What's Eating You? *Ixodes* Tick and Related Diseases, Part 3: Coinfection and Tick-Bite Prevention

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PRACTICE **POINTS**

- As tick-borne diseases become more prevalent, the likelihood of coinfection with more than one *Ixodes*-transmitted pathogen is increasing, particularly in endemic areas.
- Coinfection generally increases the diversity of presenting symptoms, obscuring the primary diagnosis. The disease course also may be prolonged and more severe.
- Prevention of tick attachment and prompt tick removal are critical to combating the rising prevalence of tick-borne diseases.

Ixodes ticks are important vectors in the transmission of human disease. In endemic areas, infection with multiple tick-borne diseases may occur. In part 3 of this review, identification and management of coinfection with multiple pathogens is discussed. Methods of tick-bite prevention and tick removal also are discussed.

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Tick-borne diseases are increasing in prevalence, likely due to climate change in combination with human movement into tick habitats.[1-3] The *Ixodes* genus of hard ticks is a common vector for the transmission of pathogenic viruses, bacteria, parasites, and toxins. Among these, Lyme disease, which is caused by *Borrelia burgdorferi,* is the most prevalent, followed by babesiosis and human granulocytic anaplasmosis (HGA), respectively.[4] In Europe, tick-borne encephalitis is commonly encountered. More recently identified diseases transmitted by *Ixodes* ticks include Powassan virus and *Borrelia miyamotoi* infection; however, these diseases are less frequently encountered than other tick-borne diseases.[5,6]

As tick-borne diseases become more prevalent, the likelihood of coinfection with more than one *Ixodes*-transmitted pathogen is increasing.[7] Therefore, it is important for physicians who practice in endemic areas to be aware of the possibility of coinfection, which can alter clinical presentation, disease severity, and treatment response in tick-borne diseases. Additionally, public education on tick-bite prevention and prompt tick removal is necessary to combat the rising prevalence of these diseases.

Coinfection

Risk of coinfection with more than one tick-borne disease is contingent on the geographic distribution of the tick species as well as the particular pathogen's prevalence within reservoir hosts in a given area (Figure). Most coinfections occur with *B. burgdorferi* and an additional pathogen, usually *Anaplasma phagocytophilum* (which causes human granulocytic anaplasmosis [HGA]) or *Babesia microti* (which causes babesiosis). In Europe, coinfection with tick-borne encephalitis virus may occur. There is limited evidence of human coinfection with *B miyamotoi* or Powassan virus, as isolated infection with either of these pathogens is rare.

In patients with Lyme disease, as many as 35% may have concurrent babesiosis, and as many as 12% may have concurrent HGA in endemic areas (eg, northeast and northern central United States).[7-9] Concurrent HGA and babesiosis in the absence of Lyme disease also has been documented.[7-9] Coinfection generally increases the

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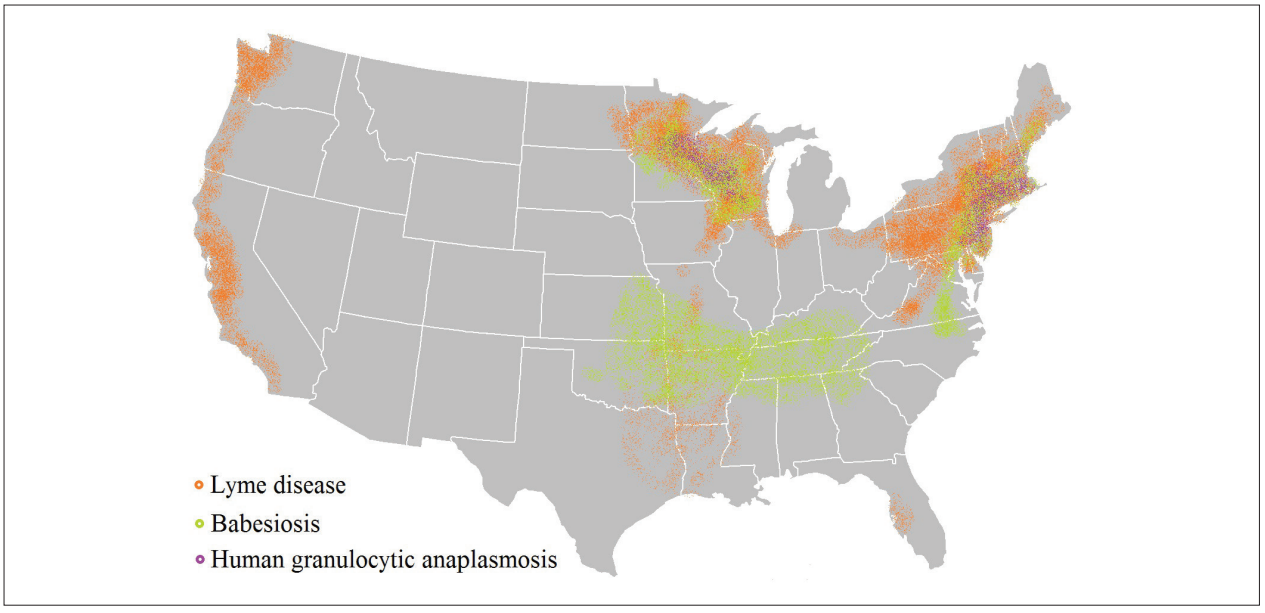

Geographic distribution of tick-borne diseases in the United States demonstrates regions at higher risk for coinfection.

diversity of presenting symptoms, often obscuring the primary diagnosis. In addition, these patients may have more severe and prolonged illness.[8,10,11]

In endemic areas, coinfection with *B burgdorferi* and an additional pathogen should be suspected if a patient presents with typical symptoms of early Lyme disease, especially erythema migrans, along with (1) combination of fever, chills, and headache; (2) prolonged viral-like illness, particularly 48 hours after appropriate antibiotic treatment; and (3) unexplained blood dyscrasia.[7,11,12] When a patient presents with erythema migrans, it is unnecessary to test for HGA, as treatment of Lyme disease with doxycycline also is adequate for treating HGA; however, if systemic symptoms persist despite treatment, testing for babesiosis and other tick-borne illnesses should be considered, as babesiosis requires treatment with atovaquone plus azithromycin or clindamycin plus quinine.[13]

A complete blood count and peripheral blood smear can aid in the diagnosis of coinfection. The complete blood count may reveal leukopenia, anemia, or thrombocytopenia associated with HGA or babesiosis. The peripheral blood smear can reveal inclusions of intra-erythrocytic ring forms and tetrads (the "Maltese cross" appearance) in babesiosis and intragranulocytic morulae in HGA.[12] The most sensitive diagnostic tests for tick-borne diseases are organism-specific IgM and IgG serology for Lyme disease, babesiosis, and HGA and polymerase chain reaction for babesiosis and HGA.[7]

Prevention Strategies

The most effective means of controlling tick-borne disease is avoiding tick bites altogether. One method is to avoid spending time in high-risk areas that may be infested with ticks, particularly low-lying brush, where ticks are likely to hide.[14] For individuals traveling in environments with a high risk of tick exposure, behavioral methods of avoidance are indicated, including wearing long pants and a shirt with long sleeves, tucking the shirt into the pants, and wearing closed-toe shoes. Wearing light-colored clothing may aid in tick identification and prompt removal prior to attachment. Permethrin-impregnated clothing has been proven to decrease the likelihood of tick bites in adults working outdoors.[15-17]

Topical repellents also play a role in the prevention of tick-borne diseases. The most effective and safe synthetic repellents are N,N-diethyl-meta-toluamide (DEET); picaridin; *p*-menthane-3,8-diol; and insect repellent 3535 (IR3535)(ethyl butylacetylaminopropionate).[16-19] Plant-based repellents also are available, but their efficacy is strongly influenced by the surrounding environment (eg, temperature, humidity, organic matter).[20-22] Individuals also may be exposed to ticks following contact with domesticated animals and pets.[23,24] Tick prevention in pets with the use of ectoparasiticides should be directed by a qualified veterinarian.[25]

Tick Removal

Following a bite, the tick should be removed promptly to avoid transmission of pathogens. Numerous commercial and in-home methods of tick removal are available, but not all are equally effective. Detachment techniques include removal with a card or commercially available radiofrequency device, lassoing, or freezing.[26,27] However, the most effective method is simple removal with tweezers. The tick should be grasped close to the skin surface

and pulled upward with an even pressure. Commercially available tick-removal devices have not been shown to produce better outcomes than removal of the tick with tweezers.[28]

Conclusion

When patients do not respond to therapy for presumed tick-borne infection, the diagnosis should be reconsidered. One important consideration is coinfection with a second organism. Prompt identification and removal of ticks can prevent disease transmission.

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