The rising challenge of Lyme borreliosis in Canada

NH Ogden, DPhil, (1), LR Lindsay, PhD, (2), M Morshed, PhD, (3), PN Sockets, PhD, (4), H Artsob, PhD, (2)

1. Foodborne, Waterborne and Zoonotic Infections Division, Public Health Agency of Canada, St-Hyacinthe, Quebec
2. Special Pathogens Division, National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, Manitoba
3. Vector-Borne Diseases and Non-Viral Serology Laboratory Services, British Columbia Centre for Disease Control, Vancouver, British Columbia
4. Foodborne, Waterborne and Zoonotic Infections Division, Public Health Agency of Canada, Ottawa, Ontario

Lyme borreliosis (LB), caused by bacteria of the Borrelia burgdorferi sensu lato complex, is the most common vector-borne disease in the temperate zone and occurs in Europe, North America and Asia(1). Early LB is characterized by a skin lesion, erythema migrans (EM), which expands further than 5 cm from the tick bite, accompanied by flu-like symptoms, arthralgias, myalgias and fever. If untreated, the disease can progress to early disseminated LB with neurological involvement (particularly cranial neuropathies) and cardiac involvement (particularly atrioventricular heart block and myopericarditis). Late disseminated LB includes central and peripheral neurological manifestations and Lyme arthritis(2,3).

Borrelia burgdorferi sensu stricto is the etiological agent of LB in North America and is transmitted by ixodid (hard-bodied) ticks. These ticks feed on the wildlife reservoir hosts of B. burgdorferi, particularly rodents and birds, as well as hosts that are not reservoirs of B. burgdorferi, such as deer. Ixodes scapularis, the blacklegged tick, is the main vector in eastern and central North America and I. pacificus, the western blacklegged tick, is the main vector in the west. Both tick species are indiscriminate in their choice of host and will feed on humans when the opportunity arises, thus potentially transmitting infections of wildlife to humans.

LB is the most commonly reported vector-borne zoonosis in the northern temperate zone, up to 23,000 cases being recorded annually in the United States (US)(4). Most of these cases occur in the north-eastern and north-central states, many of which border Canada(5). As far as we are aware, established populations of tick vectors and natural endemic cycles of B. burgdorferi s.l. appear to have a limited geographic scope in Canada at present. However, recent studies indicate that the number of established populations of I. scapularis tick vectors is increasing in Canada and that climate change is likely to accelerate this trend. In addition, passive surveillance studies suggest that there is a low possibility that Canadians may be exposed to LB tick vectors in all 10 provinces, in areas where established tick populations are unknown, from infected adventitious ticks that are carried by birds into populated areas. We review here the significance of recent studies of the distribution of LB tick vectors in Canada and consider what steps may need to be taken to prepare for the challenge of LB in the coming decades.

Geographic distribution of endemic areas in Canada: past, present and future

South-eastern and south-central Canada
In Canada in the early 1990s, only one population of *I. scapularis* was known to exist, that at Long Point peninsula on the north shore of Lake Erie, which maintained an endemic cycle of *B. burgdorferi*\(^6\). Tick populations have subsequently been identified using the protocol and criteria defined in the 1991 Canadian Consensus Conference on Lyme Disease\(^7\), i.e. a defined locality where all three feeding stages of the tick (larva, nymph and adult) are present on resident animals or in the environment for at least 2 consecutive years. The protocol to collect ticks for identification comprises a standard effort of 10 person-hours of sampling the environment for questing ticks using a 1 m\(^2\) flannel drag, and the trapping and examination of a minimum of 30 wild rodents during seasons when ticks could be expected to be active\(^7\). Identification of *B. burgdorferi* infection in ticks or reservoir host tissues is necessary to confirm that *B. burgdorferi* is endemic in a site that is endemic for its vectors. In our studies, infection was identified by means of a polymerase chain reaction (PCR) test algorithm that has evolved over the last decade with advancing knowledge of the bacterium and changes to PCR technology\(^8\). Since 1991, we have identified additional, but still isolated, populations of *I. scapularis* on the shores of Lake Erie; around Lake Ontario, in the vicinity of the Thousand Islands national park; in Nova Scotia; and in south-eastern Manitoba (Figure 1). Thus, while the distribution of recognized “endemic areas” for *B. burgdorferi* infection is still limited in Canada, it is increasing.

A number of factors can constrain the geographic distribution of *I. scapularis*:

(i) **Habitat suitability:** Ixodid ticks spend much of their life in the environment off their hosts, in the surface litter layers of the soil, while developing from one life stage to the next between the meals they take from their wild animal hosts, and on low herbage while seeking these hosts. For ticks to survive, the habitat must provide a litter layer that is capable of protecting them from drowning, dehydration, predation and prolonged deep-freezing\(^9\). Field studies suggest that many habitats in eastern Canada are indeed suitable for survival of *I. scapularis*, and this aspect of the tick's biology may not be a major constraint on its northward spread across south-eastern Canada\(^10,11\). However, it may well be an important factor in limiting any future spread of *I. scapularis* westward across the dry prairies\(^12\).

(ii) **Host abundance:** Important hosts for the tick (deer and rodents) and for *B. burgdorferi* (rodents and other small mammals and birds) must be present at suitable densities\(^13\), but these hosts appear to be abundant in south-eastern Canada\(^14\), and again this factor may not be limiting.

(iii) **Dispersal by hosts:** Ticks have very limited capacity for self-directed horizontal or long-range movement\(^15\). To expand their range, they need to be carried by their hosts, and *I. scapularis* are certainly carried into Canada on migratory birds in spring, either from endemic populations in the US or across Canada from existing Canadian populations\(^16\). It has been estimated that in the order of 3 billion land birds migrate into Canada's boreal region each year, many of which pass through *I. scapularis*-infested regions of the northern US and south-eastern Canada during their migration\(^17\); this coincides with the spring season of activity of nymphal *I. scapularis*\(^18\).

(iv) **Climate:** Temperature could be a critical factor in limiting expansion of the range of *I. scapularis* in Canada. Ambient temperature affects rates of development of ticks from one life stage to the next and has to be high enough for the ticks to complete their life cycle\(^19,20\). At present, temperature seems to impose a limit on the geographic range of establishment of reproducing *I. scapularis* populations in Canada by limiting the geographic range of locations where summers are warm enough and long enough for the ticks to complete their lifecycle (Figure 1). However, climate change is expected to drive northward range expansions for most terrestrial arthropods in the northern hemisphere\(^23\). Recent studies affirm the likelihood that *I. scapularis* will spread northwards into Canadian habitats with climate change\(^20\) (Figure 1). Furthermore, there is evidence that climate warming has already occurred over the last decade or so \(^24\), perhaps influencing the increased rate of establishment of *I. scapularis* in Canada during recent years.

**Figure 1. Geographic extent of suitable temperature conditions for Ixodes scapularis in eastern and central Canada**
Projection for the 2020s
Index of tick abundance at model equilibrium

Figure 1. A stylized diagram (after that in reference 12) of model-derived temperature limits for *I. scapularis* establishment in Canada using mean annual degree-days > 0°C as an index under current (1971-2000) and projected climate for the 2020s obtained from the Canadian Canadian Coupled Global Climate Model 2 (CGCM2)\(^{(21)}\) using emissions scenario ‘A2’ (i.e. without efforts to control greenhouse gas emissions\(^{(22)}\)). Triangles indicate the approximate location of known reproducing populations of *I. scapularis* in Canada. Populations identified by other researchers (eg. reference 25) are included.

Many bird-borne “adventitious” ticks that arrive in Canada may survive to moult to the next developmental stage (adult ticks) in areas where the duff layer provides suitable insulation for the ticks to survive the winter\(^{(10)}\). However, modelling studies suggest that, at least until recently, in many parts of Canada the summers have been too short to allow these ticks to complete their life cycle and establish self-sustaining populations\(^{(20)}\). Nevertheless, adult ticks that have moulted from nymphs carried on birds can and do feed on humans, pets and wild animals over a very wide geographic range in Canada, and approximately 12% of the ticks are infected with *B. burgdorferi*\(^{(8)}\). These ticks, therefore, provide a risk of human infection over most of populated Canada, and human cases can occur in regions considered non-endemic for the tick vector (Figure 2).

Figure 2. *Ixodes scapularis* ticks collected in passive surveillance in eastern Canada
Western Canada

Data from field studies performed by British Columbia Centre for Disease Control over the last decade provide insight into the distribution of the western vector of LB, *I. pacificus*, and of potential endemic foci of LB (Figure 3). The sources of these data are *I. pacificus* collected from trapped rodents or from the environment by flagging, and *B. burgdorferi* identified in ticks or rodent tissues by culture and PCR-confirmation of cultures, as previously described(25). Eleven sites of these field studies were revisited in 2004, when a total of 218 *Peromyscus maniculatus* mice were trapped. Immature *I. pacificus* (total 722: 625 larvae and 97 nymphs) were collected from mice at 10 of the sites (Figure 3), and 66 mice from the 10 sites were seropositive for *B. burgdorferi* as assessed by indirect fluorescent antibody testing (as described by Lindsay et al.(26)). No rodent tissues, or ticks collected from rodents, were positive by culture or PCR, suggesting that rodents were not infected or infective at the time of capture. These studies indicate that reproducing populations of *I. pacificus* already have a widespread distribution in British Columbia (BC), and bird-borne *I. pacificus* may also occur outside regions where the tick is established(27). The findings are consistent with the general pattern for *B. burgdorferi* transmitted by *I. pacificus* in western North America: because of a complex of ecological factors, transmission cycles are inefficient, and the prevalence of *B. burgdorferi* infection in host-seeking *I. pacificus* ticks is usually much lower than that found in *I. scapularis* (28-31). In addition, *I. pacificus* are less likely to bite humans, although foci of higher risk can occur(32). Therefore the risk of humans contracting LB infections in *I. pacificus*-endemic regions is usually much lower...
than in regions where *I. scapularis* populations are established.

Figure 3. The geographic distribution of *Ixodes pacificus* in British Columbia

![Map of BC locations where at least one *I. pacificus* tick was found or where samples from trapped rodents were positive for *B. burgdorferi* by PCR. Lozenges and circles represent, respectively the occurrence of *B. burgdorferi* and *I. pacificus* in data collected during the decade prior to 2004 by the BC Centre for Disease Control. Data collected in field studies in 2004 are indicated by stars, which show locations where immature *I. pacificus* ticks were found, and squares, which show where adult ticks were found. *B. burgdorferi* was not demonstrated in any of the tick or rodent samples collected in 2004.

Because the geographic range of *I. pacificus* appears to encompass the most heavily populated regions of BC, any range expansion associated with climate change may not have a significant impact on public health. More subtle and, so far, unpredictable effects of climate on the ecology of *B. burgdorferi* in western Canada cannot be ruled out, however, because some specific ecological conditions may permit “hot spots” of human infection risk(32).

**LB incidence in Canada and the US**

LB is a frequently reported disease in the US, where over 20,000 new cases per annum have been reported since 2002(4). In 2002, 12,054 cases were reported among the 50.5 million inhabitants of those states that have endemic *I. scapularis* tick populations and have borders with eastern and central Canada (i.e. Maine,
New Hampshire, Vermont, upstate New York, Pennsylvania, Michigan, Wisconsin and Minnesota, equating to an approximate annual incidence of 24 reported cases per 100,000 person-years (using contemporary census data: http://www.census.gov/statab/hist/HS-04.pdf). In eastern Canada, only 69 cases, in patients without confirmed travel to endemic areas in the US or Europe, had been reported in Ontario, Quebec and the Atlantic provinces up to the end of 2003 since recording in any of these provinces began in the late 1980s (Figure 4). Under-reporting in Canada is likely but is also common in highly endemic areas in the US, so why the difference?

Figure 4. The annual number of cases of LB in British Columbia

---

Most important, there is significantly greater risk of exposure to infected ticks in endemic areas where *I. scapularis* is the vector than in areas where only adventitious bird-borne ticks occur. While the geographic extent of adventitious ticks is very wide, the number of infected ticks per unit area of habitat is inevitably much lower than that in endemic areas. In nature, few nymphal ticks survive to be adults: for every one adult female tick there are approximately 20 nymphs in a reproducing tick population, but likely none or very few where only adventitious ticks are found. Where reproducing populations of *I. scapularis* ticks occur, nymphal ticks can be abundant and infected, and their small size increases the probability that they transmit infection before being identified and pulled off. Furthermore, 20% or more of host-seeking nymphal *I. scapularis* are infected with *B. burgdorferi* at some of these sites in Canada. In the north-eastern US endemic areas are widespread and common even in suburban gardens, so the human population is regularly exposed to habitat containing abundant infected ticks. Reproducing *I. scapularis* populations are still limited in their geographic extent in Canada, and, to our knowledge, they have so far occurred in regions of low human population density.

Nevertheless, while the annual number of reported endemic cases in central and eastern Canada (i.e. those most likely transmitted by *I. scapularis*) was never greater than 15 in the decade prior to 2004, from 2004...
to 2006 a total of 69 potentially endemic cases were reported, and the annual incidence approximately doubled in 2005 and 2006 (Figure 3). Potentially endemic cases are now roughly equal in incidence to travel-related cases (most of which were contracted in the eastern US and whose numbers are also increasing). This trend suggests that the incidence of reported human cases may well be positively correlated with the expansion of the range of *I. scapularis* populations in Canada. The number of reported cases of LB in Canada is likely to underestimate the true number of cases occurring.

Over the same period, the reported annual incidence in BC remains low with no suggestion of a temporal trend, which is consistent with *I. pacificus* being an endemic tick in much of this province but one that poses a lower environmental health hazard than *I. scapularis*. In 2001, 141 LB cases were reported in the coastal states of the US where *I. pacificus* is endemic (California, Oregon and Washington), when their total population was 44 million (http://www.census.gov/statab/hist/HS-04.pdf). This crude incidence of reported cases (0.3 cases per 100,000 person-years) is of the same order as that seen in BC, where approximately four cases are reported each year in a population of 4 million (http://www40.statcan.ca/l01/cst01/demo62k.htm), a crude incidence of 0.1 cases per 100,000 person-years.

In the west, therefore, low prevalence of infection in ticks and low rates at which endemic ticks bite humans may constrain the incidence of human infections, even though the tick vectors are widespread. In the east, low incidence has likely been associated mostly with the limited geographic range of established *I. scapularis* populations. This appears to be changing, however, and the main public health challenge may be yet to come as the geographic range of reproducing populations of *I. scapularis* expands further in eastern and central Canada. Projections of future climate and *I. scapularis* distribution (12) suggest a worst-case scenario of up to 8,000 reported LB cases a year in south-eastern and south-central Canada by 2050, assuming that by this time the incidence will be comparable to that currently seen in New England. LB alone will add a burden to health care in Canada, but *I. scapularis* transmits a number of less common but potentially more life-threatening zoonotic pathogens, including bacteria such as *Anaplasma phagocytophylum* (the causal agent of human granulocytic anaplasmosis), the protozoan *Babesia microti* (the causal agent of human babesiosis) (36) and Powassan encephalitis virus (37). Co-infection of LB and these other *I. scapularis*-borne pathogens may not be common in humans in the US, but they do occur (38).

**Linkage of diagnosis, ecology and geographic distribution**

Emergence of the LB epidemic in the US in the last three decades was accompanied by increased expertise in diagnosis and disease recognition (2), but diagnosis remains difficult. While *B. burgdorferi* has been implicated as the etiological agent for a number of clinical syndromes of LB, only EM cutaneous lesions are pathognomonic (2). Unfortunately, EM lesions are only recognized in 60% to 80% of cases, so diagnosis using this pathognomonic sign may have questionable sensitivity (2). The gold standard test of bacterial culture has low sensitivity, as does PCR amplification of target sequences of the bacterial genome in clinical material (39). Enzyme-linked immunoabsorbent assay (ELISA) used alone has limited specificity. Western blots are considered to be more specific; however this depends on the criteria for determining a blot as positive. Some band interpretations are more liberal than the widely accepted Centers for Disease Control and Prevention criteria for a positive Western blot, possibly leading to a more sensitive assay but at the risk of losing the desired specificity. One widely accepted algorithm is to employ a "two-tiered diagnostic approach" in which samples are screened using an ELISA, and only reactive or positive samples are further tested using a Western Blot procedure (2, 39). This approach does have some impact on sensitivity (2), but specificity is still a problem because of cross-reaction with antibodies to other infectious agents (40-42). For this reason there is much lower confidence that a positive result is a true, rather than false, positive in a non-endemic area, and interpretation of the two-tiered diagnostic approach rests on whether the patient has had contact with an endemic area (40).

An important aspect of clinical diagnosis, either for treatment or to identify a "surveillance case" (Table 1), therefore, is a history of potential exposure to infected ticks in an endemic area. In eastern Canada, where the distribution of endemic populations of tick vectors has been focal and limited, potential exposure to infected ticks in an endemic area has in part influenced the clinician's decision to consider LB as a diagnosis and to request and interpret serologic tests (7). However, serological confirmation is currently a cornerstone of identifying surveillance cases in non-endemic areas (7). Only the occurrence of confirmed surveillance cases (rather than suspect human cases) can identify (possibly with the assistance of field investigation for ticks) new endemic areas in Canada. There is a risk, therefore, that the non-endemic status of a geographic region in Canada is a self-fulfilling prophecy that does not account for the dynamic nature of actual and predicted spread of LB into Canada. In fact, suspect human cases (for example, those recently occurring in Nova Scotia and Manitoba) have led to enhanced passive and active field surveillance for ticks.
that confirmed the presence of new established *I. scapularis* populations and new endemic areas.

### Table 1. Case definitions for surveillance of LB according to the guidelines of the 1991 Canadian Consensus Conference on Lyme Disease (7)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Isolation of <em>B. burgdorferi</em></th>
<th>Laboratory evidence of infection*</th>
<th>EM observed by physician</th>
<th>EM described by patient</th>
<th>Late LB manifestation†</th>
<th>Exposure to an endemic area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed case 1</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed case 2</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Confirmed case 3</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Confirmed case 4</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable case 1</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable case 2</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EM = erythema migrans, LB = Lyme borreliosis

*Acceptable laboratory evidence includes (a) *B. burgdorferi* detected by immuno-staining of tissue or body fluid; (b) significant changes in confirmed antibody response to *B. burgdorferi* in sequential serum samples; (c) positive enzyme-linked immunosorbent assay according to recognized cut-off values and positive results by Western blot.

†Now termed symptoms of “disseminated Lyme borreliosis” (31), late manifestations include musculoskeletal manifestations (recurrent attacks, lasting weeks or months, of swelling of one or a few large joints or chronic progressive arthritis preceded by brief attacks), nervous system disorders (lymphocytic meningitis, cranial neuritis, facial palsy, radiculoneuropathy and, rarely, encephalomyelitis) and cardiovascular disorders (acute-onset atrioventricular conduction defects).

The changing pattern of LB endemic areas in Canada combined with the wide geographic dispersion of adventitious ticks means that the surveillance case definition needs to be modified to account for the new challenges from LB. Serology may be a useful adjunct to clinical diagnosis, but testing is not encouraged for patients who do not have clear symptoms of LB, particularly if they reside in non-endemic areas of Canada, because of the possibility of false-positive test results. Therefore, the clinical skills of medical practitioners may be paramount in responding to the emergence of LB in Canada.

### Surveillance, clinician awareness and public health

LB is a potentially preventable disease. The adoption of simple measures (wearing long trousers in habitats where *I. scapularis* occurs, application of DEET-containing products) could reduce tick bites, while careful inspection for, and removal of, attached ticks within at least 24 hours of attachment should prevent transmission of *B. burgdorferi* from infected ticks (43). In most cases LB is successfully treated with antibiotics if recognized early enough (44). Prompt treatment requires recognition of ticks, tick bites and EM lesions by the public and prompt diagnosis by clinicians (44). If LB is not recognized during the early stages, patients may suffer seriously debilitating disease, which may be more difficult to treat and require multiple courses of antibiotics (45). For these reasons, public and clinician awareness will be crucial to minimizing the impact of LB in the coming decades.

Public health objectives associated with infectious disease include surveillance, risk management, policy development, risk communication and prevention. From an LB perspective in Canada, pertinent questions include the following: (i) What surveillance methods are best used to identify new risk areas in a timely...
fashion, and (ii) What preventive methods can and should be used? Identification of human LB cases is hampered by limitations to the sensitivity and specificity of laboratory tests and uncertainty in defining boundaries of endemic areas in the light of our knowledge of bird-borne infected ticks and the expanding range of tick populations. An additional consideration is that \textit{B. burgdorferi} populations are increasingly genetically diverse\(^1\) with potential consequences for variability in clinical presentation and the performance of serologic assays\(^{46,47}\).

For arthropod-transmitted diseases such as LB, environmental indicators can be used to alert public health systems to potential risks, trigger preventive mechanisms and pre-empt human infections. Passive monitoring for tick populations remains the backbone of surveillance, despite geographic coverage that is patchy because of its dependence on an unknown threshold of human population density needed to collect and submit ticks for identification\(^8\). Because identification of endemic areas is so important for diagnosis and surveillance of human cases, it may be prudent to enhance the capacity of surveillance for ticks. Specifically, more formal systems of surveillance for ticks on humans and domesticated animals may be needed and targeted active surveillance for tick populations required to (i) check the rate of expansion of ticks in areas at particular risk of new tick populations, (ii) monitor whether reality matches predictions for range expansion of ticks, and (iii) fill the gaps in passive surveillance where human population density is low. Furthermore, it may be advisable to expand reporting of human cases to include suspect cases identified in locations that are currently outside established endemic areas yet that are highlighted as risk areas for LB emergence, to monitor potential trends in the incidence of human cases that may signal new endemic areas.

Messages concerning risk from tick exposure, particularly in LB-endemic areas, are considered an important public health preventive measure. However, the current incidence of LB in the US occurs despite dissemination of LB awareness and prevention messages to the population\(^{44}\). A variety of intervention strategies using acaricides are available in that country to control ticks\(^{48-50}\), but in Canada, because ticks have historically not presented a significant public health problem, few, if any, acaricides are currently registered for the control of ticks of public health importance. As the distribution of endemic areas for LB expands into more heavily populated regions of Canada, the availability of tick control products and the expertise to implement effective control programs will need to be enhanced in order to fully utilize this risk reduction strategy. Careful studies are needed, however, to establish the efficacy of these methods in Canada and to avoid the issues of overuse, misuse and acaricide resistance that have plagued tick control using acaricides in other parts of the world\(^{51}\).

**Conclusions**

LB can be described as an emerging disease in Canada. Many challenges remain to be faced, including difficulties in interpreting diagnostic tests, issues concerning the clinical definition of LB, symptoms and treatment, and the combined ecological challenges of expansion in the geographic range of the ticks associated with climate change and simultaneous radiative evolution of \textit{B. burgdorferi} populations in north-eastern North America\(^1\). We will need to work hard to ensure surveillance and preventive processes and activities can act swiftly, effectively and decisively in the coming decades to lessen the impact of this emerging disease.

**References**


22. Intergovernmental Panel on Climate Change (IPCC). *Climate change 2001. Third assessment report*


30. Lane RS, Quistad GB. Borreliacidal factor in the blood of the western fence lizard (Sceloporus occidentalis). J Parasitol 1998;84:29-34.


[Table of Contents] [Next]