

Guidance for Primary Care and Emergency Medicine Providers in the Management of Lyme Disease in Nova Scotia

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Health and Wellness

May, 2020

ISBN: 978-1-55457-967-9

Executive Summary:

This document has been reviewed and there are not any notable changes to highlight for 2020
There are no changes to the Lyme Disease Estimated Risk Areas Map for 2020.

In 2016, the Public Health Agency of Canada (PHAC) modified its surveillance case definition for Lyme disease. The new case definition refers to "risk areas" for acquiring Lyme disease, instead of "endemic areas for Lyme disease." Accordingly, IDEG updated its *Statement for Managing Lyme disease in Nova Scotia* in 2017. The entire province is considered an at-risk area, with certain areas in the province at moderate or higher risk of Lyme disease based on current tick and human data, and other areas at lower risk (<https://novascotia.ca/dhw/cdpc/lyme.asp>). The IDEG endorses the Infectious Diseases Society of America (IDSA) guidelines (2006) for the prevention and management of Lyme disease.¹ Although the guideline is still in the process of being updated, more recent review articles^{2,3} and the National Institute for Health and Care Excellence (NICE) guideline published in 2018 (<https://www.nice.org.uk/guidance/ng95>) are generally consistent with the IDSA diagnosis and management recommendations. IDEG continues to monitor developments in the management of Lyme disease and will update its guidance as new evidence becomes available. No management changes are recommended for this 2020 version.

We highlight the following key points pertinent to the management of tick bites and Lyme disease in Nova Scotia (NS):

- Being at risk for Lyme disease requires outdoor activity in areas of long grass, brushes, woods, including urban parks and gardens.
- The most reliable way to avoid getting Lyme disease is to prevent deer/blacklegged tick bites (see prevention measures (<https://novascotia.ca/dhw/cdpc/lyme.asp>)).
- Immediate and correct removal of an attached blacklegged tick is key to preventing the transmission of Lyme disease.
- Analysis of the blacklegged tick for the presence of infection with *Borrelia burgdorferi* does not reliably predict the risk of developing Lyme disease after a bite and is not recommended for management decisions.
- The risk of Lyme disease after a bite from an infected tick is low. Two of the most widely cited studies reported that the risk of Lyme disease in people who were found to have a blacklegged tick bite ranged from 1.2%-3.2%.^{4,5} Further, most studies have found that the infected tick needs to be attached for at least 24 hours before it can transmit disease and the risk of transmission increases after 36 hours of attachment.¹
- Routine use of antimicrobial prophylaxis for prevention of Lyme disease after a recognized blacklegged tick bite is not recommended but may be offered in specific circumstances (see [Prophylaxis section](#)).
- Serologic testing using the two-tiered algorithm described by the Centers for Disease Control and Prevention (CDC) and the Canadian Public Health Laboratory Network (CPHLN) is currently the only recommended method for making a serological diagnosis of Lyme disease.
- Sending specimens to laboratories that **1)** use interpretive criteria that are different from those of the CDC and Canadian Public Health laboratories, **2)** bypass the ELISA and use immunoblots alone, or **3)** perform IgM testing in the setting of suspected chronic infection is NOT recommended as they produce false positive results in up to 50% of cases.⁶
- Laboratory testing is not necessary in patients presenting with the typical erythema migrans (EM) rash (> 5cm) who live in or have travelled to an area where there is a risk for Lyme disease (see *Lyme Disease Estimated Risk Areas Map*: <https://novascotia.ca/dhw/CDPC/lyme.asp>) during Lyme season (anytime temperature reaches > 4°C, with the greatest risk of transmission during summer months). In this situation, the diagnosis can be made based on the presence of EM alone and treatment started.
- Patients with symptoms and signs suggestive of early disseminated and late Lyme disease should have serologic testing.

- 95 percent of cases of Lyme disease are cured with 10-28 days of oral antibiotics.
- Studies have demonstrated that longer-term antibiotic treatment is no more effective than the standard recommended course of treatment and may be associated with complications.⁷ Longer-term antibiotics are not recommended.
- Patients who have lingering symptoms after the standard recommended treatment for Lyme disease should be re-evaluated to determine if the diagnosis of Lyme disease was accurate or if they may have a different or new illness.

The following is a summary statement on Lyme disease, including appropriate laboratory testing and treatment.

Introduction:

Lyme disease is the most common tick-borne transmitted infection in NS. Factors considered by the NS Department of Health and Wellness in calling areas higher, moderate, and lower risk for Lyme disease include the presence of blacklegged ticks in the area, active and passive surveillance for the presence of *B. burgdorferi* in blacklegged ticks, and the incidence of Lyme disease in humans. The estimated risk of Lyme disease varies across Nova Scotia and is represented on the Lyme Disease Estimated Risk Areas Map available at <https://novascotia.ca/dhw/CDPC/lyme.asp>.

Blacklegged ticks are also capable of transmitting Powassan virus, *Anaplasma*, and *Babesia*. However, to date there have been only 2 cases of human granulocytic anaplasmosis (HGA) acquired in NS and no human cases of babesiosis or Powassan infection.

The clinical presentation of Lyme disease varies and is divided into early and late disease. Early disease usually presents with an acute illness characterized by the presence of localized EM. This is sometimes followed by dissemination with multiple secondary annular lesions and systemic symptoms including fever, arthralgias, headache, and lymphadenopathy. Other manifestations of early disseminated infection can include Lyme carditis with conduction abnormalities and neuroborreliosis (neurologic Lyme), which may present as aseptic meningitis or with cranial nerve involvement (especially Bell's palsy). Late disease most commonly presents as a chronic arthritis and, more rarely, chronic neuroborreliosis.

Depending on the stage and extent of the illness, there are differences in the investigations, treatment, and follow-up required.

Diagnosis of Lyme Disease:

Laboratory testing for Lyme disease in NS is done by the microbiology laboratory at the Queen Elizabeth II Health Sciences Centre (QE II HSC). It consists of first screening with an ELISA-based method to look for the presence of antibodies to specific *B. burgdorferi* proteins (VlsE1/pepC10 peptides). Specimens that screen positive or are indeterminate are forwarded to the National Microbiology Laboratory (NML) in Winnipeg for immunoblot testing, of which Western blot is one method. This "two-tier" testing is consistent with the current recommendations from both the United States (US) CDC and the CPHLN. The immunoblots are scored based on the presence or absence of a certain number of bands. The criteria used by the CDC have been well validated. Current diagnostic guidelines apply to both pediatric and adult patients.

The sensitivity of this testing approach depends on the stage of infection. In early, localized Lyme disease with EM, the sensitivity of the two-tier testing is less than 50%, but increases with the duration of infection.^{9,10,11} The sensitivity of testing for patients with early neuroborreliosis or Lyme arthritis in one study was 87% and 96% respectively.⁹ History and clinical manifestations are important for estimating the likelihood of Lyme disease before the physician decides on proceeding with testing. If the pre-test probability for Lyme disease is low, there is a much higher likelihood that the positive result is a false positive test.

IDEG Recommends:

1. Physicians need to be aware that the diagnosis of early Lyme disease with localized EM in season (anytime temperature reaches $> 4^{\circ}\text{C}$, with the greatest risk of transmission during summer months) is a clinical one. Serological tests have poor sensitivity during the first four weeks of infection and are not recommended for management decisions.
2. Patients with an EM-like rash out of season (regardless of exposure area) should undergo serological testing using the two-tiered algorithm. If the test result is negative, serological testing should be repeated in 4-6 weeks.
3. Patients presenting with a nonspecific febrile illness, but no EM-like rash, AND a recent, clear exposure in an area at moderate or higher risk for Lyme disease (<https://novascotia.ca/dhw/CDPC/lyme.asp>) should be tested and monitored for other symptoms suggestive of Lyme disease. Repeat testing in 4-6 weeks is suggested if there are still concerns that the patient has Lyme disease.
4. Patients presenting with only a nonspecific febrile illness and exposure in an area at lower risk for Lyme disease should NOT be tested.
5. Patients with signs and symptoms suggestive of early disseminated and late Lyme disease should undergo serologic testing using the two-tiered algorithm. These presentations take time to manifest and may present out of season.
6. Patients in whom there is a concern for neuroborreliosis should undergo a lumbar puncture to look for cerebrospinal fluid abnormalities, in addition to serological testing at the same time. Consultation with an infectious diseases physician or neurologist would be appropriate.

IDEG Recommends AGAINST:

1. Testing in the absence of symptoms or signs consistent with Lyme disease: the value of serologic testing is limited in the absence of symptoms or signs that support a reasonable likelihood of infection.
2. Testing in asymptomatic patients who have had a blacklegged tick bite: antibodies to *B. burgdorferi* are not detected until a few weeks after infection. Thus, there is no point in testing at the time a tick is identified on the person and/or removed. Even if the person does develop Lyme disease from the tick bite, the serology will be negative at the time the tick is removed.
3. Testing in patients with the typical EM rash ($> 5\text{cm}$ in size) in season (anytime temperature reaches $> 4^{\circ}\text{C}$, with greatest risk of transmission during summer months) and with appropriate outdoor exposure anywhere in NS or an area outside of NS that is identified as at risk for Lyme disease. The diagnosis should be made based on the presence of the EM and treatment started.
4. Repeat testing after treatment: laboratory testing cannot be used to determine "cure." Like other infections, the antibodies remain positive even after effective treatment.
5. Sending specimens to laboratories that use interpretive criteria that are different from the CDC: the most common request that physicians get is to send the specimen to I GeneX, which has different interpretive criteria for their immunoblots, which may lead to false positive test results.¹⁰
6. Bypassing the ELISA and using immunoblots alone: Immunoblots done in the absence of preceding ELISA testing have been associated with a reduction in specificity and are NOT recommended. Immunoblots are semi-quantitative tests that can produce faint bands due to non-specific reactivity, which has been demonstrated in people with no history of exposure to ticks or Lyme disease or in illnesses other than Lyme disease.¹⁰
7. The use of PCR on blood, serum, or plasma or the use of urinary antigen as a diagnostic test: these tests have not been validated.

Important Caveats to Testing:

1. Patients who are treated early for Lyme disease may have delayed seroconversion or never seroconvert (i.e., develop a positive IgG immunoblot).
2. Patients with Lyme disease who have had symptoms for greater than 4 weeks are very likely to have a positive IgG immunoblot. If the patient's symptoms have been present for greater than 4 weeks, a negative Lyme IgG immunoblot suggests that the symptoms the patient is experiencing are not due to Lyme disease.¹²
3. Diagnosis of repeat infection is often difficult as immunoblots can remain positive for years despite appropriate treatment. Suspected repeat infections requiring serological testing should be discussed with a medical microbiologist.
4. The *Borrelia* species that cause Lyme disease in Europe can be different from those that cause disease in North America. Confirmation testing may require the use of an immunoblot for those species. If the history suggests exposure in Europe, this should be documented on the requisition so that the appropriate confirmatory testing can be done.

Treatment and Chemoprophylaxis of Lyme Disease:

There have been a number of clinical trials that support treatment recommendations for Lyme disease. These form the basis for the IDSA treatment guidelines that were ratified by the IDSA Lyme disease guideline review panel¹⁴ and recommendations found in clinical reviews,^{2,3} the NICE Guideline, and the American Academy of Pediatrics Red Book.¹³

IDEG Recommends:

Lyme disease should be treated in accordance with the IDSA guidelines.

Treatment of adult patients with Lyme disease:

EM, Bell's palsy, and early disseminated disease without CNS involvement (other than Bell's palsy):

- Doxycycline 100 mg po bid X 14-21 days (contraindicated in pregnancy)
- Amoxicillin 500 mg po tid X 14-21 days
- Cefuroxime 500 mg po bid X 14-21 days

Early Lyme with CNS involvement:

- Ceftriaxone 2 g IV once daily X 14-28 days
- Pen G 4x10⁶ units IV q4h X 14-28 days
- Doxycycline 100-200 mg po bid X 28 days (alternative if others not possible)

Early Lyme with carditis:

- Same treatment as early Lyme but use IV (as with CNS involvement) initially with high grade heart block and if admission to hospital is necessary

Late Lyme without CNS involvement:

- Doxycycline 100 mg po bid X 28 days
- Amoxicillin 500 mg po tid X 28 days
- Cefuroxime 500 mg po bid X 28 days

Late Lyme with CNS involvement (late neuroborreliosis) is treated the same as early Lyme with CNS involvement.

If there is recurrent or persistent joint swelling, repeat a 4-week course of oral antibiotic as recommended above. Use of IV ceftriaxone should be reserved for relapse or persistent joint swelling without improvement with oral treatment.

Treatment of pediatric patients with Lyme disease:¹³

The American Academy of Pediatrics Committee on Infectious Diseases endorses the use of doxycycline in children younger than 8 years of age for the management of Lyme based on the low risk of dental staining in reports of treatment of young children with Rocky Mountain Spotted Fever. Use of doxycycline is therefore **preferred** for **isolated facial palsy or CNS disease** due to Lyme disease for children of any age.

Erythema migrans (single or multiple) only (no neurological/cardiac signs or symptoms):

- For patients \geq 8 years of age:
Doxycycline 4.4 mg/kg/24h PO divided q12h for 10 days
Maximum: 200mg/24h
[Round dose to nearest 25 mg (1/4 tablet)]
- For patients < 8 years of age:
Amoxicillin 50 mg/kg/24h PO divided q8h for 14 days
Maximum: 1.5 gram/24h
- If penicillin allergy:
Cefuroxime 30 mg/kg/24h PO divided q12h for 14 days
Maximum: 1 gram /24h

Isolated Facial Palsy:

- Consult Infectious Diseases
- If other neurological symptoms present, consider LP
- Corticosteroids are not recommended
- Doxycycline 4.4 mg/kg/24h PO divided q12h for 14 days for all ages
Maximum: 200mg /24h
[Round dose to nearest 25 mg (1/4 tablet)]

Amoxicillin for treatment of facial palsy due to Lyme disease has not been studied.

Lyme Arthritis:

- Consult Infectious Diseases
- For patients \geq 8 years of age:
Doxycycline 4.4 mg/kg/24h PO divided q12h for 28 days
Maximum: 200mg/24h
[Round dose to nearest 25 mg (1/4 tablet)]
- For patients < 8 years of age:
There are limited safety data on the use of doxycycline for > 21 days in children < 8 years of age
Amoxicillin 50 mg/kg/24h PO divided q8h for 28 days
Maximum: 1.5 gram/24h
- If penicillin allergy:
Cefuroxime 30 mg/kg/24h PO divided q12h for 28 day
Maximum: 1 gram /24h

Persistent Lyme Arthritis:

- Consult Infectious Diseases and Rheumatology

For persistent arthritis after first course of therapy for patients who have responded incompletely or who respond and then relapse soon after stopping therapy:

- For patients ≥ 8 years of age:
Doxycycline 4.4 mg/kg/24h PO divided q12h for 28 days
Maximum: 200mg/24h
[Round dose to nearest 25 mg (1/4 tablet)]
- For patients < 8 years of age:
There are limited safety data on the use of doxycycline for > 21 days in children < 8 years of age
Amoxicillin 50 mg/kg/24h PO divided q8h for 28 days
Maximum: 1.5 gram/24h
- If penicillin allergy:
Cefuroxime 30 mg/kg/24h PO divided q12h for 28 days
Maximum: 1 gram /24h

For patients who experience worsening of their arthritis:

- Ceftriaxone 50-75 mg/kg/day IV once daily for 14-28 days
Maximum: 2 gram /24h

Atrioventricular heart block or carditis:

- Consult Infectious Diseases
- For patients ≥ 8 years of age:
Doxycycline 4.4 mg/kg/24h PO divided q12h for 14-21 days
Maximum: 200mg/24h
[Round dose to nearest 25 mg (1/4 tablet)]
- For patients < 8 years of age:
Amoxicillin 50 mg/kg/24h PO divided q8h for 14-21 days
Maximum: 1.5 gram/24h
- OR if IV therapy required
Ceftriaxone 50-75 mg/kg/day IV once daily for 14-21 days
Maximum: 2 gram /24h
Once patient is stabilized without ongoing symptoms or signs, can be switched to oral therapy as above to finish 14-21 days
- If penicillin allergy:
Cefuroxime 30 mg/kg/24h PO divided q12h for 14-21 days
Maximum: 1 gram /24h
OR
Ceftriaxone 50-75 mg/kg/day IV once daily for 14-21 days
Maximum: 2 gram /24h
Once patient is stabilized without ongoing symptoms or signs, can be switched to oral therapy as above to finish 14-21 days

Meningitis:

- Consult Infectious Diseases
- Ceftriaxone 50-75 mg/kg/day IV once daily for 14 days
Maximum: 2g /24h
OR
Doxycycline 4.4 mg/kg/24h PO divided q12h for 14 days
Maximum: 200mg /24h
[Round dose to nearest 25 mg (1/4 tablet)]

Prophylaxis of Lyme disease:

Prophylaxis is generally not recommended but may be offered to patients when all of the following criteria are satisfied:

- The attached tick can be reliably identified as an adult or nymphal blacklegged tick that is estimated to have been attached for ≥ 36 h based on the degree of engorgement or by certainty about the time of tick acquisition.
- Prophylaxis can be started within 72 h of tick removal.
- Ecologic information indicates that the local rate of infection of these ticks with *B. burgdorferi* is $\geq 20\%$. There is insufficient information to provide a list of all counties in NS that meet this criterion. For the purposes of prophylaxis, physicians may wish to consider higher and moderate risk areas in NS (this includes all of mainland NS and Cape Breton County <https://novascotia.ca/dhw/CDPC/lyme.asp>) to have tick infection rates in this range.
- Doxycycline is not contraindicated.

Recommended prophylaxis, if above criteria are met:

- Adults: single dose of doxycycline 200 mg po
- Children of any age: doxycycline 4 mg/kg to a maximum of 200 mg PO once [Round dose to nearest 25 mg (1/4 tablet)]

Amoxicillin is not recommended for prophylaxis due to its short half life.

IDEG recommends **AGAINST**:

Prolonged courses of antimicrobials for the treatment of Lyme disease that are not in keeping with courses recommended by the IDSA treatment guidelines.

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May 30, 2011

Approved by IDEG January 6, 2012

Revised April 27, 2012
Revised June 24, 2012
Revised July 1, 2012
Revised August 24, 2015
Revised May 26, 2017
Revised April 9, 2018
Revised April 15, 2019
Reviewed May 10, 2020
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