

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

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Executive Summary:

This document has been reviewed and updated to reflect recommendations in Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease.

In 2016, the Public Health Agency of Canada (PHAC) modified its surveillance case definition for Lyme disease. The 2016 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 IDSA, AAN, and ACR guidelines (2020) for the prevention, diagnosis, and treatment of Lyme disease.¹ Two review articles^{2,3} and the National Institute for Health and Care Excellence (NICE) guideline published in 2018 (www.nice.org.uk/guidance/ng95) are generally consistent with the IDSA, AAN, and ACR recommendations. IDEG continues to monitor developments in the management of Lyme disease and will update its guidance as new evidence becomes available.

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, and 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.
- Examining the removed tick for species identification is important for anticipatory guidance and in determining if antibiotic prophylaxis to prevent Lyme diseases is appropriate. **eTick** is a tick identification platform that is available for identification of tick species within 24 hours at no cost. 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 overall risk of Lyme disease after a bite from an infected tick is low and is dependent on how long the tick has been attached. 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} However, the risk may exceed 20% when a tick has been attached ≥ 72 hours¹. Most studies have found that the infected tick needs to be attached for at least 24 hours before it can transmit disease and the majority of transmission occurs after 36-48 hours of attachment.¹
- Use of antimicrobial prophylaxis for prevention of Lyme disease is recommended only for adults when within 72 hours of removal of an identified high-risk tick bite. For children, the option of antibiotic prophylaxis for an identified high-risk tick bite OR a wait-and-watch approach is recommended. (see [Prophylaxis section](#) for details).

- Serologic testing using the standard two-tiered algorithm described by the Centers for Disease Control and Prevention (CDC) and the Canadian Public Health Laboratory Network (CPHLN) OR a validated modified two-tiered testing (MTTT) algorithm is currently the only recommended method for making a serological diagnosis of Lyme disease. As of April 1, 2021, the Queen Elizabeth II Health Sciences Centre (QEII HSC) microbiology laboratory moved to using the MTTT algorithm.
- 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% 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. (See Treatment and Chemoprophylaxis of Lyme disease for recommended treatment durations).
- 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 QE II HSC. As of April 1, 2021, serological testing for Lyme disease transitioned to the MTTT algorithm, using 2 enzyme immunoassays (EIAs). Prior to this date, serological testing for Lyme disease at the QEII HSC used the standard two tier testing (STTT) algorithm, where specimens that are reactive or indeterminate on the first step EIA are forwarded to the National Microbiology Laboratory in Winnipeg for further testing using immunoblotting. With the MTTT algorithm, specimens will first be tested using the Zeus C10/VlsE EIA (ZEUS ELISA *Borrelia* VlsE1/pepC10 IgG/IgM), with reactive specimens tested in our microbiology laboratory by a second EIA, the Zeus whole cell EIA (ZEUS ELISA *Borrelia burgdorferi* IgG/IgM), rather than an immunoblot. Specimens with positive results on both EIAs are considered to be positive. This approach has been approved by the United States Food and Drug Administration and endorsed by the CDC and the CPHLN.

The MTTT approach offers advantages over the STTT approach:

- It is more sensitive for detecting early infection (formal evaluation showed MTTT detected 28% more cases of early infection)
- It has a similar specificity compared to the STTT (99.6% with our validation)
- Both EIAs can be performed at the QEII HSC, which will significantly improve turn-around-time for results
- It simplifies the interpretation of Lyme disease serology results, which will now be reported as “positive” or “negative”

The sensitivity of this testing approach depends on the stage of infection. In early, localized Lyme disease with EM, the sensitivity of the STTT 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 While the MTTT approach has improved sensitivity for detecting early infection, it is important for clinicians to remember that patients presenting with early localized Lyme disease should be treated on the basis of a clinical diagnosis, without relying on serology. The improved sensitivity and turn-around-time may be an advantage for investigating patients where early disseminated Lyme disease is a consideration. 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.

The use of immunoblots may still have value in patients with manifestations of late stage LD, such as Lyme arthritis, or in suspect false positive cases where serologic results do not fit with the clinical presentation. In these circumstances, it is reasonable to consider performing an IgG immunoblot as patients with late stage LD have high IgG antibody responses and the immunoblot may allow for the evaluation of the response to specific Borrelial proteins, which some clinicians may find helpful.

IDEG Recommends:

1. Physicians need to be aware that the diagnosis of early Lyme disease with localized EM in season (anytime temperature reaches > 4° 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 1) 1 or more skin lesions suggestive of, but atypical for, EM or 2) an EM-like rash out of season (regardless of exposure area) should undergo serological testing using the MTTT algorithm. If the test result is negative, serological testing should be repeated at least 2-3 weeks after collection of the first (“acute-phase”) serum sample.

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 at least 2-3 weeks after collection of the first ("acute-phase") serum sample 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 MTTT 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 infection¹.
2. Testing in asymptomatic persons 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 (> 5cm in size) in season (any time temperature reaches > 4°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 MTTT).
2. Patients with Lyme disease who have had symptoms for greater than 4 weeks are very likely to have a positive MTT 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 EIAs and 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/AAN/ACR treatment guidelines¹ and recommendations found in clinical reviews,^{2,3} the NICE Guideline, the Society of Obstetrics and Gynecologists of Canada Committee Opinion¹³, and the American Academy of Pediatrics RedBook.¹⁴

IDEG Recommends:

Lyme disease should be treated in accordance with the IDSA/AAN/ACR¹ and American Academy of Pediatrics¹⁴ guidelines.

Treatment of adult patients with Lyme disease¹:

EM:

- Doxycycline* 100 mg po bid X 10 days
- Amoxicillin 500 mg po tid X 14 days
- Cefuroxime 500 mg po bid X 14 days
- Azithromycin 500 mg po once daily X 7 days (second line agent reserved for patients in whom other antibiotic classes are contraindicated)

Cranial nerve palsy:

- Doxycycline* 100 mg PO BID X 14-21 days

Meningitis or radiculopathy:

- Doxycycline* 100 mg po bid X 14-21 days
- Ceftriaxone 2 g IV once daily X 14-21 days

Lyme disease-related parenchymal involvement of the brain or spinal cord:

- Consult Infectious Diseases

Carditis:

- Doxycycline* 100 mg po bid X 14-21 days
- Amoxicillin 500 mg po tid X 14-21 days
- Cefuroxime 500 mg po bid X 14-21 days
- Ceftriaxone 2 g IV once daily X 14-21 days

Initial IV therapy is recommended for patients requiring hospital admission. Therapy can be completed orally for the same total duration.

Arthritis (initial):

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

Arthritis (recurrent or refractory):

- Doxycycline* 100 mg po bid X 28 days
- Amoxicillin 500 mg po tid X 28 days
- Cefuroxime 500 mg po bid X 28 days
- Ceftriaxone 2 g IV once daily X 14 days

(Repeat IV therapy can be extended to 28 days if inflammation is not resolving)

** The safety of doxycycline in pregnancy and breastfeeding requires more study and the decision to use it in these patients should be individualized to the likely risks and benefits of alternative antibiotics.*

Treatment of pediatric patients with Lyme disease:¹⁴

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.

EM (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 ≥ 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 in adults and children:

Prophylaxis is recommended in adults only when it can be given within 72 hours of removal of an identified high-risk tick bite, which is defined by meeting all three criteria:

- The attached tick was an identified adult or nymphal blacklegged (*Ixodes* spp.) tick
- The tick was attached for ≥ 36 h, generally based on the degree of engorgement or by certainty about the time of tick acquisition.
- It occurred in a highly endemic area. 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>) as highly endemic for prophylaxis purposes.

If a tick bite cannot be classified with a high level of certainty as a high-risk bite, a wait-and-watch approach is recommended.

For children, the option of antibiotic prophylaxis for a high-risk tick bite as identified above OR a wait-and-watch approach is recommended.

The wait-and-watch approach includes daily monitoring for the development of an expanding erythematous lesion at the site of the tick bite or other skin sites, fever, or any other unexplained illnesses for 3-30 days after the tick bite and seeking medical attention should one of these symptoms occur.

Recommended prophylaxis, if above criteria are met and there are no contraindications to doxycycline:

- 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/AAN/ACR treatment guidelines as detailed above.

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