CLINICAL GUIDANCE DOCUMENT

Management of Tick Bites and Investigation of Early Localized Lyme Disease



Please contact us at evidence@ontariohealth.ca or 1-877-280-8538 if you have

any questions or feedback about this clinical guidance document.

Box 1. Clinical Manifestations of Early Localized Lyme Disease: Erythema Migrans Rashes



Box 2. Prevalence of Symptoms in Patients Presenting With Possible Early Localized Lvme Disease[#]

- Erythema migrans rash (typical or atypical) ~70%
 - Headache 42%
- Fatigue 54%
- Myalgia 44%
- Fever/chills 39%
- Stiff neck 35%
- Decreased appetite 26%

*As a disease of public health significance, Lyme disease is reportable in Ontario under the Health Protection and Promotion Act, R.S.O. 1990, c. H.7.

Box 4. Areas of Risk for Lyme Disease

- The risk of acquiring Lyme disease varies across geographical regions. Please click to see the risks in Ontario, Canada, and the United States
- In Europe, the areas of highest risk are in Central and Eastern Europe, but infected ticks have also been found in Southern Scandinavia and up to the northern Mediterranean region

Box 5. Post-Exposure Prophylaxis

The risk of developing Lyme disease following a tick bite by an infected tick is between 1% and 3%. In Ontario, the prevalence of infected ticks varies by geographic region. In many instances, it is reasonable to adopt the "wait and see" approach and treat patients if they develop symptoms compatible with Lyme disease. Counsel patients to watch for the development of early signs and symptoms for 30 days, and advise patients that other tick-borne infections may result in signs or symptoms too.

Based on the best available evidence, post-exposure prophylaxis can be considered if these four criteria are met:

- 1. The tick was attached > 24 hours
- 2. The tick was removed within the past 72 hours
- 3. The tick was acquired in an area with a prevalence of ticks infected with *Borrelia burgdorferi* > 20% (e.g., Rouge National Urban Park and Morningside Park in the Greater Toronto

References

American Academy of Pediatrics Committee on Infectious Diseases. Lyme disease (Lyme Borreliosis, Borrelia burgdorferi sensu lato Infection). In: Kimberlin DW, Brady MT, Jackson MA, editors. Red Book (2018): report of the Committee on Infectious Diseases: American Academy of Pediatrics; 2018.

2 Cameron D.I. Johnson I.B. Maloney El. Evidence assessments and guideline recommendations in 2. Came of Devices of the commence of the commence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. Expert Rev Anti Infect Ther. 2014;12(9):1103–35.

 Canadian Paediatric Society (CPS). Lyme disease in Canada: focus on children [Internet]. Ottawa (ON): The Society; 2020 [cited 2022 Dec]. Available from: <u>https://cps.ca/documents/position/lyme-</u> disease-children

4. Centre for Effective Practice (CEP). Early lyme disease management in primary care [Internet]. Toronto (ON): The Centre; 2020 [cited 2022 Dec]. Available from: <u>https://cep.health/media/uploac CEP_EarlyLymeDisease_Provider_2020.pdf</u>

Committee on Infectious Diseases American Academy of Pediatrics, Kimberlin DW, Barnett EDSmith GN, Moore KM, Hatchette TF, Nicholson J, Bowie W, Langley JM. Committee Opinion No. 399: Management of Tick Bites and Lyme Disease During Pregnancy. J Obstet Gynaecol Can. 2020;42(5):644–53.;

6. Hatchette T, Lindsay R, on behalf of the Lyme Disease Diagnostic Working Group. Modified twotiered testing algorithm for Lyme disease serology: the Canadian context. Can Commun Dis Rep. 2020;46(5):125-31.

7. Pegalajar-Jurado A, Schriefer ME, Welch RJ, Couturier MR, MacKenzie T, Clark RJ, et al. Evaluation of Modified Two-Tiered Testing Algorithms for Lyme Disease Laboratory Diagnosis Using Well-Characterized Serum Samples. J Clin Microbiol. 2018;56(8):e01943-17.

Additional images of typical and atypical rashes are available on Health Canada's website; under "Clinical manifestations," please see "Erythema migrans rash."

Note: People with darker skin tones may present with a bruise-like rash.

Box 3. Blacklegged Ticks at Various Stages and Safe Tick Removal



For more images, please go to: Centers for Disease Control and Prevention.

For instructions, please see Centers for Disease Control and Prevention

Area, Brighton, Kingston and surrounding areas, Thousand Islands, Brockville, Perth-Smiths Falls and surrounding areas, Ottawa and surrounding areas, Rondeau Provincial Park in Morpeth, and Pinery Provincial Park in Grand Bend*)

4. Doxycycline is not contraindicated. (Doxycycline was previously contraindicated for pregnant and lactating people; however recent evidence has demonstrated that a single dose of doxycycline is safe for this population)⁵

Recommended treatment for post-exposure prophylaxis:

Adults: 1 dose of doxycycline 200 mg, by mouth

Children < 18 years of age: 1 dose of doxycycline 200 mg

dose or 4 mg/kg (up to a maximum dose of 200mg), by mouth

*Note: This is not a comprehensive list of higher-risk areas in Ontario. Infectivity rate is not uniformly collected and updated, and therefore postexposure prophylaxis decisions are sometimes made based on risk-benefit discussions with patients.

For more information, please refer to the Ontario Lyme Disease Map.

8. Lantos PM, Rumbaugh J, Bockenstedt LK, Falck-Ytter YT, Aguero-Rosenfeld ME, Auwaerter PG, et al. 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. Clin Infect Dis. 2020;72(1):e1-e48. Meissner HC, Steere AC. Management of pediatric Lyme disease: updates from 2020 Lyme guidelines. Pediatrics. 2022;149(3). Aguero-Rosenfeld ME, Wang G, Schwartz I, Wormser GP. Diagnosis of Lyme Borreliosis. Clin Microbiol Rev. 2005;18(3):484–509.

10. Nadelman RB. Erythema migrans. Infect Dis Clin North Am. 2015;29(2):211-39

11. National Institute for Health and Care Excellence (NICE). Lyme disease [Internet]. United Kingdom: The Institute; 2018 [cited 2022 Dec]. Available from: https://www.nice.org.uk/guidance/ng95

12. National Institute for Health and Care Excellence (NICE). Lyme disease: diagnosis and management. [D] Evidence review for the management of erythma migrans [Internet]. United Kingdom: The Institute; 2018 [cited 2022 Dec]. Available from: https://www.nice.org.uk/guida.ng95/evidence/d-management-of-erythma-migrans-pdf-4792271010

13. Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klempner MS, 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. Clin Infect Dis. 2006;43(9):1089–134.

14. Committee on Infectious Diseases American Academy of Pediatrics, Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH. Lyme disease (Lyme Borreliosis, Borrelia burgdorferi sensu lato Infection). Red Book: 2021–2024 report of the Committee on Infectious Diseases: American Academy of Pediatrice 2021

Box 6. Laboratory Testing

- · Laboratory testing is generally not indicated for asymptomatic patients
- Serological testing may not yield positive results during early localized Lyme disease, so management should not be based on serological testing results during this phase
- Antibiotic treatment in early disease may reduce seroconversion; testing should not be used to monitor treatment outcome
- Following exposure to Borrelia burgdorferi, immunoglobulin M (IgM) antibodies are detected within 2–4 weeks, and IgG antibodies within 4-6 weeks
- As of April 1, 2023, Public Health Ontario uses a modified two-tiered testing (MTTT) algorithm to maximize sensitivity and specificity (see Box 7)
- For serological testing, please complete the requisition fully and submit it, along with samples, to a public health laboratory for testing
- If European Lyme disease is suspected based on the patient's travel history, please order serology testing specific to European Lyme disease

Box 8. Recommendations for Treatment of Patients With Early Localized Lyme Disease

Drugs	Dosage for Adults	Dosage for Children
Preferred		
Doxycycline*	100 mg twice a day for 10–21 days [†]	For children < 18 years of age:
	Contraindicated for pregnant people	4 mg/kg, orally divided into 2 doses (maximum 200 mg/day) for 10–21 days†
Amoxicillin	500 mg three times a day for 14–21 days	For children < 18 years of age: 50 mg/kg/day orally, divided into 3 equal doses per day, maximum of 500 mg per dose for 14–21 days
Cefuroxime	500 mg twice per day for 14–21 days	For children > 8 years of age: 30 mg/kg/day divided in 2 doses (maximum 500 mg. dose) for 14–21 days
For Allergy or Int	colerance [‡]	
Azithromycin	500 mg/day for 7–17 days	For children < 18 years of age: 10 mg/kg/day, orally, once daily for 7–17 days
Clarithromycin	500 mg twice a day for 14–21 days	For children > 8 years of age:
	Relatively contraindicated in pregnant people	7.5 mg/kg twice a day (maximum 500 mg/day) for 14–21 days

Doxycycline is considered to be the preferred antibiotic treatment option by some guidelines for early Lyme disease (erythema migrans) in both children and adults based on its ability to treat potential extracutaneous manifestations of infection (particularly neurological involvement) and potential coinfection or infection with Anaplasma phagocytophilum (anaplasmosis) or Ehrlichia muris-like agent.^{9,12,14}

[†]Recent guidelines,^{3,8,14} including one by the Canadian Paediatric Society, recommend a 10-day treatment duration with doxycycline in children of all ages and adults. A 2018 guideline¹¹ recommends a 21-day treatment duration with doxycycline in children over 9 years of age and adults based on concerns with low cure rates and a lack of clear evidence for shorter courses. In addition, a longer course may be reassuring for people being treated for early Lyme disease who continue to have symptoms and the evidence suggests that adverse event rates were not increased for longer courses.12

*Patients treated with macrolides should be closely monitored to ensure resolution of clinical symptoms as macrolides are less effective.

Box 7. Sensitivity of Serological (Modified Two-Tier) Testing[†] in Patients With Lyme Disease^{6,7}

Erythema migrans, acute phase (early localized disease)	58%
Erythema migrans, convalescence phase [‡] (early localized disease)	76%
Neurological involvement (early disseminated disease)	100%
Arthritis (late disseminated disease)	100%

[†]The MTTT algorithm is based on serum sample initially tested using IgG/IgM enzyme-linked immunosorbent assay (ELISA) using a whole cell lysate (tier 1). If results of tier 1 ELISA results are reactive/ indeterminate, sample is further tested using second (tier 2) IgG/IgM ELISA assay targeting specifically VIsE1 and pepC10 antigens.

[‡]Following antibiotic treatment.