Carbapenem-Resistant and Extended-Spectrum β-Lactamase–Producing Enterobacterales in Children, United States, 2016–2020

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

[D. Peter Drotman] This podcast series is brought to you by *Emerging Infectious Diseases*, often referred to simply as EID. I'm Dr. D. Peter Drotman, Editor-in-Chief. EID is an open access, high impact, peer reviewed scientific journal published monthly by CDC. EID publishes articles on new and reemerging infectious diseases that occur anywhere around the world so as to improve the understanding of factors involved in disease emergence, control, and prevention.

[Candice Hoffmann] Welcome to the *Emerging Infectious Diseases* podcast. I'm Candice Hoffmann. On this episode, we'll be talking about antimicrobial-resistant infections in children.

[Heather Grome] My name is Heather Grome and I'm a medical epidemiologist at CDC. I work in the Division of Healthcare Quality Promotion, which is in the National Center for Emerging and Zoonotic Infectious Diseases. And currently I am leading two research activities that study the epidemiology of first invasive *E. coli*, but also ESBL-E disease, which are projects both conducted through the Emerging Infections Program. And I have a specific interest in studying the public health impact of healthcare associated infections and also what we might be able to do to prevent them.

[Candice Hoffmann] That was Dr. Heather Grome, the lead author of the article, "Carbapenem-Resistant and Extended-Spectrum β-Lactamase–Producing Enterobacterales in Children, United States, 2016–2020", which can be found in the June 2024 issue of *Emerging Infectious Diseases*.

This study sheds light on how the growing public health threat of antimicrobial resistance affects children. The two types of bacteria named in the article's title are also known by their acronyms—CREs and ESBL-Es. Dr. Grome will tell us more about them.

[Heather Grome] There are two types of antimicrobial-resistant bacteria. And thinking on a very overarching scale, antimicrobial resistance occurs when bacteria or even viruses, fungi, and sometimes even parasites just no longer are responsive to the drugs that are designed to kill them. And the problem is that infections caused by these types of bacteria can be almost impossible to treat sometimes, which increases the risk that the disease will spread or can make someone really sick or cause death. So unfortunately, these types of infections are increasing globally, and they've really become a major public health problem.

So, specifically thinking about the focus of this paper, which was CRE and ESBL-Es—CRE stands for carbapenem-resistant Enterobacterales and ESBL-E stands for extended-spectrum beta-lactamase–producing Enterobacterales—and these are two types of these antimicrobial-resistant bacteria that I mentioned that are pretty good at causing infection in humans. Generally, Enterobacterales are this group of bacteria just lives out in healthcare settings or even in the community. And sometimes they're even part of the normal intestinal flora of the human gut. But unfortunately, they're really good at developing antibiotic resistance because they can actually

pass genetic material back and forth to each other that helps to further that spread of antimicrobial resistance.

One example of that which is interesting is that ESBL-Es contain this genetic material that helps them to make a specific enzyme, also called extended-spectrum beta-lactamases. And these enzymes break down antibiotics in a class called beta-lactamases. And beta-lactamases are really commonly prescribed by providers. They include antibiotics like penicillins—penicillin, amoxicillin and stuff like that. And it's a really clinically important class of antibiotics that causes huge problems when obviously bacteria are resistant to them.

I'll say one more thing and that's CRE or carbapenem-resistant Enterobacterales, they're resistant to a totally different class of antibiotics and those are called carbapenems. And carbapenems are considered a type of broad-spectrum antibiotic or kind of these antibiotics of last resort is how you can think about them. They are effective against many types of bacteria including ones that may be resistant to other antibiotics. So, they're used to treat infections really when other antibiotics may not work, including infections caused by ESBL-E. So those are the two bacteria that were in focus for this study.

[Candice Hoffmann] Multidrug-resistant infections affect people of all ages, but this study specifically looked at infants and children who were younger than 18 years old.

[Heather Grome] So, this study was focused on children in the United States and looking at rates of two antimicrobial-resistant infections, carbapenem-resistant Enterobacterales and extended-spectrum beta-lactamase–producing Enterobacterales. And we had 10 diverse sites across the US participating through the Emerging Infections Program. We identified that there were more cases of ESBL-E compared to CRE in the pediatric population, but they were more commonly identified in females and in urine cultures, and interestingly, in infants or children less than one for both types of infection. I think that the study emphasizes how important it is to track and trend multidrug-resistant infections in children and that they really should be included in a lot of our programs that are designed to monitor for multidrug-resistant infections across the US and globally because they're impacted by antimicrobial-resistant infections just like adults.

[Candice Hoffmann] Prior to this study, not much information was available on CRE and ESBL-E in children.

[Heather Grome] We specifically wanted to focus this study on children because there's been very limited information describing mainly the epidemiology of CRE and ESBL-E in this age group. It's important because, as we all know, children have developing immune systems, so sometimes that can make them more susceptible to infections like pneumonia or meningitis, and as a result, they're frequently treated with antibiotics. But there's been very little data available that takes a look at the scope of the problem of antimicrobial resistance in children, and importantly, how that can influence prescribing practices of antibiotics by doctors or medical providers, for example. Another thing that we had noticed is that antimicrobial treatments for children don't seem to be keeping up with the trend in antimicrobial resistance. So, for example, in the last 20 years or so, there's been maybe less than 10 new antibiotics developed for children compared to nearly 40 for adults. And we hope that by focusing on children in the study, we would be able to raise awareness for how these, kind of quote, super bugs like CRE and ESBL-E

aren't just affecting adults in the US. So, by shining light on the problem, we can help push resources in this direction and help learn how to better prevent and treat them.

[Candice Hoffmann] When people get infected with CREs or ESBL-Es, it often happens when they are in a healthcare setting being treated for another condition. However, Dr. Grome and her colleagues noticed that many of the cases described in this study started somewhere else.

[Heather Grome] In this study, we were focusing only on children, and it was interesting because we found that most of the cases in this study were healthcare-associated infections with their onset in the community, or they were community-associated only. So, that means…it's a wordy way of saying that these infections were mainly identified in children from the community and not during a hospitalization. And there was even some cases that were community-associated only, meaning that those children had no history within the last year of any hospitalization or any medical procedure or surgery. And it's interesting because we often think of infections with these organisms like CRE and ESBL-E occurring mainly in hospitals. But that seems to be shifting and it's something that our study identified.

In our study looking at children and thinking about the children diagnosed with ESBL-E, we found that most of those cases were identified in urine. So, they were most likely in children that may have had a urinary tract infection. And that seems to match what we're seeing in adults, which is that we're also seeing more and more community-associated ESBL identified from urinary tract infections in adults.

[Candice Hoffmann] Dr. Grome and her colleagues encountered a few surprises when they analyzed the data.

[Heather Grome] I think the first surprise was that we found that overall, CRE and ESBL-E cases most commonly occurred in female children and from urine sources. So, we kind of suspected that might be the case, but it was good to see it confirmed. The reason we think that may have happened is because females in general have a higher number of urinary tract infections and because we do more testing and treating for those infections, we were more likely to pick up a case of CRE or ESBL in that age group, and so we saw higher numbers in that group overall, and that was for both pathogens. The second thing that we found that was surprising and important was we found a higher rate of CRE and ESBL-E infections in infants—so, we define infants as children less than one year—compared to older children, and I think that was interesting and unexpected. We think that it may be a result of different risk factors for young children and babies compared to older children. Like for example, maybe they're more likely to have longer neonatal ICU exposures if they happen to be admitted, leading to infection with CRE or ESBL-E. They're also more likely to have vertical transmission, which means transmission of one of these infections from the mother to the baby, compared to other age groups. And then, generally we just think there's overall higher rates of antibiotic-resistant Enterobacterales in this infant group overall. However, we think...we definitely need to do a more focused look at this age group to learn more about why we saw that because we couldn't identify really causality in the study, only identified the trend.

[Candice Hoffmann] For parents that might be concerned about antimicrobial-resistant infections likes CREs and ESBL-Es, Dr. Grome stresses that these infections are very rare.

[Heather Grome] The main takeaway for parents is that antimicrobial-resistant infections, such as those caused by CRE and ESBL-E, are fortunately very rare.

I think this study highlights though that they do occur and when they do, they unfortunately can be more difficult to treat. They may last longer as a result and they may make your child sicker. So, for parents, it's important to try to keep your child protected from these infections by first talking with their medical provider about how to treat certain kinds of illnesses if they're not sure when their children are sick, and that's because preventing an antimicrobial-resistant infection in the first place is so much easier than trying to treat one. So, as an example, parents should really not be giving their children antibiotics for infections caused by viruses and that's really important, and that includes things like colds, the flu, most sore throats, runny noses, and most earaches now.

And then another thing is that they should really avoid saving antibiotics for future illnesses (some people do that), and don't use antibiotics prescribed for other children for their children, or even share them. Because all of this can help protect their child from developing an antibiotic-resistant infection as best they can.

[Candice Hoffmann] Dr. Grome's team at CDC works to address antimicrobial resistance, one of the world's most urgent public health problems. Tracking drug-resistant infections and developing strategies to prevent them are important aspects of this work.

[Heather Grome] For example, within my division, we are trying to create and enhance infection control guidelines all the time to help prevent these resistant infections and we're also working on sharing knowledge and work to improve understanding about antibiotic use among prescribers to help address the problem.

But I think, really big picture, it's going to take all of us working together from public health to health care providers and even parents and caregivers of children to help try to prevent antimicrobial resistance in general and to prevent it from spreading.

[Candice Hoffmann] Being able to see the big picture of the most pressing health problems is one of the reasons Dr. Grome got into public health.

[Heather Grome] I got into public health because I started out as a clinician. So, I'm a physician by training and I saw patients on a one-on-one basis. But I really liked the idea of being able to impact more than one person at a time. So, kind of this potential for, I don't know, having greater influence on my work in helping patients and communities. And I think what I like most about my job…oh gosh, getting to work at that level every day, so getting to work with and for people. It's nice to be able to help people every day, basically. And the people I work with are great too. So that makes it really rewarding.

[Candice Hoffmann] The *Emerging Infectious Diseases* journal provides important information that helps guide public health professionals like Dr. Grome in their work combatting infectious diseases. If you found this conversation interesting, you can find much more in the journal.

[Heather Grome] Because I like that EID focuses on literally emerging infectious diseases, which is really the…that's what antimicrobial-resistance really is. It's the forefront of emerging infectious diseases almost. And I thought the audience would be really appropriate for this work.

[Candice Hoffmann] Thanks for listening to our podcast. You can read the *Emerging Infectious Diseases* journal at cdc.gov/eid. You can also follow EID on X and Instagram @eidjournal, and on LinkedIn @eid-journal.

[Outro] The conclusions, findings, and opinions expressed by authors contributing to this journal do not necessarily reflect the official position of the U.S. Department of Health and Human Services, the Public Health Service, the Centers for Disease Control and Prevention, or the authors' affiliated institutions.

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