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Lyme disease in British Columbia: Are we really missing an epidemic?

Results from surveillance and research on Lyme disease suggest there is a real but low risk of contracting this tick-borne illness in BC.

ABSTRACT: The risk of Lyme disease depends on climate, geography, the abundance of specific insect vectors, and human interaction with these. In BC, *Ixodes pacificus*, the primary tick vector for the causeative spirochete, *Borrelia burgdorferi*, has consistently been found in low numbers in populous areas, and rates of infection in this tick remain at less than 1%. Correspondingly, rates of human cases of Lyme disease in BC are less than 0.5 per 100 000 per year; this is similar to rates reported in US states with environmental epidemiology like BC's and considerably less than in high endemic areas of the eastern United States (29 per 100 000). There is no evidence to support an epidemic of Lyme disease in BC. Responses to a recent survey indicate that physicians generally are aware of the low but real risk of Lyme disease, know to treat patients with clinical symptoms, and understand that Lyme disease is preventable and treatable. Public health authorities will continue to remind residents and visitors to BC of the simple measures they can take to prevent tick bites and exposure, as well as which early signs and symptoms should lead them to seek appropriate medical treatment.

Lyme disease is a tick-borne zoonosis caused in North America by infection with the spirochete *Borrelia burgdorferi*. Humans acquire Lyme disease through the bite of an infected tick.[1] The principal tick vector in BC is the Pacific black-legged tick, *Ixodes pacificus*,[2] which is found throughout the highly populated areas of southern BC. This situation is in contrast to eastern Canada and the US, where the tick *Ixodes scapularis* is the most common vector. The low incidence of Lyme disease in BC may be explained by the fact that *I. pacificus* is a less competent vector than *I. scapularis*, is less abundant, and is less likely to feed on deer mice.[3-5] Studies have shown that infectivity rates are lower in areas where *I. pacificus* predominates than in areas where *I. scapularis* predominates. Lyme disease advocacy groups in BC have expressed concern that an

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epidemic is being ignored. Surveillance and research on Lyme disease in BC indicate this is not the case.

Tick and mouse surveillance

The BC Centre for Disease Control has actively screened ticks in over 125 areas of the province. From 1993 to 1996, 10 056 ticks were tested and 40 were found positive for *B. burgdorferi* (0.40%). From 1997 to 2007, 8602 ticks were tested and 30 ticks were found positive (0.35%), demonstrating a stable, low prevalence of infection. *I. pacificus* ticks were found most commonly in the Lower Mainland and Vancouver Island; *Dermacentor andersoni*, which is not a competent vector for Lyme disease, was the tick identified most commonly throughout BC.

On Vancouver Island, active dragging for ticks at 17 sites yielded only 41 ticks, mostly *I. pacificus*, all of which were found negative for *B. burgdorferi*. Active solicitation of ticks from veterinarians on Vancouver Island and the Gulf Islands led to 115 tick submissions, all of which were found negative for *B. burgdorferi*. In the Okanagan over 2 years, 5557 *D. andersoni* ticks were collected (no *I. pacificus* ticks were found). Of 110 ticks randomly tested for *B. burgdorferi* by culture and PCR, all were found negative. A total of 219 deer mice were trapped from the same areas and tested for antibodies to *B. burgdorferi* by the National Microbiology Laboratory in Winnipeg, and all were found to be negative.

We receive 800 to 1000 ticks from physicians, veterinarians, and the public every year. Approximately half are *I. pacificus*, of which one to two per year are found to be positive for *B. burgdorferi*.

The major mammalian reservoir for *B. burgdorferi* in BC is the deer mouse. To assess prevalence in this population we tested 3500 deer mice by culture and found 30 (0.83%) positive. We also tested 164 mice for antibodies to *B. burgdorferi* and found 6 (3.66%) positive, demonstrating a low prevalence in this reservoir.

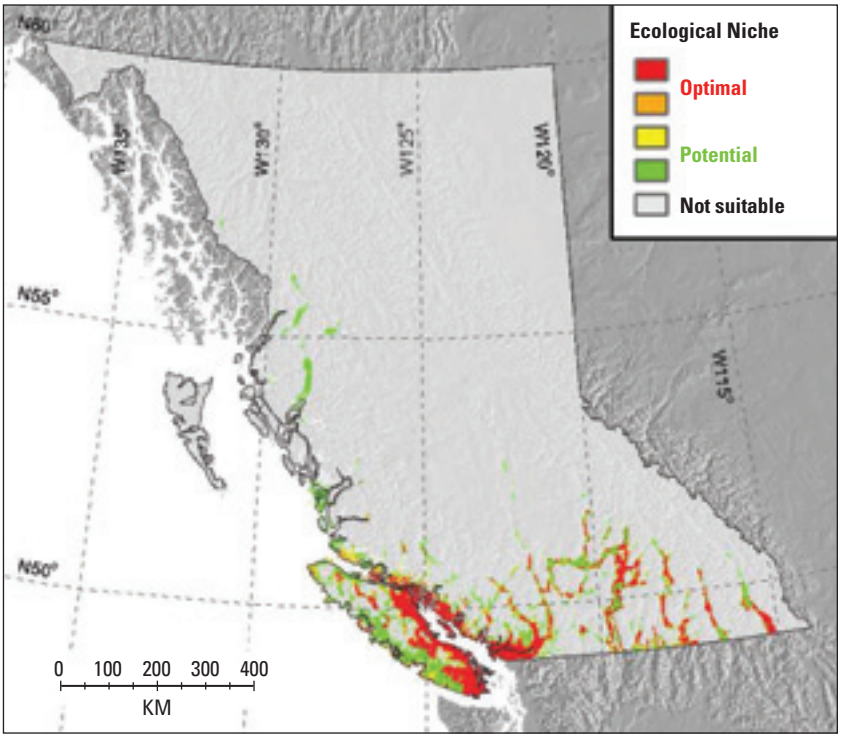

Figure 1. Forecasted ecological niche of *Borrelia burgdorferi* in British Columbia.

Ecological niche modeling

In order to identify areas with risk of Lyme disease transmission in BC, we undertook ecological niche modeling for both ticks and *B. burgdorferi* infection and assessed the potential impact of climate change. Modeling identified optimal environmental conditions in south coastal BC (i.e., Vancouver Island, Lower Mainland, and Sunshine Coast) and interior BC valley regions.[6] The habitat in these areas is characterized by low-lying vegetation such as high grass and brush, with abundant leaf litter and a nearby water source. Niche modeling demonstrates that *B. burgdorferi* is generally absent north of N51° latitude (**Figure 1**).

There is concern that global warming could lead to expansion of the ecological niche for the vector, resulting in the potential for increased exposure to infected ticks in BC.[7] Our models indicate a modest geographic range expansion for *Ixodes* ticks and *B. burgdorferi* based on 2050 climate warming projections; however, the areas where expansion might occur are sparsely populated and the densely populated centres of southern and interior BC are already within the existing ecological niche of *B. burgdorferi*. There are also variable local habitats within regions, so exact risks within a region may vary greatly.

Lyme disease may also, though rarely, be acquired from "adventitious" ticks that drop off migrating birds. These ticks pose a theoretical risk of infection during the summer months throughout the province.[8]

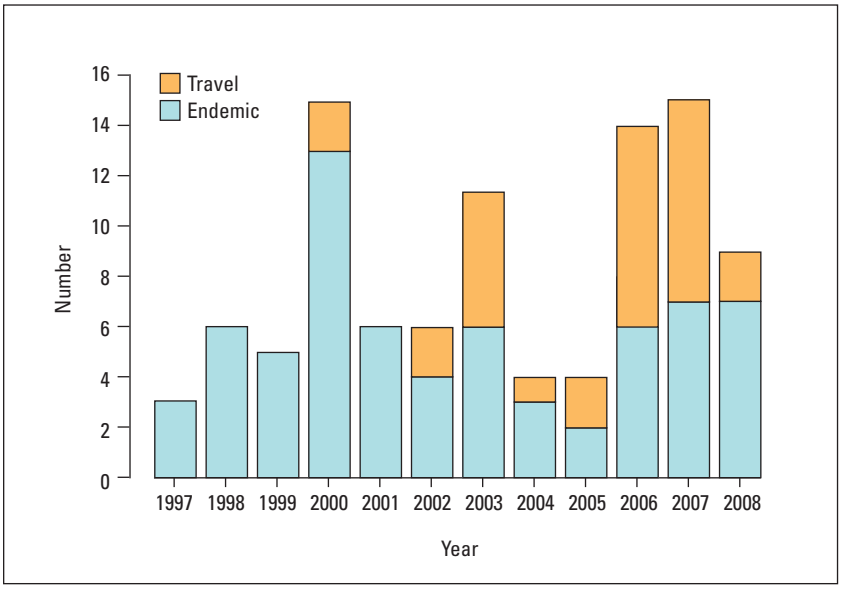

Figure 2. Number of endemic and travel-related cases of Lyme disease in BC between 1997 and 2008. Travel-related cases include patients with exposure histories in countries with endemic Lyme disease.

Human surveillance

We used capture-recapture methodology and a review of BC's three sources of passive surveillance (laboratory data, enhanced surveillance forms, and cases reported on the public health information system) to estimate the annual number of Lyme disease cases in BC between 1997 and 2008, to develop a more accurate estimate of the burden of disease, and to compare BC with Washington, California, and high-endemic areas in the eastern US.

Ninety-three cases of Lyme disease were identified over the 12-year period (**Figure 2**); 45 patients (48.4%) were male and most were between 41 and 70 years of age (mean age 43.7 years, range 3.5–80.6). One-third of patients acquired their illness outside of BC. The mean age of patients with travel-related disease was 40.4 years, younger than those who acquired Lyme disease in BC (mean age 44.8 years).

The annual incidence rate of Lyme disease in BC ranged from 0.1 to 0.3 per 100 000 population, a rate similar to that of Washington and California, with yearly incidence rates of less than 0.5 per 100 000 population (including travel-related cases). These rates have remained stable over the past 10 years. In contrast, the incidence of Lyme disease in the 10 highly endemic states in US is 29.2 per 100 000 people,[9] indicating important differences in both disease risk and burden of illness.

Capture-recapture methods show underreporting of Lyme disease does occur in BC. The best model places the corrected number of cases in BC between 1997 and 2008 at 142 (95% CI:111-224), for a maximum incidence of 0.5 per 100 000 population. Underreporting is common for rare diseases when surveillance is passive.[10] Whether underreporting results from clinical cases being treated without testing and not reported or whether cases are truly not diagnosed is not known. To help gain insight into this question we looked at physician awareness of Lyme disease in BC.

Physician awareness

In 2008 we conducted a survey of physicians in BC. We modified a previously validated questionnaire[11] to collect data on respondent demographics and general knowledge of Lyme disease. The survey included questions about geographic risk perception, laboratory testing, and three clinical scenarios. Physicians were also asked whether they were aware that Lyme disease is reportable.

We sent questionnaires to all pediatricians, internists, and family practitioners who gave a BC address as their practice address. The response rate was 32% (1673/5199). Of these respondents, 148 (8%) recalled diagnosing 221 cases of Lyme disease in 2007, while 58% of family physicians and 66% of specialists indicated they knew Lyme disease is reportable.

Physicians scored high on the knowledge questions, with over 90% correctly identifying the signs and symptoms of Lyme disease as well as the causative agent and incubation period. Fewer were aware that erythema migrans (**Figure 3**) on its own is diagnostic. The mean overall knowledge score was 74% (8.9/12).

Three clinical scenarios were presented: Scenario 1 involved a patient with erythema migrans and no laboratory testing; more than half (57%) of all respondents answered correctly ("give antibiotics at this time"), while one-third opted to first test for Lyme disease. Scenario 2 involved an asymptomatic patient with history of a tick bite; 56% indicated correctly they would educate and reassure the patient. Scenario 3 involved a patient with arthritis, no history of erythema migrans, and multiple negative tests for Lyme disease; 82% correctly reported they would investigate causes other than Lyme disease, or refer the patient to a specialist.

Several questions addressed phy-

sicians' perceptions of risk in their community of practice. When asked about their patients' risk of developing Lyme disease after a tick bite, 94% of respondents indicated they believed their patients faced some risk. Logistic regression modeling showed that physicians have a good understanding of the spatial distribution of risk within the province, with greater risk perceived in areas where ecological conditions are most suitable for disease transmission.

The final questions of the survey addressed physician perceptions of patients requesting evaluation for Lyme disease because of nonspecific symptoms such as fatigue and musculoskeletal pains. While a majority (79% of family physicians and 72% of specialists) indicated they believed that their patients' symptoms were caused by something other than Lyme disease, 31% of family physicians and 12% of specialists reported they had treated such patients for Lyme disease because of patient concern.

This survey shows physicians are knowledgeable about and aware of the risk of Lyme disease in BC, despite the province being a low endemic area. It is also apparent physicians in BC are comfortable with treating patients empirically, in many cases based on patient concern. More cases are clinically diagnosed and treated than are reported to public health.

Clinical picture

Ticks are most likely to transmit infection after being attached for more than 24 hours of feeding, making prompt detection and removal of ticks a key way to prevent Lyme disease. A tick attached for less than 24 hours is unlikely to transmit infection, even if it is infected with *B. burgdorferi*.[12]

Erythema migrans diagnosed on physical examination, even in the absence of other Lyme-specific signs or symptoms and positive laboratory tests, establishes the diagnosis of Lyme disease.[13] Erythema migrans is an annular, slowly expanding erythematous lesion, usually 5 cm or greater in diameter, that may exhibit partial central clearing or central necrosis, giving a bull's-eye appearance. Erythema migrans typically occurs 7 to 14 days after infection (range 3 to 30 days), and in some cases secondary lesions may occur.[14] In contrast, a localized tick-bite reaction occurs within hours of the bite, expands over hours, and resolves within 48 hours. In studies, erythema migrans rash occurs in at least 80% of all patients with Lyme disease and 90% of children.[15] Patients can also experience symptoms of fatigue, chills, fever, headache, and migratory arthralgias, and lymphadenopathy, which may last several weeks if untreated.

Untreated infection can spread over several weeks or months and lead to three main syndromes:

- Neurological. Neurological abnormalities can include aseptic meningitis, cranial neuritis, Bell palsy, and radiculoneuritis. Such abnormalities affect about 5% of untreated patients.
- Musculoskeletal. Musculoskeletal manifestations can include migratory joint and muscle pains without objective signs of swelling.
- Cardiac. Rarely occurring cardiac manifestations can include atrioventricular block and acute myopericarditis.

Weeks to years after onset of infection (mean 6 months) episodes of swelling and pain in large joints (especially the knees) can occur in up to 60% of untreated patients, leading to chronic arthritis. Some patients develop chronic axonal polyneuropathy or encephalopathy. Lyme disease is rarely fatal, although patients with late disseminated disease can have severe, chronic, and disabling symptoms.[16]

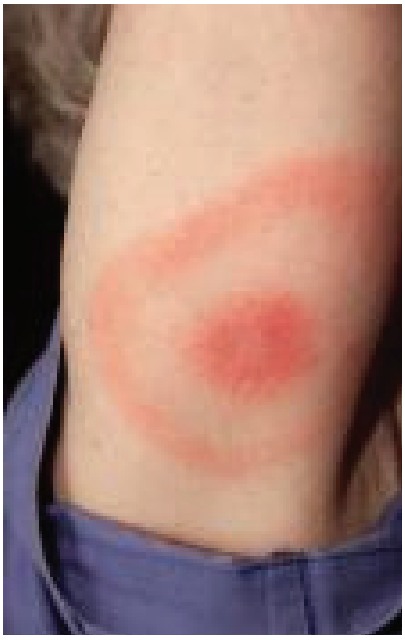

Figure 3. Erythema migrans.

Source: CDC/James Gathany

Most cases of Lyme disease are successfully treated with antibiotics. Treatment is most effective if begun early in the course of illness. However, a small percentage of patients have lingering symptoms that last months to years even after appropriate treatment. Symptoms include muscle and joint pain, arthritis, cognitive defects, sleep disturbance, and fatigue. The cause of these symptoms is not known, although there is some evidence that they result from an autoimmune response. Long-term antibiotic treatment has been found to be of no benefit in patients with long-term symptoms, and has been associated with sometimes severe adverse effects, including death.[17,18]

In addition, a group of patients with nonspecific symptoms such as fatigue, memory changes, and musculoskeletal pain have been identified by some physicians as suffering from "chronic Lyme disease" despite multiple negative laboratory tests and no

history of acute disease. This syndrome is the subject of ongoing scientific research, with a number of possible infectious and noninfectious causes being investigated. One recently discovered virus, Xenotropic murine leukemia virus, has been associated with a similar syndrome in some studies[19] but not in others.[20] There is a need for further research into the cause of this syndrome and therapeutic options for people who are suffering from its debilitating symptoms.

Early treatment prevents late complications and should be initiated on clinical suspicion pending laboratory results.

Diagnostic testing in BC

With the exception of direct detection of *B. burgdorferi* from biopsy specimens of erythema migrans rash, there is no validated direct test for the *B. burgdorferi* bacterium in blood or other samples and the organism cannot be easily cultured. Laboratory testing for Lyme disease relies on detection of antibodies in blood. Because antibodies to *B. burgdorferi* proteins can be induced by infection with microbes other than *B. burgdorferi*,[13] antibody tests can yield false-positive results unless properly interpreted.

A two-step process to test for evidence of Lyme disease is used by the Public Health Laboratories of the BC Provincial Health Services Authority (PHSA), following recommendations by the US Centers for Disease Control and Association of State and Territorial Public Health Laboratory Directors.

- **Step 1: Enzyme immnoassay (EIA)** (VIDAS, BioMériux, France). This is a very sensitive test, meaning it will detect almost all true cases of Lyme disease but will also react if a patient has certain other diseases, including mononucleosis, lupus, and various microbial infections.
- **Step 2: Western blot (WB)** (MARDX, Trinity Biotech Co., CA, US). This test is conducted on a specimen that yields positive or equivocal/indeterminate EIA results. It is a very specific test that can distinguish between true-positive and false-positive results from the EIA. Western blot IgM is considered reactive when two markers (out of three required markers) are identified, and Western blot IgG is considered reactive when five markers (out of ten required markers) are identified.

These tests, taken together, show whether a patient has ever been exposed to *B. burgdorferi*. Positive results do not demonstrate active infection and must be interpreted in light of patient history and symptoms.

Some commercial laboratories use either discredited tests (such as urine antigen tests) or interpret tests in non-standard and unproven ways. As a result, these laboratories can return a positive result that is not reproducible by public health laboratories following the internationally recognized protocols. For example, some private US labs use only one marker for IgM and only three markers for IgG Western blot tests, which can result in a false-positive result and a high rate of cross-reactivity with other infections.[21] This can lead not only to unnecessary treatment for Lyme disease, but can also prevent patients from receiving treatment for the condition that is actually causing their symptoms.

Antibody tests may be negative early after infection by *B. burgdorferi*, as it may take several weeks to develop antibodies. If the diagnosis is unclear and acute serology is negative, a convalescent test 2 to 4 weeks later may aid in diagnosis. Because erythema migrans is considered diagnostic for Lyme disease, a patient presenting with this distinctive rash requires no further testing. However, a patient with erythema migrans treated early with antibiotics may not develop antibodies. If the patient presents with other symptoms of Lyme disease and erythema migrans is atypical or absent, serologic testing should be done at initial presentation and repeated after 2 weeks. Early treatment prevents late complications and should be initiated based on clinical suspicion pending laboratory results.

Even after curative antibiotic treatment, antibodies may persist in the blood for years, meaning that a positive antibody test after treatment does not indicate treatment failure. Because of long-term persistence of antibodies, asymptomatic patients should not be retested, as a positive test result can be misleading.

In BC for the past 10 years, PHSA laboratories have consistently received about 3000 patient samples for

serological testing for Lyme disease yearly. Of these specimens, about 90 have had positive or indeterminate results on EIA and 7 to 12 cases of Lyme disease have subsequently been confirmed by WB.

Conclusions

There is no evidence to support an epidemic of Lyme disease in BC. The primary vector, *I. pacificus*, is found in populous areas in consistently low numbers, and rates of infection in the tick population remain less than 1%. Human case rates in BC are less than 0.5 per 100 000.

A recent survey of clinicians confirms doctors have good knowledge of Lyme disease, are comfortable making a diagnosis given clinical signs and symptoms, and appropriately use laboratory testing to assist in diagnosis for those patients suffering nonspecific signs and symptoms.

Further research is needed to develop diagnostic tests and treatment protocols for patients suffering from nonspecific, debilitating symptoms that some physicians attribute to "chronic Lyme disease." Otherwise, Lyme disease is a preventable and treatable illness, and public health authorities will continue to remind residents and visitors to the province of the simple measures they can take to prevent tick bites and exposure as well as the signs and symptoms of acute illness so they can seek appropriate medical treatment.

Competing interests

None declared.

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