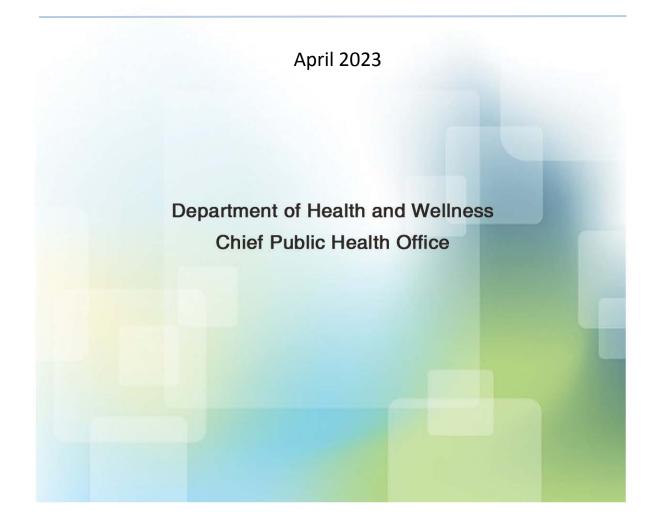


# Prince Edward Island Guidelines for the Management and Control of Lyme disease



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# **Case Definition (9)**

#### **Confirmed Case**

Clinical evidence of illness with laboratory confirmation by one of the following methods:

- Isolation of *Borrelia burgdorferi* (*B. burgdorferi*) from a clinical specimen as specified by current guidelines (1,8).
- Detection of B. burgdorferi DNA by PCR testing on synovial fluid, cerebrospinal fluid, erythema migrans (EM) tissue biopsies or blood and by methods specified by current guidelines.

OR

Clinical evidence of illness *with* a history of residence in, or visit to, a <a href="Lyme disease risk">Lyme disease risk</a> area; and laboratory evidence of infection in the form of a positive serologic test using the two-tiered approach. The two-tiered testing approach consists of a screening EIA followed by an immunoblot assay.

#### **Probable Case**

Clinical evidence of illness *without* a history of residence in, or visit to, a Lyme disease risk area; and laboratory evidence of infection in the form of a positive serologic test as defined above under confirmed cases.

#### OR

Clinician-observed erythema migrans (>5cm) *without* laboratory evidence but *with* history of residence in, or visit to, a Lyme disease risk area\*.

\* Lyme disease risk areas in Canada are defined as a locality in which there is evidence for the occurrence of reproducing populations of known tick vector species (particularly *Ixodes scapularis* [known as the deer or black legged tick] and *Ixodes pacificus* [western black-legged tick]) and the likely transmission of *B. burgdorferi* as determined by one of the methods noted in Appendix A.

Endemic or *risk areas for the Ixodes* ticks in Canada include Southern British Columbia, southeastern Manitoba, southeastern Ontario to southern Quebec along the St. Lawrence River, southern New Brunswick Moncton-Saint John and bordering areas along the Bay of Fundy) and Nova Scotia.

Areas with *moderate-high risk of Lyme disease* in the tick population include northeastern United States and Wisconsin; Kingston, Ontario and surrounding area; New Brunswick Counties

of Saint John, Charlotte, Kings, Albert, and Westmorland (Moncton) and all of Nova Scotia except for Cape Breton.

For at-risk areas, visit <u>Lyme disease risk areas</u> or visit the websites of the relevant provincial and territorial public health organizations. Information on areas outside Canada where Lyme disease risk occurs can be found at <u>Lyme and other tick-borne diseases</u>: <u>International resources</u> and <u>Tickborne Diseases Abroad</u>.

# **Reporting Requirements (7)**

#### **Health Care Providers**

Health care providers shall in accordance with the Prince Edward Island (PEI) Public
Health Act report clinical and suspect cases to the Chief Public Health Officer (CPHO)
when observed, and in any case not later than 24 hours after observation.

#### **Laboratories**

• The Provincial Laboratory shall in accordance with the PEI *Public Health Act*, report all laboratory confirmed case results to the CPHO (or designate) by phone and mail, fax, or electronic transfer as soon as the result is known.

# Etiology (2)

Clinical evidence of Lyme disease is documented in Europe as early as 1883 by German physician Dr. Alfred Buchwald. He described the skin rash characteristic of Lyme disease in Europe, subsequently known as acrodermatitis chronica atrophicans (ACA). Nearly a century later, in 1976 in the United States, clusters of children with juvenile rheumatoid arthritis in Lyme, Connecticut were diagnosed with a condition called Lyme disease. In 1982, Dr. Alan Steere at Yale University and colleagues first identified *Borrelia burgdorferi* as the causative bacterium of Lyme disease in North America. In Europe, three *Borrelia* species are known to cause disease; *B. burgdorferi* sensu stricto, *B. garinii* and *B. afzelii*. The latter two species are also found in Asia.

# **Clinical Presentation (15)**

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. 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. In addition, manifestations of Lyme disease may depend on the infecting *Borrelia* species, which have been shown to have a predilection for specific organs and sites. For example, infections with *Borrelia species* in Europe mainly result in localized erythema

migrans (EM), whereas in the United States and Canada, disseminated illness with chronic arthritis is a more frequent manifestation.

In the absence of antibiotic treatment, some *Borrelia* infections will spontaneously resolve and generalized systemic symptoms will decrease. However in some patients, the organism can survive for several years in isolated niches within the body subsequently causing relapsing arthritis, polyneuropathy or other systemic symptoms.

#### 1) Stage 1 - Early (Localized) Infection

Within 3 to 30 days of a tick bite, a distinctive rash, erythema migrans (EM), occurs at the site of the tick bite in about 70-80% of individuals. EM is a round or oval expanding erythematous area of the skin greater than 5cm in diameter that enlarges 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 red, whereas others have prominent central clearing or a distinctive target-like appearance. 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. On the lower extremities, the lesion may be partially purpuric.

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.

Note: An erythematous skin lesion present while a tick vector is still attached or that has developed within 48 hours of detachment is most likely a tick bite hypersensitivity reaction (i.e., a non-infectious process), rather than EM. Tick bite hypersensitivity reactions are usually less than 5 cm in diameter, sometimes have an urticarial appearance and typically begin to disappear within 24-48 hours. Diagnosis of EM requires careful examination by a health care provider (HCP) to eliminate alternative types of skin rash. Note that it is recommended that HCPs would normally treat patients with EM and recent travel history to Lyme risk areas (without recourse to serological testing) since specific antibodies may not be detectable in early Lyme disease. (1)

#### 2) Stage 2 – Early (Disseminated) Infection

The most commonly reported manifestation of disseminated infection is multiple EMs. 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. These lesions reflect spirochetemia

with cutaneous dissemination and usually fade within three to four weeks (range: one day to fourteen months).

Systemic symptoms such as fatigue and lethargy are often constant, while musculoskeletal symptoms such as: Lyme arthritis, which presents as a monoarticular or oligoarticular form of arthritis, most commonly involving the knee. Other large joints or the temperomandibular joint can be affected as well. 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 twelve months or more is not a usual presentation (2).

After several weeks to months, approximately 15% of untreated individuals will develop other symptoms of early disseminated illness. Early neurological Lyme disease encompasses acute peripheral nervous system involvement, including radiculopathy, cranial neuropathy and mononeuropathy multiplex (multifocal involvement of anatomically unrelated nerves), and CNS involvement, including lymphocytic meningitis and, rarely, encephalomyelitis (parenchymal inflammation of brain and/ or spinal cord with focal abnormalities) (2).

Cardiac manifestations 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 the early stages of the disease. Cardiac symptoms develop in up to 5% of untreated cases and may last 3 days to 6 weeks. Cardiac involvement is uncommon in children.

#### 3) 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 and may occur weeks to years (average 6 months) after the onset of EM. Attacks may last from a few weeks to months with periods of complete remission in between. Arthritis may occur without prior signs and symptoms of illness (including EM). Chronic arthritis is uncommon in children who are treated with antimicrobial agents in the early stage of the disease.

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

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

Acrodermatitis chronica atrophicans 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 *Borrelia* has been cultured from such lesions as much as ten years after their onset in the untreated patient.

#### 4) 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. There is no ongoing infection in these cases.

#### 5) <u>Post-Lyme Disease Syndrome</u>

Most people with early Lyme disease who receive appropriate antibiotics recover completely. However, some patients may continue to have persistent symptoms following treatment.

Persistence of objective findings following treatment, especially high fever, may be due to co-infection with another pathogen transmitted by Ixodes ticks. This calls for investigation for co-infection if the initial antibiotic is not effective against these pathogens.

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. 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 paresthesias, 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. However, other reasons that may explain a lack of response are as follows:

The initial diagnosis of Lyme disease was incorrect.

- There is another condition that persists (for example, fibromyalgia, depression, patellofemoral joint disease).
- An autoimmune process may have been triggered (for example, in the case of knee synovitis of Lyme disease that persists for months after antibiotic therapy).
- Permanent tissue damage may have occurred (in patients with previous neurologic involvement).

# Diagnosis

Diagnosis is based on the clinical picture, epidemiological information and laboratory results, as a helpful adjunct. A clinical diagnosis 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 or risk area is indicated.

#### Serology

All blood testing for Lyme disease on PEI is now done in Halifax at the QEII using the Modified Two-Tier Testing (MTTT) algorithm using 2 enzyme immunoassays (EIAs). This approach has been approved by the FDA and endorsed by the CDC in Atlanta and the Canadian Public Health Laboratory Network.

The MTTT approach offers the following advantages:

- It has a similar specificity compared to the STTT (99.6%)
- It is more sensitive for detecting early infection (formal evaluation showed that the MTTT approach detected 28% more cases of early infection)
- Both EIAs can be performed at the QEII HSC Microbiology Laboratory, which will significantly improve turn-around-time for results.
- It simplifies the interpretation of Lyme disease serology results, which will now be reported as "positive" or "negative"

While the MTTT approach has improved sensitivity for detecting early infection, it is important for clinicians to remember that patients presenting with early localized Lyme diseases should be treated on the basis of a clinical diagnosis, without relying on serology. The improved sensitivity and turn-around-time may be an advantage for investigating patients where early disseminated Lyme disease is a consideration.

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

#### **Other Supplementary Tests**

#### 1) 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 and CSF of serologically positive patients. Testing is available from the NML by special request by the Provincial Lab only. This is a rarely performed test

#### 2) Urine Antigen Detection

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

#### 3) Culture

*B. burgdorferi* has been isolated from EM lesions, joints, blood and CSF but is not used for clinical diagnostic purposes.

Clinical and epidemiological history need to be taken into account when interpreting all laboratory results. Consultation with the infectious disease consultant 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. There are other tick-associated and zoonotic conditions other than Lyme that can produce similar symptoms.

# **Epidemiology (15)**

#### 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. The spread of *B. burgdorferi* into new geographic areas requires the presence of suitable vectors and hosts. Infected hosts can move the disease into areas with uninfected vectors and vice versa. Two species of Ixodid ticks act as the primary reservoirs for Lyme disease in Canada: *Ixodes scapularis* in the east (known as the blacklegged or deer tick) and *Ixodes pacificus* (western blacklegged tick) on the west coast.

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.

Ixodes ticks have been found to also carry other parasites such as *Babesia microti* and *Anaplasma phagocytophilum*, which cause the human diseases babesiosis and anaplasmosis, respectively. Ixodes ticks can also carry the Powassan virus and Francisella tularensis (Tularemia).

In PEI, the *Ixodes* tick is not known to be endemic. The adults are not believed to survive winter and/or reproduce sufficiently on PEI due to the absence of deer or other large mammals. Carriage on migrating birds is thought to be the primary vehicle for ticks found on PEI.

#### Transmission (12)

Lyme disease is a tickborne disease. Infection is transmitted most often through the bite of infected nymphs. Transmission does not occur between infected female ticks and their eggs. In order to transmit disease, the tick must have its mouthparts buried in the skin for 36 hours (24-72hrs).

#### Incubation Period

The incubation period from infection to the onset of EM is typically seven to fourteen days, but may be as short as three days and as long as thirty days.

#### Period of Communicability

There has been no conclusive evidence of natural transmission from person to person although there is a theoretical transmission risk as bacterium has been found in breast milk and stored blood from blood donations in the United States.

#### Host susceptibility

It is believed that susceptibility is universal. Re-infection has occurred in those previously treated with antibiotics for early disease. Infection with Lyme disease does not produce lifelong immunity. Untreated Lyme disease during pregnancy may cause complications; fetal death is extremely rare.

#### Occurrence

#### General (2, 12)

Lyme disease occurs mainly in temperate regions of the Northern Hemisphere including Canada, United States, Europe, Russia, China, and Japan. Lyme disease has also been reported in some African and South American countries. The risk of getting a tick bite starts when the weather warms up in the spring, through the fall. Ticks can also be active in the winter, if the winter is mild and there is not much snow. However, the greatest risk occurs during the spring and summer months.

Lyme disease is the most commonly reported vector-borne infection in the US, concentrated along the upper Atlantic coast, the upper Midwest, and on the West Coast. 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.

#### Canada (12, 15)

Lyme disease was made nationally notifiable in Canada since 2009. The rates of Lyme disease in Canada have been increasing over the past several years.

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

#### **Prince Edward Island**

Although the rates of LD in Canada have been increasing over the past several years, the rates of lab-confirmed and probable cases in PEI have remained steady at 0-7 and 0-4 cases respectively.

#### Control

#### **Prophylaxis**

Prophylaxis treatment can be started if the patient meets all of the following criteria.

- 1. The tick can be reliably identified as an *lxodes* blacklegged tick and is estimated to have been attached for more than 24-36 hours.
  - This is based on the degree of engorgement or by certainty of when the individual was bitten.
- 2. Prophylaxis must be started within 72 hours after the feeding tick has been removed. Strong recommendation for prophylaxis if the individual has been recently traveling to Lyme disease risk areas.
- 3. Doxycycline is not contraindicated.

If all of the above criteria are met, a single dose of 200 mg of doxycycline may be given to:

- adults
- children

It should be given at 4.4 mg/kg for patients under 45 kg, up to a maximum dose of 200 mg. Doxycycline is not recommended for pregnant women.

There may be other circumstances where prophylaxis could be considered. This can be discussed on a case by case basis with the CPHO or Infectious Diseases Consultant.

#### Treatment of a case (12, 14)

The treatment regimens listed in the chart below are guidelines for localized (early) Lyme disease. The regimens may need to be adjusted depending on a patient's:

- age
- allergies
- medical history
- pregnancy status
- underlying health conditions
- Important treatment considerations

Some patients may be unable to tolerate the drugs listed in the chart.

In this case: a macrolide from the following list can be used, although it will have lower efficacy azithromycin

erythromycin

clarithromycin

Patients who are treated with a macrolide should be closely monitored to ensure their symptoms are resolved.

Large population studies of pregnant women with Lyme disease who received treatment have shown no increased risk of adverse outcomes. If further assistance is required, you may discuss with the Chief Public Health Office.

Table 1. Treatment of early localized disease (14)

Age Category	Line	Drug	Dosage	Frequency	Maximum	Duratio n
A abadta	4 st	Damendina	100 mag avallar	Turing /day	NI/A	1
Adults	1 <sup>st</sup>	Doxycycline	100 mg orally	Twice/day	N/A	21*
	2 <sup>nd</sup>	Cefuroxime axetil	500 mg orally	Twice/day	N/A	21*
		Amoxicillin	500 mg orally	Three times/day	N/A	21*
Children (< 18 yrs)	1 <sup>st</sup>	Doxycycline	4 mg/kg orally	Daily, 2 divided doses	100 mg per dose	21*
( ,	2 <sup>nd</sup>	Amoxicillin	50 mg/kg orally	Daily, 3 divided doses	500 mg per dose	21*
		Cefuroxime axetil	30 mg/kg orally	Daily, 2 divided doses	500 mg per dose	21*

<sup>\*</sup>https://cep.health/media/uploaded/CEP\_EarlyLymeDisease\_Provider\_2020.pdf

Special populations:

 Pregnant women: Doxycycline is contraindicated during pregnancy and should not be used for the treatment of early Lyme disease in pregnant women. Pregnant women should be treated using appropriate antibiotics for their stage of pregnancy.

• **Children**: A growing consensus accepts the safety of doxycycline use with children <8 years old, for 21 days or less. Historically doxycycline has been contraindicated in children <8 years old due to its potential to cause teeth staining.

If further assistance is required or for individual patient treatment decisions, including contraindications or extended therapies, please consult an Infectious Diseases Consultant.

#### Management of contacts (12)

- Lyme disease is not passed from person to person, however, it may be prudent to identify others who may have been exposed to the same source 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 a paediatric infectious disease specialist.

#### Preventative measures (12)

- Educate the public about ways to reduce transmission of tick-borne diseases, including:
  - o removing brush and leaf litter
  - o creating a buffer zone of wood chips or gravel between forest and lawn
  - o avoiding tick-infested areas when possible
  - wearing long sleeved shirts and long pants that are tight at the wrist and ankles or tucked into gloves or socks
  - wearing light coloured clothing which can aid in the detection of ticks that have not yet attached
  - wearing a hat where contact with vegetation cannot be avoided such as in dense woods, high grasses, or thickets
  - applying insect repellents containing 20–30% N,N-diethyl-3-methylbenzamide
     (DEET) to the skin (adults) or icaridin (hydroxyethyl isobutyl piperidine carboxylate, also known as picaridin)
- For children age 2 to 12 years, insect repellent with <10% DEET may be used up to 3 times per day and once per day for children 6 months to 2 years of age. It is not recommended for use on children under 6 months of age. However, the efficacy of 5% to 10% DEET to repel ticks is not certain.
- Icaridin is considered to be the repellent of first choice by the Public Health Agency of Canada's Canadian Advisory Committee on Tropical Medicine and Travel for travellers six months to 12 years of age. Products containing up to 20% icaridin are considered to be safe and efficacious.
  - o Daily inspection and prompt removal of ticks for pets that spend time outdoors.
- Consult with a veterinarian about the best tick repellent medications for pets.

- If working or playing in a tick-infested area, daily inspection and prompt removal can prevent transmission.
  - Removal of ticks within 36 hours of attachment usually prevents transmission of B. burgdorferi.
  - O Showering after being in an area where ticks are present can cause them to detach before they firmly attach.
  - 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.
- Remove any attached ticks carefully without crushing.
  - 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.
  - Afterwards, wash the bite site with soap and water or disinfect with alcohol hand sanitizer.
  - Check the bite area daily for at least two weeks.
  - o If a red rash appears or the bite appears to be infected, seek medical attention.
  - Protect hands with gloves, cloth or tissue when removing ticks from humans or animals.
  - Wash hands thoroughly following tick removal.
- For more information see Appendices B, C and D and the <u>Public Health Agency of</u> Canada's website.

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#### Appendix A

#### Methods of determining risk areas for Lyme disease in Canada (9)

A Lyme disease risk area in Canada is defined as a locality in which there is evidence for the occurrence of reproducing populations of known tick vector species (particularly *Ixodes scapularis* and *Ixodes pacificus*) and the likely transmission of *B. burgdorferi* as determined by one of the following methods:

- i) active field surveillance involving capture of wild rodent reservoirs as well as drag sampling on multiple occasions to ensure that ticks have become established (as evidenced by demonstration of all three feeding stages of the tick over more than one year) and that B. burgdorferi is being transmitted (as evidenced by molecular detection or culture of ticks or rodent samples);
- ii) active field surveillance involving only drag sampling for ticks;
- iii) evidence from passive tick surveillance when using field-validated methods of analysis of these data to improve their specificity in detecting tick populations (these may include high numbers of submitted ticks, immature ticks and multiple ticks found feeding on humans or animals);
- iv) field-validated signals from human case surveillance; or
- v) field-validated ecological/niche models that predict risk. Method (i) is recommended to confirm the first occurrence of Lyme disease risk areas in Provinces and Territories where these have not been identified to date.

Methods (ii), (iii), (iv) and (v) are recommended only for those Provinces and Territories after the occurrence of one or more reproducing populations of tick vectors, and *B. burgdorferi* transmission, has been confirmed using method (i).

# **Appendix B**

#### **PHAC Lyme Disease Poster**



PEI Guidelines for the Control and Management of Lyme Disease

# Appendix C

# **Tick Prevention Landscape Checklist (12)**

He	re a	re some ways to limit exposure to ticks near your home:
		Mow the lawn regularly to keep the grass short
		Remove leaf litter, brush and weeds at the edge of the lawn and around stonewalls and
		woodpiles
		Stack firewood neatly and in a dry area
		Put barriers to exclude deer (if applicable) around your home and seal stonewalls and
		small openings to discourage rodent activity
		Place children's recreational playground sets, patios and decks away from the yard
		edges and trees. Place them on a woodchip or mulch foundation and in a sunny
		location, if possible.
		Treat pets that are commonly exposed to ticks with oral or topic acaricides (as
		recommended by your veterinarian) as they could carry ticks into the home
		Keep bird feeders away from play areas and home/building, and clean up spilled bird
		food

### **Appendix D**

#### **Tick Check Poster**



#### Image from:

http://www.healthvermont.gov/sites/default/files/images/2017/06/HS ID Tick shower card.jpg