similar type of illness, but STEC O157 is usually a bit more severe.

[Sarah Gregory] Just curious, I know that reptiles have a lot of *Salmonella* in their intestines, as do backyard poultry. Do backyard poultry and reptile pets, or reptiles, have *E. coli* in their intestines also?

[Katherine Marshall] Well actually, STECs…they can live in the guts of animals. And it's really cattle primarily that they live in, and other types of animals. And so, because of that…it's funny, we actually see that beef is the most common source of STEC O157 outbreaks. And that's because cattle are the primary reservoir for…for STECs.

[Sarah Gregory] I see, okay. So what are the symptoms, and can it be deadly? I think it's deadly, right?

[Katherine Marshall] Yes. So, STECs can cause diarrhea, which is sometimes bloody, and then some cramping and vomiting and fever sometimes as well. But the range of symptoms can really vary. So, some people might experience a mild illness, but others might get so sick that they need to be hospitalized. And sadly, sometimes people do die from STEC infection. There's also a small proportion of people who are diagnosed with STEC infection that go on to develop a potentially life-threatening complication that's called hemolytic uremic syndrome, or HUS, and it's a condition that affects the kidneys.

[Sarah Gregory] So, where do leafy greens fall in on the spectrum of STEC outbreaks? And tell us again what exactly STEC is.

[Katherine Marshall] So, STEC stands for Shiga toxin-producing *E. coli*. And as we discuss in our paper, leafy greens are the second most common source of STEC O157 outbreaks. Beef is the most common, and…and that makes sense because STEC lives in the guts of certain animals—primarily cattle. So, it makes sense that we see beef as the most common source of STEC O157 outbreaks. But leafy greens are often grown out in the open and are exposed to the environment, so they can be vulnerable to contamination.

[Sarah Gregory] Okay, and what are considered leafy greens and which one is the most common culprit?

[Katherine Marshall] So, leafy greens can include different types of lettuce—like romaine and iceberg—but it also includes cabbage, spinach, kale, and there's other greens like chard, collard, and mustard greens…so that sort of thing. So, in our study, we found that among STEC outbreaks with a single type of leafy green that was identified as the outbreak's source, most were linked to romaine.

[Sarah Gregory] And why is this? Why would leafy greens be affected with *E. coli*? Obviously they don't have it in their systems.

[Katherine Marshall] Right. So, leafy greens can become contaminated with poop from cattle or other wild animals that could be carrying or spreading STEC bacteria. And…and they can do that directly or indirectly—so, through contaminated irrigation water, for example, through flooding runoff, or even dust. And…and so, we don't know exactly why we saw romaine as the most common leafy green type here, but we have a few potential factors that could be

contributing to this. So, the first is the popularity of romaine. So one hypothesis we had was that romaine might just be more popular than other types of leafy greens. So, we looked at some data around the popularity of romaine versus other types of lettuce and how that's changed over time. And we found that romaine and iceberg—maybe not surprisingly—are the most popular types of lettuce. But they're…they're pretty similar, so we don't think this explains why we're seeing more STEC outbreaks linked to romaine versus other types. And the second factor that could be contributing is the shape of the lettuce. So, if you picture a head of romaine lettuce, it's…it's a little bit taller, the leaves are sort of loosely clumped together, and it's a bit more open at the top of the plant. So, then if you picture iceberg, it's kind of more of this closed ball kind of shape. And so, we wonder if the open shape of romaine could allow it to become contaminated more easily, and maybe that closed ball shape of iceberg helps protect it. But ultimately, we need more research to really understand what's happening here.

[Sarah Gregory] Is there a difference in these outbreaks between organic and non-organic?

[Katherine Marshall] That's a good question, but that's not something that we actually looked at in these outbreaks, unfortunately.

[Sarah Gregory] I'm always surprised when I see that there's an outbreak in an organic farm. But I guess maybe pesticides and not pesticides doesn't have much to do with poop spread.

Are environmental investigations done at the time of the outbreak?

[Katherine Marshall] Ideally they are. But an environmental investigation can only take place on a farm where the contaminated lettuce is grown, but only if investigators are able to determine where the contaminated lettuce came from. And that requires detailed information that's collected from interviews with sick people—that's what we call epidemiologic data—and detailed information that's collected from records that show how the contaminated lettuce moved through the supply chain. And that's traceback data. So, many times investigators aren't able to collect enough of that really important, detailed information to be able to figure that out. But, environmental investigations are important and they can help give us clues about how lettuce became contaminated in the first place. So for example, in one investigation in our study, investigators found the same strain of bacteria that made people sick in an irrigation canal that was close to romaine farms that were identified during traceback. And, it was also near a cattle

operation. So, you know, we don't know for sure that contaminated irrigation water caused the outbreak, but it's a pretty big clue.

[Sarah Gregory] Are these outbreaks seasonal?

[Katherine Marshall] Our data certainly suggests that most outbreaks tend to begin in…in the fall and spring season. And then, within those seasons, more outbreaks began in October and April than any other month.

[Sarah Gregory] Is there a reason for this that you've been able to identify?

[Katherine Marshall] We don't know. You know, we need more research to be able to understand this finding.

[Sarah Gregory] What about geographic location? Were these outbreaks mostly originate in one particular part of the country or countries?

[Katherine Marshall] Well, about 98% of the leafy greens that are grown in the United States come from just two states, and that's California and Arizona. So, we often aren't able to figure out exactly where the contaminated leafy greens linked to outbreaks are from. But a few of them in this study were linked to growers in Arizona and California.

[Sarah Gregory] And how many outbreaks have there been over the decade you studied?

[Katherine Marshall] Well, we found 40 STEC outbreaks that were linked to leafy greens in both the United States and in Canada. And we identified just about 1,200 ill people that were linked to these outbreaks. There were 420 people who were hospitalized, 77 people who developed HUS, and, sadly, 8 people died. But the number of people who actually got sick in these outbreaks is likely much higher. These are just the ones that we know about. So, for example, if you ate food that was contaminated with STEC and you got sick, but you didn't go to your doctor or you went to your doctor but no testing was done, investigators wouldn't know about your illness.

[Sarah Gregory] What about age? Is there an age group more impacted than another?

[Katherine Marshall] So, for leafy green outbreaks, people of all ages were linked to them—so that includes children less than 1 all the way up to older adults—but most people were in their 20s. But some people can be more likely to develop HUS or experience more severe symptoms, and that includes people who have weakened immune systems or young children.

[Sarah Gregory] But most people were in their 20s…is that what you just said?

[Katherine Marshall] Yes.

[Sarah Gregory] That's so surprising. Do they eat more lettuce? Or, for some bizarre reason, more susceptible, do you think?

[Katherine Marshall] I think that it's probably that they just ate more lettuce.

[Sarah Gregory] Huh. What's the economic toll of all of this?

[Katherine Marshall] So, in general, we estimate that there's about 265,000 STEC illnesses that occur each year in the United States at a cost of about 280 million dollars. But beyond the cost of illness itself, outbreaks can result in a lot of cost to companies that end up having to recall contaminated food. So, the economic toll is not only impacting people who get sick and the healthcare system, but it impacts food companies as well.

[Sarah Gregory] Well, what kinds of actions are taken when *E. coli* is found in a food source to warn the public? What happens? What's the chain of communication, here?

[Katherine Marshall] So if investigators are….able to identify the food source for an outbreak, there's a few different actions that they can take, and that includes actions to remove contaminated food from the marketplace and warning consumers. So, FDA, or the Food and Drug Administration, will work with companies that produce contaminated food and recall it. And then CDC, FDA, and state and local health departments might all issue warnings to consumers advising them to throw away the product and not eat the contaminated food. But they also might warn restaurants and retailers to not serve or sell the recalled food. And then for multistate outbreaks, CDC will post announcements on their website and on social media and sometimes issues press releases as well to make sure the public is aware.

[Sarah Gregory] Are stores, store chains, pretty good about getting this stuff off the shelf, do you think?

[Katherine Marshall] So actually, FDA will work with retailers to ensure that product is recalled from the market.

[Sarah Gregory] Ah, good. That's comforting. How is the cause of the outbreak tracked down? What's the process? I mean, it seems like it must be extremely difficult.

[Katherine Marshall] Yes, investigating foodborne outbreaks is…is a complex and…and difficult job. There are five common steps in a foodborne outbreak investigation, some of which might happen at the same time. So, the first step is to detect a possible outbreak; the second step is to define and find cases; the third step is to generate hypotheses about the likely sources; the fourth step is to gather traceback and laboratory data and then test that hypothesis; and then the fifth step is to take action and control the outbreak. So, I can walk us through the search in each one of these steps.

So, the first step, to detect the possible outbreak, we do that using public health surveillance methods, including PulseNet, which is the national molecular subtyping network, and it captures DNA fingerprints of the bacteria that's cultured from sick people. We also might learn of an outbreak through formal reports of illnesses or informal reports of illnesses.

So in step two, defining and finding cases, that really helps us understand the size, the timing, severity, and even possible sources of an outbreak. And that's typically when we develop a case definition that defines who's going to be included in the outbreak. And usually, again, that's based on that DNA fingerprint of the bacteria that people are infected with.

So during hypothesis generation, investigators in a local or state health department will interview sick people to find out what foods they ate that week before they became sick. So, that data that's reported by sick people is then analyzed to see if there's any foods that are being reported more frequently than we would expect, or if sick people are reporting eating at the same restaurants or shopping at the same grocery stores. So if investigators find something in common, they'll dig a bit deeper for more specific information—like brands or to see if people ate the same food at the same restaurant. And all of this is what we call epidemiologic data.

So once we have that hypothesis, investigators will gather some additional traceback and laboratory data to help see if there's a common point of contamination in the distribution chain. And so, investigators in states and FDA will review records that are collected from restaurants and stores where sick people ate or shopped. And at the same time, investigators might also collect and test the suspect food from somebody's home, retail location, or where the food was produced. And if they find that same bacteria that caused illness in that suspect food or a production environment, that's called laboratory data. So, investigators will assess all three of

these types of data—epidemiologic, traceback, and laboratory—to identify and confirm a food is the source of the outbreak.

And then during that last step, that's when public health officials might issue public warnings and companies might recall contaminated food to help stop the outbreak and prevent additional people from becoming sick. And throughout this whole process, we're in constant communication with other federal agencies and our state and local health partners to ensure there's a consistent flow of information so that we can work together to promptly identify a potential source, and then take those important steps to protect the health of the public.

[Sarah Gregory] Thank goodness for public health. This is just amazing that all this complicatedness can be pulled together into figuring these things out, and there's so often more than one outbreak going on at a time, so….

[Katherine Marshall] That's right.

[Sarah Gregory] Wow. So give us a brief summary of your study, the time frame you studied, and how you went about it and who was involved, that sort of thing.

[Katherine Marshall] So for this study, we worked together with our colleagues and public health officials at the Public Health Agency of Canada and in the state of California, and worked with regulatory officials at FDA and the Canadian Food Inspection Agency. And we reviewed epidemiologic, laboratory, and traceback data from STEC outbreaks that occurred in the United States and in Canada that were linked to leafy greens during 2009 to 2018. And to do that, we analyzed data from CDC's Foodborne Disease Outbreak Surveillance System for U.S. outbreaks, and we worked with our Canadian colleagues to identify outbreaks using their internal database for tracking outbreaks. So, we found 40 outbreaks that were linked to leafy greens that resulted in 1,200 reports of ill people, 420 people hospitalized, 77 people who developed HUS, and, sadly, 8 people who died. And what we found is that there were more outbreaks that were linked to romaine than any other type of lettuce; that more outbreaks began in the fall and the spring than any other season; and we also discussed some important barriers to gathering epidemiologic, traceback, and laboratory data. We also highlighted some of the changes that the leafy green industry has made in response to some of these recent outbreaks. But ultimately, more research will need to be done to evaluate how effective these changes are.

[Sarah Gregory] Are there any important gaps in what we know about these outbreaks, what causes them, and how we can quickly identify them?

[Katherine Marshall] Well, while technological advancements—like whole-genome sequencing—are allowing us to learn more than ever before about these types of outbreaks, there's…there's really still lot that we need to learn. So while we found that more outbreaks began in the fall and the spring, we don't know exactly why that is or what's driving that, and we also don't know why we're seeing more outbreaks linked to romaine than other types of leafy greens. So more research around these findings could help us better understand why these outbreaks are happening, and provide clues on what we can do to prevent them from happening in the first place.

[Sarah Gregory] So, what kinds of improvements are needed to more quickly halt these outbreaks?

[Katherine Marshall] Well, there are two categories of improvements that could be made—so, improvement to address epidemiologic barriers and improvement to address traceback barriers. So, one of the epidemiologic barriers that we discuss in our paper is the time that it takes to be notified of a possible outbreak and to begin an investigation. So, by the time investigators try to identify a potential food source, sick people might not clearly remember what they ate before they got sick. And that can be 3 to 4 weeks in the past. And that delay occurs because it takes time for people to get sick and to seek medical care, and for laboratories to complete testing and DNA fingerprinting.

Another epidemiologic barrier is that leafy greens are widely consumed, and…and that makes it harder to show that they're the source of an outbreak and to pinpoint the exact leafy greens that made a person sick. So I mean, as…as you can guess, leafy greens are eaten by many people, and in fact about half of Americans report eating romaine lettuce in the past week. And furthermore, the people who eat leafy greens also typically eat various different types in a single week. So, all of that combined can make it more difficult for investigators to find an association between leafy greens and illness, and then to determine which specific leafy greens are the cause of their illness.

So to help overcome these epidemiologic barriers more quickly, to identify the source of an outbreak, outbreak investigators should continue to use some successful strategies—like using

shopper cards and loyalty cards—which can provide more detailed information about foods people ate that they might not remember, and then also to continue to develop new strategies to solve outbreaks as quickly as possible to prevent additional illnesses. But improvement should really also address some of the traceback barriers that we highlight, and the first is the lack of complete and detailed records. So records of shipment lots are often missing really important details that are needed for traceback. So without the right type of information, investigators are unable to trace the contaminated product to its source.

There's also challenges around identifying which leafy greens were grown on which farms. So because leafy greens from different farms are often mixed together throughout the distribution chain, such as when they're added to prepackaged bags. That can make it difficult for investigators to identify one specific lot or source. So to help overcome these traceback barriers and speed efforts to help stop outbreaks faster, the leafy green industry and retailers should keep complete and detailed records of transactions for each point along the farm to fork supply chain. To help with that, FDA has recently launched the new era of food safety, which is a new approach that's designed to leverage technology and other tools to help create a safer and more digital, traceable food system. And for leafy greens specifically, FDA has developed a 2020 leafy green action plan to help prevent and respond to leafy green outbreaks and address some of these knowledge gaps in leafy green safety.

[Sarah Gregory] We're in the midst of two big *Salmonella* outbreaks right now. How are *Salmonella* and *E. coli* outbreaks different?

[Katherine Marshall] Yes, we are. So there's…there's the outbreak linked to onions and peaches, and these are two more examples of foodborne outbreaks linked to produce. But they are caused by a different germ, and that's *Salmonella*. So, *Salmonella* infections are a bit more common than STEC infections. So we estimate there are about 1.35 million *Salmonella* infections each year in the U.S., and that's compared to about 265,000 STEC infections. Most people who get ill from *Salmonella* have diarrhea, fever, stomach cramps—many of the symptoms that are similar to STEC. But STEC infections are generally more severe, and what I mean by that is that the proportion of people who are hospitalized due to STEC is generally higher than for *Salmonella* infections. But foodborne outbreaks that are caused by *Salmonella* are still investigated the same way as outbreaks that are caused by STECs.

[Sarah Gregory] What do you think is the most significant public health aspect of your study?

[Katherine Marshall] Well, STEC outbreaks that are linked to leafy greens continue to occur. And in fact, the largest recent STEC outbreak in the U.S. was an outbreak that was linked to leafy greens in 2018. A lot of people eat leafy greens, and they are an important part of a healthy diet. And since many leafy greens aren't cooked and we usually eat them raw, we need to prevent them from becoming contaminated in the first place. So, we still have work to do to make leafy greens safer to eat. Improving traceability of leafy greens could help us solve outbreaks faster and enable us to conduct those important environmental assessments to help us understand how and why outbreaks occurred. And understanding why romaine was linked to more outbreaks and why more outbreaks happen in the fall and spring could help us understand what causes these outbreaks and what we can do to prevent them. And we can all work together to improve the safety of leafy greens—public health officials, the leafy green industry, retailers, and researchers all have an important role to play in this.

[Sarah Gregory] Okay, well what can people do to protect themselves from getting *E. coli* from romaine and these other leafy greens? I love romaine but, frankly, I'm pretty much afraid to eat it anymore.

[Katherine Marshall] So, even though we identified 40 outbreaks over a 10 year period, they're still relatively rare events. The U.S. food supply is one of the safest in the world, and millions of servings of leafy greens are eaten safely every day. Leafy greens are an important part of a healthy, balanced diet. But there are a few things that you can do to help reduce your risk of *E. coli* infection.

So when you are buying leafy greens, choose leafy greens that aren't bruised or damaged. For leafy greens that are not labeled pre-washed, you should discard the outer leaves and then wash the remaining leafy greens under running water. And during an outbreak linked to leafy greens, consumers should follow the advice of health officials. And that might include throwing out a recalled product, not eating a specific type of leafy green, and cleaning all the surfaces in your kitchen that have been in contact with the contaminated leafy greens.

[Sarah Gregory] Okay. Tell us about your job at CDC and what you find most exciting about it.

[Katherine Marshall] So I'm an epidemiologist in the Outbreak Response and Prevention Branch. And I always wanted a career where I could help people, and…and I feel like public health gives me the opportunity to do that on a large scale. So for the past couple of years, I've been investigating multistate outbreaks of *Salmonella*, STEC, and Listeria infections, and it's like being a detective. You're working on a really great team to put together pieces of a really complicated puzzle to try and solve the outbreak. But you get to see the results of your work right away, which is really rewarding. Now I work on preventing outbreaks, and taking all of those lessons learned from outbreak investigations and then applying them to make changes to the food safety system. And when we're successful, we prevent illness. And I think that's exciting and rewarding.

[Sarah Gregory] What are you doing for fun and relaxation in these difficult pandemic times?

[Katherine Marshall] I like to hike and explore the city with my husband and our two dogs. And we've also always played a lot of board games, so we're doing that more these days—we've got a growing collection of games. And we've also learned to adapt and to play with friends over Zoom lately.

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

[Katherine Marshall] Thank you for having me.

[Sarah Gregory] And thanks for joining me out there. You can read the October 2020 article, Investigations of Shiga Toxin-Producing *E. coli* Outbreaks Linked to Leafy Greens, United States and Canada, 2009–2018, online at cdc.gov/eid.

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

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