THE CHANGING LANDSCAPE OF
TICKBORNE DISEASE IN MINNESOTA:

A spotlight on emerging diseases

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The risk for tickborne disease in Minnesota has expanded over the years, not only geographically, but also in terms of the number of infections possible. Of particular interest are some of the newer and emerging tickborne diseases like Powassan virus, *Ehrlichia muris eauclairensis*, *Borrelia mayonii* and *Borrelia miyamotoi*. In addition to learning how to recognize these infections in patients, providers need to know how to test for them, offer appropriate and effective treatment and help patients reduce or prevent further exposure to ticks.

Over the last 30 years, the risk of tickborne diseases has changed. While Lyme disease is still the most common tickborne disease, both in Minnesota and nationwide, it is now just one of several diseases possible after the bite of an infected tick. The primary vector tick in Minnesota is *Ixodes scapularis*, more commonly known as the blacklegged or deer tick, and as the distribution of this tick has changed, the picture of disease has changed as well. More than just a pest, this tick has become a significant disease threat to people living around, working in and enjoying the great outdoors while in forested areas of the state (Figure 1). In addition to spreading Lyme disease, anaplasmosis and babesiosis, this tick has been shown to be the vector of several additional diseases over the past 20 years (Figure 2). Powassan virus was reported in a Minnesota resident in 2008, and the first case of *Ehrlichia muris eauclairensis* in Minnesota was reported in 2009. The index case of *Borrelia mayonii*, a new form of Lyme disease, was identified in a Minnesota child in 2013, and *Borrelia miyamotoi*, also known as hard tick relapsing fever, was first identified in Minnesota in 2016. Much less is known about these new pathogens and the illnesses they cause, but the more cases that are identified, the more a "typical" clinical course emerges.

Powassan virus

Powassan virus (POW) is a tickborne flavivirus that can cause severe disease in humans. The disease is considered rare, and although human cases have traditionally only been reported sporadically, it is becoming more common. Most cases report exposure in the northeastern United States and in the upper Midwest. POW typically presents with neurologic symptoms, most commonly encephalitis or meningitis, after an incubation period of one to four weeks. Milder, even subclinical, infections occur, although they are likely underreported. Long-term sequelae after infection occur in approximately 50 percent of cases and 10-15 percent are fatal.

From 2008 through 2018, Minnesota reported 37 cases of POW, with an average of three cases per year. Cases were 73 percent male and the median age was 60 years (range, 0–75 years). Clinically, 89 percent of cases had meningitis or encephalitis with fever, headache, confusion and weakness also commonly reported. Two of Minnesota's cases were fatal.

Diagnostic testing for POW is not widely available, and is primarily performed at public health laboratories or the Centers for Disease Control (CDC). Serologic and molecular testing can be ordered through the Minnesota Department of Health (MDH). There is no vaccine to prevent POW and treatment is primarily supportive care.

Ehrlichia muris eauclairensis

Ehrlichia muris eauclairensis was first identified in 2009 by researchers at Mayo Medical Laboratories, and was initially referred to as *Ehrlichia muris*-like agent, or EML. Unlike the more well-known *Ehrlichia chaffeensis*, which is transmitted by the lone star tick, *E. muris eauclairensis* is transmitted by the blacklegged tick. The index patients were from Minnesota and Wisconsin and subsequent cases have primarily occurred in the upper Midwest.

Clinically, illness caused by *E. muris eauclairensis* is indistinguishable from the closely related and much more common illnesses of anaplasmosis or ehrlichiosis caused by *E. chaffeensis*. Patients com-

monly report fever, headache, malaise and myalgia, and laboratory studies often note thrombocytopenia and elevated transaminases. From 2009 through 2018, Minnesota has reported 60 cases of *E. muris eauclairensis*, 22 percent of which required hospitalization.

Laboratory diagnosis of *E. muris eauclairensis* is made by PCR and molecular methods are the only way to reliably differentiate different species. Unlike for anaplasmosis and ehrlichiosis caused by *E. chaffeensis*, there is no commercially available serologic test for this bacteria and peripheral smears are not recommended for diagnosis due to insensitivity. As with anaplasmosis and other rickettsial diseases, doxycycline is the preferred treatment for infection with *E. muris eauclairensis*.

Borrelia mayonii

Borrelia mayonii is a recently identified bacteria closely related to *Borrelia burgdorferi*. It was first identified in a Minnesota resident in 2013. Since then, a small number of cases have been found in people who have been exposed to ticks in Minnesota or Wisconsin. The illness *B. mayonii* causes is very similar to Lyme disease caused by *B. burgdorferi*, although there are some differences. For instance, nausea and vomiting are associated with *B. mayonii*, but are not commonly reported symptoms in infections with *B. burgdorferi*.

A total of 10 cases have been reported in Minnesota through 2019, with an average of one to two cases reported each year. Of the 10 cases reported, 80 percent were among males, the median patient age was 45 years (range, 6–61 years), and 90 percent had likely tick exposure in Minnesota or Wisconsin (one case unknown). All cases experienced a febrile illness, with 50 percent of illness onsets occurring in July. Four cases involved brief hospitalizations. Five patients experienced a rash, although only one patient's rash was described as erythema migrans. Other common symptoms included headache, myalgia and fatigue. All patients experienced clinical improvement after treatment with amoxicillin or doxycycline.

Currently, testing for *B. mayonii* is not widely available and is limited to molecular methods. All cases have tested positive by PCR for the disease agent. Limited information suggests that patients may develop detectable antibodies after infection with *B. mayonii*, so infections may be detected on traditional Lyme disease serology, but serologic testing cannot distinguish between *B. mayonii* and *B. burgdorferi*.

Borrelia miyamotoi

Borrelia miyamotoi is closely related to the bacteria that cause tickborne relapsing fever. It was first identified as a cause of human illness in 2011 in a patient from Russia and the first case in the United States was reported in 2013. Since 2016, 13 cases have been reported in Minnesota, with an average of three cases each year.

Of the 13 Minnesota cases, 69 percent were among males, median patient age was 57 years (range, 33–77 years) and 92 percent had likely tick exposure in Minnesota or Wisconsin (one case unknown). All patients experienced a febrile illness with 38 percent of illness onsets occurring in August. Three (23 percent) cases involved brief hospitalizations. None of those affected experienced a rash. Nationally, the most commonly reported symptoms are fever, chills and headache, as well as fatigue, myalgia and arthralgia.

Currently, both molecular and serologic testing is available for *B. miyamotoi* at commercial laboratories and CDC can assist with diagnostic testing. *B. miyamotoi* infections have been successfully treated with a two- to four-week course of doxycycline. Amoxicillin and ceftriaxone have also been effective.

While these new diseases have emerged, the incidence of more well-known diseases, like Lyme disease, anaplasmosis and babesiosis, has also increased over the same period. It is important for providers to think broadly about tickborne diseases in patients with compatible symptoms and exposures and to consider testing with broader disease panels, rather than focusing on specific tests. The symptoms of tickborne diseases can be non-specific and co-infections may occur. Patients with outdoor occupations or recent outdoor activities, either around forested areas at home or away from home, are at particular risk. Providers should encourage prevention, like regular use of EPA-registered repellents and daily tick checks, to reduce risks.

In Minnesota, the highest risk season for tickborne diseases is from late spring into mid-summer, coinciding with peak activity of the adult and nymphal stages of the blacklegged tick. A smaller, secondary peak occurs again in the fall when adult ticks are active again. Routine surveillance of ticks in Minnesota has provided data since 2005 on six different disease agents (Figure 3). Results have shown that infec-

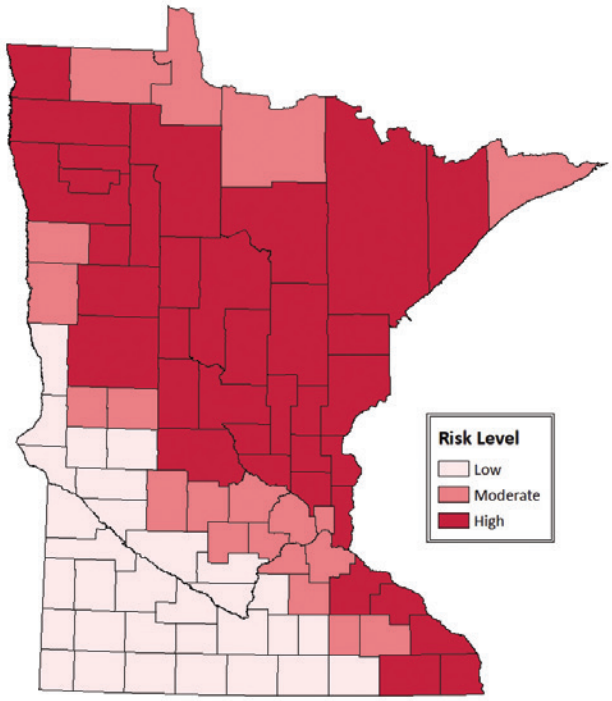

FIGURE 1

Minnesota Tickborne Disease Risk

Tickborne disease risk in Minnesota by county, based on average incidence (cases/100,000 population) of anaplasmosis, babesiosis and Lyme disease, 2007–2018 (MDH).

tion prevalence can vary from site to site and year to year but, on average, about one in three adult blacklegged ticks and one in five blacklegged tick nymphs are infected with *B. burgdorferi*. Prevalence of other pathogens is considerably lower, with about 6-8 percent of ticks infected with anaplasmosis or babesiosis and only 1-3 percent of ticks infected with *E. muris eauclairensis*, *B. miyamotoi* or *B. mayonii*. While testing of individual ticks is not generally recommended, tick data collected during field studies are useful in understanding the tickborne disease risk from a tick bite in Minnesota. Understanding when and where the risks for disease occurs can help patients avoid infection and can help providers understand the epidemiology of these important infections. MM

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FIGURE 2

Timeline of the discovery of the seven human pathogens transmitted by blacklegged ticks (Eisen and Eisen, 2018).

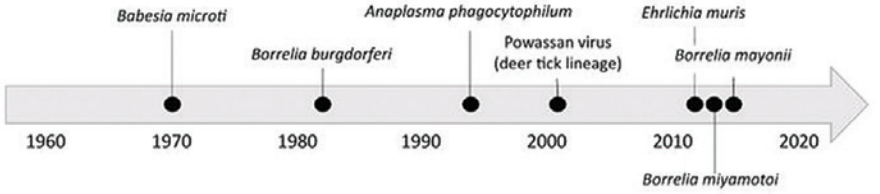
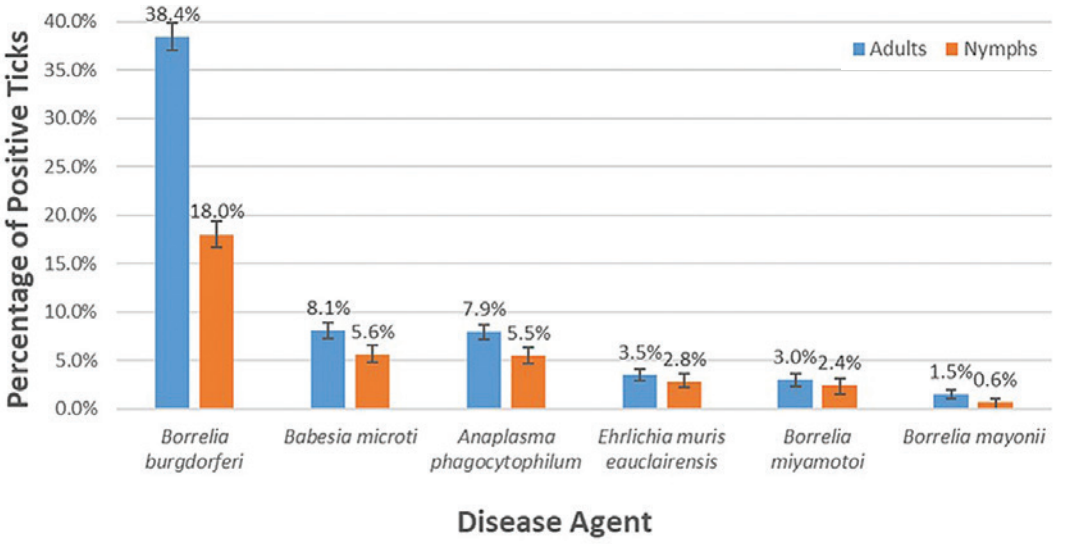


FIGURE 3

Average infection prevalence of blacklegged tick adults and nymphs for six different pathogens

Based on testing 7,634 ticks from Minnesota, 2005–2019 (MDH).



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For more information

MDH vectorborne disease epidemiologists are available for clinical consultations or facilitating testing at MDH or CDC by calling (651) 201-5414 or emailing health.bugbites@state.mn.us. MDH also offers complimentary tick-identification services using the mailing instructions listed on the online Submission Form for Tick Identification (https://www.health.state.mn.us/diseases/tickborne/ticksubform.pdf). For further information on vectorborne diseases in Minnesota and to earn free continuing education credit, on March 17, 2020, tune into a live webinar, "Ticks, Mosquitoes, and Our Health," designed specifically for health care providers in Minnesota. Registration and details are available on the MDH website www.health.mn.gov/ticks.