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#### Diagnosing and Managing Early Lyme Disease in Ontario

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May 14, 2019

Public Health Ontario Grand Rounds

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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**

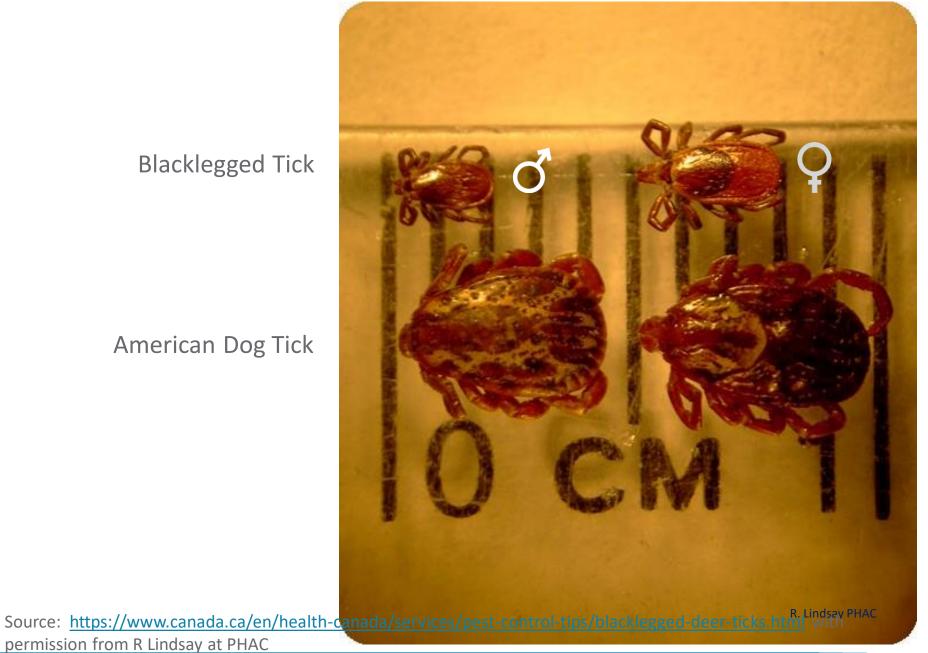
The blacklegged tick (*Ixodes scapularis*) is the vector responsible for transmitting Lyme disease in Ontario



Source: <u>https://www.canada.ca/en/health-canada/services/pest-control-tips/blacklegged-deer-</u> <u>ticks.html</u> with permission from R Lindsay at PHAC

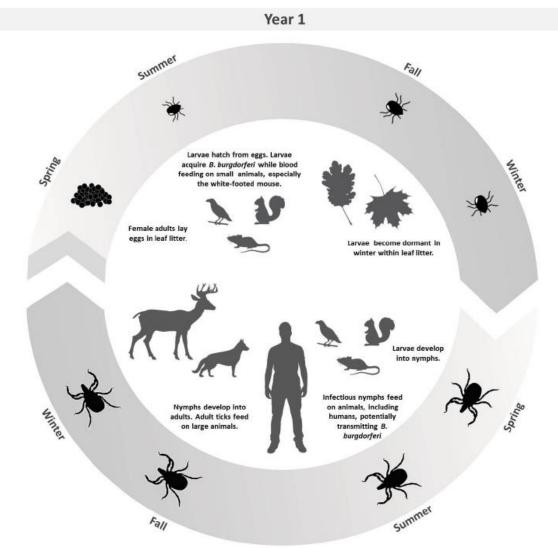


#### American Dog Tick



permission from R Lindsay at PHAC

# Life Cycle of a Blacklegged Tick



#### Year 2

Source: Ontario Agency for Health Protection and Promotion (Public Health Ontario). Technical report: update on Lyme disease prevention and control. 2<sup>nd</sup> ed. Toronto, ON: Queen's Printer for Ontario; 2016. Available from: <u>http://www.publichealthontario.ca/en/eRepository/Technical\_report\_update\_on\_Lyme\_disease\_prevention\_and\_control.pdf</u>

#### 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

Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, et al. Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5539539/</u> Shapiro ED. *Borrelia burgdorferi* (Lyme disease). Pediatr Rev. 2014;35(12):500-9. Available from: <u>https://pedsinreview.aappublications.org/content/35/12/500.long</u>

# **Blacklegged Tick Size Comparison**





Source: <u>https://www.canada.ca/en/health-canada/services/pest-control-tips/blacklegged-deer-ticks.html</u> with permission from R Lindsay at PHAC

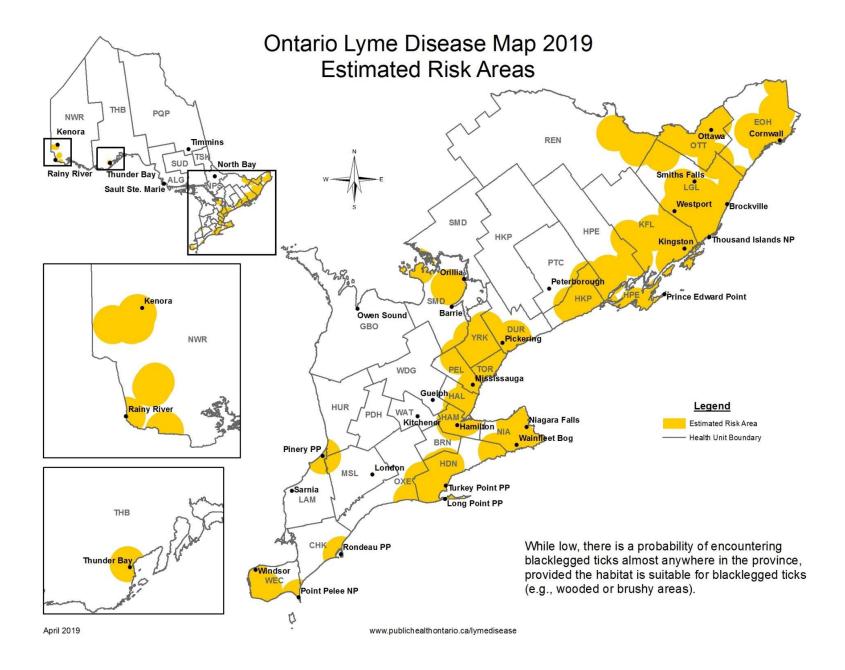
# Lyme Disease Surveillance in Ontario

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)

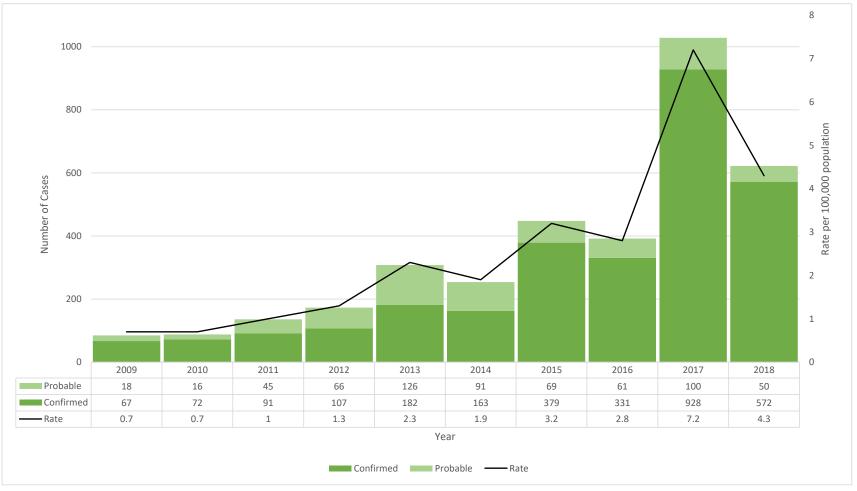
Active Surveillance (looking for ticks in the environment)

- Tick dragging determine estimated risk areas
- Small mammal trapping trapping rodents to test them and their ticks for *B. burgdorferi*



Ontario Agency for Health Protection and Promotion (Public Health Ontario). Ontario Lyme disease map 2019: estimated risk areas. Toronto, ON: Queen's Printer for Ontario; 2019. [cited 2019 May 10]. Available from: <a href="https://www.publichealthontario.ca/-/media/documents/lyme-disease-risk-area-map-2019.pdf?la=en">https://www.publichealthontario.ca/-/media/documents/lyme-disease-risk-area-map-2019.pdf?la=en</a>

#### Annual Lyme Disease Confirmed and Probable Case Counts and Incidence Rate per 100,000 Population: Ontario, 2009-2018



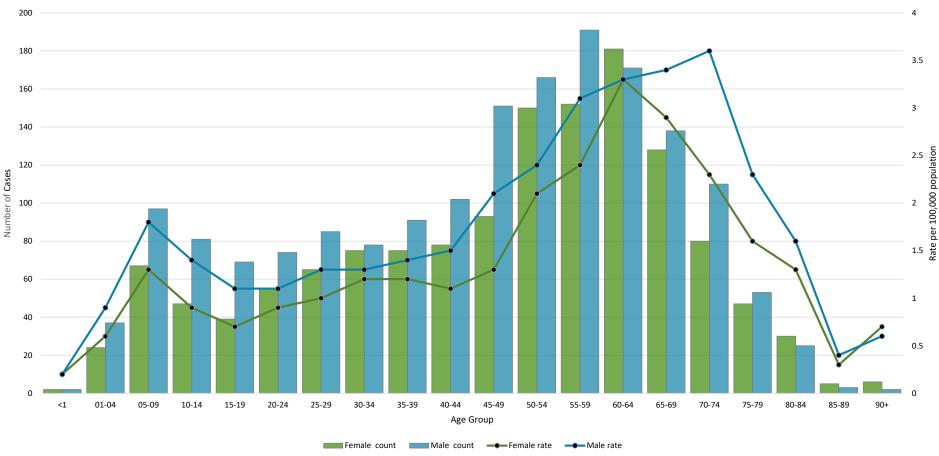
Ontario Cases: Ontario. Ministry of Health and Long-Term Care. Integrated Public Health Information System (iPHIS) [database]. Toronto, ON: Queen's Printer for Ontario [producer and distributor]; [data extracted 2019 Apr 24].

Ontario Population: Statistics Canada. Population Projections 2017-2018 and Estimates 2009-2016 [data file]. Ottawa ON: Government of Canada [producer], Toronto, ON: Ontario. Ministry of Health and Long-Term Care, IntelliHEALTH Ontario [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





#### 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

Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, et al Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5539539/</u> Shapiro ED. *Borrelia burgdorferi* (Lyme disease). Pediatr Rev. 2014;35(12):500-9. Available from: <u>https://pedsinreview.aappublications.org/content/35/12/500.long</u>

#### **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 7<sup>th</sup>)
    - Meningitis or episodic headaches
  - Systemic symptoms
    - Can include fever, myalgia, arthralgia, headache, or fatigue
  - Cardiac symptoms
    - Atrioventricular (AV) node block
  - Arthritis

Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, et al Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5539539/</u> Shapiro ED. *Borrelia burgdorferi* (Lyme disease). Pediatr Rev. 2014;35(12):500-9. Available from: <u>https://pedsinreview.aappublications.org/content/35/12/500.long</u>

#### 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

Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, et al Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5539539/</u> Shapiro ED. *Borrelia burgdorferi* (Lyme disease). Pediatr Rev. 2014;35(12):500-9. Available from: https://pedsinreview.aappublications.org/content/35/12/500.long

#### **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

Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, et al Lyme borreliosis. Nat Rev Dis Primers. 2016;2:16090. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5539539/

# **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. burgdoferi* infection rate in ticks is  $\geq 20\%$
    - 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 endemicity 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



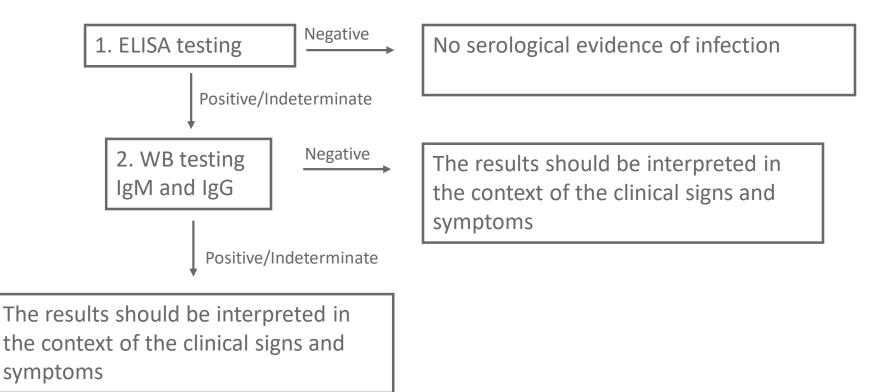
### Performance Characteristics of Each Assay in Patients with Lyme Disease

 Slide presents data on test performance (Whole cell) ELISA, IgM, IgG, two-tier testing) from "Table 4. Reactivities obtained using different methods to detect antibodies to B. burgdorferi in Lyme borreliosis in patients from the United States" from Aguero-Rosenfeld ME, Wang G, Schwartz I, Wormser GP. Diagnosis of Lyme borreliosis. Clin Micro Rev. 2005;18(3):484-509. Available from: https://cmr.asm.org/content/18/3/484.full

Aguero-Rosenfeld ME, Wang G, Schwartz I, Wormser GP. Diagnosis of Lyme borreliosis. Clin Micro Rev. 2005;18(3):484-509. Available from: https://cmr.asm.org/content/18/3/484.full

#### **Testing Algorithm at PHO's Laboratories**

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



#### **Challenges Posed by Private Laboratories in USA**

- Private labs uses variety of different 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: <u>https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5405a6.htm</u>

#### 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

CDC. Notice to readers: caution regarding testing for Lyme disease. MMWR Morb Mortal Wkly Rep. 2005;54(5):125. Available from: <a href="https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5405a6.htm">https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5405a6.htm</a>

Duerden BI. Unorthodox and unvalidated laboratory tests in the diagnosis of Lyme borreliosis and in relation to medically unexplained symptoms [Internet]. London, UK: Crown Copyright; 2006 [cited 2019 May 9]. Available from:

https://webarchive.nationalarchives.gov.uk/20080205204935/http://www.dh.gov.uk/prod\_consum\_dh/idcplg?IdcService=GET\_FILE&dID=3278&Rendition=Web

## 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 speciality 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:
  - Fallon BA, Pavlicova M, Coffino SW, Brenner C. A comparison of Lyme disease serologic test results from 4 laboratories in patients with persistent symptoms after antibiotic treatment. Clin Infect Dis. 2014;59(12):1705-10. Available from: <u>https://academic.oup.com/cid/article/59/12/1705/2895616</u>

#### **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



#### **Clinical Guidance Document**

GRACIA MABAYA & LACEY PHILLIPS | MAY 14, 2019





Let's make our health system healthier

# **Clinical Guidance Document**

### **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**

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

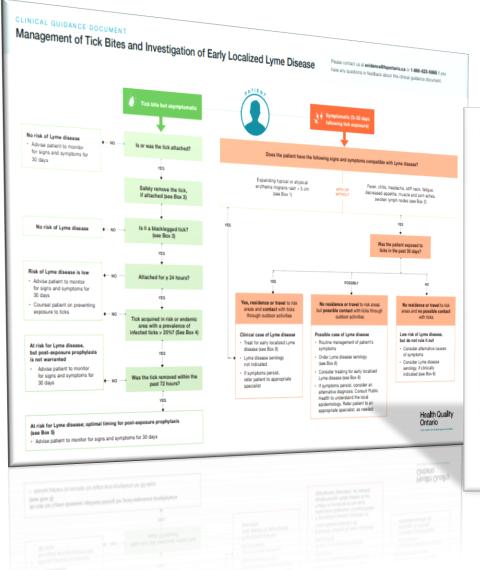
Mid December 2017:

WG review of draft table of contents

Mid November 2017:

First Working Group (WG) meeting

### Lyme Disease Clinical Guidance Document



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



· Headarbs 276

· Ferminia 125

· Still muck 25%

· Decreated appetite 20%

Box 2. Prevalence of Symptoms in Patients

No. a disease of public health significance. Lyne disease is reportable in Oritana upday the Health Protection and Protection Act, R.S.D. 1980, c. H.

geographical regions. Please click to see the risks in

In Europe, the areas of highest risk are in Central and

found in Southern Scandinavia and up to the northern

Eastern Furnne, but infected ticks have also been

Box 4. Areas of Risk for Lyme Disease The risk of acquiring Lyme disease varies across

Ontario, Canada, and the United States.

Presenting With Possible Early Localized Lyme Disease\*

Frothams mineses cash

Fatigue 54%

Musipia 44%

(typical or stypical) -70%

rashes are available on Health Canada's. uninity please see "Early local disease (< 30 days)." Note: Passile with darker skin tones may esent with a bruise-like rash

nal images of typical and atypics





National Urban Park and Morninesida Park in the Greater

Toronto Area, Brighton, Kingston and surrounding areas

surrounding areas, Ottaws and surrounding areas, and

contraindicated for pregnant people and for children

< 8 years old. There is insufficient evidence for the

Adults: 1 dose of documptine 200 mp, by mouth

up to a maximum dose of 200 mg, by mouth

Children a 8 years: 1 dose of doxycycline 4 mg/kg.

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National Voltavie for Health and Case Excellences. (price disease (internel) London (England): The Healthale, 2014 (clinic 2014 Heal), Available Stars

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righylactic use of other medications, such as amosicilly

Thousand Islands, Brockville, Perth-Smiths Falls and

Rondway Provincial Park in Morpeth\*

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#### Mediterranean region. Box 5. Post-Exposure Prophylaxis

The risk of developing Lyme disease following a tick bits by an infected tick is between 1% and 2%. In Ontario, the prevalence of infected ticks varies by peographic region. in many instances, it is reasonable to adopt the "wait and see" approach and treat patients if they develop symptoms tible with Lyme classes. Counsel patients to watch for 4. Descenarios is not contraindicated (Descenarios is the development of early signs and symptoms for 30 days, and advise patients that other tick-borne infactions may sault in signs or symptoms too. Based on the best available evidence, post-expo prophylaxis can be considered if these four criteria are met: 1. The lick was attached - 24 hours. 2. The tick was removed within the past 72 hours 3. The tick was accuired in an area with a prevalence of ticks. nfected with Bornella burgdonleri > 20% (e.g., Rouge

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Aguero Assanctista ME, Narry G, Schwartz I, Morrower GP, Dagnosia of Lyree-Reventions. Clin Microsoft New 2000;10(5):101–1018. Converse DJ, Advances LB, Wallance, GL, Southerne assessments and publishin reconstructed provide the disease the clinical management of income for the organized signess andreas and parentinet classion. Expert New Arts theor Tra-2014;20(1):212–25.

Human GP, Datheyjer AJ, Shapiro GD, Yalgarit JJ, Steen AC, Klengrav MG, 4 at The chiral assessment tractions, and smeather of Letter disease. Notes Automation 74, Dyther para telep Da Cia Sarti An. 2010 DECOV-38

#### Box 6. Laboratory Testing

Laboratory testing is not indicated for asymptomatic Semiopical testing may not vield positive results during early localized Lyme disease, so management should no 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 Borrella burodorferi immunoplobulin 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)

aboratory for testing

Drugs

ecific to European Lyme disease

For serological testing, please complete the upplic fully and submit it, along with samples, to a public health Two-ter testing algorithm is based on service cample is itially tested using erzyme-linked immunisorbein assay (0.154) method. If results of 0.154 If European Lyme disease is suspected based on the method are read forwinderterminate, separate tabl and tab Western bar text patient's travel history, please order serology testing

as jafotted **Falsaing artitions** to

Box 7. Sensitivity of Serological (Two-Tier) Testing

29-40%

22-78%

87%

87%

in Patients With Lyme Disease

Erothama miseana, anula nhase

Neurological involvement (early

Arthritis (late disseminated disease)

Erythema migrana, convaleacence phase!

(early localized disease)

learly localized disease!

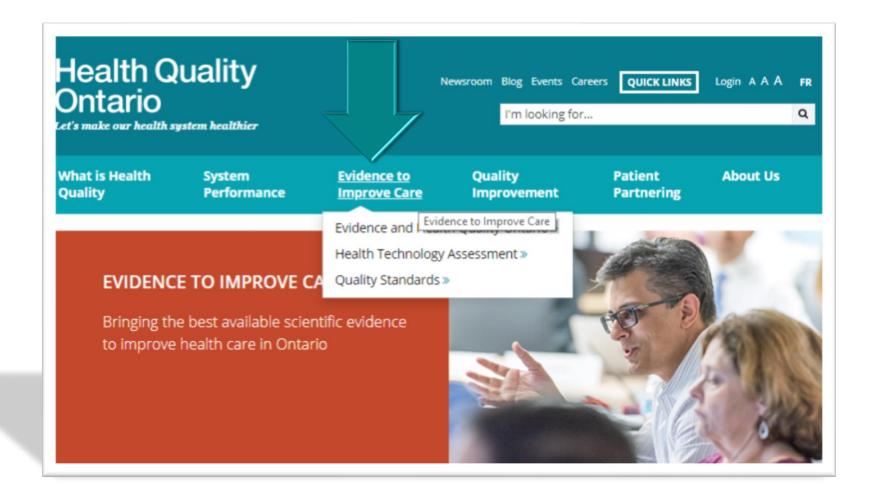
disseminated disease)

#### Box 8. Recommendations for Treatment of Patients With Early Localized Lyme Disease Desages for Adults Desage for Children

Preferred		
Desycycline	100 mg taice a day for 21 days	Not recommended for children < 8 years of age
	Contraindicated for pregnant or lactating people	For children aged 3-12 years of age < 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
		For severe infections, up to 5 mg/kg/day for 21 days
Amoxicilin	1 g three times a day for 21 days	For children s 12 years of age s 33 kg 30 mg/kg three times a day for 21 days
Cefurosime	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	tolerance <sup>8</sup>	
Azithromycin	500 mg/d for 17 days	For children x12 years of age x 50 kg: 10 mg/kg/day for 17 days
Clarithromycin	500 mg twice a day for 14-21 days	For children > 8 years of age: 7.5 mg/kg teice a day (maximum 500 mg/day) for 14–21 days
	Relatively contraindicated in pregnant people	
Erythromycin	500 mg four times a day for 14-21 days	For children > 8 years of age: 12.5 mg/kg tour times a day (maximum dose 500 mg day) for 14-21 days

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### Lyme Disease Clinical Guidance Document

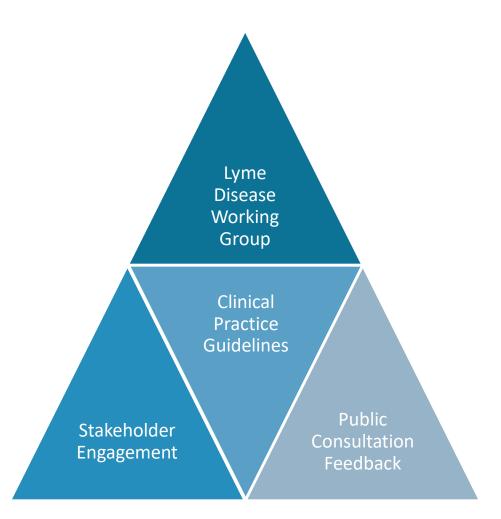


### **Scope of Clinical Guidance Document**

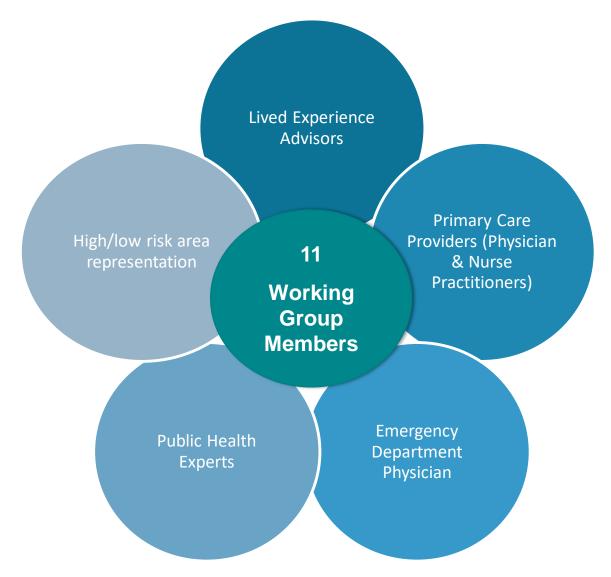
Inclusion Criteria	Exclusion Criteria
<ul> <li>Patient Population <ul> <li>Children and adults</li> </ul> </li> <li>Tick bite management</li> <li>Diagnosis and management of early localized disease (&lt;30 days) <ul> <li>Including post-exposure prophylaxis</li> </ul> </li> <li>Clinical setting <ul> <li>Primary care and emergency department</li> </ul> </li> </ul>	<ul> <li>Prevention of Lyme disease</li> <li>Diagnosis and management of early and late disseminated disease (≥ 30 days but &lt; 3 months or ≥ 3 months)</li> <li>Including indication for laboratory testing</li> <li>Diagnosis and management of coinfections</li> </ul>

# Clinical Guidance Document Development Process

# **Key Development Inputs**



## **Working Group Composition**



### Lyme Disease Clinical Practice Guidelines

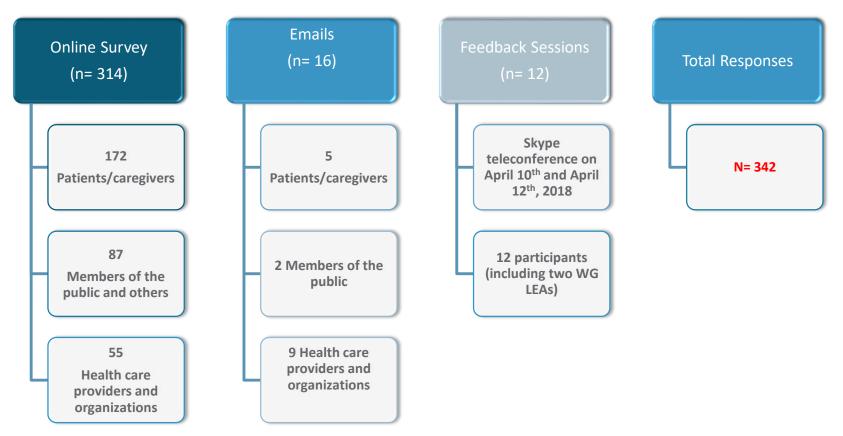
	Year	Author	Country	Title
1	2006	Infectious Diseases Society of America (IDSA)	United States of America	The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America
2	2014	International Lyme and Associated Diseases Society (ILADS)	International	Evidence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease
3	2018	National Institute for Health and Care Excellence (NICE)	United Kingdom	Lyme Disease

# **Additional Documents**

- Canadian Public Health Laboratory Network. The laboratory diagnosis of Lyme borreliosis: guidelines from the Canadian Public Health Laboratory Network. Can J Infect Dis Med Microbiol. 2007;18(2):145-8. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2533539/</u>
- 2. British Infection Association. The epidemiology, prevention, investigation and treatment of Lyme borreliosis in United Kingdom patients: a position statement by the British Infection Association. J Infect. 2011;62(5):329-38.
- 3. Hu LT. Lyme disease. Ann Intern Med. 2016;164(9):ITC65-80.
- Sanchez E, Vannier E, Wormser GP, Hu LT. Diagnosis, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: a review. JAMA. 2016;315(16):1767-77.
- Moore A, Nelson C, Molins C, Mead P, Schriefer M. Current guidelines, common clinical pitfalls, and future directions for laboratory diagnosis of Lyme disease, United States. Emerg Infect Dis. 2016;22(7):1169-77. Available from: <a href="https://wwwnc.cdc.gov/eid/article/22/7/15-1694\_article">https://wwwnc.cdc.gov/eid/article/22/7/15-1694\_article</a>

## **Public Consultation Process**

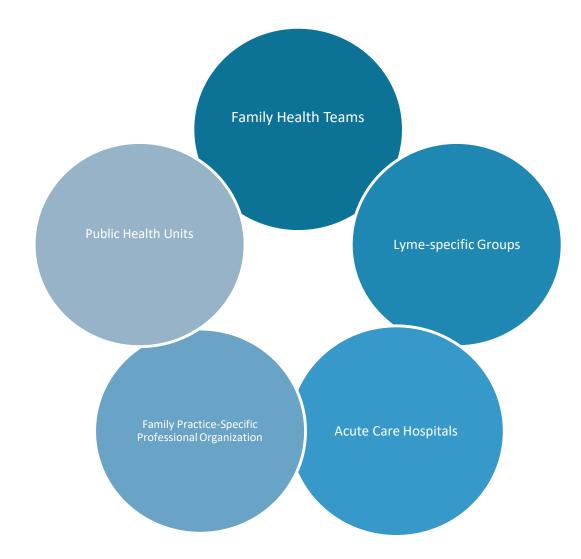
### March 23 – April 16, 2018



# Feedback from Health Care Professionals, Clinicians, and Researchers



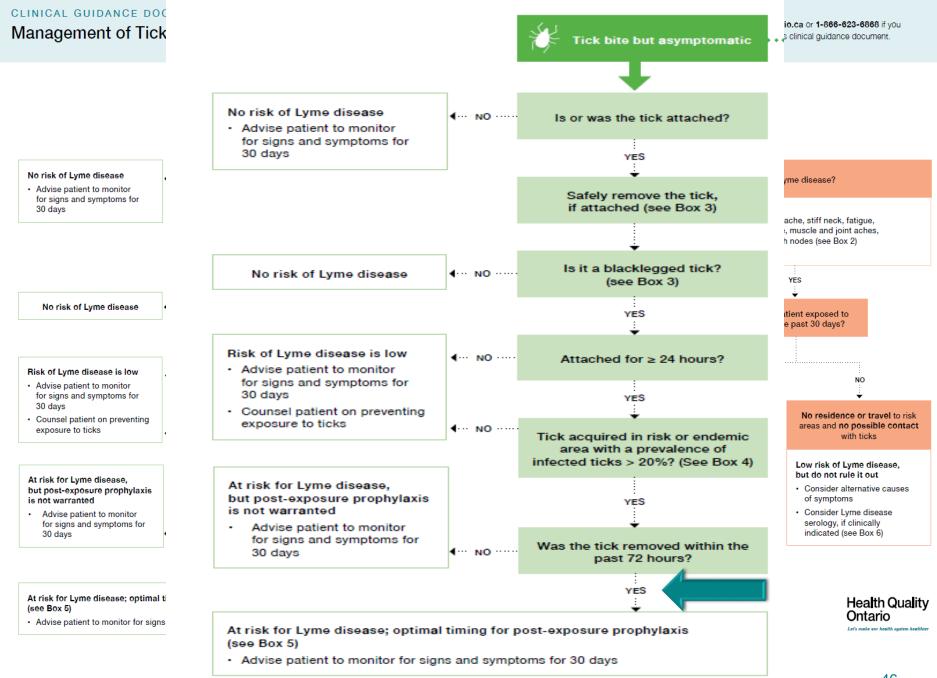
### **Feedback from Organizations**



# **Case Studies**

- 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?

- 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?



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



Decreased appetite 26%

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

- Erythema migrans rash (typical or atypical) ~70% Fever/chills 39%
- Fatigue 54%
   Stiff neck 35%
- Myalgia 44%
- Myaigia 44%

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 <u>Ontario, Canada</u>, and the <u>United States</u>.
- 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
- The tick was acquired in an area with a prevalence of ticks infected with *Borrelia burgdorferi* > 20% (e.g., Rouge

#### Bibliography

Aguero-Rosenfeld ME, Wang G, Schwartz I, Wormser GP. Diagnosis of Lyme Borreliosis. Clin Microbiol Rev. 2005;18(3):484–509.

Cameron DJ, Johnson LB, Maloney EL. Evidence 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.

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

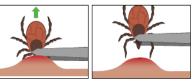
Additional images of typical and atypical rashes are available on <u>Health Canada's</u> <u>website</u>; please see "Early localized Lyme disease (< 30 days)."

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

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



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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\*)

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- Antibiotic treatment in early disease may reduce seroconversion; testing should not be used to monitor treatment outcome
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#### Box 8. Recommendations for Treatment of Patients With Early Localized Lyme Disease

Drugs	Dosage for Adults	Dosage for Children
Preferred		
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Azithromycin	500 mg/d for 17 days	For children ≤12 years of age ≤ 50 kg: 10 mg/kg/day for 17 days
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	Relatively contraindicated in pregnant people	7.5 mg/kg twice a day (maximum 500 mg/day) for 14–21 days
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Patients treated with macrolides should be closely monitored to ensure resolution of clinical symptoms as macrolides are less effective.

Box 7. Sensitivity of Serological (Two-Tier) Testing:

\*Two-tier testing algorithm is based on serum sample initially tested using

enzyme-linked immunosorbent assay (ELISA) method. If results of ELISA

method are reactive/indeterminate, separate IgM and IgG Western blot tests

29-40%

29-78%

87%

97%

in Patients With Lyme Disease

Ervthema migrans, convalescence phase<sup>‡</sup>

Erythema migrans, acute phase

Neurological involvement (early

Arthritis (late disseminated disease)

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- A 30 year old **asymptomatic** patient presented with a tick that was attached to her for over a day
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- Prophylaxis or no prophylaxis?
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- What if it was a 6-year-old boy?

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



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

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

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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 > 24 hours
- 2. The tick was removed within the past 72 hours
- The tick was acquired in an area with a prevalence of ticks infected with *Borrelia burgdorferi* > 20% (e.g., Rouge

#### Bibliography

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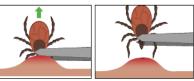
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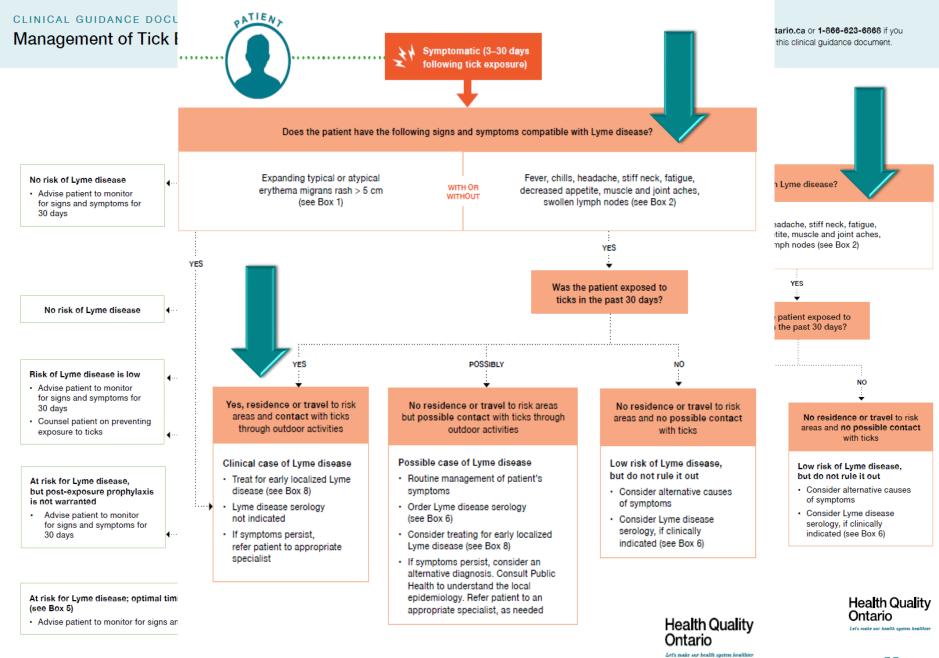
- 68-year-old retired nurse living in Ottawa area was bitten by a tick while gardening
- She took the tick to her local public health unit
- Tick was not sent to the laboratory at Public Health Ontario for identification
- A few days later she developed a rash and "flu-like" symptoms
- Upon examination 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?

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Erythema migrans rash 
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 (typical or atypical) ~70%
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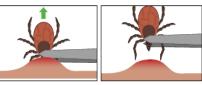
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Box 7. Sensitivity of Serological (Two-Tier) Testing<sup>1</sup> in Patients With Lyme Disease

Erythema migrans, acute phase (early localized disease)	29-40%
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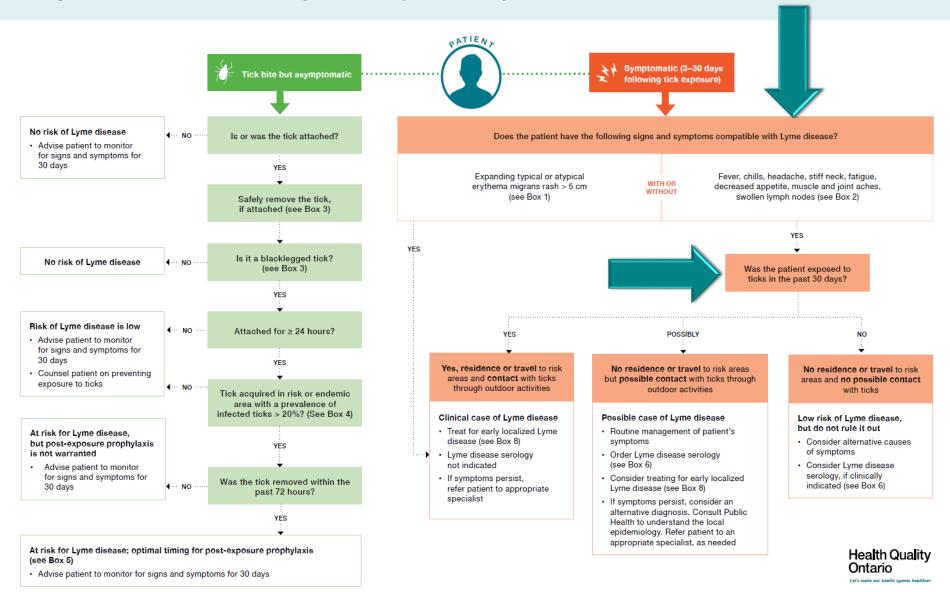
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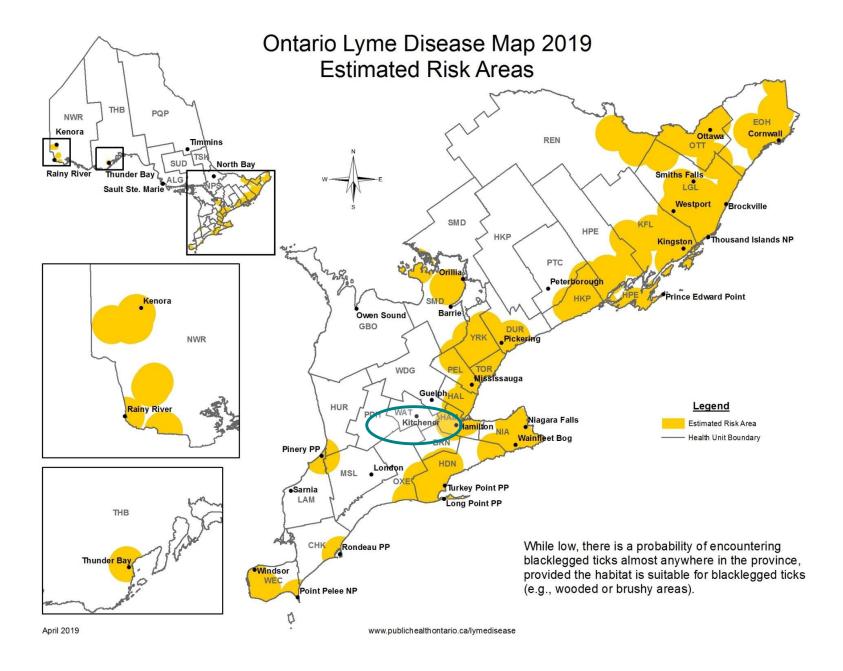
- 19 year old student lives in Kitchener
- Presented to a doctor with history of rash (circular erythematous patch) for ~1 week in April
- General "flu-like" symptoms (i.e., fatigue, chills, fever, headache, muscle and joint aches, and swollen lymph nodes)
- No travel history to risk areas and no possible contact with ticks in past month
- Initial thoughts and work-up?

### CLINICAL GUIDANCE DOCUMENT

### Management of Tick Bites and Investigation of Early Localized Lyme Disease

Please contact us at evidence@hqontario.ca or 1-866-623-6868 if you have any questions or feedback about this clinical guidance document.



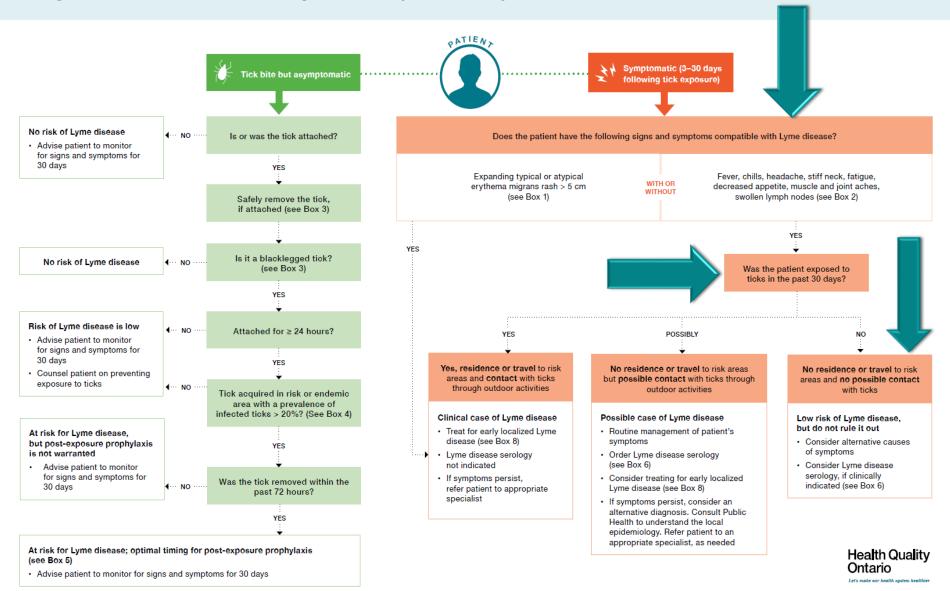


Source: Ontario Agency for Health Protection and Promotion (Public Health Ontario). Ontario Lyme disease map 2018 estimated risk areas [Internet]. Toronto, ON: Queen's Printer for Ontario; 2018 [cited 2018 June 14]. Available from: <a href="http://www.publichealthontario.ca/en/eRepository/Lyme\_disease\_risk\_areas\_map.pdf">http://www.publichealthontario.ca/en/eRepository/Lyme\_disease\_risk\_areas\_map.pdf</a>

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## 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.

### LET'S CONTINUE THE CONVERSATION:

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You Tube

- HealthQualityOntario
- F) @HQOntario
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### Health Quality Ontario

Let's make our health system healthier

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