

Tick Bite Infections in Austria

[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. Mateusz Markowicz, a researcher at the Medical University of Vienna in Austria. We'll be discussing the risk of tickborne infections after a tick bite.

Welcome, Dr. Markowicz.

[Mateusz Markowicz] Hello.

[Sarah Gregory] How many different pathogens are there in ticks?

[Mateusz Markowicz] So, we conducted our study in Austria. And in Austria we find in ticks, first of all, *Borrelia burgdorferi* sensu lato, and this is the most common infectious pathogen. And we also find some other rare pathogens like *Anaplasma phagocytophilum*, *Candidatus Neoehrlichia mikurensis*, and relapsing fever borreliae (like *Borrelia miyamotoi*) and a variety of *Rickettsia* species. So, these are pathogens which are taken up by the tick during the blood meal because the ticks need the blood of different animals in order to develop in order to keep a life cycle. And in this situation, they take up the pathogens which might cause diseases in humans. So, the origin of the pathogens are animals.

[Sarah Gregory] What are they?

[Mateusz Markowicz] The biggest group are bacteria, and our study focused on bacterial pathogens, but we also find viruses like tickborne encephalitis virus and parasites like *Babesia*. But the biggest group of pathogens are bacterial pathogens. And some of them are intracellular pathogens, like *Rickettsia* species and *Anaplasma*, and so they are quite difficult to cultivate in the routine laboratory.

[Sarah Gregory] Apparently many new tick pathogens have emerged. Do you know why this is?

[Mateusz Markowicz] Yes, this is a good question. When we look at Lyme borreliosis, which is known for quite a long time, the first cases of infections were described in Vienna in 1912. So, I have read a publication on erythema migrans which was described by a doctor in Vienna, and these are very good descriptions, very detailed descriptions of a disease which was not known (so far). And a pathogen was described and calculated 70 years later, so it took a lot of time. And today we find new pathogens which were not known, basically because of the progress in molecular testing. So, we do not need to wait 70 years, but we are quite much faster. But some of the pathogens are really new. For example, *Borrelia miyamotoi* were first reported—so, the human cases of *Borrelia miyamotoi* infections—were reported in Russia in 2011, and the other pathogen which we were interested in, *Candidatus Neoehrlichia mikurensis*, was found in 2010. And I guess infections may have occurred earlier, but it was not known (the pathogen was not known). Due to better diagnosis and progress in molecular testing, we are able to detect such bacterium, and we even detect new species of *Rickettsia*, which is a very big group of bacteria. So, with our methods, we could detect a new *Rickettsia* species in a tick from Tyrol when we were doing...when we have been performing the study. So, I think this is a technical progress which enables to find new bacteria which are difficult to cultivate, like intracellular bacteria.

[Sarah Gregory] Are some pathogens more infectious to people than others? And which ones stood out for you?

[Mateusz Markowicz] Yes, this is an interesting question because it's difficult to study this question under controlled conditions. So, what are the factors which were responsible for transmitting a pathogen from a tick to human? So, of course, the pathogen must be in the tick, so the tick must have been infected with this pathogen. And the other question is how many ticks (or what is the prevalence) of the pathogen in the ticks. We know for *Borrelia burgdorferi* that this is (in Austria) about 20–30%. We know for *Rickettsia* species that we have about 10–20 *Rickettsia*-positive ticks. So, the pathogen must be in ticks and it must be transmitted. And there are some conditions which are responsible for successful transmission. This might be, for example, time—so, the duration of the blood meal, which is important for *Borrelia*. We know that it takes hours to transmit *Borrelia* from a tick to human, but there are some pathogens which do not need such long time periods. So, each pathogen is different. Therefore, it is not possible to say which pathogen is the one which is most infectious because we cannot have comparable observations, comparable conditions to study. But from the clinical perspective, we know that Lyme borreliosis is the most common infection, which was also shown in our study.

[Sarah Gregory] So, what are some other factors that increase the risk of infection? There seem to be several according to your article.

[Mateusz Markowicz] Yes, so in our study, we investigated the risk factors for Lyme borreliosis because this was the most common infection, and we had enough cases (enough infections) to perform a statistical analysis. So, what we wanted to know from our patients was how long was the tick attached after the bite, just to have an estimated duration of blood meal. We also investigated the ticks under with a microscope just to see their engorgement level (we wanted to know how big they are). We documented the site of the body where the tick was biting the participants, and we analyzed, and we did a risk analysis just to see what variables are predictive for infection. And what stood out was that the engorgement level of the ticks was a main predictor for the infection. So, if a tick was fully engorged, the risk was then much higher to get the infection. And also, the PCR detection of *Borrelia burgdorferi* sensu lato in ticks was also a factor which was predicted for the infection.

We did not find a correlation with an estimated time of blood meal duration, so maybe the reports of the patients were not precise enough, because it is difficult to estimate how long the tick was in the skin. And so, we found that the engorgement level of the tick and the PCR confirmation of *Borrelia* in ticks was predictive.

[Sarah Gregory] And what was the aim of your study?

[Mateusz Markowicz] So, the aim of our study was to analyze the outcome of tick bites in general and we focused on bacterial tickborne infections. We wanted to know what infections would develop in our participants if symptoms occurred or if there were also asymptomatic infections, and we wanted to analyze risk factors for *Borrelia burgdorferi* infections because we expected that *Borrelia* would be the most common (the most frequent) infection in our study cohort. And we analyzed different risk factors.

[Sarah Gregory] And how did you conduct your study?

[Mateusz Markowicz] So, our study was a prospective study which was performed in two centers in Austria (in our university in Vienna and also in Tyrol). And we asked participants who were bitten by ticks to come to our center with the tick and we investigated the tick for different bacterial pathogens, and we also took blood from the patients and we repeated the blood

investigation after approximately six weeks. This was because we wanted to know if specific antibodies would develop after the tick bite. And we also analyzed the blood for the pathogens by PCR methods.

Then, we also asked the patients to report if there was erythema migrans. So, we wanted to know how many participants will develop erythema migrans, which is the most common clinical manifestation of Lyme borreliosis. So, this is how it worked, and we could include about 500 participants in Vienna and in Austria who were bitten by >1,200 ticks. So, there were several persons who had more tick bites, and we investigated all ticks for pathogens which were brought by patients.

[Sarah Gregory] So all the ticks that you studied were brought by patients who had been bitten by ticks, okay.

[Mateusz Markowicz] Yes.

[Sarah Gregory] How do you analyze a tick? I mean, how do you get the blood out of a tick?

[Mateusz Markowicz] Yes, so our institute has big experience in tick investigations and analysis of ticks. We previously performed studies when my colleagues collected ticks from the vegetation, and we have different methods to find pathogens. So, we use PCR, we use sequencing, and in case of our study, the ticks which were removed by participants were analyzed. So, the participants of the study were asked to collect the ticks and to bring the ticks to our institute and to give their blood for more investigations and tests.

[Sarah Gregory] But I mean physically, what do you do with the ticks to analyze them? I mean, do you cut them apart? Stick a little tiny syringe and pull the blood out?

[Mateusz Markowicz] The tick must be cut apart, yes, in order to analyze the pathogens which are inside. So, we have procedures to do that. Our technicians are quite experienced in this kind of work.

[Sarah Gregory] Very skillful small motor skills.

[Mateusz Markowicz] Yes.

[Sarah Gregory] Why do you feel your study is important?

[Mateusz Markowicz] I believe that our study is a good overview of possible outcome of tick bites in Europe, so I think we had a representative sample of persons who were bitten by ticks during recreational activities or during occupational activities. So, there have been many studies where ticks were analyzed for pathogens. So, we had a quite good overview of what pathogens can be found in ticks. However, studies which showed the infections after the tick bite are not very frequent. And we wanted to combine the tick screening, the tick testing, and the testing of patients just to see what is the frequency of pathogens in ticks and what is the frequency of pathogens which can be found in patients after a tick bite.

So, the advantage of the study is that we also concentrated on different pathogens, not only on Lyme borreliosis but also on the emerging pathogens like relapsing fever borreliae, like *Neoehrlichia*, and these pathogens are relatively new, and they are known just since several years. And of course, we also focused on risk analysis for *Borrelia* infection which might be important for further studies, for example, on prophylactic measures, how to prevent Lyme

borreliosis. So, we have identified a specific group of patients or specific conditions in which the risk for infection is higher.

[Sarah Gregory] You mentioned testing for antibodies earlier in one of your answers. Is it possible for people to develop antibodies to prevent a future infection from this same pathogen?

[Mateusz Markowicz] Yes. So, the antibodies which develop after a *Borrelia* infection are not protective for 100% because in Europe we have many different species of *Borrelia burgdorferi* sensu lato which cause human infection. This is different in comparison to the North America, and in Europe, we have patients who develop *Borrelia* infection for several times. So, you can get erythema migrans after a new tick bites again. So, even if you have antibodies after the infection, so they are not protective like, for example, after vaccination.

[Sarah Gregory] You mention in your article that you think tick bite infections are underestimated. What needs to happen so accurate data is reported?

[Mateusz Markowicz] It is important to think about pathogens in patients who have specific symptoms. For example, fever is a symptom which might be caused by different infections. And I am not sure if testing is performed by doctors for these infections because these pathogens are new, and they may be not known very well. So, it would be important to test patients with fever for these infections and to have epidemiological surveillance, which is missing. And of course, it would be important to have a surveillance system for patients with specific symptoms after a tick bite. For example, fever, it would be interesting to investigate or to test patients with fever for emerging pathogens. So, I think a complete surveillance is missing in many countries currently.

[Sarah Gregory] How do you think this study applies to tickborne infections in other parts of the world? I think you mentioned that you thought it was applicable to Europe but tell us a little bit more about that.

[Mateusz Markowicz] Yes, so in our country and in central Europe, *Ixodes ricinus* is the tick species which is responsible for which bites people very frequently. So, in our study almost all ticks were *Ixodes ricinus*. So, I think that our results are comparable to other regions of Europe where *Ixodes ricinus* is active. And there are some other studies from Scandinavia, and they show that the risk for infection with Lyme borrelia is about 5%, which was also shown in our report. So, we have very comparable results. In North America, there are different tick species which bite people. Therefore, I don't think that our results would be the same, yeah, and also there are different *Borrelia* species. So, I think for Europe, our results would be similar in other parts of our region.

[Sarah Gregory] Were you surprised by any of the findings you discovered?

[Mateusz Markowicz] Yes. So, the project took four years and I had contact with many participants and I was very surprised that some of the people were bitten by a very high number of ticks. So, we had some persons who had...we had one participant who was bitten by 150 ticks, and some ladies who were bitten by 50 or 60 ticks. So, obviously there are some people who attach ticks more than the others. And this, of course, raises additional research questions. So, what are the factors responsible for such...what are the factors why these people are so attractive for ticks?

What also was surprising in our study was that *Candidatus Neohhrlichia mikurensis*, which is an emerging pathogen, occurred quite frequently after a tick bite in humans. So, this was the second common infection after Lyme borreliosis—so, 2.5% of participants had the pathogen after a tick

bite. This was quite surprising, and what also was surprising was that some persons had a persistent infection. So, we found three persons with a persistent *Neoehrlichia* infection, and all of them were asymptomatic. So, these were persons who were healthy, but we found the infection only because we tested all participants systematically by PCR. And what was also interesting is that we found *Rickettsia helvetica* quite frequently in our ticks, which was known, but there were no human infections. So, this pathogen occurs in ticks but obviously it is not very dangerous to people because we did not find any case, either by seroconversion nor by PCR. Yeah, so these were the main findings which I did not expect before the study was carried out.

[Sarah Gregory] So, earlier you said risk factors were time, engorgement, that sort of thing. But my mind boggles at having 50 or 60 or 100 ticks on you at one time. Was more ticks related to a higher infection level?

[Mateusz Markowicz] Yes, this was also significantly. So, at least in our study, we did not document this kind of relationship, but the point is that maybe not all patients knew about all ticks which had bitten them. So, they only brought those ticks which they have detected on their skin. So, you do not observe or notice all ticks which bite. That's the problem here.

[Sarah Gregory] So, what were some of the challenges? I guess that was a challenge, knowing how many bites a person actually had, but were there any other challenges?

[Mateusz Markowicz] Yes. So, when we started with the project in 2015, the problem was that we did not include many participants because it was not known. We had the chance to announce our project on media one year later, and after that we really had very nice numbers of participants who came to our center. But before it was quite disappointing because the number of participants was not very satisfying. And the other thing which...challenging was that in May and in June there were many tick bites, and we had simultaneously many participants who came to our department. And of course, this was a challenge for the laboratory to test all the ticks, because we had really hundreds of ticks in a very short period of time. And in patients or for participants who were bitten by many ticks, it was difficult to document all body sites because we wanted to know for each tick what was the site of the tick bite. And it was quite difficult if there was a person with 20 tick bites, just to document all the sites of the tick bites for these persons.

[Sarah Gregory] Can you remind us of the best ways to avoid tick bites?

[Mateusz Markowicz] Yes. So, avoiding tick bites, the best way to avoid tick bites is to check your body after being outdoors, I think. If the tick is removed quickly or even if it does not have a chance to attach, then the risk of infection is very low. The other possibility is to take a shower and to check clothing and to change clothing after being outdoors. And also, repellents can be used. However, in Europe, we do not have evidence-based data about the efficacy of repellants. But maybe for some persons they are helpful.

[Sarah Gregory] Oh, that's interesting. Okay. What should someone do if they discover ticks on themselves? Do they need to remove them themselves? Or should they rush off to see a doctor immediately?

[Mateusz Markowicz] There are many persons who are able to remove ticks themselves. If it is not possible, then of course one should get to a doctor. But normally, this is not a problem. And after that, it is enough to observe the skin to see if erythema migrans develops (so, if there is a rash). And this rash can develop even several weeks after a tick bite, so it may take time. There

are also some other symptoms which one should think about, for example, fever. If there is fever, the infection with some other emerging pathogens may be possible, like *Anaplasma* or *Neoehrlichia*. And then of course one should go to a doctor to make a test. But our study showed that often 95% of tick bites, no infection develops. So, there is rather a high chance to stay healthy after a tick bite than to get any of these infections.

[Sarah Gregory] Your article was chosen as a MedScape Continuing Medical Education article by EID. Why do you think it is? EID only chooses about two a month.

[Mateusz Markowicz] Yes, I'm happy that our study was, and I think this is because ticks and tick bites are relevant for patient care. So, I think that the outcome of tick bites is very well-documented in our study, and this information may be useful for doctors who see patients after tick bites. And this study is a simple study, it is a very simple design, and it is easy to follow, I think. And I think it is good to know that after most tick bites, there is no infection. So, in our study 95% of participants did not develop any infection. And on the other hand, there are also some rare pathogens aside from Lyme borreliosis which might not be widely known, and our study shows the frequency of these infections on a quite big sample of participants. And the knowledge about the epidemiology of such infections is rather limited so far.

[Sarah Gregory] So, tell us about your job. What about it matters most to you?

[Mateusz Markowicz] So, I'm working at the Medical University of Vienna, and our institute is the Institute for Hygiene and Applied Immunology. And we are the reference center for Lyme borreliosis and for other bacterial tickborne infections in Austria. So, our main research topic is Lyme borreliosis and tickborne infections, and I personally take care of clinical projects and I also work in an outpatient department and try to advise patients and to treat patients if they have an infection with any of these pathogens. And we have also many other clinical projects on host-pathogen interaction in Lyme borreliosis patients. So, there are some other ongoing projects currently, which are also very interesting.

[Sarah Gregory] Have you done anything differently during the pandemic than before it hit? Anything new that you will continue as we slowly emerge?

[Mateusz Markowicz] I must admit that I'm happy that we carried out this study before the pandemic hit, because it would be not possible to include so many participants because the people had to come to the outpatient department for giving their blood. And I'm really happy that we could finish our project in 2018 before the pandemic began. But we are not directly working with COVID, so I think Lyme borreliosis and tickborne diseases is a different topic, and it will be also important after the pandemic because ticks and tick bites and tickborne infections will be here after the pandemic also. A very important topic.

[Sarah Gregory] Well thank you for taking the time to talk with me today, Dr. Markowicz.

[Mateusz Markowicz] Thank you.

[Sarah Gregory] And thanks for joining me out there. You can read the April 2021 article, Infections with Tickborne Pathogens after Tick Bite, Austria, 2015–2018, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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