Borrelia miyamotoi: The Newest Infection Brought to Us by Deer Ticks

It's not just Lyme disease anymore. Residents and visitors in many parts of the northeastern, north-central, and far western United States have more than one reason to avoid bites from hard-bodied (ixodid) ticks. The latest addition to the list of infections transmitted to humans by the same ixodid ticks that are vectors of Lyme disease is *Borrelia miyamotoi*. Although *B. miyamotoi* is in the same genus as *B. burgdorferi*, it is more closely related to species that cause relapsing fever than to Lyme disease agents (1). Discovered in *Ixodes persulcatus* ticks in Japan in 1994 and subsequently documented in ticks and rodents in North America and Europe, *B. miyamotoi* was not recognized as a human pathogen until a report from Russia in 2011 (2). It has since been reported in patients in the United States, Europe, and Japan (3–8). In this issue, Molloy and colleagues report the first large case series in the United States and provide important new information about the epidemiology and clinical presentation of human disease caused by this pathogen (8).

Whole blood samples from patients in the northeastern United States with suspected tickborne illness during April to November in 2013 and 2014 were tested with polymerase chain reaction (PCR) for 4 tickborne pathogens. Amplifiable DNA of *B. miyamotoi*, *Anaplasma phagocytophilum*, *B. burgdorferi*, or *Babesia microti* was detected in approximately 1%, 1%, 2%, and 3%, respectively, of 11 515 samples from individual patients. The frequency of infection with *B. burgdorferi,* which is primarily a fixed-tissue pathogen, should be greatly underestimated on the basis of PCR of the blood alone. Furthermore, the relative frequencies of these 4 infections vary across different regions of the northeastern United States, so different results might have been obtained with samples from other locations. Nevertheless, on the basis of the current report and previous data, the frequency of *B. miyamotoi* infection seems to be similar to that of *A. phagocytophilum* and *B. microti* (3, 6, 8).

The researchers provide clinical information for 51 patients infected with *B. miyamotoi*. Of note, the peak incidence of positive assay results for *B. miyamotoi* was in August, with probable onsets of illness continuing into September, which is about a month after the peak incidence of Lyme disease. This temporal peak is similar to that observed in naturally infected white-footed mice in Connecticut and corresponds to the questing activity of *Ixodes scapularis* larvae in the northeastern United States (3). Acquisition of *B. miyamotoi* infection from unfed larval ticks is possible because of transovarial transmission of the pathogen from an infected female (9). Bites from larval deer ticks have not been considered as a health threat, but this needs to be reevaluated. Larval transmission of *B. miyamotoi* has implications for checking for ticks and continuing tick precautions even after the risk for Lyme disease has abated. Human-to-human transmission by blood transfusion is theoretically possible (3), but a transfusion-associated case has not been reported to date.

The clinical manifestations of *B. miyamotoi* among the 51 infected American patients are similar to those described for patients with undifferentiated acute febrile illness, including fever and headache as the most prominent findings (2–8). Recurrence of fever was noted in 4% of patients in this case series and 10% in the original case series from Russia (2). Higher relapse rates might have been observed if antibiotic therapy had been delayed or omitted. A rash was noted in 8% of the American patients, but none was described as an erythema migrans rash. Symptoms were often severe, resulting in hospitalization for about one quarter of the patients. None of the patients developed complications, however, presumably because of prompt antibiotic treatment. Meningoencephalitis due to *B. miyamotoi* has been described in 2 immunocompromised patients in separate reports from the United States and the Netherlands (4, 7). Jarisch–Herxheimer reactions, which consist of fever and chills with occasional hypotension after the first dose of an antibiotic, were not described in this case series, although such reactions were observed in a minority of previously reported patients with *B. miyamotoi* (2–4). Leukopenia, thrombocytopenia, and elevated liver enzyme concentrations were reported, as has been documented previously (2).

The diagnosis of *B. miyamotoi* in this case series was based on PCR testing and subsequent sequencing of the product. *Borrelia miyamotoi* antibody testing using the glycerophosphodiester phosphodiesterase (GlpQ) antigen was noted to be relatively insensitive in diagnosing acute illness, but it is a reasonable test to confirm the diagnosis if convalescent sera are available (5, 6, 8). Antibodies to a *Borrelia* GlpQ protein are not observed in Lyme disease because *B. burgdorferi* does not make the protein; however, there may be cross-reactive antibodies with other forms of relapsing fever (10). Both PCR and GlpQ antibody assays for *B. miyamotoi* are available from commercial and university laboratories, but to date no *B. miyamotoi* tests have been approved by the U.S. Food and Drug Administration. Although not examined in this report, a Wright- or Giemsa-stained blood smear is a routinely performed procedure that may reveal *B. miyamotoi* spirochetes in the blood during febrile episodes. Doxycycline, amoxicillin, and ceftriaxone seem to be effective in alleviating symptoms and preventing complications (2–8). Such therapy would also be effective against co-infection with *B. burgdorferi*. Doxycycline is the preferred initial therapy in patients with suspected *B. miyamotoi* infection because it effectively treats Lyme disease and human granulocytic anaplasmosis, which may be the cause of illness or co-infection with *B. miyamotoi*.

This article was published online first at www.annals.org on 9 June 2015.

An official name for *B. miyamotoi* infection has not yet been adopted. The term "*Borrelia miyamotoi* disease," which Molloy and colleagues suggest, is one option. As an alternative, we suggest "hard tick–borne relapsing fever," which accurately indicates the class of pathogens to which the agent belongs but also distinguishes it from the other types of vectors for this group of species—namely, soft tick–borne relapsing fever and louseborne relapsing fever (2). Regardless of the nomenclature, Molloy and colleagues' report provides important new information about a bacterial zoonosis that may be as common as babesiosis or human granulocytic anaplasmosis in the northeastern United States and may require hospitalization for severe illness (2, 3, 8).

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Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M15-1219.

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Ann Intern Med. 2015;163:141-142. doi:10.7326/M15-1219

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