Continued Circulation of Tick-Borne Encephalitis Virus Variants and Detection of Novel Transmission Foci, the Netherlands

[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. Helen Esser, an assistant professor at Wageningen University. We'll be discussing tick-borne encephalitis virus presence and prevalence in potential new foci in the Netherlands.

Welcome, Dr. Esser.

[Helen Esser] Well, thank you for having me.

[Sarah Gregory] What is tick-borne encephalitis as opposed to any other encephalitis?

[Helen Esser] Tick-borne encephalitis (or for short, TBE) is a disease caused by a virus (the virus is called tick-borne encephalitis virus). And as the name already implies, it's spread in ticks.

[Sarah Gregory] Is it common?

[Helen Esser] Well luckily, it's not very common. So in contrast to, for example Lyme disease, it's actually quite rare. So where, for example, if we look at the Netherlands, about one in every five ticks is infected with the bacterium that causes Lyme disease. If we look at TBE, then it's only one in 5,000 ticks that's infected. So it's pretty rare.

[Sarah Gregory] How is it spread? Can you get it only if you are bitten by a tick that carries it? Or could you get it from touching an animal or another person who has it?

[Helen Esser] So most people get infected because they're bitten by an infected tick. But there are indeed other ways in which you can get infected. So in some cases, people get infected because they drink or eat infected dairy products—milk or cheese that's not pasteurized maybe from goats or sheep, sometimes also cows. And in very rare cases, you can also get it because, for example, a blood transfusion or donation of an organ or slaughtering an animal. But those are very rare cases. It's mostly by being bitten by an infected tick. But maybe noteworthy recently, there was kind of a big outbreak in France in a village that had not seen this disease before, and then suddenly 43 people got sick at the same time because they ate unpasteurized goat cheese from one specific source.

[Sarah Gregory] So one more reason not to eat or drink unpasteurized dairy products, right?

[Helen Esser] Exactly.

[Sarah Gregory] Is there a specific tick species that carries it?

[Helen Esser] There's actually multiple tick species, but there's a few of them that are most important. So in Europe, it's mostly the Castor Bean tick (*Ixodes ricinus*), and in Russia it's mostly *Ixodes persulcatus*, both of which are very closely related. But there's other tick species as well that can potentially transmit it, such as *Dermacentor reticulatus*. So multiple species involved, but the majority of cases it's really one specific tick species.

[Sarah Gregory] And what are the signs that someone is sick with TBE virus?

[Helen Esser] Well, it starts out with some very general flu-like symptoms—so, headache, fever, maybe vomiting. But then as the disease progresses, that's when it becomes more dangerous. So then you can have encephalitis (so that's inflammation of the brain) or meningitis (inflammation of the membranes that surround the brain or the spinal cord). And so the people that develop encephalitis or meningitis, about 1% actually don't make it; they die of the infection. And about half of the people that recover, they don't recover fully. They have long-lasting symptoms which are neurological—so, it could be constant fatigue or headaches, even paralysis. So that's a pretty large impact on people that get sick.

[Sarah Gregory] Some of the other tick-borne diseases can be treated with antibiotics, like Lyme disease. But this is a virus. So are there any effective treatments for this one?

[Helen Esser] Yes. So indeed, antibiotics don't work for viruses, and unfortunately there's no specific treatment for tick-borne encephalitis. There is, however, a very effective vaccine that you can take.

[Sarah Gregory] So what regions of the world is TBEV found in?

[Helen Esser] A fairly large region. So lots...a big part of Europe and Asia, mostly Russia but also some Central Asian areas. So it has a huge distribution.

[Sarah Gregory] What role do ecologic and climate aspects play in the spread of this disease?

[Helen Esser] So there's a lot of different ecological and climatic aspects that play a role. If we consider the ecological ones then, well, the virus can only occur where its tick vector occurs, right? And ticks can only occur where the abiotic conditions (so, the temperature and humidity) are right, as well as the biotic conditions (so, the presence of specific wildlife species). So these ticks are very sensitive to location. So regions need to be not too cold or too warm, too dry or too wet. And they need deer, because that's what the adult ticks need for reproduction (they use deer for the blood meal for developing eggs), as well as rodents (that's what the larvae and the nymphal ticks feed on). So we generally see that TBEV is very strongly linked to forested areas with abundance of wildlife and lots of deer.

And as for the climatic aspect, that's kind of a pretty complex topic (lots of discussion going on there). For a very long time, it was thought that TBEV can only occur in regions with very specific climatic conditions that are linked to continental climates—so, regions with very cold winters and rapid increases in temperature during Spring. But the problem is TBEV now occurs in countries such as the Netherlands, but do not have a continental climate but an oceanic climate. We don't have these rapid increases in temperature in Spring; it goes very slowly here. And yet we do have TBEV. So the impact of climate I think needs to be reconsidered. And at the same time, there's discussion going on what the impact of climate change could be. And we definitely see that ticks now occur in regions that did not have TBEV or ticks before because they've become warmer in cold regions in Scandinavia (so, more northern latitudes) as well as regions higher up in the mountains (so, in the Alpine regions) where ticks and TBEV are now creeping upwards in the mountains. So lots of different things to consider here, both ecological and climatological.

[Sarah Gregory] And your study is about the circulation of TBEV variants in the Netherlands. Tell us about those variants and what they tell us.

[Helen Esser] Yes. In the publication, we describe that we found three different variants of TBEV. By now we've actually found a fourth one, and the interesting thing is that it seems that every time we have a new location where we find TBEV, it's a different variant circulating there. And that indicates that there were independent introductions of the virus, and possibly also that these introductions are ongoing. And it's possible that migratory birds play a role there, or maybe even rodents if they are being transported in, I don't know, maybe trucks or other machines...cars that travel long distances.

[Sarah Gregory] And when and where was it first discovered in the Netherlands?

[Helen Esser] So in the Netherlands, it was first discovered in 2016. But we have indication that it has been there for longer because what happened with that in 2016, they screened roe deer serum samples from roe deer that were shot in 2010. So it was a retrospective study. They were sampling or analyzing samples that had been collected six years before. And then they discovered that some of these roe deer from one specific location had antibodies to the virus. And they went to that location to collect ticks, and indeed they found infected ticks. So even though they'd discovered the virus in 2016, it was probably already present in 2010.

[Sarah Gregory] In your opinion, is it emerging or was it just not recognized before 2015 or 16?

[Helen Esser] Well...so at least we know that it has been there since 2010, but then indeed that raises the question, "Was it even there before 2010?", right? Has it...has been there for such a long time or...that we didn't notice it? Or is it really just emerging? I think it might actually be emerging because prior to 2010, there was a study conducted in 2005 where they sampled wildlife, domestic animals and ticks, tested these for the presence of the virus and did not find it. Also, patients that had TBE were all linked to international travel. So all these people who were sick...well, there were not that many, but the few people that had TBEV all went abroad for holiday to regions where TBEV occurs. So there's no evidence that the virus was in the Netherlands prior to 2010.

[Sarah Gregory] Why don't you tell us briefly about your study and what you were specifically looking for and why did you choose to sample rodents in your study, and how the roe deer are involved in all of this?

[Helen Esser] So our study was actually a response to a second study that was basically a roe deer follow up study from the first one. And in that follow up study, they sampled roe deer that was shot in 2017 (so, basically seven years after the first roe deer were sampled). And that study indicated that the virus had potentially increased the distribution in those seven years. So now they found evidence of the virus (so, antibodies) in roe deer that were collected from the border with Germany and Belgium (so, more locations than during the first study). The problem, however, with roe deer samples is that roe deer can potentially travel far distances, particularly young males when they're in search of new territory. So potentially, roe deer collected along the border could have come from either Germany or Belgium.

And the other thing is, of course, that antibodies only tell you something about past exposure. You know that these roe deer have been exposed to the virus at one point in life but not exactly when that was, and whether that virus is still there. So that's why we went to those locations to see if the virus was still there, and you can do that by testing either the ticks or rodents, which have very small territories and don't live that long. So that's what we did, collecting and testing both ticks and rodents.

[Sarah Gregory] Are deer and rodents spreading it back and forth, and how does this impact people?

[Helen Esser] So deer themselves are not so-called 'competent hosts'. So they do not transmit the virus to feeding ticks. They are 'dead end' hosts. Rodents, on the other hand, do play an important role. So either they can become infected themselves and then transmit the virus to an infected feeding tick. But probably more importantly, these rodents function as a trench and bridge, so to speak. Ticks that are infected and feed on a rodent can directly transmit the virus to other uninfected ticks that feed simultaneously on that rodent, and that's because the virus, when it enters the skin cells of the rodent, is able to travel through those skin cells to evade the rodent immune system and then infect a tick that feeds nearby. So it's a pretty smart virus, in that sense. So rodents do play an important role in the transmission of that virus.

[Sarah Gregory] How did you go about your study—collecting ticks, sampling rodents, all that stuff?

[Helen Esser] Right. So yeah, we went to lots of different locations (48). And in each of those locations, we aimed to collect about 1,000 ticks (sometimes that was more easy than in other instances), and we did so by drag sampling. So you basically have this white cotton cloth (about a square meter), and you drag it through the leaf litter and through the vegetation. Ticks that are in that vegetation think that this is a potential host, so they cling to the cloth. And it's a white cloth, you can then easily see those ticks and collect them. And as for the rodents, we used these little live traps, quite similar to the Sherman traps that are often used in the US. These are a little bit different; we fill them with hay and food to attract the rodents, and then the next day we check the traps and then collect the rodents.

[Sarah Gregory] And when we say rodents, are these mice or are they rats? Or both?

[Helen Esser] So rats are too big to enter the trap, so it really targets small rodents. And the rodents that we found, those are mostly true mice (wood mice, they're called) as well as voles. So small rodents.

[Sarah Gregory] Okay. I was thinking that rats usually are too smart to fall for going into a trap, so that makes sense.

[Helen Esser] Actually, that's true too. It's much more difficult to trap rats than rodents, yeah.

[Sarah Gregory] Yeah. And what did you find? Were there any surprising findings?

[Helen Esser] I think the most surprising finding was that we found all of these different variants, and that these variants were very similar to variants abroad (so, from Sweden and Germany), some places like really far away. They were much more closely related to variants abroad than to each other. And that suggests that this virus is spread over really long distances.

[Sarah Gregory] What are the public health implications of your findings?

[Helen Esser] So I think the bad news is that the virus actually does have a wider distribution than previously thought. It's present in quite a few places in the Netherlands. But the good news is that it's relatively rare, so chances of being bitten by an infected tick are really low. And as I said before, the majority of people who are bitten by an infected tick do not become sick. It's a pretty small percentage of people who do get sick. But then if you get sick, then it can be pretty severe.

[Sarah Gregory] Did you come across any challenges when you were conducting this study?

[Helen Esser] Well, there were some logistical challenges as well as typical challenges related to field work, such as setting out safety traps and then not catching any rodents the next day, even though you've pre-baited those traps. So that means that, you know, you've already put food in there for several days to get these rodents used to the traps so that they lose their fear, and they enter the trap. Sometimes you just happen to sample an area where at that moment, there's very few rodents.

And I think the other logistical challenge has more to do with acquiring all the permits for sampling there. I had just not realized how many different organizations were involved as landowners in the Netherlands. Really, it's such a tiny country, but then having these forest patches being divided over multiple different landowners made it sometimes quite complex to figure out, "Okay, this specific plot within the forest...who does it belong to?". So that was a surprise.

[Sarah Gregory] Oh, that's very interesting. Yeah, that's something I would not have thought of.

Well Dr. Esser, tell us about your job and how you became interested in tick-borne diseases.

[Helen Esser] So I'm a disease ecologist. That means that I am strictly interested in the ecological interactions between arthropod vectors such as ticks, the wildlife hosts, and the pathogens that they carry. And I think I've...yeah, when did I become interested in tick-borne diseases? I've always had an interest and a passion for wildlife, nature, small critters, from a very young age. And I think that my interest specifically in tick-borne disease started during my master's studies.

I went to Panama (so, a very tropical place) to study the impact of hunting on wildlife communities and seed dispersal. And there, I realized that in locations where there was lots of hunting and relatively few mammals, there were also few ticks. I had very few tick bites, whereas my colleagues that were working on an island where there was no hunting, they were covered in ticks each day. But that island also lacked large predators. So there were lots and lots of medium- to large-size mammals (deer, peccary). And it was such a big contrast in the number of ticks between those locations that I thought, "Wow, this would be a really interesting study to follow up on and see how can we explain that". And that's basically how I started my PhD project on ticks. So yeah, the rest is history.

[Sarah Gregory] Well, it is definitely a very interesting topic. I always enjoy it when we talk about climate and impact on the environment and disease.

So you live in the Netherlands. Were you raised in the Netherlands?

[Helen Esser] I was born in Aruba, which is a really tiny Caribbean Island. But I only spent there a couple of years during my childhood. And then, the rest of my childhood was spent in different places in the Netherlands. And then after my study, I immigrated to Panama. So I lived there for almost three years. So yeah, I find it really hard to say where I really grew up or have my roots. It's just a mix of different places. My heart is really with the tropical and more mountainous countries abroad.

[Sarah Gregory] Thank you for taking the time to talk with me today, Dr. Esser.

[Helen Esser] Yeah, you're very welcome.

[Sarah Gregory] And thanks for joining me out there. You can read the December 2022 article, Continued Circulation of Tick-Borne Encephalitis Virus Variants and Detection of Novel Transmission Foci, the Netherlands, online at cdc.gov/eid.

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

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