Clinical Insights

Increasing Risk for Tick-Borne Disease: What Should Clinicians Know?

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Many of the diverse tick-borne diseases (TBD) in the US appear to be increasing in incidence, leading to concern that factors such as climate change may create challenging scenarios. The 18 TBD and 1 syndrome that cause illnesses in US residents present varying public health burdens (**Table**). For US clinicians, the most common TBD of concern is Lyme disease (estimated at about 476 000 cases each year[1]), with babesiosis, human granulocytic anaplasmosis (HGA), Rocky Mountain spotted fever, monocytic ehrlichiosis (HME), and alpha gal allergy (ie, red meat allergy) annually accounting for hundreds to thousands of cases. The remaining TBD are either rare (≤50 cases/y) or diagnosed sporadically every few years, although some of these carry severe morbidity or mortality. TBD cases have increased within the last decade, but the cause for this trend is multifactorial. Changes in case reporting and case definitions have contributed to the increase,[2] as have improved diagnostic capacity, demographic shifts, urbanization, and an expansion in the range and local abundance of tick vectors.

For some TBD, notably babesiosis, HGA, and Powassan encephalitis, the aging US population (>60 years) has contributed to the increased reporting of cases. Age is a significant determinant for severe disease and an increasing aged population means more at risk. An increasing population of immunocompromised people is likely to be another factor.

Changes in tick range and abundance will increase the incidence of Lyme disease, babesiosis, and alpha gal syndrome. The deer tick (northern lineage of *Ixodes scapularis*) is the primary vector for Lyme disease and babesiosis and has expanded its range over the last 20 years.[3] Alpha gal syndrome, an allergy to red meat, is now commonly diagnosed where Lone Star ticks are found,[4] including sites in southern New England, Long Island, New Jersey, and south to Florida, to Texas, and northwards to Illinois. The abundance of deer ticks and Lone Star ticks depends on that of white-tailed deer, which have proliferated within the last 50 years. Urbanization and habitat fragmentation promote the local abundance of these ticks, be-

Table. Currently Recognized Tick-Borne Diseases in the United States

Disease	Agent	Tick vector	Incidence, cases/y	Trend	Distribution
Lyme disease	*Borrelia burgdorferi*	Deer tick, Western BLT	10 000-300 000	Rising	Northeast, Mid Atlantic, Midwest, Upper Midwest, Northern California/Pacific Northwest
Babesiosis	*Babesia microti*	Deer tick, Western BLT	100-500	Rising	Northeast, Mid Atlantic, Midwest, Upper Midwest
HGA	*Anaplasma phagocytophilum*	Deer tick, Western BLT	100-500	Rising	Northeast, Mid Atlantic, Midwest, Upper Midwest, Northern California/Pacific Northwest
Ehrlichiosis	*Ehrlichia muris*	Deer tick	<50	Stable	Upper Midwest
Borrelia miyamotoi disease/hard tick-borne relapsing fever	*Borrelia miyamotoi*	Deer tick, Western BLT	<50	Stable	Northeast, Mid Atlantic, Midwest, Upper Midwest, Northern California/Pacific Northwest
Powassan encephalitis	Powassan virus lineage II	Deer tick	<50	Rising	Northeast, Mid Atlantic, Midwest, Upper Midwest
RMSF	*Rickettsia rickettsii*	Dog/Wood tick	100-500	Rising[a]	Eastern, Midwest, Central, Southern, some areas of Southwest
Tularemia	*Francisella tularensis*	Dog/Wood tick, Lone Star tick	50-100	Stable	All US, but mainly southcentral states
Colorado tick fever	Coltivirus	Lone Star tick, Wood tick	<50	Stable	Western
Ehrlichiosis	*Ehrlichia chaffeensis, E ewingii*	Lone Star tick	100-500	Rising[a]	Eastern, Midwest, Southern
Alpha gal allergy	No infectious agent	Lone Star tick	10 000-20 000	Rising	Eastern, Midwest, Southern
STARI/Masters disease	*Borrelia lonestari*[a]	Lone Star tick	<50	Stable	Eastern, Midwest, Southern
Heartland virus disease	Phlebovirus	Lone Star tick	<50	Rising[a]	Eastern, Midwest, Southern
Bourbon virus disease	Thogotovirus	Lone Star tick	Sporadic	Stable	Eastern, Midwest, Southern
Rickettsiosis	*Rickettsia parkeri*	Gulf Coast tick	<50	Stable	Southern, focal in Northeast/Midwest
Babesiosis	*Babesia MO-1*	*Ixodes dentatus*[a]	Sporadic	Stable	Eastern, Midwest, and Pacific Northwest
Babesiosis	*Babesia duncani (WA1)*	*Dermacentor albipictus*	Sporadic	Stable	Northern California, Pacific Northwest
Powassan encephalitis	Powassan virus lineage I	*Ixodes cookii, I marxi*	Sporadic	Stable	Northern/Northeastern
Relapsing fever	*Borrelia hermsi, B turicatae*	*Ornithodoros hermsii, O turicatae*	<50	Stable	Western, Southern/Southcentral

Abbreviations: BLT, blacklegged tick; HGA, human granulocytic anaplasmosis; RMSF, Rocky Mountain spotted fever; STARI, Southern tick-associated rash illness.

[a] Uncertainty as to whether this agent, tick vector, or trend is correct.

cause deer are now common backyard wildlife, and difficult to manage in residential settings by hunting. TBD may be acquired in backyards as frequently as during hikes.

Climate change is often suggested as a main driver for increased TBD risk.[5] Climate change may allow ticks to populate sites previously thought too cold and also to extend the season of TBD risk. For example, the expansion of deer ticks and increased TBD risk into Canada has been attributed to more permissive temperature regimes. However, warmer temperatures may not be the primary driver of the expanding range of deer ticks.[6] In addition to climate change, reforestation, habitat fragmentation, and increases in deer population density are also contributing factors that have allowed the Lone Star tick to reinvade New England. Thus, multiple environmental factors influence current and future trends in TBD risk.

TBD diagnosis has improved within the last decade: patients and clinicians are more aware of TBD, informed by the internet and other media. Enhanced patient awareness can help inform clinical suspicion, but it can also lead to unnecessary antibiotic therapy or clinical testing.[7] Lyme disease diagnosis has been streamlined with improvements in serologic testing. The modified 2-tier test, which includes a screening enzyme-linked immunosorbent assay (EIA) with confirmation of a positive or borderline result by a second EIA using a specific recombinant antigen, eliminates subjective evaluation of immunoblots.[8] The Infectious Disease Society of America[9] has issued clear indications for requesting confirmatory or diagnostic testing, which should be consulted for more detail.[9] Testing for exposure to *Borrelia burgdorferi,* the bacteria that causes Lyme disease, should be reserved for tick-exposed patients presenting with fever without respiratory signs or symptoms, particularly during tick season (May to September) and within sites of known endemicity (New England to Virginia; upper Midwest; northern California). Those with a rash diameter greater than 5 cm that was observed to expand over days (erythema migrans, EM) do not require confirmatory testing because a clinical diagnosis of Lyme disease is established. Other TBD can be cotransmitted by deer ticks and should be considered in the differential diagnosis of the tick-exposed patient with fever and flu-like symptoms. Polymerase chain reaction (PCR) testing for *B microti* should be considered when a patient remains febrile after the first week of treatment with doxycycline because that parasite is not susceptible to this drug. All of the other deer tick-transmitted nonviral infections (HGA, ehrlichiosis, *B miyamotoi* disease) are susceptible to doxycycline.

There are no clinical laboratory options for directly detecting *B burgdorferi* from patient samples, either from the acutely ill or those with more persistent manifestations. Serology remains the only confirmatory test, and even with a highly sensitive and specific test, false positives are common in areas of low endemicity. Validated serologic tests cannot routinely confirm a diagnosis of extracutaneous (no EM) Lyme disease during the antibody window period, nor confirm bacterial clearance after antibiotic therapy. However, current validated laboratory methods (PCR and serology) for virtually all other TBD are routinely available. When ordered and interpreted correctly, tests are sensitive and specific for confirming a diagnosis. In addition, there are panel assays that capture evidence of infection by multiple tick-borne agents. Once validated for clinical use, these panels will greatly enhance diagnosis and management of the patient with fever who was exposed to a tick.

At the individual level, risk of TBD may be substantially reduced by tick awareness, prompt removal of attached ticks, use of repellants (DEET, picaridin, IR3535) as directed by the label, and wearing permethrin-treated clothing.[10] Patients in endemic areas should be educated about the need to seek medical advice for any fever without obvious cause during tick season. Prompt diagnosis and treatment enhances the likelihood of full recovery.

TBD risk and reported cases have increased in the last decade and will likely continue to increase, particularly in the eastern US. Environmental interventions such as deer management or habitat modification should be pursued, but simple personal protective measures also reduce risk of TBD.

ARTICLE INFORMATION

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