

Tickborne *Ehrlichia* in North Carolina

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

[Sarah Gregory] Hi, I'm Sarah Gregory, and today I'm talking with Dr. Ross Boyce, an infectious disease physician at the University of North Carolina at Chapel Hill. We'll be discussing *Ehrlichia* in North Carolina. Welcome, Dr. Boyce.

[Ross Boyce] Thank you for having me.

[Sarah Gregory] So, what is *Ehrlichia* and how is it different from other tickborne diseases?

[Ross Boyce] *Ehrlichia* is a genus of bacteria, generally considered weakly gram-negative, an intracellular bacteria that was originally discovered around the turn of the last century in South Africa, but is something that we commonly refer to as a tickborne disease in the United States.

[Sarah Gregory] I understand that *Ehrlichia* is an intracellular disease, the same as leprosy. But what does that actually mean?

[Ross Boyce] *Ehrlichia*, specifically in regard to the tickborne disease, infects the monocytes and macrophages, and can only be found in those cells, which is where it gets the term "intracellular bacteria." And you can compare this to, for example, anaplasma, which is another tickborne disease which infects the granular sites, or rickettsia, which often infects the endothelial cells. This does have some implications for diagnoses, because it's harder to isolate the bacteria from the peripheral blood.

[Sarah Gregory] So, how does a new tick disease get introduced into an area? How does it spread?

[Ross Boyce] I think you have to consider three different factors when you're thinking about the spread of a tickborne disease. Obviously, the first is the tick. The other is the geography of the area. And the other is humans or animals, which often serve as the reservoir of the infection. One of the reasons, I think, that we have seen a spread in tickborne disease, as was noted recently in one of the CDC's announcements over the summer, is that people are moving into suburban areas that are often wooded, and becoming in closer contact with both the tick and a lot of the animal reservoirs, such as deer and mice.

[Sarah Gregory] What diseases have been linked to ticks in North Carolina?

[Ross Boyce] If you were to ask someone here in North Carolina, I think the most common response you would receive is Rocky Mountain spotted fever. I'm not so sure that that is true, and we can discuss that later, but clearly the spotted fever rickettsia group, which includes Rocky Mountain spotted fever, is common. There is increasing evidence of some Lyme disease being spread in the northwest part of the state. And then alpha-gal, which you may have heard about, which is commonly referred to as a meat allergy, which is actually not an infection, but the transmission of a carbohydrate from the lone star tick.

[Sarah Gregory] What made you initially suspect that *Ehrlichia* was being underdiagnosed? Is it actually new to North Carolina or has it been there a while and just not noticed?

[Ross Boyce] I first encountered *Ehrlichia* taking care of a young woman in our intensive care unit here at Chapel Hill. She had presented with high fevers, fatigue, and a skin rash and it hadn't

not yet been diagnosed. She had had a test for the rickettsial species, including Rocky Mountain spotted fever, sent that was negative, but it was only after the test for *Ehrlichia* came back, almost a week later, that was positive, that we identified what was the cause. Fortunately, she had been on the appropriate treatment and recovered well. The experience, however, really made me think about what it is we're testing for, when we think about tickborne disease here in North Carolina. I think it's unlikely that *Ehrlichia* is new to North Carolina; I think it has just been largely underdiagnosed. In fact, it gets its name, *Ehrlichia chaffeensis*, from Fort Chaffee in Arkansas, where it was first discovered in 1989.

[Sarah Gregory] So, to investigate this, your study looked at patient records from UNC hospitals and clinics in the summer of 2016. What specifically were you looking for?

[Ross Boyce] I really wanted to see what doctors were doing when they thought about ticks. When they saw a patient who they suspected there might be a tickborne disease, I was curious what they were testing for. Were they looking for Rocky Mountain spotted fever, were they looking for *Ehrlichia*, or were they testing for other things? In addition, I was curious how they were handling treatment decisions.

[Sarah Gregory] And what did you find?

[Ross Boyce] Well, what we found is that about three quarters of patients were tested for the spotted fever group rickettsia; about two thirds were tested for Lyme disease; but only one third were tested for *Ehrlichia*. Now what we did, because the serum was stored in all those patients for 90 days after the testing was performed, is we went back and we tested those individuals who did not have *Ehrlichia* testing performed initially. We call this retrospective testing. And in the cohort of those who had retrospective testing performed, we found that the prevalence of reactive antibodies to *Ehrlichia* was very similar to that seen with the spotted fever group. And while it's not a perfect comparison, it does suggest that what we're seeing is that *Ehrlichia* is equally as prevalent as the spotted fever rickettsia.

[Sarah Gregory] Does *Ehrlichia* present differently? I mean, the symptoms are exactly the same as these other diseases?

[Ross Boyce] The symptoms are not exactly the same, but most tickborne diseases that we see here in North Carolina present with very nonspecific symptoms. And these are things that can look like flu, a cold, or more common illnesses. They're things like fever, headache, body aches, occasionally rashes, especially with *Ehrlichia* and the spotted fever group rickettsia. But also, it can be very nonspecific things like diarrhea and upset stomach.

[Sarah Gregory] So, at what point would somebody go to an infectious disease doctor for testing for these things? I mean, if I had flu symptoms or cold symptoms, I'd just think I had a cold or a flu and stay home.

[Ross Boyce] That was one of the interesting findings to me in our study is that the vast majority of patients were initially seen by what I would consider front-line providers. So these are primary care physicians, your internists and family medicine doctors, and emergency room physicians. Only about five percent of them were seen by infectious disease physicians.

[Sarah Gregory] So, why do you think doctors were less likely to order testing for *Ehrlichia* than Lyme or rickettsia?

[Ross Boyce] I think that physicians and the patients are more aware of both Rocky Mountain spotted fever and Lyme disease because of what you can find on the internet and in the media. Certainly, Rocky Mountain spotted fever can be fatal and I think that physicians are rightfully concerned about that when they're worried about tickborne diseases. However, where I think there's a disconnect is when you look at the population of the ticks. Some of my colleagues here at the University of North Carolina and at North Carolina State University have done some studies where they go out and just look at what sort of ticks are being pulled off of people. And what you find is that the ticks that carry Lyme disease and Rocky Mountain spotted fever are uncommon—we're talking five percent, 10 percent of all the ticks that are pulled off of people. In contrast, the lone star tick is about 90 percent of the ticks that's being pulled off of people. Now, this has implications because the lone star tick does not carry, or at least is not a competent vector of Rocky Mountain spotted fever or Lyme disease. So, if we're seeing that most of the ticks are lone star ticks, then what you should expect is that most of the diseases are going to be diseases that are carried by the lone star tick. And I think that that message has not yet been communicated or taken up by the medical community, perhaps because it's an entomology issue as opposed to a medical issue.

[Sarah Gregory] So, what other, besides *Ehrlichia*, what other diseases are carried by the lone star ticks?

[Ross Boyce] *Ehrlichia* is probably the most common disease that we're seeing here carried by the lone star tick. The STARI, the southern tick-associated rash illness, has also been associated with the lone star tick, as well as alpha-gal, which is the meat allergy that I mentioned previously.

[Sarah Gregory] How will these results affect care for tickborne illnesses in North Carolina?

[Ross Boyce] So, first let me say that our results should not affect the way providers treat patients when there's a high suspicion for tickborne disease. It takes up to a week or two weeks for someone to develop antibodies to a tickborne disease. Therefore, if physicians have a high suspicion, they should treat patients empirically, which means regardless of the test results. And typically, that is five to 10 days of doxycycline. Now, that doesn't mean that testing does not have a role and it is especially important in trying to understand the epidemiology of tickborne disease here in North Carolina. And that itself is important in understanding the best ways that we can advise residents about avoidance, prevention, and ultimately, control measures.

[Sarah Gregory] So, how can this lack of testing be overcome? Should people who have symptoms be more aware of these diseases or is it up to doctors and clinicians to be more aware of the possibility of various tickborne diseases, not just Lyme and rickettsia?

[Ross Boyce] I don't think that it should be a burden on the patients. Certainly, physicians and providers should be more aware of the diseases that are endemic in their areas. On the other hand, I'm also someone who believes that we can make this a little bit simpler. One of the things that I've recommended here, and we're perhaps in the process of slowly adapting, are things like tickborne panels or reflex testing. And what I mean by that is that, if you think that your patient might be at risk of a tickborne disease and you want to order that test, you automatically get the spotted fever group rickettsia and *Ehrlichia*. Alternatively, you could have reflex testing where, if you order a Rocky Mountain spotted fever test, then it's negative, then it automatically gets

reflexed to an *Ehrlichia* test, as well. I think this would significantly improve our understanding and the reporting of these diseases.

[Sarah Gregory] Okay, so, Dr. Boyce, what's your specialty? I know you're an infectious disease physician. Is there any area particularly that you're more interested in and how were you interested in tickborne diseases in North Carolina? And do you have any personal experience with it?

[Ross Boyce] Well, growing up here in North Carolina, I think everyone has some experiences with ticks if you've been out in the woods at all. I am actually a researcher and the main topic that I research is malaria in western Uganda. However, as you may know, malaria is not very prevalent here in North Carolina, but a lot of the principles of malaria control and understanding the relationship between people and insects apply to ticks. And so, when I'm here in the U.S., it's a area of interest.

[Sarah Gregory] So you travel a good bit?

[Ross Boyce] I do.

[Sarah Gregory] Okay, well, thank you so much, Dr. Boyce, for being on our podcast today. Listeners can read the November 2018 article, *Ehrlichia* Infections, North Carolina, USA, 2016. I'm Sarah Gregory for *Emerging Infectious Diseases*.

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