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New Hampshire Tickborne Disease (TBD) Update, 2019

Key Points and Recommendations:

1. Tickborne diseases (TBDs) are increasing nationally with Lyme disease accounting for 82% of all TBDs in the U.S.: <https://www.cdc.gov/mmwr/volumes/67/wr/mm6717e1.htm>.
2. NH continues to have a high-incidence of Lyme disease (*Borrelia burgdorferi* infection), and also has increasing numbers of *Anaplasma* and *Babesia* infections.
3. Two additional emergent TBDs are present in NH: Powassan virus and *Borrelia miyamotoi*.
 - *Borrelia miyamotoi* was identified in two NH residents in 2018. Infection usually presents with symptoms of fever, headache, myalgia, fatigue, and arthralgia.
 - Powassan was identified in three NH residents in 2013, 2016 and 2017. Infection often presents with neurologic illness, including meningoencephalitis.
4. Healthcare providers are encouraged to use the CDC's "Tickborne Diseases of the United States: A Reference Manual for Healthcare Providers" to aid with TBD diagnosis and testing: <https://www.cdc.gov/ticks/tickbornediseases/TickborneDiseases-P.pdf>.
5. Providers should consider testing for TBDs in patients presenting with compatible signs and symptoms, especially if there are risk factors for tick bites. Further details about disease-specific testing are outlined below in the "Diagnostic Testing" section.
6. Ticks and TBDs are very difficult to control due to the tick life cycle, abundant habitat, and animal reservoirs. Prevention needs to focus on personal protective measures (see information below). Additional educational resources can be found here: <https://www.dhhs.nh.gov/dphs/cdcs/lyme/publications.htm?>
7. Providers should report all TBDs, confirmed or suspected, to the Bureau of Infectious Disease Control at 603-271-4496 (after hours 603-271-5300).

Background Epidemiology:

New Hampshire has identified local transmission of five tickborne diseases (TBDs): Lyme disease (*Borrelia burgdorferi*), anaplasmosis (*Anaplasma phagocytophilum*), babesiosis (*Babesia spp.*), *Borrelia miyamotoi*, and Powassan virus, all of which are transmitted by the bite of the blacklegged tick (*Ixodes scapularis*). Lyme disease is the most common and has been identified in all 10 NH counties. Although the lifespan of this tick is two years, people are most likely to be infected between April and August when the aggressive nymph stage is active. Nymphs are very small (< 2mm) and difficult to see unless they become engorged with blood.

Symptoms:

Many TBDs present initially with nonspecific flu-like symptoms that may include fever, chills, malaise, headache, muscle and joint pains, and lymphadenopathy. Some may also present with

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other systemic symptoms (neurological, cardiovascular, gastrointestinal symptoms). Powassan virus infection, in particular, can progress to meningoencephalitis and ~10% of Powassan encephalitis cases are fatal. About half of those that survive clinical disease have permanent neurological sequelae.

For more information about specific clinical syndromes associated with the different TBDs, please review the following:

- Lyme disease: https://www.cdc.gov/lyme/signs_symptoms/index.html
- Anaplasmosis: <https://www.cdc.gov/anaplasmosis/symptoms/index.html>
- Babesiosis: <https://www.cdc.gov/parasites/babesiosis/disease.html>
- *Borrelia miyamotoi*: <https://www.cdc.gov/ticks/miyamotoi.html>
<https://www.ncbi.nlm.nih.gov/pubmed/26053877>
- Powassan: <https://www.cdc.gov/powassan/symptoms.html>

The CDC has published a reference for healthcare providers on the diagnosis and treatment of TBDs found in the US: <https://www.cdc.gov/ticks/tickbornediseases/index.html>.

Diagnostic Testing:

Providers should consider testing for TBDs in patients presenting with non-specific flu-like symptoms (i.e., fever, chills, headache, malaise, fatigue, myalgia, arthralgia), especially if there are risk factors for tick bites. Testing varies by organism:

- Lyme disease: diagnosed by detection of IgM or IgG antibodies in serum on a two-stage testing algorithm, including a confirmatory Western Blot. If symptom onset was more than a month prior, diagnosis relies on IgG positivity because an isolated positive IgM at this point is often a false-positive.
 - An erythema migrans rash (i.e., an expanding ring of erythema at the site of a tick bite that is usually 5 cm in diameter or larger) is classic for Lyme disease and no testing is necessary because serology is often negative at this early stage of disease; these patients should be treated for Lyme disease based on the presence of the erythema migrans rash alone.
- Anaplasmosis: diagnosed by PCR (most sensitive during the first week of illness), or a 4-fold increase in IgG antibody titers (first titer obtained the first week of illness followed by a second titer 2-4 weeks later); IgM tests alone should not be used for diagnosis.
- Babesiosis: diagnosed by peripheral blood smear (thick and thin blood smear) and PCR. An IgG antibody titer can be supportive evidence, but positive antibody tests do not differentiate between recent and past infection.
- *Borrelia miyamotoi*: diagnosed by PCR and antibody based tests (see attachment for more information).
- Powassan: diagnosed by finding virus-specific IgM antibodies in serum or cerebrospinal fluid (CSF); testing is performed through our State Public Health Laboratories.

Additional testing information:

- In patients presenting with early symptoms, antibody-based tests may be negative and repeat testing may be necessary several weeks after onset of illness. Testing for Lyme disease after an erythema migrans rash is usually not necessary.

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- Because antibody tests can remain positive for months or years after an infection (sometimes decades with Lyme disease), single antibody titers do not necessarily differentiate between recent and past infection, so clinical judgement is needed when ordering and interpreting tests.

For Lyme disease, anaplasmosis, and babesiosis providers should use their already established clinical testing networks. Powassan virus testing should be coordinated through New Hampshire's Public Health Laboratories by calling the Bureau of Infectious Disease Control. For testing information on *Borrelia miyamotoi*, please see attachment 1.

If you suspect another tickborne disease for which testing may be limited or not accessible, please contact the Bureau of Infectious Disease Control at 603-271-4496 (after hours 603-271-5300).

Treatment:

For guidelines on treatment of Lyme disease, anaplasmosis, and babesiosis, please see the most current IDSA guidelines: <https://academic.oup.com/cid/article/43/9/1089/422463>. The Lyme disease guidelines are currently being updated and may be released within the next year.

A more recent review (published in JAMA 2016) provides an update on diagnosis, treatment, and prevention of Lyme disease, anaplasmosis and babesiosis, and may also be a helpful resources for clinicians: <https://www.ncbi.nlm.nih.gov/pubmed/27115378>.

Newer evidence suggests that early Lyme disease can be treated with doxycycline for as short as 10 days (<https://www.cdc.gov/lyme/treatment/index.html>). Antibiotic treatment durations beyond 3-4 weeks (duration is dependent on clinical syndrome) are not indicated, and the need for re-treatment is rare. A minority of patients who undergo treatment for Lyme disease will report persistent symptoms of fatigue, musculoskeletal pain, and neurological or cognitive symptoms; this heterogeneous syndrome has been termed Post-Lyme Disease Syndrome (PLDS), but persistent infection with *Borrelia burgdorferi* has not been found to be a cause. Antibiotic therapy beyond the recommended durations has not been shown to have long-term benefit in numerous randomized clinical trials. Additionally, longer durations of therapy beyond the recommend courses have been shown to have potential adverse health consequences:

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5657841/>
- <https://academic.oup.com/cid/article/67/10/1568/4972864>

Data on treatment for *Borrelia miyamotoi* is limited, but case reports suggest treatment is likely similar to that of Lyme disease. In patients diagnosed with *Borrelia miyamotoi*, we suggest consultation with an Infectious Disease specialist.

There is no specific treatment for Powassan infection and care is supportive.

The CDC has published diagnosis and management guidelines for anaplasmosis and other rickettsial diseases in the May 13, 2016 Morbidity and Mortality Weekly Report (MMWR): <https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6502.pdf>.

Prevention Messages for Patients:

- Avoid tick-infested areas when possible and stay on the path when hiking to avoid brush.
- Wear light-colored clothing that covers arms and legs so ticks can be more easily seen.
- Tuck pants into socks before going into wooded or grassy areas.

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- Apply insect repellent (20-30% DEET) to exposed skin. Other repellent options may be found here: https://www.epa.gov/insect-repellents/find-insect-repellent-right-you#search_tool
- Permethrin is highly effective at repelling ticks on clothing; it is not meant for use on skin.
- Outdoor workers in NH are at particular risk of tickborne diseases and they should be reminded about methods of prevention.
- Perform daily tick checks to look for ticks on the body, especially warm places like behind the knees, the groin, and the back and neck.
- Pets returning inside may also bring ticks with them. Performing tick checks and using tick preventatives on pets will minimize this occurrence.
- Encourage landscape or environmental management to reduce tick habitat and encounters.
- Shower soon after returning indoors to wash off any unattached ticks and check clothes for any ticks that might have been carried inside. Placing dry clothes in the dryer on high heat for ten minutes (one hour for wet or damp clothes) effectively kills ticks.
- Remove ticks promptly using tweezers. Tick removal within 36 hours of attachment can prevent Lyme disease, but transmission of other tick-borne diseases can occur with shorter periods of attachment time.
- Monitor for signs and symptoms of tickborne diseases for 30 days after a tick bite. Patients should contact their healthcare provider if symptoms develop.

There are several resources available to educate your patients about how to reduce their risk of tick encounters and tick bites.

State of New Hampshire Tickborne Disease Webpage:
<https://www.dhhs.nh.gov/dphs/cdcs/lyme/>

State of New Hampshire Tickborne Disease Prevention Plan:
<https://www.dhhs.nh.gov/dphs/cdcs/lyme/documents/tbdpreventionplan.pdf>

University of New Hampshire Cooperative Extension's Biology and Management of Ticks in New Hampshire:
https://extension.unh.edu/resources/files/Resource000528_Rep1451.pdf

Connecticut Agricultural Experiment Station's Tick Management Handbook:
<https://portal.ct.gov/-/media/CAES/DOCUMENTS/Publications/Bulletins/b1010pdf>

CDC Tick Bite Prevention:
<https://www.cdc.gov/ticks/avoid/index.html>

Reporting Tickborne Diseases:

Clinicians should report suspected and confirmed cases of all tick-borne diseases to the Bureau of Infectious Disease Control by submission of a case report form or by calling 603-271-4496 (after hours 603-271-5300). Please be sure to record the date of symptom onset and exposure history. Completed forms can be mailed or faxed to the Bureau of Infectious Disease Control at 29 Hazen Drive, Concord, NH, 03301 (Fax: 603-271-0545).

Please utilize the following case report forms:

- Lyme disease: <http://www.dhhs.nh.gov/dphs/cdcs/documents/lymediseasereport.pdf>
- Tickborne Rickettsial Diseases: https://www.cdc.gov/ticks/forms/2010_tbrd_crf.pdf
- Babesia: <https://www.cdc.gov/parasites/babesiosis/resources/50.153.pdf>
- Other tickborne diseases:
<https://www.dhhs.nh.gov/dphs/cdcs/documents/diseasereport.pdf>

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For any questions regarding the contents of this message, please contact NH DHHS, DPHS, Bureau of Infectious Disease Control at 603-271-4496 (after hours 603-271-5300).

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Originating Agency: NH Department of Health and Human Services, Division of Public Health Services

Attachments:

1. *Borrelia miyamotoi* lab testing table,
2. Lyme disease prophylaxis guidelines

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ATTACHMENT 1

***Borrelia miyamotoi* lab testing**

Confirmation of a diagnosis relies on 1) the use of polymerase chain reaction (PCR) tests that detect DNA from the organism (preferred) or 2) antibody-based tests. Both types of tests are under development and not widely commercially available but can be ordered from a limited number of CLIA-approved laboratories.

Less sensitive and specific methods for detecting *B. miyamotoi* and agents of tickborne relapsing fever include identification of spirochetes in peripheral blood films and spinal fluid preparations and serologic testing.

Lab	Test	Specimen	Volume	Storage	Shipping	Turnaround time	Comments
Imugen	<i>Borrelia</i> PCR	CSF, Synovial Fluid or EDTA Whole Blood	2.0 ml (0.5 ml minimum)	Refrigerate	Ambient	24-48 hours from receipt	Doesn't differentiate between <i>B. burgdorferi</i> and <i>B. miyamotoi</i>
Imugen	<i>B. miyamotoi</i> serology (IgM and IgG)	Serum or CSF	2.0 ml (0.5 ml minimum)	Refrigerate	Ambient	24-48 hours from receipt	Most patients acutely symptomatic with <i>Borrelia miyamotoi</i> infection are seronegative. If the clinical history strongly suggests infection, collect/submit a convalescent specimen 3-4 weeks later.
Mayo	<i>B. miyamotoi</i> PCR	EDTA whole blood	1.0 ml (0.3 ml minimum volume)	Refrigerate	Ambient	Unknown	
Quest	<i>B. miyamotoi</i> PCR	CSF, synovial fluid, whole blood (EDTA)	1.0 ml (0.3 ml minimum volume)	Refrigerate	Ambient	Unknown	

ATTACHMENT 2

Tick bites and single-dose doxycycline as prophylactic treatment for Lyme disease in NH (Based on the 2006 Infectious Disease Society of America guidelines)

A **single** dose of doxycycline (200 mg) may be offered to adult patients and to children ≥ 8 years of age (4 mg/kg up to a maximum dose of 200 mg) when ALL of the following conditions exist:

1. The attached tick is a blacklegged tick (deer tick, *Ixodes scapularis*). Tick identification is most accurately performed by an individual trained in this discipline. However, blacklegged ticks are very common in southeastern and central New Hampshire and there are many images available online to help identification.

AND

2. The tick has been attached for at least 36 hours. This determination can be made by asking the patient about outdoor activity in the time before the tick bite was noticed to estimate attachment time, or by asking about degree of engorgement. Unengorged (unfed) blacklegged ticks are typically flat. Any deviation from this “flatness,” which is often accompanied by a change in color from brick red to a gray or brown, is an indication that the tick has been feeding.

AND

3. Prophylaxis can be started within 72 hours of the time that the tick was removed. This time limit is suggested because of an absence of data on the efficacy of prophylaxis for tick bites following longer time intervals after tick removal.

AND

4. Doxycycline prophylaxis is not contraindicated. Doxycycline is relatively contraindicated in pregnant women and children less than 8 years old. The other common antibiotic treatment for Lyme disease, amoxicillin, is not recommended for prophylaxis because of an absence of data on an effective short-course prophylaxis regimen, the likely need for a multi-day regimen along with its possible adverse effects, and the excellent efficacy of treatment if signs or symptoms do develop.

Note that single-dose doxycycline is not 100% effective for prevention of Lyme disease; consequently, patients who receive this therapy should monitor themselves for the development of Lyme disease as well as other tickborne diseases including anaplasmosis and babesiosis.

Adapted from: Wormser GP, et al. The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America. *Clinical Infectious Diseases*; 2006; 43:1089 –1134. Available online at: <http://cid.oxfordjournals.org/content/43/9/1089.full>