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Lyme Disease and Other Tickborne Diseases in New Hampshire

Key Points and Recommendations:

1. New Hampshire continues to have one of the highest rates of Lyme disease in the nation and ~60% of blacklegged ticks sampled in NH are infected with *Borrelia burgdorferi*, the bacterium that causes Lyme disease.
2. Prevent tickborne disease through the use of DEET insect repellent, wearing long pants and sleeves outdoors, and daily tick checks followed by prompt removal of any ticks.
3. Healthcare providers can diagnose early Lyme disease when an erythema migrans rash is present based solely on clinical presentation because diagnostic serologies (including IgM) may not yet be positive.
4. Report all tickborne diseases, confirmed or suspected, to the NH DPHS Bureau of Infectious Disease Control at 603-271-4496 (after hours 1-800-852-3345, x5300).

Background:

Lyme disease (*Borrelia burgdorferi*), babesiosis (*Babesia microti* and other species), anaplasmosis (*Anaplasma phagocytophilum*), and Powassan virus are transmitted by the bite of the deer tick (*Ixodes scapularis*), also known as the blacklegged tick. Although these ticks have a 2-year life cycle, the greatest risk for human acquisition of tickborne diseases is between May and August when the aggressive nymph stage of the blacklegged tick is active. Nymphs are very small (< 2mm) and easy to miss unless they become engorged with blood.

Epidemiology:

Over the last decade, reported Lyme disease cases have increased significantly in NH. In 2014, there were an estimated 1,415 new cases of Lyme disease in NH. The highest disease rates occurred in Rockingham, Strafford and Hillsborough counties. Compared to national data from 2013 (the most recent available), the Centers for Disease Control and Prevention (CDC) reports that NH had the second highest incidence rate of Lyme disease in the United States (100.0 confirmed cases per 100,000 population). Only Vermont had a higher rate of reported disease in 2013. NH Lyme disease data and maps by county and town from 2006-2013 are available at <http://www.dhhs.nh.gov/dphs/cdcs/lyme/publications.htm>. In 2014, 130 cases of anaplasmosis, and 40 cases of babesiosis were reported. The only case of locally-acquired Powassan virus infection was reported in 2013.

The risk of Lyme disease for any individual depends on their outdoor activities and the abundance of infected ticks. Tick surveillance performed during 2007-2010 in NH counties showed that >50% of ticks tested in most counties were infected with the bacteria causing Lyme disease with the exception of slightly lower rates (40%) in Belknap and Carroll counties, and very low numbers of ticks collected in Coos County, precluding prevalence assessment. *Babesia* and *Anaplasma* have been detected in ticks in NH, though reliable prevalence data for these pathogens in ticks is not available.

Lyme Disease

Clinical Presentation: Lyme disease is caused by the bacteria *Borrelia burgdorferi*. In approximately 70-80% of patients, illness first manifests with a red “bull’s-eye” rash that expands slowly, often with central clearing (erythema migrans [EM]), within the first 30 days after a tick bite. At this stage, serologic testing is often negative and treatment should be based on clinical diagnosis. Early treatment generally leads to complete and rapid recovery, and may prevent seroconversion (so that later testing is negative). Early systemic manifestations may also include malaise, fever, headache, stiff neck, muscle and joint pains, and lymphadenopathy. Patients who are not treated in the early stage of infection may develop a variety of syndromes weeks to months after onset of symptoms, including aseptic meningitis, encephalitis, cranial neuritis, and cardiac abnormalities such as heart block or myopericarditis. Without treatment, a patient may develop chronic or intermittent episodes of arthritis or neurological symptoms months to years after onset.

In 2013, CDC released a report of three Lyme disease carditis cases in the northeastern United States that resulted in sudden cardiac death. While rare, these cases highlight the importance of prompt diagnosis and treatment for Lyme disease. Healthcare providers should ask patients with suspected Lyme disease about cardiac symptoms and obtain an electrocardiogram (EKG) if indicated. Healthcare providers should also ask patients with unexplained heart block about possible exposure to infected ticks. The full report on this rare clinical presentation is available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6249a1.htm>

Testing: Laboratory testing should be used to support clinical suspicion of disease based on presenting signs and symptoms and a history of possible exposure to infected ticks. Within 4 weeks of infection, *Borrelia burgdorferi* antibodies can be detected using FDA-approved serologic testing. The CDC currently recommends a two-stage testing approach with the first step involving an ELISA as the screening test, and if positive or equivocal confirmed by Western Blot. A Western Blot should not be run if the initial ELISA test is negative. A patient is considered to have a positive Lyme Western Blot test if 2 of 3 IgM bands are reactive (24, 39, 41 kDa) OR if 5 of 10 IgG bands are reactive (18, 21, 28, 30, 39, 41, 45, 58, 66, 93 kDa). An isolated positive IgM (without a positive IgG) in a patient with tick exposure more than 8 weeks prior is likely to be a false positive test, since IgG antibodies are produced within 4-8 weeks after exposure. Only laboratories with validated and FDA-approved testing methods for Lyme ELISA and confirmatory Western blot should be used for diagnosis of disease.

Treatment: The Infectious Disease Society of America (IDSA) updated guidelines for tickborne diseases in 2006. The IDSA guidelines were confirmed by an independent panel (recommendations published in 2010) and are the best available synthesis of the medical literature on the diagnosis and treatment of Lyme disease. A summary of treatment recommendations based on these guidelines is attached and the full guidelines are available at: <http://cid.oxfordjournals.org/content/43/9/1089.full.pdf+html>

Antibiotic Prophylaxis: Based on the high prevalence of Lyme disease in NH, providers can consider prescribing single dose doxycycline prophylaxis (200 mg) for patients who meet all four criteria outlined in the attached Lyme disease prophylaxis guidelines. 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. It is also a reasonable course of action to ask the patient to monitor the bite site and call back for further medical evaluation if a rash or any systemic symptoms develop. Testing the tick for tickborne infectious agents is available in certain labs but is not recommended for guiding individual prophylaxis or treatment decisions.

Anaplasmosis

Clinical Presentation: Anaplasmosis (human granulocytic anaplasmosis [HGA], previously known as human granulocytic ehrlichiosis) is an infection of neutrophils caused by the rickettsial bacteria *Anaplasma phagocytophilum*, and is transmitted by the blacklegged tick. Symptoms typically occur 5-21 days following the bite of an infected tick, and may include fever, chills, headache, and myalgia. Some people, particularly elderly persons or those with weakened immune systems, may have a more severe illness. Laboratory abnormalities may include leukopenia, lymphopenia, thrombocytopenia, and mild elevation in liver enzyme levels.

Testing: Identification of the characteristic intragranulocytic inclusions on blood smear is the most rapid diagnostic method, but requires lab expertise. Acute and convalescent antibody assays are the most sensitive diagnostic method.

Treatment: Doxycycline is the first line therapy for anaplasmosis (see attached treatment guideline table). If co-infected with Lyme disease, doxycycline will treat both infections. Antibiotic therapy should not be delayed in a patient with a suggestive clinical presentation pending the results of diagnostic testing.

Babesiosis

Clinical Presentation: Babesiosis is caused by the intraerythrocytic protozoan *Babesia microti* (or other *Babesia* species) and is transmitted by the blacklegged tick. Clinical presentation can range in severity from asymptomatic to a rapidly fatal illness. Most people infected with *Babesia* present with a viral-like illness with fever, chills, sweats, myalgia, arthralgias, anorexia, nausea, vomiting, and/or fatigue within 1-6 weeks after infection. Severe and fatal cases most often occur in patients who are older or have a weakened immune system, particularly those without a spleen. Complications of *Babesia* can include acute respiratory failure, congestive heart failure, renal failure, and disseminated intravascular coagulation. Rare cases of relapsing disease have been reported. Laboratory abnormalities may include findings of a hemolytic anemia, thrombocytopenia, elevated liver enzymes, and renal dysfunction.

Testing: Diagnosis is based on identification of *Babesia* parasites in a blood smear or by PCR amplification of babesial DNA.

Treatment: Babesiosis can be successfully treated with antimicrobial therapy (see attached treatment guideline table). RBC exchange transfusion may also be needed in cases with a high parasitemia ($\geq 10\%$), or in persons with severe clinical disease.

Powassan Virus Infection

Clinical Presentation: Powassan (POW) virus is an RNA virus of the genus *Flavivirus* with an incubation period of 7-30 days following bite of an infected tick. Although most infections are subclinical, symptoms may include fever, headache, vomiting, and generalized weakness that can progress to meningoencephalitis. About half of survivors have permanent neurological sequelae.

Testing: Cerebrospinal fluid (CSF) findings include normal or mildly elevated protein, normal glucose concentration, and lymphocytic pleocytosis typically with <500 white blood cells/mm³. Brain magnetic resonance imaging (MRI) reveals changes consistent with microvascular ischemia or demyelinating disease in the parietal or temporal lobes. Electroencephalography (EEG) shows generalized slow wave activity.

Diagnosis can be made by the detection of POW virus-specific IgM antibody in serum or CSF, combined with a consistent clinical presentation. Currently, POW virus testing is not commercially available but can be arranged through the NH Public Health Laboratories.

Treatment: Treatment is supportive.

Reporting Tickborne Diseases:

Clinicians should report suspected and confirmed cases of Lyme disease, anaplasmosis, babesiosis, and Powassan virus infection to the NH DPHS Bureau of Infectious Disease Control at 603-271-4496 (after hours 1-800-852-3345, x5300). When filling out the Lyme disease case report form, it is important to record the date of symptom onset because this information is used to determine whether a case meets the CDC case definition for surveillance. A copy of the most recent Lyme disease case report form is attached. The case report form is also available at: <http://www.dhhs.nh.gov/dphs/cdcs/documents/lymediseasereport.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.
- Apply insect repellent (20-30% DEET) to exposed skin. Other repellent options may be found here: <http://www.epa.gov/pesticides/insect/choose.htm>
- Outdoor workers in NH are at particular risk of tickborne diseases and they should be reminded about methods of prevention.
- Do 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.
- Shower soon after returning indoors to wash off any unattached ticks and check clothes for any ticks that might have been carried inside. Placing clothes in the dryer on high heat for an hour effectively kills ticks.
- Remove ticks promptly using tweezers. Tick removal within 36 hours of attachment can prevent disease.
- Monitor for signs and symptoms of tickborne diseases for 30 days after a tick bite. Patients should contact their healthcare provider if symptoms develop.

Additional background information about tickborne diseases and prevention can be found in the State of New Hampshire Tickborne Disease Prevention Plan at:

<http://www.dhhs.nh.gov/dphs/cdcs/lyme/documents/tbdpreventionplan.pdf>

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 1-800-852-3345 ext.5300).

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From: Benjamin Chan, MD, MPH- State Epidemiologist
Originating Agency: NH Department of Health and Human Services, Division of Public Health Services

Attachments: 1. Tickborne diseases treatment table, 2. Lyme disease prophylaxis guidelines, 3. Lyme disease case report form

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ATTACHMENT 1

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 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>

ATTACHMENT 2

**NH DPHS Treatment Recommendations for Tickborne Diseases
 Summary of 2006 Infectious Disease Society of America Guidelines**

Disease	Treatment Regimens for Adults	Treatment Regimens for Children
Lyme disease	Oral Options	
	Doxycycline 100 mg PO twice daily*	Doxycycline 4 mg/kg/day in 2 divided doses (max 100 mg/dose) only if 8 years and older
	Amoxicillin 500 mg PO three times daily	Amoxicillin 50 mg/kg/day in 3 divided doses (max 500 mg/dose)
	Cefuroxime axetil 500 mg PO twice daily	Cefuroxime axetil 30 mg/kg/day in 2 divided doses (max 500 mg/dose)
	Parenteral options	
	Preferred: Ceftriaxone 2g IV Once daily	Preferred: Ceftriaxone 50-75 mg/kg IV Once daily (max 2g)
	Alternative: Cefotaxime 2g IV every 8 hrs	Alternative: Cefotaxime 150-200 mg/kg/day IV in 3-4 divided doses (max 6g/day)
	Alternative: Penicillin G 3-4 million units IV every 4 hrs	Alternative: Penicillin G 200,000-400,000 U/kg/day divided every 4 hr (max 18-24 million units per day)
Note: Choice of regimen, route and length of treatment for Lyme disease depends on symptoms and stage of disease.		
Anaplasmosis	<p>Doxycycline 100 mg PO twice daily for 10 days*</p> <p>Alternatives:</p> <p><u>mild disease:</u> Rifampin 300 mg PO twice a day for 7-10 days (note: rifampin is not effective for Lyme disease. If coinfection exists, Amoxicillin or Cefuroxime would need to be <i>added</i> for treatment of Lyme disease as well)</p>	<p>8 years and older: Doxycycline 4 mg/kg/day PO in 2 divided doses for 10 days (max 100 mg/dose)</p> <p>Under 8 years old (without concomitant Lyme disease): <u>Severe disease:</u> Doxycycline (dose as above) for 4-5 days, with close monitoring after for resolution of symptoms.</p> <p><u>Mild disease:</u> Rifampin 10 mg/kg PO twice daily (max 300 mg/dose) for 7-10 days, with close monitoring after for resolution of symptoms.</p> <p>Under 8 years old (with concomitant Lyme disease): --If Doxycycline is used for 4-5 days (dose as above) then complete a 14 days course with Amoxicillin OR Cefuroxime axetil (doses as above) after treating with doxycycline. --If Rifampin is used for mild disease, Amoxicillin or Cefuroxime would need to be <i>added</i> for treatment of Lyme disease as well.</p>
Babesiosis	Atovaquone 750 mg PO every 12 hrs + Azithromycin 500-1000 mg on day 1, then 250 mg PO daily thereafter	Atovaquone 20 mg/kg PO every 12 hrs (max 750 mg/ dose) + azithromycin 10 mg/kg/day once daily on day 1 (max 500 mg/dose) then 5 mg/kg once daily (max

	<p><u>Severe disease:</u> Clindamycin 300-600 mg IV every 6 hrs (or 600 mg PO every 8 hrs) + Quinine 650 mg PO every 6-8 hrs. Consider exchange transfusion.</p> <p>Note: patients with coinfection with <i>B. burgdorferi</i> or <i>A. phagocytophilum</i> should be treated with additional antibiotics as described above.</p>	<p>250 mg/dose) thereafter.</p> <p><u>Severe disease:</u> Clindamycin 7-10 mg/kg every 6-8 hrs PO or IV (max 600 mg/dose) + Quinine 8 mg/kg PO every 8 hrs (max 650 mg/dose). Consider exchange transfusion.</p> <p>Note: patients with coinfection with <i>B. burgdorferi</i> or <i>A. phagocytophilum</i> should be treated with additional antibiotics as described above.</p>
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***NOTE: For pregnant women, doxycycline should not be used.**

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