Lyme Disease (Lyme Borreliosis)

Manitoba
Public Health Branch

1. Case Definition

The following are National surveillance definitions and not intended to guide clinical management (1).

1.1 Confirmed case

One of the following:

1. Clinical evidence of illness with laboratory confirmation:
   - isolation of *Borrelia burgdorferi* (or *B. burgdorferi*) from an appropriate clinical specimen

     OR
   - detection of *B. burgdorferi* DNA by PCR
2. Clinical evidence of illness with a history of residence in, or visit to, an endemic area*, and with laboratory evidence of infection:
   - positive serologic test using the two-tier ELISA and Western Blot criteria

1.2 Probable case

One of the following:

1. Clinical evidence of illness without a history of residence in, or visit to, an endemic area* and with laboratory evidence of infection:
   - positive serologic test using the two-tier ELISA and Western Blot criteria
2. Clinician-observed erythema migrans (EM) without laboratory evidence but with history of residence in, or visit to, an endemic area*

Note*: PHAC's definition of an endemic area has two requirements: a reproducing population of *Ixodes scapularis* or *Ixodes pacificus* ticks; and evidence of *B. burgdorferi* infection in that population (1).

For more information about the case definitions, please see
http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09vol35/35s2/Lyme-eng.php.

2. Reporting and Other Requirements

In 2009, all probable and confirmed cases became reportable to the Public Health Agency of Canada.

Laboratory:

- All positive laboratory tests for *Borrelia burgdorferi* (serology, isolation or nucleic acid detection) are reportable by laboratory.
- Equivocal serology (defined as a positive ELISA, positive IgM Western Blot and negative/borderline IgG Western Blot) is also reportable.

Health Professional:

- Clinical cases of Lyme disease are to be reported to Manitoba Health using the Lyme Disease Clinical Case Report Form (http://www.gov.mb.ca/health/lyme/pdf/lyme_reportfrm.pdf) and submitted by fax to the Environmental Health Policy Unit at (204) 948-2190 (secure fax line). It is important to supply a travel history or any exposure to ticks that is as complete as possible. Public health practitioners may contact physicians/clinicians for further information on reported cases.

3. Clinical Presentation/Natural History

This tickborne, spirochetal, zoonotic disease can be characterized by a distinctive skin lesion, systemic symptoms and neurologic, rheumatologic and cardiac involvement, occurring in varying combinations, over a period of weeks to years.

Early localized Lyme Disease - Erythema Migrans (days to weeks after infection)

- Erythema migrans (EM) appears in 60 to 80 per cent of patients within three to 30 days after exposure to an infected nymph or adult *Ixodes* tick (2,3). EM is an expanding round or oval, erythematous skin lesion, usually more than five cm in diameter, occurring at the site of the tick bite (1,4). EM skin lesions can vary in

appearance: some are homogeneously erythematous, whereas others have prominent central clearing or a target appearance (5,6,7); rarely vesicles or pustules can be present (<5%) (8). Typical signs of inflammation, including itchiness, swelling, pain, scaling and exudation are not usually associated with EM (1,9).

- The EM rash is specific to Lyme disease and if recognized, when associated with the appropriate exposure, is sufficient for a clinical diagnosis and initiation of treatment for Lyme disease (4). Most patients do not recall a tick bite due to the very small size of the ticks.
- Within 48 hours of tick detachment, or while a tick is attached to the skin, an erythematous lesion less than five cm in diameter may appear. This could be a tick bite hypersensitivity reaction rather than EM and should disappear in 24-48 hours after tick removal (1,4).

Early disseminated disease (days to months after infection) may manifest as:

- Additional early symptoms of Lyme disease concurrent with EM may include fatigue, fever, headache, mildly stiff neck, arthralgia or myalgia, and lymphadenopathy in untreated infection (2,10,11). Multiple EM lesions which may be less than 5 cm are believed to be secondary to hematogenous spread (12). Multiple EM represents the earliest disseminated disease and may appear within several days to weeks of onset of illness (10,11). EM appearing months or years after the initial EM is likely to be caused by a new infection.
- Cardiac symptoms present in a small percentage of patients, usually within 2 months of infection, and can include intermittent atrioventricular heart block often involving the atrioventricular node (although heart block may occur at multiple levels) and sometimes associated with myopericarditis (1,4).
- Neurological symptoms affecting the acute peripheral nervous system, including radiculopathy, cranial neuropathy and mononeuropathy multiplex (multifocal involvement of anatomically unrelated nerves); and the central nervous system (CNS), including lymphocytic meningitis and, rarely, encephalomyelitis (parenchymal inflammation of brain and/ or spinal cord with focal abnormalities) (1,2,4).

Late Lyme Disease (months to years after infection) may occur in untreated patients.

- Lyme arthritis is a monoarticular or oligoarticular form of arthritis most commonly involving the knee, but other large joints or the temporo-mandibular joint may be involved (1,4). Large effusions that are out of proportion to the pain are typical. Lyme arthritis is often intermittent if untreated, with episodes of joint inflammation spontaneously resolving after a few weeks to a few months. Persistent swelling of the same joint for 12 months or more is not a usual presentation. Lyme arthritis usually resolves completely within several years, even in untreated patients (13).
- In rare instances, neurological symptoms can present months to years after infection and after long periods of latent infection (13). Late Lyme disease-associated peripheral neuropathy may present as reduced vibratory sensation of the distal lower extremities, intermittent limb paresthesias or radicular pain (4). Encephalomyelitis is severe, may be unifocal or multifocal (14,15), principally involves white matter and is monophasic and slowly progressive (4). Lyme disease-associated encephalopathy is a mild syndrome involving subtle cognitive disturbances (16,17).

Post-Lyme disease syndrome

- A small percentage of patients develop subjective pain, neurocognitive or fatigue symptoms lasting months to years after resolution of objective Lyme disease symptoms with antibiotic therapy (18). This phenomenon, sometimes known as Post-Lyme disease syndrome, has no well-accepted diagnostic criteria, making it difficult to

evaluate the prevalence, pathogenesis and treatment requirements. In order to provide a framework for future research in this area, the Infectious Disease Society of America has suggested a definition of Post-Lyme disease syndrome (4). The suggested definition may be found in Table 5 of the 2006 IDSA guidelines at http://www.idsociety.org/Lyme/.

Co-infection

- *Anaplasma phagocytophilum*, the agent of Human granulocytic anaplasmosis (HGA), and *Babesia microti*, the agent of babesiosis, can be transmitted by blacklegged ticks. Co-infection with *B. burgdorferi* and one or both of *A. phagocytophilum* and *B. microti* may lead to more severe acute illness (19,20). Both *A. phagocytophilum*, and rarely *B. microti*, have been isolated from blacklegged ticks in Manitoba. Co-infection should be considered in patients who present with initial symptoms which are more severe than commonly observed with Lyme disease, especially when a high grade fever is present for more than 48 hours despite effective Lyme disease treatment, or when thrombocytopenia, leukopenia, or anemia are present despite resolved EM and flu-like symptoms.

Patients with travel history to Europe may exhibit additional symptoms not included in this protocol; please see the 2006 clinical practice guidelines of the Infectious Disease Society of America at http://www.idsociety.org/Lyme/ for details (4).

4. Etiology

Lyme disease is a tick-borne infection caused by the spirochete *Borrelia burgdorferi* and transmitted in Manitoba by *Ixodes scapularis*, the blacklegged tick. Lyme disease is caused by three pathogenic *Borrelia* species (*Borrelia burgdorferi sensu lato*). To date, all North American strains have belonged to the first group, *Borrelia burgdorferi sensu stricto*, while strains in the other two species, *Borrelia garinii* and *Borrelia afzelii*, are found only in Europe and Asia (13).

5. Epidemiology

5.1 Vectors and Reservoir

The vectors of Lyme disease are certain ixodid tick species of the *Ixodes ricinus* complex (21). In eastern and central North America (including Manitoba), the primary vector tick is *Ixodes scapularis*, and *Ixodes pacificus* is the vector in British Columbia and the western United States (13,22). Wild rodents (especially *Peromyscus spp*., commonly known as deer mice) and birds maintain the enzootic transmission cycle as reservoir hosts (22). Deer, which are not involved in the transmission cycle, nonetheless serve as important mammalian hosts for the tick vectors and may be necessary for their survival (13). Larval and nymphal ticks prefer to feed on small mammals, while adult ticks feed primarily on larger animals such as deer (13,22).

5.2 Transmission

Lyme disease is transmitted when an infected tick takes a blood meal. In experimental animals, transmission of *B. burgdorferi* by *I. scapularis* rarely occurs unless the tick has been attached for 36 hours or more (23,24). This is also thought to be true in humans (4). In Europe and Asia however, *I. ricinus* can often transmit *B. afzelii* in less than 24 hours (25,26).

5.3 Occurrence

General: Lyme disease is the most common vector-borne disease in the United States and Europe (27,28), with more than 25,000 confirmed or probable cases each year since 2007 in the United States (29). In the United States, most human cases are associated with two primary endemic foci along the upper Atlantic coast, and in the upper Midwest. Endemic areas are being redefined both by increasing recognition of the disease and by range expansion of *I. scapularis* out of these two primary foci (30). Elsewhere, it is common in the temperate zone in Europe and Asia, with the highest reported frequencies of infection occurring in Austria, the Czech Republic, Germany, Slovenia and the northern countries bordering the Baltic Sea (31).

Adult *I. scapularis* ticks quest primarily during spring and fall, while nymphs are active throughout the summer (13). The small size of nymphal ticks (less than 2 mm) increases their probability of transmitting infection before being identified and removed (32). In the United States, the largest number of confirmed Lyme disease cases between 2001 and 2010 had onset of illness in the months of June, July and August, corresponding to periods of high nymph activity (33).

Canada: Lyme disease became nationally reportable to the Public Health Agency of Canada (PHAC) in 2009. The highest numbers of provincially reported Lyme disease cases occur in Ontario, which reported between 95 and 110 cases each year between 2008 and 2010 (34), and 140 cases in 2011 (35). Nova Scotia reported 54 cases of Lyme disease in 2011, and between 13 and 17 cases each of the three years prior (36). British Columbia reported between 7 and 20 cases each year between 2008 and 2011 (37).

The vast majority of Lyme disease cases in Canada are reported in the provinces where there are established populations of infected *I. pacificus* (British Columbia) or *I. scapularis* (Manitoba, Ontario, Quebec, New Brunswick and Nova Scotia) ticks. In recent years, the number of endemic areas in Canada has been expanding; for a current list of endemic areas in Canada, see http://www.phac-aspc.gc.ca/id-mi/tickinfo-eng.php. It is expected that the range of *I. scapularis* will continue to expand in the coming years, and that this process may accelerate with climate change (38,39). It has been estimated that northward expansion of *I. scapularis* range will occur at a rate of approximately 46 km/year in the coming decade, but climate change could increase this rate of spread (40). Based on these estimates, the proportion of the human population of Canada from Manitoba eastward inhabiting areas with established *I. scapularis* populations is expected to increase from 18% in 2010 to over 80% in 2020 (40).

Manitoba: Between 1999 and 2008, 24 cases were reported in Manitoba based on previous case definitions. Beginning in 2009, all cases in Manitoba (including those not meeting the PHAC case definitions for confirmed and probable cases) have been reported on the Manitoba Health website at http://www.gov.mb.ca/health/lyme/stats.html. Between 2009 and 2012, 22 confirmed and 25 probable cases of Lyme disease were reported in Manitoba.

In Manitoba, blacklegged ticks are most commonly found in:

- wooded areas
- areas where forests meet plains
- places with thick, woody shrubs and other vegetation
- areas with plenty of leaf litter and high humidity

Areas with established blacklegged tick populations carry the highest Lyme disease risk. However, because ticks can attach to migrating birds, it is possible to find blacklegged ticks in other areas of Manitoba. The disease risk outside endemic areas is relatively low. As of July, 2012, surveillance activities have identified confirmed or suspected established populations of infected blacklegged ticks (endemic areas for Lyme disease) in the following areas of Manitoba:

- the **southeastern corner of the province**
- the **Pembina escarpment** in south-central Manitoba, including the Stanley/Thompson Trails
- the **Pembina Valley**, from the United States border to approximately La Rivière
- the area around **St. Malo** in south-central Manitoba
- **Arbakka** (south of Vita)
- **Beaudry Provincial Park**, west of Headingley

For updated information about established populations of blacklegged ticks in Manitoba, and a more detailed description of the areas listed here, see http://www.gov.mb.ca/health/lyme/surveillance.html.

5.4 Incubation Period

The incubation period for EM can range from three to 30 days after tick exposure. However, the early stages of the illness may be asymptomatic, with the patient presenting with later manifestations.

5.5 Susceptibility and Resistance

All persons are considered susceptible. Reinfection has occurred in those treated with antibiotics for early disease, as well as in other, non-treated individuals (4).

5.6 Period of Communicability

There is no evidence of natural transmission from person-to-person, except in the rare case reports of congenital transmission in the mid-1980s, with two infants dying during the first week of life (10). However, no further cases of congenital transmission were documented in subsequent prospective studies (41).

6. Laboratory Investigation

- A serum specimen (red top or serum separator tube), should be sent to Cadham Provincial Laboratory (CPL).
- The volume should be 5-10 cc for adults and 2-3 cc for children.
- Serologic testing involves a two-tier approach to measure antibodies: 1) ELISA (enzyme-linked immunosorbent assay); if positive, then 2) a Western Blot test is performed to confirm a positive test for Lyme disease.
- Travel history or any exposure to ticks should be noted on the requisition. For example, travel to Europe or Asia requires a different test kit.

Early localized Lyme disease or early disseminated disease: Both acute and convalescent serum samples (minimum 3-4 weeks apart) are recommended. Serologic tests for Lyme disease may be negative early in the infection (within the first six weeks after infection). Some individuals treated early in the infection may not seroconvert or may never meet the positivity criteria on western blot, hence remaining negative or equivocal. Ensure that the convalescent sample is taken 6 weeks after the onset of symptoms.

Late Lyme disease: Single serum sample is sufficient.

Other Laboratory tests: The United States Centers for Disease Control and Prevention (CDC) has cautioned against the use of alternative testing procedures offered by some for-profit laboratories (42,43).

7. Key Investigations

Positive laboratory and equivocal serology results are referred to the health region of residence for public health investigation. Results of the investigation are to be reported to Manitoba Health using the *Lyme Disease Clinical Case Report Form* (http://www.gov.mb.ca/health/lyme/pdf/lyme_reportfrm.pdf) and submitted by fax to the Environmental Health Policy Unit at (204) 948-2190 (secure fax line). It is important to complete the form as fully as possible, with emphasis on:

- history of erythema migrans
- travel history (including local excursions) within 30 days prior to symptom onset
- known tick exposure within 30 days prior to symptom onset

Public Health will consider travel history and patient residence in order to determine potential endemic area exposure.

8. Control

8.1 Management of Cases

Early diagnosis and treatment is important to prevent development of late complications. **Treatment should be initiated based on clinical suspicion of the disease.** Consultation with an infectious disease specialist is recommended for all complex cases.

TREATMENT FOR EARLY DISEASE

Dosage for adults	Dosage for children
Erythema migrans	
• **Doxycycline** (contra-indicated in pregnant or lactating women or children < eight years old) 100mg PO BID for two to three weeks OR • **Amoxicillin** 500mg PO TID for two to three weeks OR • **Cefuroxime axetil** 500mg PO BID for two to three weeks can be used for patients with penicillin allergies or who are unable to take tetracyclines	• **Amoxicillin** 50mg/kg/day in three divided oral doses (max. 500mg/dose) for two to three weeks • **Cefuroxime axetil** 30mg/kg/day in two divided oral doses (max. 500mg/dose) for two to three weeks
Early neurologic disease – cranial nerve palsy	
• Oral regimen as described for EM	
Early neurologic disease – meningitis or radiculopathy	
• **Ceftriaxone** 2g IV once daily for two to four weeks	• **Ceftriaxone** 50-75mg/kg IV in a single dose (maximum, 2g) for two to four weeks
Cardiac disease	
• Oral regimen as described for EM in ambulatory patients • Parenteral regimen for two to three weeks as described for meningitis or radiculopathy in hospitalized patients; an oral regimen may be substituted to complete a course of therapy	

TREATMENT FOR LATE DISEASE

Dosage for adults	Dosage for children
Arthritis without neurologic disease	
• Oral regimen as described for EM for four weeks	
Recurrent arthritis after oral antibiotic regimen	
• Oral regimen as described for EM for four weeks OR • Parenteral regimen as described for meningitis or radiculopathy	
Central or peripheral nervous system disease	
• Parenteral regimen as described for meningitis or radiculopathy	

* Please see the most current IDSA guidelines for additional information and updates at http://www.idsociety.org/Lyme/, including: alternative therapies for patients who are intolerant of the antibiotics or regimens listed here; treatment of symptoms rarely seen in North America; and treatment of antibiotic-refractory arthritis and post-Lyme disease syndrome (4).

Routine prophylactic treatment in the absence of objective symptoms of Lyme disease is **not** recommended (4). If a patient presents with recent history of a tick bite (whether it is known to be *I. scapularis* or not), but without early symptoms of Lyme disease, they should be educated and asked to return should symptoms appear.

8.2 Management of Contacts

No public health management of contacts is required as person-to-person spread does not occur.

8.3 Preventive Measures

Educate the public about transmission by ticks and personal protection, including the following:

- After spending time outdoors, inspect yourself and your children for ticks and remove any ticks found as soon as possible. Bathing soon after coming indoors is a good way to find ticks.
- Apply an appropriate repellent (it should state 'for use against ticks' on the product label) on clothing and exposed skin. Always read and follow instructions for use.
- Use trails, whenever possible, and stay to the centre of hiking trails or paths.
- Wear light-coloured clothing to make it easier to see ticks crawling on your clothing.
- Wear long pants and a long-sleeved shirt so that most exposed skin is covered.
- Tuck your shirt into your pants and your pants into your socks; this will make it more difficult for the ticks to attach to your skin.
- Regularly inspect pets for ticks, as they can bring ticks into the home.
- If a tick is attached to the skin, remove it with tweezers:
  - Grasp the tick close to the skin with tweezers and pull slowly upward with steady pressure; avoid twisting or crushing the tick. Other methods such as using a match, petroleum jelly, soap, etc. are not recommended.
  - Cleanse the skin around the tick bite with soap and water or disinfectant.
  - Mark the date and location of the tick bite on a calendar for future reference.
  - If symptoms develop, see your doctor.

In areas where blacklegged tick populations are established, a large number of landscape management strategies can be employed to help reduce the abundance of ticks (44). In general, tick numbers can be lowered by reducing cover and shade, through activities such as keeping grass mowed short, removing leaf litter and trimming other vegetation (shrubs and trees) to minimize shade cover in commonly used areas. Also, 'tick unfriendly' habitats can be created by using drier, less water-demanding materials such as mulch, gravel, decks or cement in commonly used areas. For more detailed information, relevant sections of Stafford's Tick Management Handbook (44) can be accessed at

http://www.gov.ns.ca/hpp/publications/Pages_from_Tick_Management_Handbook.pdf.

Tick Surveillance:

- Further information can be found on the Manitoba Health website at www.gov.mb.ca/health/lyme.

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