National Surveillance of Human Ehrlichiosis Caused by *Ehrlichia ewingii*, United States, 2013–2021

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[Candice Hoffmann] Welcome to the *Emerging Infectious Diseases* podcast. I'm Candice Hoffmann. In this episode, we'll be discussing the article "National Surveillance of Human Ehrlichiosis Caused by *Ehrlichia ewingii*, United States, 2013–2021" which was published in the February 2025 issue. We spoke with two authors of this paper: Sydney Adams, and Dr. Johanna Salzer.

[Sydney Adams] My name's Sydney Adams. I'm an ORISE fellow with the Rickettsial Zoonoses Branch. I focus mainly on surveillance. I do a lot of work with ehrlichiosis and murine typhus, but I work closely with our surveillance epidemiologist on our nationally notifiable conditions. That includes ehrlichiosis, anaplasmosis, spotted fever, group rickettsiosis and Q fever.

[Dr. Joanna Salzer] I'm Dr. Johanna Salzer. I'm a veterinary medical officer and I also lead the epidemiology team in the Rickettsial Zoonoses Branch, which is within the Division of Vector-Borne Diseases, where we do surveillance of a large number of rickettsial diseases and also work on alpha-gal syndrome. So, I'm a veterinarian and I have a PhD in disease ecology. I've been at CDC since '08. I've always worked on zoonotics—so mpox, anthrax, brucellosis. I've done a fair amount of global health work. Working on rickettsial disease to me is so exciting because it's…it's adding this new element, which is the vector. So, it's taking what I already loved, which were complex zoonotic diseases, and then making them even more complex when you add a vector. I also love my job because there's a number of diseases we work on, that the way that you protect people is improving the lives of animals. And so specifically with Rocky Mountain spotted fever, we protect and improve the lives of dogs in order to protect and improve the lives of people, specifically children.

[Candice Hoffmann] To start, we'll discuss the *Ehrlichia* bacteria that are responsible for spreading the disease, ehrlichiosis.

[Sydney Adams] So there's three species primarily responsible for human disease in the US, and that's *Ehrlichia ewingii*, *Ehrlichia chaffeensis*, and *Ehrlichia muris eauclairensis*. *Ehrlichia chaffeensis* and *Ehrlichia ewingii* are spread through the bite of the lone star tick, or *Amblyomma americanum. Ehrlichia muris eauclairensis* is spread through the bite of the blacklegged tick, and that's *Ixodes scapularis. Ixodes scapularis*, or the blacklegged tick, is found throughout the eastern United States, but human cases of *Ehrlichia muris eauclairensis* have been geographically isolated to residents or travelers to Minnesota and Wisconsin. The lone star tick, which is the main vector for *Ehrlichia chaffeensis* and *Ehrlichia ewingii*, is found throughout the eastern United States and southeastern and South-Central United States.

[Candice Hoffmann] Ehrlichiosis can sometimes be deadly, especially when not treated early with doxycycline, a type of antibiotic. However, the severity of disease differs depending on the species of *Ehrlichia* bacteria causing the illness.

[Sydney Adams] So, *Ehrlichia chaffeensis* usually results in the most severe disease. So, the case fatality rate for *Ehrlichia chaffeensis* is about 1%. Case fatality rates for *Ehrlichia chaffeensis* ehrlichiosis are highest among those less than five years old and over the age of 65 and individuals with weakened immune systems. *Ehrlichia muris eauclairensis* has had no fatal cases reported, and *Ehrlichia ewingii* ehrlichiosis has long been thought to be less severe than *Ehrlichia chaffeensis* ehrlichiosis and results in less severe manifestations.

[Candice Hoffmann] The authors of this study wanted to better understand *Ehrlichia ewingii* ehrlichiosis.

[Sydney Adams] *Ehrlichia ewingii* ehrlichiosis is an emerging pathogen in the United States, and little is known about its geographic distribution and clinical presentation. So, this analysis was undertaken to get a better understanding of the geographic spread of *Ehrlichia ewingii* ehrlichiosis and the demographic characteristics of patients infected with this pathogen.

[Candice Hoffmann] They found that cases have increased in recent years and learned more about the demographic characteristics of the patients.

[Sydney Adams] Compared to the 2008 to 2012 surveillance summary published by CDC, there is an approximately two-fold increase in the average number of reported cases from 2013 to 2021. States that reported the most cases were Missouri, Arkansas, Kansas, New Jersey, Tennessee, Virginia, Maryland, Oklahoma, Delaware and Kentucky. And Missouri alone accounted for 48% of all reported cases. The first identified human cases of *Ehrlichia ewingii* ehrlichiosis back in 1999 were actually among Missouri residents, so it was first identified there. The demographic characteristics of patients…for most of the patients, they were mostly male, mostly white, mostly non-Hispanic and mostly older, so over the age of 65.

[Candice Hoffmann] Missouri had the highest number of reported cases of ehrlichiosis caused by *Ehrlichia ewingii*, and this might be because the lone star tick is common there and doctors in that state are more familiar with the disease and are testing for it more often.

[Sydney Adams] Healthcare providers are probably more familiar in that state with the diagnostic methods to diagnose a person with ehrlichiosis. So, I would say they're probably identifying more cases because they're using PCR more often and they have a lot of lone star ticks in Missouri and a lot of lone star tick-associated diseases in Missouri. So, that may be why most cases are probably in that state. I think Arkansas had the second highest case count. So, Missouri was number one and then Arkansas was number two.

[Dr. Johanna Salzer] I think Missouri being a hotbed for lone star-associated diseases, not just ehrlichiosis, but it's also where Heartland was found as well. They appear to have a large number of alpha-gal syndrome cases as well.

[Candice Hoffmann] During the study's reporting period, many states reported cases of *Ehrlichia ewingii* ehrlichiosis for the first time.

[Sydney Adams] So, 24 jurisdictions reported more than one case of *Ehrlichia ewingii* ehrlichiosis and 15 of these states reported cases for the first time during this period, indicating increasing geographic distribution and incidence. And then the states that reported the most cases

reflected 86% of all reported cases during this time period. So, Missouri, Arkansas, Kansas, New Jersey, Tennessee, Virginia, Maryland, Oklahoma, Delaware and Kentucky made-up 86% of all cases during the time period. And then, again, Missouri alone made-up over 40%.

[Candice Hoffmann] Ehrlichiosis following a tick bite might be difficult to diagnose, because it shares symptoms with other diseases.

[Sydney Adams] So, the signs and symptoms are pretty nonspecific. They are fever, headache, myalgia, nausea, vomiting, diarrhea, confusion and headache for *Ehrlichia ewingii.* So, the symptoms of ehrlichiosis are pretty similar across all three species that cause human disease. Gastrointestinal symptoms like nausea, vomiting, diarrhea has been more commonly reported with infection associated with *Ehrlichia chaffeensis* compared to *Ehrlichia ewingii*. But generally, fever, headache, malaise, myalgia, nausea, vomiting and diarrhea, early in illness.

[Candice Hoffmann] These non-specific symptoms might make it difficult for healthcare providers to recognize cases of ehrlichiosis. But there may be clues that would lead a healthcare provider to this diagnosis.

[Sydney Adams] In addition to those nonspecific signs and symptoms, there are some abnormal laboratory findings that healthcare providers could look for that can maybe indicate that the patient has ehrlichiosis. So, leukopenia, thrombocytopenia and elevated hepatic transaminases, those are key indicators that maybe a patient is infected with an *Ehrlichia* species causing ehrlichiosis. Time of year is also important. Ticks are the vector of these pathogens. So, you know, during peak tick activity months, you know healthcare providers could have ehrlichiosis on the differential for patients presenting with these nonspecific signs and symptoms.

[Candice Hoffmann] If a healthcare provider suspects ehrlichiosis, diagnostic testing can be performed. PCR testing, also referred to as molecular testing, is one type. Serology is another. Dr. Salzer discussed the differences between the different types of tests.

[Johanna Salzer] So, ehrlichiosis can be very challenging to diagnose and that is why it's important for healthcare providers to understand the different tests available and when they would maybe use one test or another or possibly both. So, PCR is detecting DNA, which is one reason why you're able to differentiate between *Ehrlichia ewingii, Ehrlichia chaffeensis* and *Ehrlichia muris eauclairensis*. And so, when you detect DNA through PCR, then you're able to clearly identify what species of *Ehrlichia* this person's infected with. With serology, we're detecting antibodies, and the antibodies are all cross-reactive. So, it's impossible to say which species of *Ehrlichia* this person was infected with because they just have these more generic antibodies to *Ehrlichia*.

[Candice Hoffmann] The timing of the test may influence which test is most helpful, as Sydney Adams explains.

[Sydney Adams] So, the optimal test depends on timing relative to symptom onset and the types of specimens available. So, PCR on whole blood is the best method for confirming ehrlichiosis infection. It's most sensitive within the first week of illness and within 48 hours of starting doxycycline. After 48 hours, the test isn't as sensitive or specific. Serology can't provide a species-specific result for patients, but it can be useful if, you know, the patient presents to their doctor later in illness. It also requires two specimens be collected to confirm illness. So, for serology you would need to collect a serum sample within the first week of the patient's illness,

and then the patient would need to return two to 10 weeks later after that acute sample is collected for a convalescent sample in order to confirm infection.

[Candice Hoffmann] While serology can be useful, the authors stressed the importance of molecular testing, such as PCR, to ensure accurate diagnosis.

[Sydney Adams] So, one of our important findings was just emphasizing the reliance on serologic testing to diagnose patients is leading to an underestimation of ehrlichiosis cases, specifically *Ehrlichia ewingii* ehrlichiosis cases, because molecular methods are required for diagnosis. Molecular testing for *Ehrlichia ewingii* is available at several commercial laboratories in the United States. So, want to make sure healthcare providers know that these tests are available, and molecular tests are the only way to provide a species-specific result for your patient. Molecular methods and PCR testing are a great way to get the patient a quick definitive diagnosis early in illness where you don't have to return for an additional result, but they also help us on the public health side by helping us get a better understanding of the geographic distribution of these cases and a better understanding of the clinical presentation and the severity of these *Ehrlichia ewingii* cases. There have been very few reported over this this surveillance summary period—only 234 cases. But if more PCR testing is done, it'll help us in public health get a better understanding of the severity of this disease and a better idea of how to target our messaging. So, if more PCR testing is used, and we get a better idea of the actual burden of this disease, then we can target messaging to maybe groups or populations that are more risk of severe outcomes. So, if we identify that a certain population is really at risk for severe disease or fatal disease, then we can target messaging on the public health side to healthcare providers and to those populations to make sure, you know, we're preventing severe and fatal illness associated with ehrlichiosis.

[Candice Hoffmann] Early treatment for ehrlichiosis can reduce the risk of severe and fatal outcomes for the patient.

[Sydney Adams] So doxycycline is the treatment of choice for patients of all ages.
It's usually given twice per day for five to seven days and until 72 hours after fever subsides and evidence of clinical improvement. And without doxycycline treatment, ehrlichiosis can progress to a severe and fatal illness. So, it's very important that if a healthcare provider suspects that their patient has ehrlichiosis, that they treat them with doxycycline without waiting for test results. They shouldn't withhold treatment pending test results. And even if serology, like a negative… early acute serology result is negative, they should not stop treatment based on a negative serology result alone. It’s very important that as soon as a healthcare provider suspects ehrlichiosis, they prescribe doxycycline pending that test result.

[Candice Hoffmann] CDC has resources for healthcare providers who want to learn more about ehrlichiosis. The article discussed in this episode also offers continuing medical education.

[Sydney Adams] CDC has a free continuing education module on ehrlichiosis and anaplasmosis available to healthcare providers through CDC TRAIN that's online, available to anyone. We also have additional information on the CDC website.

[Candice Hoffmann] In addition to their recommendations for clinicians, the authors also wanted to stress the importance of preventing tick bites.

[Sydney Adams] You know, if a tick never bites you, then you don't have to worry about a tickborne disease. So, making sure you wear EPA-registered insect repellent, you know, DEET-based repellent or picaridin for your skin, and then permethrin-treated clothing.

[Candice Hoffmann] If, however, you do get bitten by a tick, here's how to remove it.

[Sydney Adams] So as soon as someone sees a tick attached, they should remove it as soon as possible by using tweezers and grabbing as close to the mouth parts as possible or other tick removal devices, making sure to get the tick as close to the mouth parts as possible and then pulling straight up.

[Candice Hoffmann] This article sheds light on *Ehrlichia ewingii*, but there is more to learn about this emerging pathogen. Sydney Adams has this advice for future researchers interested in learning more about *Ehrlichia.*

[Sydney Adams] I think specific to *Ehrlichia ewingii*, I think it would be great to expand our understanding of the clinical presentation of this disease and severity. You know, *Ehrlichia chaffeensis* we know can be very severe. But *Ehrlichia ewingii* is still relatively new. It was just discovered in 1999 and wasn't included in the surveillance case definition until 2008, and there are just very few cases. So, the more research we can do to understand the clinical presentation of this disease and severity, I think will improve patient outcomes and help target messaging. So, anything that we can do to further that along, I think would be beneficial.

[Candice Hoffmann] We hope you have enjoyed listening to this podcast, and that you will become a regular reader of EID like Sydney Adams and Dr. Salzer.

[Sydney Adams] I regularly read *Emerging Infectious Diseases*. I definitely look for articles related to our pathogens. I know there was recently, maybe a couple months ago, an article published by Anne Kjemptrup on the new species of *Rickettsia* identified out of California. So, love reading things that are related to my work. I also just find new and emerging diseases very interesting, and I definitely think EID is a great resource and great publisher of those emerging infectious disease articles. We chose EID, we just thought this would be a great fit for this emerging disease. I think the readership would be very interested in this. And yeah, I just think it's a great place to put this emerging tickborne disease.

[Dr. Johanna Salzer] I've been reading EID since I was in vet school in 2007. I had a professor who studied the emergence of Lyme disease in Illinois, and he would have a stack in his office, and he would give me the ones that he was done reading with.

[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 you can find us on LinkedIn.

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