Alberta Public Health Disease Management Guidelines

Lyme Disease

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Health and Wellness Promotion Branch

Public Health and Compliance Branch

Alberta Health

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Case Definition

Confirmed Case

Clinical illness[A] with a history of residence in, or visit to, an endemic area[B] and with laboratory evidence of infection:

- Positive serologic test[C] for *Borrelia burgdorferi* following the two-tier algorithm of enzyme immunoassay (EIA) (ELISA) and Western Blot

OR

Clinical evidence of illness[A] with laboratory confirmation:

- Detection of *B. burgdorferi* DNA by molecular diagnostic methods (i.e., polymerase chain reaction [PCR]) from an appropriate clinical specimen (e.g., skin biopsy, synovial fluid or CSF)[D]

  OR

- Isolation of *B. burgdorferi*[C] from an appropriate clinical specimen (e.g., skin biopsy, synovial fluid or CSF)[D]

Probable Case

Clinical illness[A] without a history of residence in, or visit to, an endemic area[B] and with laboratory evidence of infection:

- Positive serologic test[C] using the two-tier EIA and Western Blot algorithm

  OR

- Clinician-observed EM that occurred within the previous 12 months, without laboratory evidence, but with history of residence in, or visit to, an endemic area[B]

[A] For purposes of surveillance, erythema migrans (EM) is defined as a round or oval expanding erythematous area of the skin greater than 5 cm in diameter and enlarging slowly over a period of several days to weeks. It appears one to two weeks (range 3–30 days) after infection and persists for up to eight weeks. Some lesions are homogeneously erythematous, whereas others have prominent central clearing or a distinctive target-like appearance. On the lower extremities, the lesion may be partially purpuric. Signs of acute or chronic inflammation are not prominent. There is usually little pain, itching, swelling, scaling, exudation or crusting, erosion or ulceration except that some inflammation associated with the tick bite itself may be present at the very centre of the lesion. Note: An erythematous skin lesion present while a tick vector is still attached or which has developed within 48 hours of detachment is most likely a tick bite hypersensitivity reaction (i.e., a non-infectious process), rather than EMs. Tick bite hypersensitivity reactions are usually <5 cm in largest diameter, sometimes have an urticarial appearance, and typically begin to disappear within 24–48 hours.

OR

Objective evidence of disseminated Lyme disease includes any of the following when an alternative explanation is not found:

- Neurological: Early neurological Lyme disease: acute peripheral nervous system involvement including radiculopathy, cranial neuropathy, and mononeuropathy multiplex (multifocal involvement of anatomically unrelated nerves), and central nervous system (CNS) involvement including lymphocytic meningitis and, rarely, encephalomyelitis (parenchymal inflammation of brain and/or spinal cord, with focal abnormalities). Late neurologic Lyme disease may present as encephalomyelitis, peripheral neuropathy, or encephalopathy.
- Musculoskeletal: 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. 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.
- Cardiac: Cardiac involvement associated with Lyme disease includes intermittent atrioventricular heart block often involving the atrioventricular node, (although heart block may occur at multiple levels), and sometimes associated with myopericarditis. Carditis can occur in early stages of the disease.

[B] An endemic area is defined as a locality in which two or more locally-acquired human cases have been reported OR a reproducing population of Ixodes scapularis or I. pacificus tick vectors is known to occur, which has been demonstrated by molecular methods to support transmission of *B. burgdorferi* at that site (see Incidence).

[C] Includes the genospecies *B. burgdorferi*, *B. afzelii* and *B. garinii*.

[D] Consult the Public Health Laboratory (ProvLab) Microbiologist-on-Call. Refer to the ProvLab Guide to Services for current specimen collection and submission information.

Table 1: Case Classification Summary

Case Classification	Clinical evidence of illness[A] required	Exposure to an endemic area[B] required	Laboratory Criteria	Testing	Clinician Diagnosis Required?
Confirmed	Yes*	Yes	Yes	Two Step Testing Process: 1. EIA Positive or Indeterminate AND 2. Western Blot (IgM and/or IgG) Positive[C]	Yes
	Yes*	No	Yes	PCR or culture	Yes
Probable	Yes*	No	Yes	Two Step Testing Process: 1. EIA Positive or Indeterminate AND 2. Western Blot (IgM and/or IgG) Positive[C]	Yes
	Yes*	Yes	Not Required		Yes

*EM may be present or absent.

Reporting Requirements

Physicians, Health Practitioners and Others

Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed and probable cases by mail, fax or electronic transfer within 48 hours (two business days).

Laboratories

All laboratories shall report all confirmed positive laboratory results by mail, fax or electronic transfer within 48 hours (two business days) to the:

- Chief Medical Officer of Health (CMOH) (or designate), and
- MOH (or designate) of the zone.

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- The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed and probable cases to the CMOH (or designate) within two weeks of notification and the final NDR (amendment) within four weeks of notification.
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days):
  - name,
  - date of birth,
  - out-of-province health care number,
  - out-of-province address and phone number,
  - positive laboratory report, and
  - other relevant clinical/epidemiological information.

Epidemiology

Etiology

The causative spirochete of Lyme disease in North America is solely *B. burgdorferi sensu lato*, first identified in 1982 by Steere and colleagues.[1] Historically, there was published clinical evidence of Lyme disease in Europe, with the description of acrodermatitis chronica atrophicans (ACA) in 1883 by Buchwald[2,3] and only much later in the United States in 1976, after clusters of children diagnosed with juvenile rheumatoid arthritis, subsequently found to have Lyme disease, were reported.[4]

Currently, 19 genospecies have been described within *B. burgdorferi sensu lato*; three of these have been definitively associated with disease in humans, namely *B. burgdorferi, B. garinii and B. afzelii*.[5] In North America *B. burgdorferi sensu stricto* is the only genospecies, whereas in Europe, *B. burgdorferi sensu stricto*, *B. garinii* and *B. afzelii*[1] also occur, with two recently described pathogens – *B. spielmanii* and *B. bavariensis*[5] – associated with occasional infections. *B. garinii and B. afzelii* are also found in Asia.[6]

The spirochete produces a number of differentially expressed outer surface proteins, such as OspA through OspF, which are key to its adaptation, survival and infection in many different mammalian and arthropod hosts.[6]

Clinical Presentation

Lyme disease is a multi-system inflammatory disease that ranges from asymptomatic or mild illness to chronic, debilitating illness and may manifest in three stages: early localized, early disseminated, and late persistent infection (refer to Appendix 1 for a summary of manifestations by stage). A small proportion of infected individuals have no recognized illness or rash or manifest only non-specific symptoms, making the clinical diagnosis of Lyme disease difficult.[1] In addition, manifestations of Lyme disease may depend upon the infecting *Borrelia* genospecies, which have been shown to have a predilection for specific organs and sites.[6] For example, infections with *B. burgdorferi sensu lato* in Europe mainly result in localized EM, whereas in the United States and Canada, disseminated illness with chronic arthritis is a more frequent manifestation.[7] Similarly, *B. afzelii* frequently causes the skin lesions of lymphadenosis benigna cutis and ACA,[1] whereas *B. garinii* gravitates towards the CNS, causing chronic encephalomyelitis.[8]

In the absence of antibiotic treatment, the intact immune response will usually begin to control a disseminated infection, and generalized systemic symptoms will decrease.[9] However, the organism can survive for several years in isolated niches within the body, subsequently causing relapsing arthritis, polyneuropathy or other systemic symptoms. Few cases have had relapses beyond five years.[10]

Following is a brief description of the three stages of Lyme disease, as well as other manifestations.

Stage 1 - Early (Localized) Infection

Within three to 32 days of a tick bite, which many individuals do not remember,[6] a distinctive rash, EM, occurs at the site of the tick bite in about 70–80% of individuals.[11] The EM expands slowly in an annular (ring shaped) manner, with central clearing and is generally about 5 cm in diameter. EM lesions can vary greatly in location, size and shape, have vesicular or necrotic areas in the centre, or only partial central clearing and can be confused with cellulitis.[6,11] Central clearing of the erythema is more common in European cases than North American cases.[12,13] This is likely because it is identified at earlier stages in North American cases. The rash can be hot to the touch and may be described as burning, itchy or painful.[6]

With or without EM, early symptoms may also include malaise, fatigue, fever, headache, stiff neck, myalgia, migratory arthralgias, and/or lymphadenopathy, possibly lasting several weeks or more in untreated persons.[1,14]

Stage 2 – Early (Disseminated) Infection

The most commonly reported manifestations are multiple EMs.[6,11] They may develop within several days to weeks of the onset of the initial EM and may be similar to but smaller than the primary lesion.[6] These lesions reflect spirochetemia with cutaneous dissemination and usually fade within three to four weeks (range: one day to 14 months).[6]

Systemic symptoms such as fatigue and lethargy are often constant, while arthralgia, musculoskeletal pain, headache, encephalopathy, hepatitis and lymphadenopathy or splenomegaly may intermittently occur in approximately 18% of untreated individuals at this stage.[6,15,16]

After several weeks to months, approximately 15% of untreated individuals will develop other symptoms of early disseminated illness, including palsies of the cranial nerves (Bell's palsy), meningitis, motor and sensory radiculoneuritis, cerebellar ataxia, myelitis and/or conjunctivitis.[6,11]

Cardiac manifestations (e.g., arrhythmias, heart block and syncopal episodes due to impaired conduction to the atrioventricular node) may develop in up to 5% of untreated cases[17] and may last three days to six weeks.[6] Cardiac involvement is uncommon in children.[11]

Stage 3 – Late (Persistent) Infection

The most commonly reported symptom in 60% of untreated individuals is relapsing arthritis that usually affects the large joints, especially the knees,[6,11,17] and may occur weeks to years (average six months) after the onset of EM.[1,18] Attacks may last from a few weeks to months with periods of complete remission in between.[6] Arthritis may occur without prior signs and symptoms of illness (including EM).[11] Chronic arthritis is uncommon in children who are treated with antimicrobial agents in the early stage of the disease.[6]

CNS manifestations may also occur, including polyneuropathy, leukoencephalitis[6] and encephalopathy, which may include such non-specific manifestations as sleep disturbance, behavioural changes and headaches.[18]

About 5% of untreated individuals may develop chronic neurological manifestations such as spinal radicular pain or distal paresthesias.[6]

ACA, described mainly in European Lyme disease cases, begins with red violaceous lesions that become sclerotic or atrophic. These lesions, which may be the presenting manifestation of the disease, may last for many years, and *B. burgdorferi* has been cultured from such lesions as much as 10 years after their onset in the untreated patient.[6]

Antibiotic-Refractory Lyme Arthritis

While the majority of patients with Lyme arthritis respond to appropriate antibiotic treatment, approximately 10% may have persistent joint inflammation for months or years after completion of treatment.[18,19]

Post-Lyme Disease Syndrome

Reference 6 applies to this section.

A small percentage of patients complain of pain, and neurocognitive, or fatigue symptoms for months or years afterwards, despite resolution of the objective manifestations of the initial infection with antibiotic therapy.[20] Indistinguishable from chronic fatigue syndrome or fibromyalgia, these patients tend to have more generalized or disabling symptoms: marked fatigue, severe headache, diffuse musculoskeletal pain, multiple symmetric tender points in characteristic locations, pain and stiffness in many joints, diffuse paresthesia, difficulty with concentration, or sleep disturbance.

Patients with these conditions lack evidence of joint inflammation; they have normal neurologic test results, and they usually have a greater degree of anxiety and depression. At the present time there is no evidence that persistent subjective symptoms after recommended courses of antibiotic therapy for Lyme disease are caused by active *B. burgdorferi* infection.[20,21]

Diagnosis

The diagnosis of early Lyme disease should be based on the clinical picture and epidemiological information (i.e., history of exposure to ticks or travel to Lyme-endemic area).[22] In order to prevent long-term sequelae from Lyme disease, early treatment is the best option. Laboratory testing early in the disease process, prior to the formation of antibodies, will result in a higher number of false negative results (negative when the person is actually a case). A clinical diagnosis (i.e., no laboratory testing required) can be made early in the disease course if the characteristic skin rash (EM) is observed and a history of travel to, or living in, an endemic area is indicated.[17,18] Consultation with an infectious disease specialist is recommended, as

differential diagnoses among Lyme arthritis, encephalopathy or polyneuropathy and other syndromes such as chronic fatigue or fibromyalgia is difficult and the management differs significantly. In addition, the Microbiologist-On-Call at ProvLab should be consulted prior to specimen collection to determine how and when specimens should be collected. Refer to Table 1 for Testing and Treatment Strategy Recommendations.

Table 1: Recommendations for Testing and Treatment Strategy[26]

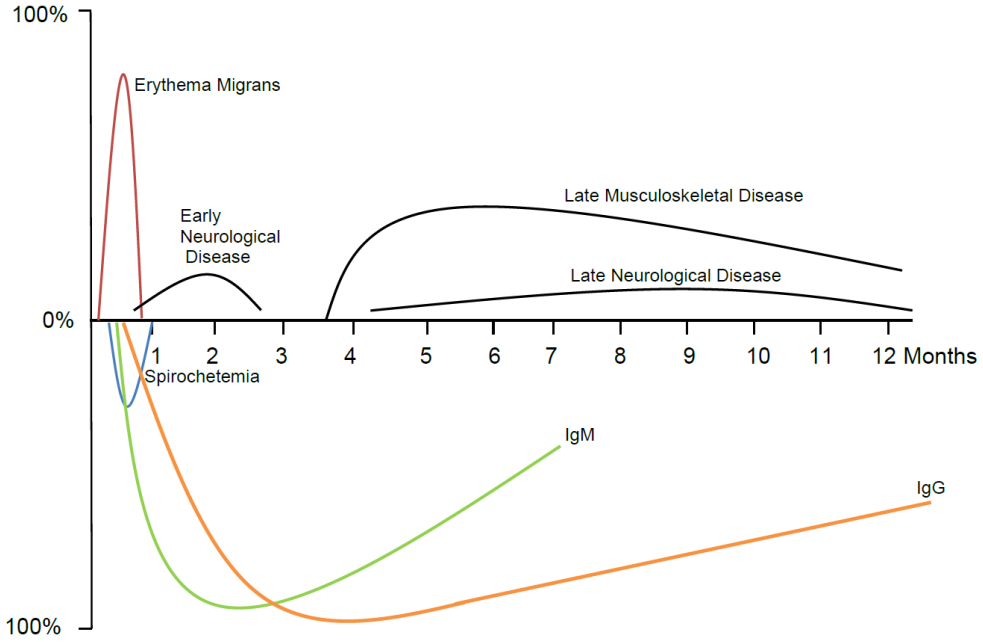
Stage of Infection	Recommendation
Stage 1 (Acute): EM (seasonal occurrence, tick-endemic area)	Clinical diagnosis and empirical treatment may be considered (in consultation with an infectious disease specialist)
Stage 1 (Acute): EM (out of season, not a tick-endemic area)	EIA* - repeat in four weeks if negative; treatment at physician's discretion
Stage 2/3 (Early Disseminated /Late Infection): Characteristic neurological, cardiac or joint involvement	EIA* - consider PCR of synovial or spinal fluid
No objective findings	Testing or treatment not recommended
Persistent symptoms following recommended treatment	Testing or further treatment not recommended

**EIA with an approved-in-Canada kit and Western Blot confirmation*

Currently, antibody detection and laboratory confirmation follows a two-step testing approach,[23] in keeping with the recommendations of the Public Health Agency of Canada and the United States Centers for Disease Control, to decrease the possibility of reporting false positives as cases of confirmed infections.[18,24,25]

Untreated individuals who remain seronegative, despite continuing symptoms for six to eight weeks, are unlikely to have Lyme disease; thus other potential diagnoses should be actively pursued.[22]

IgM antibodies generally appear within two to four weeks of EM onset and peak around six weeks. IgG antibodies appear within four to six weeks of EM onset and peak around two to three months. IgM antibodies usually decline to undetectable levels after four to six months, while IgG can remain detectable for prolonged periods despite treatment.[27,28]



Adapted from Morrison[29]

Enzyme Immunoassay

The first test of the two-step testing approach is screening for antibodies to *B. burgdorferi, B. afzelii* and *B. garinii* by C6 EIA. This test is performed at the ProvLab; however, this assay cannot distinguish between the three genospecies. The C6 EIA that is used in Alberta is more sensitive (66.5% versus 35.2%, p<0.001) than whole cell sonicate EIAs in patients with early Lyme disease (i.e., it can detect antibodies earlier).[30,31] In addition, the C6 peptide sequence is highly specific to *Borrelia* strains causing Lyme disease, further reducing the cross-reactivity to other infectious organisms seen with previous whole cell sonicate EIAs.

Serologic (EIA) test sensitivity is low during the first several weeks of infection and usually remains negative in persons treated early with antibiotics.[1,11,18] Approximately 16% of individuals with EM will test positive during the first week of illness.[32,33] Sensitivity increases to ~50% as individuals progress to the convalescent stage two to four weeks later. After four weeks and with the presence of other symptoms (e.g., arthritis, acute neurologic or cardiac abnormalities), EIA test sensitivity increases to >99%. Cross-reacting antibodies may cause false-positive reactions on EIA in persons with other spirochetal infections (e.g., syphilis, leptospirosis, relapsing fever), viral infections (e.g., Epstein–Barr virus, varicella), immunodeficiency (e.g., HIV) and autoimmune diseases (e.g., systemic lupus erythematosus, rheumatoid arthritis).[1,31,34-39]

In some individuals, IgM responses may persist for many years after treatment;[40] therefore a positive IgM response should not be interpreted as recent infection or reinfection unless the appropriate clinical picture is also present.[6] If patients with resolved past or asymptomatic Lyme infection have symptoms caused by another illness, the danger is that the current symptoms may be attributed incorrectly to Lyme disease.

Sera that screen as reactive (positive) or equivocal/indeterminate are referred to the National Microbiology Laboratory (NML) in Winnipeg for the second test of the two-step approach: confirmation by western blot (WB) testing, and when appropriate, for the species identity. Results are generally available within two weeks of referral. Sera that test negative in the screening assay performed at ProvLab are not referred to NML.[41]

Western Blot

The WB test has high specificity and should not be performed without a reactive (positive) or equivocal/indeterminate EIA result because of the increased risk of false positive results.[17] Infrequently, false-positive IgM WB tests can also occur for unknown reasons. If signs and symptoms have been present for 30 days or less, both IgM and IgG WB testing can be performed; if signs and symptoms have been present for more than 30 days, only IgG WB testing should be performed.

Travel history is obligatory as the WB assay for *B. garinii* and *B. afzelii* is only performed if travel outside of North America is provided; there is no or minimal serologic cross-reactivity between these three genospecies by the individual WB assays in the acute stage of infection (refer to NML Guide to Services).[41]

Molecular Detection

Polymerase chain reaction (PCR testing has been used to detect *B. burgdorferi* DNA in a variety of samples. Skin lesions have the highest yield, followed by a much lower rate in joint fluids[11] and CSF[18] of serologically positive patients. Testing is available from the NML by special request, and the ProvLab Microbiologist-On-Call must be contacted prior to submission of samples.[41]

Urine Antigen Detection

Results obtained from the Lyme urine antigen test have been unreliable and are not recommended in the diagnosis of Lyme disease.[6]

Culture

Isolating *B. burgdorferi* from EM lesions, joints, blood and CSF via culture is possible, but results are not available in a timely manner and therefore lack clinical usefulness.[18]

Treatment

Treatment with an appropriate antibiotic should be started prior to laboratory confirmation if clinical exam and exposure history are suggestive of Lyme disease. Consultation with an infectious disease specialist is recommended.

Reservoir

The survival and spread of *B. burgdorferi* depends on the availability of a suitable tick vector, as ticks are the primary means by which the bacteria can move from one habitat to another. Movement of the organism into new geographic areas requires the presence of both suitable vectors and hosts. Infected hosts can move the disease into areas with uninfected vectors and vice versa.[42] Two species of Ixodes ticks act as the primary reservoirs for Lyme disease in Canada: *Ixodes scapularis* (blacklegged tick) in the east and *Ixodes pacificus* (western blacklegged tick) on the west coast.[43] The primary vector of Lyme disease in Europe is the sheep tick, *I. ricinus* and in Asia is the taiga tick, *I. persulcatus*.[6]

In North America, the nymphal stage of *I. scapularis* is most active in biting small mammals and humans in late spring and summer. The adult stage is more active in biting large mammals such as deer, elk and moose which allow it to survive over the winter.[6]

In Europe and Asia, the preferred host of *I. ricinus* is largely debated; however, small rodents are important reservoirs for *B. afzelii* and birds are important for *B. garinii*.[44]

Ixodes ticks have been found to also carry other parasites such as *Theileria microti* and *Anaplasma phagocytophilum*, which cause the human diseases babesiosis and anaplasmosis, respectively.

Other tick species, such *I. angustus,* have been or are being put forth as capable of being a reservoir for or transmitting *B. burgdorferi*; however more field research is needed in this area.[45]

Transmission

Lyme disease is a tick-borne disease. Infection is transmitted most often through the bite of infected nymphs; and in order to transmit disease, the tick must have its mouthparts buried in the skin for between 36–72 hours.[1,6,46]. Transmission does not occur between infected female ticks and their eggs. Vector suitability results from molecular and biological factors rather than the number of hosts; Alberta has many ticks that are not competent Lyme disease vectors.

Lyme disease is not transmitted from person to person, with some exceptions: The bacterium has been found in breast milk[47] and stored blood from blood donations in the United States[6] resulting in a theoretical remote risk. Transplacental transmission resulting in extremely rare fetal death has been documented.[48]

Incubation Period

The incubation period from infection to the onset of EM is typically seven to 14 days, but may be as short as three days and as long as 30 days.[46,49]

Period of Communicability

There has been no conclusive evidence of person-to-person transmission.[1]

Host Susceptibility

It is believed that susceptibility is universal. Re-infection has occurred in those previously treated with antibiotics for early Lyme disease,[6] as infection with Lyme disease does not necessarily produce lifelong immunity.[50,51]

Incidence

General

Lyme disease occurs mainly in temperate regions of the Northern Hemisphere, including Canada, United States, Europe, Russia, China and Japan.[6] Lyme disease has also been reported in some African[52] and South American countries.[53] The disease is typically acquired in the spring and summer, when ticks are most active.

Lyme disease is the most commonly reported vector-borne infection in the United States, focused along the upper Atlantic coast, the upper Midwest, and on the West Coast.[54] Over 30,000 cases are reported in the United States each year.[55] Potential factors contributing to this increase include growing populations of deer that support the tick vector, increased residential development of wooded areas, tick dispersal to new areas, improved disease recognition, and enhanced reporting.

Borrelia burgdorferi is the predominant strain in North America. Although *B. burgdorferi* is also present in Europe, *B. afzelii* and *B. garinii* cause most European cases of Lyme disease.[56]

For more information on endemic locations refer to:

- United States Centers for Disease Control and Prevention
- European Centre for Disease Prevention and Control

Canada

Lyme disease was made nationally notifiable in Canada in 2009.

Established *I. scapularis* populations (endemic areas) have been identified in southern Ontario, Nova Scotia, New Brunswick, southeastern Manitoba and *I. pacificus* in parts of southern British Columbia.[43] The prevalence of *B. burgdorferi* in *I. pacificus* is much lower than in *I. scapularis*.[43,57-59] In addition, up to 12% of bird-borne "adventitious" nymph ticks that survive and moult into adults may be infected with *B. burgdorferi.*[60]

For more information on incidence and endemic areas in Canada refer to: www.canada.ca/en/public-health/services/diseases/lyme-disease/risk-lyme-disease.html

Alberta

Between 1991 and 2020, 132 cases of Lyme disease were reported in Alberta, and all cases were acquired outside the province.

Alberta has an enhanced tick surveillance program, and people are encouraged to submit a photograph of any tick found on themselves, their pets or the environment to eTick. The Submit-a-Tick program will help Alberta Health better understand the risk of acquiring Lyme disease in Alberta. Only ticks that have been requested to be submitted to the lab following photo identification through eTick will be accepted for testing at the lab. Any blacklegged ticks speciated are tested for *B.burgdorferi*. To date no supporting evidence for the establishment of the major Lyme disease vectors (*I. scapularis* and *I. pacificus*) in Alberta has been found.

Physicians/clinicians can also submit ticks to the ProvLab for speciation if it is required to assist in the diagnosis of their patients. Any blacklegged ticks found are then sent to the NML to be tested for *B. burgdorferi*. Refer to the ProvLab's Guide to Services.

More information on Lyme disease and tick surveillance can be found on Alberta Health's website.

Public Health Management

Key Investigation

- Determine history of recent tick exposure. Risk factors include:
  - travel to a known endemic area,
  - residential exposure during property maintenance, recreation, and leisure activities in known endemic areas,
  - living or working in areas surrounded by woods or overgrown brush infested by known tick vectors,
  - participating in recreational activities such as hiking, camping, fishing, and hunting in tick habitat, and
  - engaging in outdoor occupations such as landscaping, brush clearing, forestry, and wildlife and parks management in endemic areas.
- Determine presence or history of EM-like rash or other clinical symptoms.
- Identify others who may have been exposed to the same source.

Management of Contacts

- Lyme disease is not transmitted from person-to -person; however, it may be prudent to identify others who may have been exposed to the same source (e.g., endemic location) so they can be educated in order to monitor for the signs and symptoms of Lyme disease.
- Infants born to women infected with Lyme disease while pregnant should be assessed by an infectious disease specialist.

Post-Exposure Prophylaxis after a Tick Bite

- A single dose of doxycycline may be offered to adult patients (200 mg dose) and to children older than eight years of age (4 mg/kg up to a maximum dose of 200 mg) when all of the following circumstances exist:[62-64]
  - the attached tick can be reliably identified as an *I. scapularis* tick that is estimated to have been attached for over 36 hours on the basis of the degree of engorgement of the tick with blood or of knowledge about the time of exposure to the tick,
  - prophylaxis can be started within 72 hours of the time that the tick was removed,
  - ecologic information indicates that the local rate of infection of these ticks with *B. burgdorferi* is >20% (e.g., known endemic areas; refer to Incidence), and
  - doxycycline treatment is not contraindicated (e.g., pregnant, less than eight years of age).

Preventive Measures

- A Lyme disease vaccine is no longer available. The vaccine manufacturer discontinued production in 2002 after anecdotal reports of joint reactions associated with vaccination, accompanied by lawsuits, resulted in insufficient consumer demand and sales.[1]
- Educate the public about ways to reduce transmission of tick-borne diseases, including:
  - removing brush and leaf litter from around the home, and
  - creating a buffer zone of wood chips or gravel between forest and lawn around the home.
- Avoid tick-infested areas when possible (see Incidence).
- Use personal protective measures to minimize exposure and reduce the risk of tick bites, as follows.
  - Wear long sleeved shirts and long pants that are tight at the wrist and ankles or tucked into gloves or socks.
  - Light coloured clothing can aid in the detection of ticks that have not yet attached.
  - Wear a hat where contact with vegetation cannot be avoided, such as in dense woods, high grasses, or thickets.
  - Apply permethrin to tents, pant legs, and sleeves. Do not apply directly to skin.
  - Apply insect repellent containing 20–30% N,N-diethyl-3-methylbenzamide (DEET) (adults only) or up to 20% Picardin (anyone over six months of age) to the skin.[65]

    - DEET is not recommended for use on children under six months of age.
    - For children age two to 12 years, insect repellent with < 10% DEET may be used up to three times per day.
    - For children six months to two years of age, insect repellent with < 10% DEET may be used once per day.
- If working or playing in a tick-infested area, daily inspection and prompt removal can prevent transmission of disease.
  - Removal of ticks within 24 hours of attachment usually prevents transmission of *B. burgdorferi*.[57,66]
  - Ticks often attach to moist or hairy areas of the body such as the groin, axillae, neck or head.
  - In small children, ticks may be found on the head and neck, which are uncommon places for them to attach in adults.
  - Pets that spend time in tick-infested areas require daily inspection and prompt removal of ticks.
- Remove any attached ticks carefully, without crushing them.
  - Grasp gently with tweezers as close to its mouth as possible (the part sticking into the skin).
  - Slowly pull the tick straight out without jerking or twisting.
  - Check the bite area daily for at least two weeks.
  - If a red rash appears seek medical attention.
  - Protect hands with gloves, cloth or tissue when removing ticks from humans or animals.
  - Wash hands thoroughly following tick removal.

Appendix 1: Stages and Manifestions of Lyme Disease

Reference 6 applies to this appendix.

Body System[†]	Early Infection		Late Infection
	Localized Stage 1*	Disseminated Stage 2	Persistent Stage 3
SKIN	Erythema migrans – with or without central clearing	Secondary annular lesions	Acrodermatitis chronica atrophicans
		Malar rash	Localized scleroderma-like lesions
		Diffuse erythema or urticaria	
		Evanescent lesions	
		Lymphocytoma	
MUSCULOSKELETAL		Migratory pain in joints, tendons, bursae, muscle, bone	Prolonged arthritis attacks
		Brief arthritis attacks	Chronic arthritis
		Myositis[‡]	Peripheral enthesopathy
		Osteomyelitis[‡]	Periostitis or joint subluxations below acrodermatitis
		Panniculitis[‡]	
NEUROLOGIC		Meningitis	Chronic encephalomyelitis
		Cranial neuritis, facial palsy	Spastic parapareses
		Motor or sensory radiculoneuritis	Ataxic gait
		Subtle encephalitis	Subtle mental disorders
		Mononeuritis multiplex	Chronic axonal polyradiculopathy
		Pseudotumor cerebri	
		Myelitis[‡]	
		Cerebellar ataxia[‡]	
LYMPHATIC	Regional lymphadenopathy	Regional or generalized lymphadenopathy	
		Splenomegaly	
HEART		Atrioventricular nodal block	
		Myopericarditis	
		Pancarditis	
EYES		Conjunctivitis	Keratitis
		Iritis[‡]	
		Choroiditis[‡]	
		Retinal hemorrhage or detachment[‡]	
		Panophthalmitis[‡]	
LIVER		Mild or recurrent hepatitis	
RESPIRATORY		Nonexudative sore throat	
		Nonproductive cough	
KIDNEY		Microscopic hematuria or proteinuria	
GENITOURINARY		Orchitis[‡]	
CONSTITUTIONAL SYSTEMS	Minor	Severe malaise and fatigue	Fatigue

From Steere AC. Lyme disease. N Engl J Med. 1989;321:586.

† *The systems are listed from the most to the least commonly affected.*

* *The staging system provides a guideline for the expected timing of the different manifestations of the illness, but this may vary in an individual case.*

‡ *Because the inclusion of these manifestations is based on one or a few cases, they should be considered possible but not proven manifestations of Lyme disease.*

Appendix 2: Revision History

Revision Date	Document Section	Description of Revision
November 2021	General	• Updated Template • Etiology, Clinical Presentation, Diagnosis and Treatment sections moved to Epidemiology • Key Investigation section moved to Public Health Management (formerly called Control) • Updated web links
	Incidence	• Updated Canada and Alberta epidemiology and added relevant web links

References

(1) Heymann DL. Control of Communicable Diseases Manual. 20th ed. Washington, DC: American Public Health Association; 2014.

(2) Buchwald A. Ein Fall von diffuser idiopathischer Haut-Atrophie. Vierteljahresschrift für Dermatologie und Syphilis 1883;10(1):553-556.

(3) Chodynicka B. Acrodermatitis Chronica Atrophicans. 2014; Available at: emedicine.medscape.com/article/1051695-overview.

(4) Steere AC, Malawista SE, Snydman DR, al e. Lyme arthritis: an epidemic of oligoarticular arthritis in children and adults in three Connecticut communities. Arthritis Rheum 1977;20:7.

(5) Mannelli A, Bertolotti L, Gern L, Gray J. Ecology of Borrelia burgdorferi sensu lato in Europe: transmission dynamics in multi-host systems, influence of molecular processes and effects of climate change. FEMS Microbiol Rev 2012 Jul;36(4):837-861.

(6) Steere AC. Lyme disease (Lyme borrelia) due to Borrelia burgdorferi. In: Bennet JE, Dolin R, Blaser MJ, editors. Mandell, Douglas and Bennett's principles and practice of infectious diseaes. 8th ed. Philadelphia, PA: Elsevier Saunders; 2014. p. 2725-2735.

(7) Jones KL, Muellegger RR, Means TK. Higher mRNA levels of chemokines and cytokines associated with macrophage activation in erythema migrans skin lesions in patients from the United States than in patients from Austria with Lyme borreliosis. Clin Infect Dis 2008;46(1):85-92.

(8) Steere AC, Coburn J, Glickstein L. Lyme borreliosis. In: Goodman GL, Dennis DT, Sonenshing DE, editors. Washington, DC: ASM Press; 2005. p. 176-206.

(9) Steere AC. Lyme disease. N Engl J Med 1989;321:586.

(10) Steere AC, Schoen RT, Taylor E. The clinical evolution of Lyme arthritis. Ann Int Med 1987;107:725.

(11) American Academy of Pediatrics. Lyme Disease. In: Pickering LL, Baker CJ, Kimberlin DW, Long SS, editors. The Red Book: 2012 Report of the Committee on Infectious Diseases. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012. p. 474-479.

(12) Strle F, Nadelman RB, Cimperman J, Nowakowski J, Picken RN, Schwartz I, et al. Comparison of culture-confirmed erythema migrans caused by Borrelia burgdorferi sensu stricto in New York State and by Borrelia afzelii in Slovenia. Ann Intern Med 1999 Jan 5;130(1):32-36.

(13) Tibbles CD, Edlow JA. Does this patient have erythema migrans? JAMA 2007 Jun 20;297(23):2617-2627.

(14) Steere AC, Dhar A, Hernandez J, Fischer PA, Sikand VK, Schoen RT. Systemic symptoms without erythema migrans as the presenting picture of early Lyme disease. Am J Med 2003 01;114(1):58-62.

(15) Steere AC, Sikand VK. The presenting manifestations of Lyme disease and the outcomes of treatment. N Engl J Med 2003 06/12;348(24):2472-2474.

(16) Steere AC, Bartenhagen NH, Craft JE, Hutchinson GJ, Newman JH, Rahn DW, et al. The early clinical manifestations of Lyme disease. Ann Intern Med 1983 07;99(1):76-82.

(17) Canadian Paediatric Society. Lyme disease in Canada: Q & A for paediatricians. Paediatr Child Health 2009;14(3):103-105.

(18) 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):145-148.

(19) Steere AC, Levin RE, Molloy PJ, Kalish RA, Abraham JH I, Liu NY, et al. Treatment of Lyme arthritis. Arthritis Rheum 1994 06;37(6):878-888.

(20) Feder Jr H, Johnson BJ, O'Connell S, al e. A critical appraisal of "chronic Lyme disease". N Engl J Med 2007(357):1422.

(21) Sigal LH, Hassett AL. Contributions of societal and geographical environments to "chronic Lyme disease": the psychopathogenesis and aporology of a new "medically unexplained symptoms" syndrome. Environ Health Perspect 2002(110):607.

(22) Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klempner MS, et al. The clinical assessment, treatment, and prevention of lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2006 11/01;43(9):1089-1134.

(23) Ledue TB, Collins MF, Craig WY. New laboratory guidelines for serologic diagnosis of Lyme disease: evaluation of the two-test protocol. J Clin Microbiol 1996;34(10):2343-2350.

(24) Centers for Disease Control and Prevention (CDC). Notice to Readers Recommendations for Test Performance and Interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease. MMWR Morb Mortal Wkly Rep 1995;44(31):590-591.

(25) Public Health Agency of Canada (PHAC). Lyme disease fact sheet. 2015; Available at: www.phac-aspc.gc.ca/id-mi/lyme-fs-eng.php.

(26) Lindsay LR, Bernat K, Dibernardo A. Laboratory diagnostics for Lyme disease. Can Commun Dis Rep 2014;40(11).

(27) Depietropaolo DL, Powers JH, Foy AJ. Diagnosis of Lyme disease. Am Fam Physician 2005;72(2):297-304.

(28) Craft JE, Grodzicki RL, Steere AC. Antibody response in Lyme disease: evaluation of diagnostic tests. J Infect Dis 1984 May;149(5):789-795.

(29) Morrison C, Seifter A, Aucott JN. Unusual presentation of Lyme disease: Horner syndrome with negative serology. J Am Board Fam Med 2009 Mar-Apr;22(2):219-222.

(30) Wormser GP, Schriefer M, Aguero-Rosenfeld ME, Levin A, Steere AC, Nadelman RB, et al. Single-tier testing with the C6 peptide ELISA kit compared with two-tier testing for Lyme disease. Diagn Microbiol Infect Dis 2013 Jan;75(1):9-15.

(31) Johnson BJB. Laboratory diagnostic testing for Borrelia burgdorferi infection. In: Halperin JJ, editor. Lyme disease: An evidence-based approach Oxfordshire, UK: CAB International; 2011. p. 73-88.

(32) Steere AC, McHugh G, Damle N, Sikand VK. Prospective study of serologic tests for lyme disease. Clin Infect Dis 2008 07/15;47(2):188-195.

(33) Bacon RM, Biggerstaff BJ, Schriefer ME, Gilmore RD J, Philipp MT, Steere AC. Serodiagnosis of Lyme disease by kinetic enzyme-linked immunosorbent assay using recombinant VlsE1 or peptide antigens of Borrelia burgdorferi compared with 2-tiered testing using whole-cell lysates. J Infect Dis 2003;187(8):1187-1199.

(34) Johnson BJB, Biggerstaff BJ, Bacon RM, Schriefer ME. Correspondence/Reply: Cost-effectiveness of peptide-antigen immunoassays for Lyme disease. J of Infect Dis 2004;189:1962-1964.

(35) Johnson B. Lyme disease: serological assays for antibodies to Borrelia burgdorferi. In: Detrick B, Hamilton R, Folds J, editors. Manual of molecular and clinical laboratory immunoblotting. 7th ed. Washington, D.C.: ASM Press; 2006.

(36) Burkot TR, Schriefer ME, Larsen SA. Cross-reactivity to Borrelia burgdorferi proteins in serum samples from residents of a tropical country nonendemic for Lyme disease. J Infect Dis 1997 Feb;175(2):466-469.

(37) Grodzicki RL, Steere AC. Comparison of immunoblotting and indirect enzyme-linked immunosorbent assay using different antigen preparations for diagnosing early Lyme disease. J Infect Dis 1988 Apr;157(4):790-797.

(38) Magnarelli LA, Miller JN, Anderson JF, Riviere GR. Cross-reactivity of nonspecific treponemal antibody in serologic tests for Lyme disease. J Clin Microbiol 1990 Jun;28(6):1276-1279.

(39) Russell H, Sampson JS, Schmid GP, Wilkinson HW, Plikaytis B. Enzyme-linked immunosorbent assay and indirect immunofluorescence assay for Lyme disease. J Infect Dis 1984 Mar;149(3):465-470.

(40) Kalish RA, McHugh G, Granquist J, Shea B, Ruthazer R, Steere AC. Persistence of immunoglobulin M or immunoglobulin G antibody responses to Borrelia burgdorferi 10-20 years after active Lyme disease. Clin Infect Dis 2001 09/15;33(6):780-785.

(41) Fonseca K, Provincial Laboratory for Public Health. 2009 08/01;Personal Communication.

(42) Fitzgerald D, Alberta Agriculture and RD, Communication P. 2009 08/01.

(43) Ogden ND, Lindsay LR, Morshed M, al e. The rising challenge of Lyme borreliosis in Canada. Canada Communicable Disease Report 2008;34(1):1-19.

(44) Kurtenbach K, De Michelis S, Etti S, Schafer SM, Sewell HS, Brade V, et al. Host association of Borrelia burgdorferi sensu lato--the key role of host complement. Trends Microbiol 2002;10(2):74-79.

(45) Peavey CA, Lane RS, Damrow T. Vector competence of Ixodes angustus (Acari: Ixodidae) for Borrelia burgdorferi sensu stricto. Exp Appl Acarol 2000 Jan;24(1):77-84.

(46) National Advisory Committee on Immunization (NACI). Statement on immunization for Lyme disease. 2000; Available at: www.phac-aspc.gc.ca/publicat/ccdr-rmtc/00pdf/acs26-3-4-5.pdf.

(47) Schmidt BL, Aberer E, Stockenhuber C, al e. Detection of Borrelia burgdorferi DNA by polymerase chain reaction in the urine and breast milk of patients with Lyme borreliosis. Diagn Microbiol Infect Dis 1995;21(3):121-128.

(48) Schlesinger PA, Duray PH, Burke BA, al e. Maternal-fetal transmission of the Lyme disease spirochete, Borrelia burgdorferi. Ann Intern Med 1985;103(1):67-68.

(49) Wormser GP. Clinical practice. Early Lyme disease. N Engl J Med 2006(354):2794-2801.

(50) Nowakoski J, Schwartz I, Nadelman RB, al e. Culture-confirmed infection and reinfection with Borrelia burgdorferi. Ann Int Med 1997;127(2):130-132.

(51) Krause PJ, Foley DT, Burke GS, al e. Reinfection and relapse in early Lyme disease. Am J Trop Med Hyg 2006;75(6):1090-1094.

(52) Jowi JO, Gathua SN. Lyme disease: report of two cases. East Afr Med J 2005;82(5):267-269.

(53) Yoshinari NH, Oyafuso LK, Monteiro FG, de Barros PJ, da Cruz FC, Ferreira LG. Lyme disease. Report of a case observed in Brazil]. Rev Hosp Clin Fac Med Sao Paulo 1993 07;48(4):170-174.

(54) Centers for Disease Control and Prevention (CDC). Surveillance for Lyme disease - United States, 1992-2006. Morb and Mort Wkly Rep 2008;57(ss-10):2014-06-25.

(55) Centers for Disease Control and Prevention (CDC). Summary of Notifiable Diseases – United States, 2011. Morb and Mort Wkly Rep 2013;60(53):2014-06-25.

(56) Stanek G, Fingerle V, Hunfeld KP, Jaulhac B, Kaiser R, Krause A, et al. Lyme borreliosis: clinical case definitions for diagnosis and management in Europe. Clin Microbiol Infect 2011 Jan;17(1):69-79.

(57) Brown RN, Lane RS. Lyme disease in California: a novel enzootic transmission cycle of Borrelia burgdorferi. Science 1992;256(5062):1439-1442.

(58) Clover JR, Lane RS. Evidence implicating nymphal Ixodes pacificus (Acari: ixodidae) in the epidemiology of Lyme disease in California. Am J Trop Med Hyg 1995;53(3):237-240.

(59) Ogden NH, Lindsay LR, Morshed M, al e. The emergence of Lyme disease in Canada. 2009; . Accessed 12, 180.

(60) Ogden NH, Trudel L, Artsob H, al e. Ixodes scapularis ticks collected by passive surveillance in Canada: Analysis of geographic distribution and infection with the Lyme borreliosis agent Borrelia burgdorferi sensu latu. J Med Entomol 2006(43):600-609.

(61) Alberta Health. Communicable Disease Reporting System (CDRS). 2015.

(62) Onyett H. Lyme disease in Canada: Focus on children. Can Paed Soc 2014;19(7):379-383.

(63) Infectious Diseases Society of America (IDSA). Final report of the Lyme Disease Review Panel of the Infectious Diseases Society of America (IDSA). 2010; Available at: www.idsociety.org/Lyme_Final_Report/.

(64) Public Health Agency of Canada (PHAC). Lyme disease and other tick-borne diseases: Information for healthcare professionals. 2015; Available at: www.phac-aspc.gc.ca/id-mi/tickinfo-eng.php#sec-1.10b.

(65) Public Health Agency of Canada (PHAC). Statement on Personal Protective Measures to Prevent Arthropod Bites - Update. Can Commun Dis Rep 2012;38(ACS-3).

(66) Schwann TG, Piesman J. Vector interations and molecular adaptations of Lyme disease and relapsing fever spirochetes associated with transmission by ticks. Emerging Infect Dis 2002(8):115-121.