Diagnosing and Managing Early Lyme Disease in Ontario

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Gracia Mabaya, Health Quality Ontario
May 14, 2019
Public Health Ontario Grand Rounds
Authors

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Overview

• Epidemiology of Lyme disease in Ontario
• Description of the three clinical stages of Lyme disease
• Diagnostic testing for Lyme disease
• Use of the Health Quality Ontario Clinical Guidance Document: Management of Tick Bites and Investigation of Early Localized Lyme Disease
• Case studies
Lyme Disease (Lyme borreliosis)

- Vector-borne disease caused by infection with the spirochaete *Borrelia burgdorferi* in North America
- In Ontario, *B. burgdorferi* is transmitted by the bite of an infected blacklegged tick (*Ixodes scapularis*) that has been attached for sufficient time to a human host (> 24 hours)
- Has a range of clinical manifestations and is diagnosed through clinical symptoms and serological testing
The Blacklegged Tick

The blacklegged tick (*Ixodes scapularis*) is the vector responsible for transmitting Lyme disease in Ontario.

Source: [https://www.canada.ca/en/health-canada/services/pest-control-tips/blacklegged-deer-ticks.html](https://www.canada.ca/en/health-canada/services/pest-control-tips/blacklegged-deer-ticks.html) with permission from R Lindsay at PHAC
Blacklegged Tick

American Dog Tick

Source: https://www.canada.ca/en/health-canada/services/pest-control-tips/blacklegged-deer-ticks.html with permission from R Lindsay at PHAC
Life Cycle of a Blacklegged Tick

Year 1
- Spring: Female adults lay eggs in leaf litter.
- Summer: Larvae hatch from eggs. Larvae acquire *B. burgdorferi* while blood feeding on small animals, especially the white-footed mouse.
- Fall: Larvae become dormant in winter within leaf litter.
- Winter: Larvae develop into nymphs.
- Summer: Nymphs develop into adults. Adult ticks feed on large animals.
- Fall: Infectious nymphs feed on animals, including humans, potentially transmitting *B. burgdorferi*.

Year 2

Lyme Disease Transmission

• Nymphal ticks are most likely to transmit *B. burgdorferi* because they are:
  • active at times when humans are most often in areas where ticks live
  • small so easy to miss on the person

• The incidence rate of Lyme disease in humans peaks in late spring/summer, when nymphal ticks are active

Blacklegged Tick Size Comparison

Source: [https://www.canada.ca/en/health-canada/services/pest-control-tips/blacklegged-deer-ticks.html](https://www.canada.ca/en/health-canada/services/pest-control-tips/blacklegged-deer-ticks.html) with permission from R Lindsay at PHAC
Lyme Disease Surveillance in Ontario

Passive Surveillance

- Ticks are submitted by the public or physicians
- Ticks are identified at the species level
- Tick testing – blacklegged ticks tested for *Borrelia burgdorferi*
- Human case surveillance – cases reported through reportable disease system (iPHIS)

Active Surveillance (looking for ticks in the environment)

- Tick dragging – determine estimated risk areas
- Small mammal trapping – trapping rodents to test them and their ticks for *B. burgdorferi*
While low, there is a probability of encountering blacklegged ticks almost anywhere in the province, provided the habitat is suitable for blacklegged ticks (e.g., wooded or brushy areas).
Annual Lyme Disease Confirmed and Probable Case Counts and Incidence Rate per 100,000 Population: Ontario, 2009-2018

Ontario Cases: Ontario. Ministry of Health and Long-Term Care. Integrated Public Health Information System (iPHIS) [database]. Toronto, ON: Queen’s Printer for Ontario [producer and distributor]; [data extracted 2019 Apr 24].


*Case counts account for the 2009 change in the Lyme disease case definition.
Human Lyme Disease Case Counts and Rates for All Ages, by Sex in Ontario, 2005-2018

Lyme disease case count and rates for all ages, by sex in Ontario, 2005-2018

Data source:
Ontario. Ministry of Health and Long-Term Care, Integrated Public Health Information System (iPHIS)[database]. Toronto, ON: Queen’s Printer for Ontario [producer and distributor]; 2018 [data extracted 2019 Apr 10].
Lyme Disease Clinical Features

• Three different stages
  • Early localized
  • Early disseminated
  • Late disseminated

• Post-treatment Lyme disease syndrome (PLDTS)
Early Localized Lyme Disease

• Time frame 3-30 days after tick bite (usually 7-14 days)

• Rash (erythema migrans)
  • Usually occurs at site of tick-bite
  • Only present in subset (~70%) of patients
  • ‘Bull’s eye’ rash occurs in minority of patients

• Other potential symptoms:
  • Headache, fatigue, myalgia, arthralgia, malaise, fever, regional lymphadenopathy


Early Disseminated Lyme Disease

• Within days to weeks, *B. burgdorferi* can spread to other sites/organs if untreated
  • Additional skin lesions (multiple erythema migrans)
  • Peripheral/central nervous system
    • Cranial nerve palsies (often 7th)
    • Meningitis or episodic headaches
  • Systemic symptoms
    • Can include fever, myalgia, arthralgia, headache, or fatigue
  • Cardiac symptoms
    • Atrioventricular (AV) node block
  • Arthritis

Late Disseminated Lyme Disease

• Weeks to months after the initial infection, late symptoms can occur if untreated, including:
  • Arthritis
    • Often monoarticular
    • Usually involves large joints, especially the knee
  • Neurological
    • Encephalitis/encephalopathy
    • Polyneuropathy
    • Stroke-like illness

Post-Treatment Lyme Disease Syndrome (PTLDS)

- After treatment for Lyme disease, ~10% of patients report symptoms for at least six months
- PTLDS can be defined by symptoms that began within six months of treatment of Lyme disease infection and persist for at least six months. These include:
  - Fatigue
  - Cognitive complaints
  - Musculoskeletal pain

Diagnosis of Lyme Disease
Tick bites and Prevention of Lyme Disease

• For prevention of Lyme disease after a tick bite:
  • Routine abx prophylaxis and serological testing is not recommended
  • A single dose of doxycycline can be offered if:
    • Tick can be identified as black legged tick
    • Attached for at least 24-36 hours
    • Prophylaxis can be started within 72 hours
    • Prevalence of *B. burgdorferi* infection rate in ticks is ≥ 20%
    • Doxycycline is not contraindicated

• Persons should be monitored for signs and symptoms for up to 30 days for development of rash at the site of bite
What is the Role of Tick testing in Diagnosis of Lyme Disease?

• **IDSA guidelines**
  • Testing ticks for tick borne pathogens is not recommended
  • Primarily used for research and surveillance
  • Health care practitioners in areas of endemcity should learn how to identify black legged ticks and differentiate level of engorgement

• PHOL currently identifies ticks and where appropriate send it to NML for Borrelia testing.
Diagnosis of Lyme Disease

Acute: Clinical presentation with epidemiological link
Late: Clinical presentations with laboratory testing
Performance Characteristics of Each Assay in Patients with Lyme Disease

Testing Algorithm at PHO’s Laboratories

2-tier testing (Recommended by IDSA/CDC and CPHLN)

1. ELISA testing
   - Negative: No serological evidence of infection
   - Positive/Indeterminate: The results should be interpreted in the context of the clinical signs and symptoms

2. WB testing
   - IgM and IgG
     - Negative: The results should be interpreted in the context of the clinical signs and symptoms
     - Positive/Indeterminate: The results should be interpreted in the context of the clinical signs and symptoms
Challenges Posed by Private Laboratories in USA

- Private labs use various assays to diagnose Lyme disease.
- None of them are scientifically validated.
- In 2005, the CDC placed a notice in their Morbidity and Mortality Weekly Report (MMWR) cautioning about using these private laboratories: [https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5405a6.htm](https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5405a6.htm)

**UNORTHODOX AND UNVALIDATED LABORATORY TESTS IN THE DIAGNOSIS OF LYME BORRELIOSIS AND IN RELATION TO MEDICALLY UNEXPLAINED SYMPTOMS**

Professor Brian I. Duerden, BSc, MD, FRCPath, FRCPEdin
Inspector of Microbiology and Infection Control
Department of Health


Alternative Testing Leads to High False-Positive Results

• Slide presents data on false positive and test discordance rates for testing (ELISA, WB IgM (CDC), WB IgM (Lab), WB IgG (CDC), WB IgG (Lab), 2 tier testing) at a university reference laboratory versus commercial or specialty laboratories on 40 medically health control patients from “Table 2. Number and Percentage of False-Positive Serologic Test Results and Discordant Pairs for 40 Medically Healthy Controls (University Reference Laboratory Versus Commercial and Lyme Specialty Laboratories)” from:

Tests That Should Be Avoided

Some laboratories offer Lyme disease testing using assays whose accuracy and clinical usefulness have not been adequately established. Unvalidated tests available as of 2011 include:

- Capture assays for antigens in urine
- Culture, immunofluorescence staining, or cell sorting of cell wall-deficient or cystic forms of *B. burgdorferi*
- Lymphocyte transformation tests
- Quantitative CD57 lymphocyte assays
- “Reverse Western blots”
- In-house criteria for interpretation of immunoblots
- Measurements of antibodies in joint fluid (synovial fluid)
- IgM or IgG tests without a previous ELISA/EIA/IFA
- Cytokine biomarkers
Lyme Disease

Clinical Guidance Document

GRACIA MABAYA & LACEY PHILLIPS | MAY 14, 2019
Project Objectives

• Health Quality Ontario (HQO) and Public Health Ontario (PHO), in collaboration with clinical experts, patients, and caregivers across the province, jointly developed a clinical guidance document on tick bite management and the diagnosis and treatment of early localized Lyme disease.

• The clinical guidance document was developed for use in primary care, community-based care, and emergency department settings.
Development Timeline

Mid November 2017:
First Working Group (WG) meeting

Mid December 2017:
WG review of draft table of contents

Late January 2018:
Second WG meeting (finalize draft for public consultation)

Late March 2018:
Post for public consultation (3 weeks) and hold patient focus group

Mid April – Early May 2018:
Third WG meeting (review consultation results and finalize draft)
Lyme Disease Clinical Guidance Document
Lyme Disease Clinical Guidance Document
## Scope of Clinical Guidance Document

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
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| • Patient Population  
  • Children and adults  
  • Tick bite management  
  • Diagnosis and management of early localized disease (<30 days)  
  • Including post-exposure prophylaxis  
  • Clinical setting  
  • Primary care and emergency department | • Prevention of Lyme disease  
  • Diagnosis and management of early and late disseminated disease (≥ 30 days but < 3 months or ≥ 3 months)  
  • Including indication for laboratory testing  
  • Diagnosis and management of coinfections |
Clinical Guidance Document Development Process
Key Development Inputs

- Lyme Disease Working Group
- Clinical Practice Guidelines
- Stakeholder Engagement
- Public Consultation Feedback
Working Group Composition

11 Working Group Members

- Lived Experience Advisors
- Primary Care Providers (Physician & Nurse Practitioners)
- Emergency Department Physician
- Public Health Experts
- High/low risk area representation
# Lyme Disease Clinical Practice Guidelines

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<tr>
<th>Year</th>
<th>Author</th>
<th>Country</th>
<th>Title</th>
</tr>
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<tbody>
<tr>
<td>2006</td>
<td>Infectious Diseases Society of America (IDSA)</td>
<td>United States of America</td>
<td>The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America</td>
</tr>
<tr>
<td>2014</td>
<td>International Lyme and Associated Diseases Society (ILADS)</td>
<td>International</td>
<td>Evidence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease</td>
</tr>
<tr>
<td>2018</td>
<td>National Institute for Health and Care Excellence (NICE)</td>
<td>United Kingdom</td>
<td>Lyme Disease</td>
</tr>
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Additional Documents


Public Consultation Process

March 23 – April 16, 2018

- **Online Survey** (n= 314)
  - 172 Patients/caregivers
  - 87 Members of the public and others
  - 55 Health care providers and organizations

- **Emails** (n= 16)
  - 5 Patients/caregivers
  - 2 Members of the public
  - 9 Health care providers and organizations

- **Feedback Sessions** (n= 12)
  - Skype teleconference on April 10th and April 12th, 2018
  - 12 participants (including two WG LEAs)

- **Total Responses**
  - N= 342

March 23 – April 16, 2018
Feedback from Health Care Professionals, Clinicians, and Researchers

- LHIN Clinical Leads/VP Clinical
- Medical Officers of Health
- Public Health Inspectors
- Researcher/Senior Epidemiologist/Educator
- Naturopathic Doctor
- ED Physicians (Medical Directors)
- Infectious Diseases Physicians/Specialist
- Primary Care Providers/Peds MD
- Public Nurses/Infectious Disease

55 Health Care Professional, Clinicians, and Researchers
Feedback from Organizations

- Family Health Teams
- Lyme-specific Groups
- Acute Care Hospitals
- Family Practice-Specific Professional Organization
- Public Health Units
Case #1

• A 30 year old **asymptomatic** patient presented with a tick that was attached to her for over a day

• She was hiking in Kingston area two days ago

• Prophylaxis or no prophylaxis?

• How long should symptoms be monitored for?

• What if it was a 6-year-old boy?
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Management of Tick Bites

**Tick bite but asymptomatic**

- **No risk of Lyme disease**
  - Advise patient to monitor for signs and symptoms for 30 days

  - **Is or was the tick attached?**
    - **No**
    - **Yes**
      - Safely remove the tick, if attached (see Box 3)

  - **Is it a blacklegged tick? (see Box 3)**
    - **No**
      - **Risk of Lyme disease is low**
        - Advise patient to monitor for signs and symptoms for 30 days
        - Counsel patient on preventing exposure to ticks
      - **Yes**
        - Attached for ≥ 24 hours?
          - **No**
            - **At risk for Lyme disease, but post-exposure prophylaxis is not warranted**
              - Advise patient to monitor for signs and symptoms for 30 days
            - **Yes**
              - Tick acquired in risk or endemic area with a prevalence of infected ticks > 20%? (See Box 4)
                - **No**
                  - **Was the tick removed within the past 72 hours?**
                    - **Yes**
                      - Advise patient to monitor for signs and symptoms for 30 days
                    - **No**
                      - **At risk for Lyme disease; optimal timing for post-exposure prophylaxis (see Box 5)**
                        - Advise patient to monitor for signs and symptoms for 30 days
                - **Yes**
                  - **At risk for Lyme disease; optimal timing for post-exposure prophylaxis (see Box 5)**
                    - Advise patient to monitor for signs and symptoms for 30 days
Box 1. Clinical Manifestations of Early Localized Lyme Disease: Erythema Migrans Rash

Additional images of typical and atypical rashes are available on Health Canada’s website; please see “Early localized Lyme disease (≤ 30 days).” Note: People with darker skin tones may present with a bruse-like rash.

Box 2. Prevalence of Symptoms in Patients Presenting With Possible Early Localized Lyme Disease

- Erythema migrans rash (typical or atypical) - 70%
- Headache - 42%
- Fatigue - 54%
- Myalgia - 44%
- Decreased appetite - 26%

*Note: 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 3. Blacklegged Ticks at Various Stages and Safe Tick Removal

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

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 5%. 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 for 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 Area, Brantford, Kingston, and surrounding areas, Thousand Islands, Brockville, Fitch-Smiths Falls and surrounding areas, Ottawa and surrounding areas, and Rondeau Provincial Park in Mopeth)

4. Doxycycline is not contraindicated (Doxycycline is contraindicated for pregnant women and for children < 8 years old. There is insufficient evidence for the prophylactic use of other medications, such as amoxicillin, in these populations)

Adults: 1 dose of Doxycycline 200 mg, by mouth
Children ≥ 8 years: 1 dose of doxycycline 4 mg/kg, up to a maximum dose of 200 mg, by mouth

*Note: This is not a comprehensive list of riskier areas in Ontario. For more information, please refer to the Ontario Lyme Disease Map.

Bibliography


Box 6. Laboratory Testing

- Laboratory testing is 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
- Public Health Ontario uses a two-step testing 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 7. Sensitivity of Serological (Two-Tier) Testing in Patients With Lyme Disease

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sensitivity (%)</th>
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<tbody>
<tr>
<td>Erythema migrans, acute phase</td>
<td>29–40%</td>
</tr>
<tr>
<td>Erythema migrans, convalescence phase</td>
<td>29–76%</td>
</tr>
<tr>
<td>Neurological (early disseminated disease)</td>
<td>87%</td>
</tr>
<tr>
<td>Arthritis (late disseminated disease)</td>
<td>97%</td>
</tr>
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The two-tier testing algorithm is based on serum sample initially tested using enzyme-linked immunosorbent assay (ELISA). If results of ELISA method are reactive/inconclusive, separate IgM and IgG Western blot tests are performed.

Following antibiotic treatment.

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

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<td></td>
<td>Contraindicated for pregnant or lactating people</td>
<td>For children aged 9–12 years of age &lt; 45 kg: 5 mg/kg/day in 2 divided doses on day 1, followed by 2.5 mg/kg/day in 1 or 2 divided doses, for a total of 21 days</td>
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<td>For severe infections, up to 5 mg/kg/day for 21 days</td>
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<td>Amoxicillin</td>
<td>1 g three times a day for 21 days</td>
<td>For children ≤ 12 years of age ≤ 33 kg: 30 mg/kg three times a day for 21 days</td>
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<td>Cefuroxime</td>
<td>500 mg twice per day for 14–21 days</td>
<td>For children &gt; 8 years of age: 30 mg/kg/day divided in 2 doses (maximum 500 mg/dose) for 14–21 days</td>
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<td>For Allergy or Intolerance</td>
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Patients treated with macrolides should be closely monitored to ensure resolution of clinical symptoms as macrolides are less effective.

References Available at: [https://www.who.int/inf-dis-watch/0001](https://www.who.int/inf-dis-watch/0001)
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Based on the best available evidence, post-exposure prophylaxis can be considered if these four criteria are met:
1. The tick was attached for > 24 hours.
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National Urban Park and Morningside Park in the Greater Toronto Area, Brighten, Kingston and surrounding areas, Thousand Islands, Brockville, Fresh Smith Falls and surrounding areas, Ottawa and surrounding areas, and Rondeau Provincial Park in Moosonee). 4. Doxycycline is not contraindicated. Doxycycline is contraindicated for pregnant or lactating people.

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• What if it was a 6-year-old boy?
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 Area, Brighton, Kingston and surrounding areas, Thousand Islands, Brockville, Perth-Smiths Falls and surrounding areas, Ottawa and surrounding areas, and Rondeau Provincial Park in Morpeth)

4. Doxycycline is not contraindicated (Doxycycline is contraindicated for pregnant people and for children < 8 years old. There is insufficient evidence for the prophylactic use of other medications, such as amoxicillin, in these populations)

Adults: 1 dose of doxycycline 200 mg, by mouth

Children ≥ 8 years: 1 dose of doxycycline 4 mg/kg, up to a maximum dose of 200 mg, by mouth

*Note: This is not a comprehensive list of higher-risk areas in Ontario. For more information, please refer to the Ontario Lyme Disease Map."
Case #2

- 68-year-old retired nurse living in Ottawa area was bitten by a tick while gardening
- She took the tick to her local public health unit
- Tick was not sent to the laboratory at Public Health Ontario for identification
- A few days later she developed a rash and “flu-like” symptoms
- Upon examination – erythematous rash at the site of the lesion measuring 8 cm
- Treated with amoxicillin for two weeks
- Doctor did not test her for Lyme disease antibodies
Case #2 Questions

• What evidence supports the diagnosis of early localized Lyme disease?
• Should the physician have ordered serology?
• Was the choice of antibiotic appropriate for treatment of early localized Lyme disease?
• Patient returns and insists on getting tested for Lyme disease. How would you counsel her?
Case #2 Questions

• What evidence supports the diagnosis of early localized Lyme disease?
• Should the physician have ordered serology?
• Was the choice of antibiotic appropriate for treatment of early localized Lyme disease?
• Patient returns and insists on getting tested for Lyme disease. How would you counsel her?
Management of Tick Bites

Symptomatic (3–30 days following tick exposure)

Does the patient have the following signs and symptoms compatible with Lyme disease?

- Expanding typical or atypical erythema migrans rash > 5 cm (see Box 1)
- Fever, chills, headache, stiff neck, fatigue, decreased appetite, muscle and joint aches, swollen lymph nodes (see Box 2)

No risk of Lyme disease

- Advise patient to monitor for signs and symptoms for 30 days

Risk of Lyme disease is low

- Advise patient to monitor for signs and symptoms for 30 days
- Counsel patient on preventing exposure to ticks

At risk for Lyme disease, but post-exposure prophylaxis is not warranted

- Advise patient to monitor for signs and symptoms for 30 days

At risk for Lyme disease; optimal timing (see Box 5)

- Advise patient to monitor for signs and symptoms for 30 days

Was the patient exposed to ticks in the past 30 days?

- Yes
- Possibly
- No

Yes, residence or travel to risk areas and contact with ticks through outdoor activities

Clinical case of Lyme disease

- Treat for early localized Lyme disease (see Box 8)
- Lyme disease serology not indicated
- If symptoms persist, refer patient to appropriate specialist

No residence or travel to risk areas and possible contact with ticks through outdoor activities

Possible case of Lyme disease

- Routine management of patient’s symptoms
- Order Lyme disease serology (see Box 8)
- Consider treating for early localized Lyme disease (see Box 8)
- If symptoms persist, consider an alternative diagnosis. Consult Public Health to understand the local epidemiology. Refer patient to an appropriate specialist, as needed

No residence or travel to risk areas and no possible contact with ticks

Low risk of Lyme disease, but do not rule it out

- Consider alternative causes of symptoms
- Consider Lyme disease serology, if clinically indicated (see Box 6)

Low risk of Lyme disease, but do not rule it out

- Consider alternative causes of symptoms
- Consider Lyme disease serology, if clinically indicated (see Box 6)
Case #2 Questions

• What evidence supports the diagnosis of early localized Lyme disease?

• Should the physician have ordered serology?

• Was the choice of antibiotic appropriate for treatment of early localized Lyme disease?

• Patient returns and insists on getting tested for Lyme disease. How would you counsel her?
Box 1. Clinical Manifestations of Early Localized Lyme Disease: Erythema Migrans Rash
- Additional images of typical and atypical rashes are available on Health Canada's website: see "Early Localized Lyme disease (< 30 days)."
- Note: People with darker skin tones may present with a bruise-like rash.

Box 2. Prevalence of Symptoms in Patients Presenting With Possible Early Localized Lyme Disease
- Erythema migrans rash (typical or atypical) 70%
- Headache 42%
- Fever/chills 33%
- Fatigue 54%
- Myalgia 44%
- Decreased appetite 26%
- "As a result 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 3. Blacklegged Ticks at Various Stages and Safe Tick Removal
- For more images, please go to: Centers for Disease Control and Prevention

Box 4. Areas of Risk for Lyme Disease
- The risk of acquiring Lyme disease varies across geographical regions. Please click for the risks in Ontario, Canada, and the United States.
- In all, 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 in 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 Area, Brighten, Kingston, and surrounding areas, Thousand Islands, Brockville, Kent-Smith Falls, and surrounding areas, Ottawa, and surrounding areas, and Rondeau Provincial Park in Morpeth)
- 4. Doxycycline is not contraindicated (Doxycycline is contraindicated for pregnant or lactating people if children are < 8 years old. There is insufficient evidence for the prophylactic use of other medications, such as amoxicillin, in these populations)
- Adults: 1 dose of doxycycline 200 mg, by mouth
- Children: 1 dose of doxycycline 4 mg/kg, up to a maximum dose of 200 mg, by mouth
- Note: This is a non-exhaustive list of the areas at an elevated risk of acquiring Lyme disease.
- For more information, please refer to the Ontario Lyme Disease website.

Box 6. Laboratory Testing
- Laboratory testing is 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.
- Public Health Ontario uses a two-step testing 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 7. Sensitivity of Serological (Two-Tier) Testing in Patients With Lyme Disease
- Erythema migrans, acute phase (early localized disease) 29-40%
- Erythema migrans, convalescence phase (early localized disease) 29-78%
- Neurological involvement (early disseminated disease) 87%
- Arthritis (late disseminated disease) 97%

Two-tier testing algorithm is based on serum sample initially tested using enzyme-linked immunosorbent assay (ELISA). Results of ELISA method are reactive/determined, specific IgM and IgG Western blot test are performed.
- Following antibiotic treatment.

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage for Adult</th>
<th>Dosage for Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline</td>
<td>100 mg twice a day for 21 days</td>
<td>Not recommended for children &lt; 8 years of age</td>
</tr>
<tr>
<td></td>
<td>Contraindicated for pregnant or lactating people</td>
<td>For children aged 9-12 years of age &lt; 45 kg: 5 mg/kg/day in 2 divided doses on day 1, followed by 2.5 mg/kg/day in 1 or 2 divided doses, for a total of 21 days</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>1 g three times a day for 21 days</td>
<td>For children &lt; 12 years of age ≤ 33 kg: 30 mg/kg three times a day for 21 days</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>500 mg twice per day for 14-21 days</td>
<td>For children &gt; 8 years of age: 500 mg/kg/day divided in 2 doses (maximum 500 mg/dose) for 14-21 days</td>
</tr>
</tbody>
</table>

For Allergy or Intolerance
- Azithromycin: 500 mg/dl for 17 days
- Clarithromycin: 500 mg twice a day for 14-21 days
- Erythromycin: 500 mg four times a day for 14-21 days
- Azithromycin: 7.5 mg/kg twice a day for 14-21 days (maximum 500 mg/day) for 14-21 days
- Erythromycin: 12.5 mg/kg four times a day for 14-21 days (maximum 500 mg/dose) for 14-21 days

Patients treated with macrolides should be closely monitored to ensure resolution of clinical symptoms as macrolides are less effective.
Case #3

• 19 year old student lives in **Kitchener**
• Presented to a doctor with history of rash (circular erythematous patch) for ~1 week in April
• General “flu-like” symptoms (i.e., fatigue, chills, fever, headache, muscle and joint aches, and swollen lymph nodes)
• No travel history **to risk areas and no possible contact with ticks** in past month
• Initial thoughts and work-up?
While low, there is a probability of encountering blacklegged ticks almost anywhere in the province, provided the habitat is suitable for blacklegged ticks (e.g., wooded or brushy areas).

Management of Tick Bites and Investigation of Early Localized Lyme Disease

**Tick bite but asymptomatic**

- **Is or was the tick attached?**
  - **YES**
    - Safely remove the tick, if attached (see Box 3)
  - **NO**
    - **Is it a blacklegged tick?** (see Box 3)
      - **YES**
      - Attached for ≥24 hours?
        - **YES**
          - Ticks acquired in risk or endemic area with a prevalence of infected ticks > 20%? (See Box 4)
            - **YES**
              - **Was the tick removed within the past 72 hours?**
                - **YES**
                  - Clinical case of Lyme disease
                    - Treat for early localized Lyme disease (see Box 8)
                    - Lyme disease serology not indicated
                    - If symptoms persist, refer patient to an appropriate specialist
                - **NO**
                  - Possible case of Lyme disease
                    - Routine management of patient’s symptoms
                    - Order Lyme disease serology (see Box 8)
                    - Consider treating for early localized Lyme disease (see Box 8)
                    - If symptoms persist, consider an alternative diagnosis. Consult Public Health to understand the local epidemiology. Refer patient to an appropriate specialist, as needed
            - **NO**
              - **Was the patient exposed to ticks in the past 30 days?**
                - **YES**
                  - Yes, residence or travel to risk areas and contact with ticks through outdoor activities
                  - **POSSIBLE**
                  - **NO**
                    - No residence or travel to risk areas but possible contact with ticks through outdoor activities
        - **NO**
          - No residence or travel to risk areas and no possible contact with ticks

- **No risk of Lyme disease**
  - Advise patient to monitor for signs and symptoms for 30 days

- **Risk of Lyme disease is low**
  - Advise patient to monitor for signs and symptoms for 30 days
  - Counsel patient on preventing exposure to ticks

- **At risk for Lyme disease, but post-exposure prophylaxis is not warranted**
  - Advise patient to monitor for signs and symptoms for 30 days

- **At risk for Lyme disease; optimal timing for post-exposure prophylaxis** (see Box 5)
  - Advise patient to monitor for signs and symptoms for 30 days

**Symptomatic (3–30 days following tick exposure)**

- Does the patient have the following signs and symptoms compatible with Lyme disease?
  - Expanding typical or atypical erythema migrans rash > 6 cm (see Box 1)
  - Fever, chills, headache, stiff neck, fatigue, decreased appetite, muscle and joint aches, swollen lymph nodes (see Box 2)

- **Was the patient exposed to ticks in the past 30 days?**
  - **YES**
    - Yes, residence or travel to risk areas and contact with ticks through outdoor activities
  - **NO**
    - No residence or travel to risk areas but possible contact with ticks through outdoor activities
  - **POSSIBLE**
    - No residence or travel to risk areas and no possible contact with ticks

Please contact us at evidence@hqontario.ca or 1-866-823-6888 if you have any questions or feedback about this clinical guidance document.
**Differential**

- Parvovirus
- Enterovirus
- Syphilis
- Epstein-Barr Virus
- Cellulitis
- Ringworm
- Eczema or atopic dermatitis
- List goes on

- If nothing else found and symptoms worsen, consider ordering Lyme serology
Questions?
Acknowledgements (Public Health Ontario)

Thanks to the following individuals for their assistance in developing this presentation:

- Mark Nelder
- Curtis Russell
- Vithusha Ravirajan
- Jennifer Pritchard
- Bryna Warshawsky
Thank you.

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