Tick-borne diseases are a growing public health concern across much of North America.\textsuperscript{1} Black-legged ticks, in particular, continue their range of expansion in the northeast and upper midwestern United States, bringing with them an impressive list of human pathogens. Dr Mead puts the consequences of this phenomenon into context in our first article, entitled, “Epidemiology of Lyme disease.” East of the Mississippi, the vector tick \textit{Ixodes scapularis}, commonly called the deer tick, may transmit seven different pathogens. In the western United States and Canada, \textit{Ixodes pacificus}, the western black-legged tick, transmits Lyme disease, \textit{Borrelia miyamotoi} infection, and anaplasmosis, but with far fewer reported cases overall. In this issue of the \textit{Infectious Disease Clinics of North America}, our authors provide expert reviews of the illnesses these ticks cause, with a particular emphasis on the most common, and, in some respects, most contentious, Lyme disease. Recognition of the seven diseases associated with black-legged tick infections is relatively recent, with the first clinical reports of babesiosis (1970) and Lyme disease (1977) followed in rapid succession by anaplasmosis (1994), deer tick virus (or Powassan virus lineage 2) encephalitis (2009), and infections due to \textit{Ehrlichia muris eauclairensis} (2009), \textit{B} \textit{miyamotoi} (2013), and \textit{Borrelia mayonii} (2016).

While the emphasis here is on pathogens transmitted by North American black-legged ticks, reference is also made to the differences in the epidemiology and clinical presentation of Lyme disease and other diseases transmitted by related \textit{Ixodes} tick species (ie, \textit{Ixodes ricinus} and \textit{Ixodes persulcatus}) in Europe and Asia.

The next five articles provide current, evidence-based reviews of the clinical features of Lyme disease, such as erythema migrans, neurologic sequelae of early disseminated Lyme disease, Lyme carditis, and Lyme arthritis as well as rare neurologic complications of late disease. The article by McCarthy and colleagues highlights aspects of the presentation and clinical course of Lyme disease and other diseases transmitted by black-legged ticks in children. The article by Kobayashi and Auwaerter provides a review of sero-diagnostics for Lyme disease, including a discussion of the recent Food and Drug Administration endorsement of a modified two-tier diagnostic strategy.
We also extend our discussion to less-well-understood aspects of *B burgdorferi* infection, including current research on possible causes for posttreatment Lyme disease symptoms (article by Marques). For clinicians and their patients, the medical and/or social framing and public representation of Lyme disease are often contradictory and confusing, sometimes to the detriment of good patient care. We have included a discussion of the challenges the infectious disease specialist must meet when the consultation includes discussion of disparate views and public misperceptions of the scope and treatment of Lyme disease (article by Dejace).

Four subsequent articles provide overviews of major infections other than *B burgdorferi* transmitted by these ticks: anaplasmosis (MacQueen and Centellas); babesiosis (Waked and Krause); Powassan virus encephalitis (Plantadosi and Solomon); and infection by *Borrelia mayonii* or *Borrelia miyamotoi* (Rodino and Pritt). In a minority of cases, these pathogens may be transmitted as coinfections, presumably from a single tick bite. The commonest of these coinfections involves *B burgdorferi* and *Anaplasma phagocytophilum* or *Babesia microti*.

Molecular detection led to recent discoveries of human infection by *B mayonii* and *E muris eauclairensis* in patient blood samples from the upper Midwest. Subsequent studies led to their detection in black-legged ticks in this region, the presumed vector for these infections. Over a fourth of the 100 or more identified cases of *E muris eauclairensis* occurred in immune-compromised patients, but the clinical presentation and course have otherwise been similar to that of anaplasmosis and infection by the most common cause of ehrlichiosis, *Ehrlichia chaffeensis*. Ehrlichiosis, which with the rare exception noted above, is transmitted by bites from the lone star tick, *Amblyomma americanum*, and is therefore not represented by a separate article in this issue.

Three species of ticks account for most transmission of human pathogens in the eastern and midwestern United States (Figure 1). The American dog tick (*Dermacentor variabilis*) is widely distributed, but its importance as a vector of disease (i.e., Rocky Mountain spotted fever, tularemia) varies regionally. Northward range expansion of the lone star tick (*A americanum*) in the northeast United States has led to a larger geographic overlap with the black-legged tick. The growing regional complexity of exposure to tick-transmitted pathogens, coupled with human mobility, leads to a challenging panoply of tick-transmitted diseases for consideration in the acutely ill patient. If a patient presents with a combination of fever and leucopenia and/or thrombocytopenia, the initial differential diagnosis may include anaplasmosis, ehrlichiosis, *B miyamotoi* or *B mayonii*, babesiosis, and rickettsial diseases. Knowledge of regional epidemiology, and potential patient risk factors often helps to narrow the possibilities.

Our understanding of the scope and public health burden of these diseases continues to evolve, and substantial gaps in our knowledge and ability to diagnose and treat them remain.

With the marked increase in incidence of anaplasmosis and babesiosis in the northeastern United States, it is notable that we have only one well-studied antibiotic available to treat severe anaplasmosis and just two combination therapies in use for babesiosis. Powassan encephalitis, caused by a lineage of Powassan virus or deer tick virus, is a severe and life-threatening infection for which no treatment is available.

Given increased attention to current gaps in diagnosis and treatment of infections transmitted by black-legged ticks, and rapid advances in the clinical science that underpins their diagnosis and treatment, we encourage our readers to use these state-of-the-art reviews as a framework for continuing assessment of new insights and strategies as they are published in the peer-reviewed literature.
Prevention remains a challenge. Effective control strategies for the tick vectors often require a nuanced understanding of local ecologic and epidemiologic realities. Behaviors to prevent tick bites can be helpful, but difficult to sustain. To date, no preventive vaccines for these diseases are approved, although research efforts are underway on this front. Through a combination of informed medical care for those ill with tick-borne infections, and implementation of existing and novel strategies for their prevention, the rise in public health burden of these infections can be stemmed.

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REFERENCES


