Bill C-442: Shining the limelight on the Lyme-like?

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On June 11, 2014, The House of Commons passed Bill C-442, *An Act Respecting a Federal Framework on Lyme Disease* (1), and on June 12, 2014, this was introduced as a First Reading into the Senate. This act is a private members' bill introduced by Member of Parliament Elizabeth May and aims to develop a Federal plan surrounding the diagnosis and management of Lyme disease in Canada. The Federal Framework on Lyme disease dictates that a conference be held with provincial and territorial ministers and a range of stakeholders to establish an enhanced surveillance program and to develop prevention, identification and management guidelines, and standardized educational materials for public health care providers in Canada.

As detailed in the preamble (1), motivation for this bill stems from concerns that increasing cases of Lyme disease are expected to occur in the ensuing years due to the evolving distribution of the vector black-legged (*Ixodes scapularis*) and western blacklegged (*Ixodes pacificus*) ticks, and the spread of the pathogen *Borrelia burgdorferi* in Canada. In addition, the Bill C-442 preamble asserts that current diagnostic and management approaches are inadequate and explicitly claims that use of current Canadian guidelines "severely limit the diagnosis of acute Lyme disease and deny the existence of continuing infection, thus abandoning sick people with a treatable illness" (1).

Lyme disease has been a nationally reportable disease in Canada since 2009. Surveillance data from the Public Health Agency of Canada indicate that the vectors and pathogen are established in parts of New Brunswick and Nova Scotia, southeastern Quebec, southern and eastern Ontario, southeastern Manitoba and southern British Columbia (2). Human disease cases reported for the first five years of national surveillance have significantly increased annually and are as follows: 2009 (128 cases), 2010 (132 cases), 2011 (258 cases), 2012 (315 cases), and 2013 (anticipated ≥500 cases pending confirmation) (2).

Field surveillance and modelling studies have identified existing confirmed and suspected endemic risk areas and potential future risk areas within Canada (2-4). In fact, confirmed populations of *I. scapularis* increased from one to 13 regions between 1997 and 2006 (5). While predicting areas of future risk is difficult and challenged by many variables including climate change, habitat, distribution of wild animal reservoirs and bird migration routes, potential marked further increased distribution of the vector and, hence, risk areas for Lyme disease in the coming decades is reasonably expected (4,6).

Lyme disease has a broad range of potential symptoms, signs and severity. Early localized infection may be asymptomatic, associated with a nonspecific flu-like illness or, most commonly, associated with the presence of erythema migrans (7,8). Untreated cases may then progress to disseminated disease manifested by cardiac, neurological, dermatological and/or rheumatological abnormalities.

Appropriate antimicrobial therapy with doxycycline, penicillins, and second- or third-generation cephalosporins is highly effective at resolving clinical disease and eradicating the organism (9-11). However, in a minority of patients following successful treatment, prolonged symptoms of fatigue, musculoskeletal and neurocognitive complaints,

and/or adverse effects on functioning and quality of life occur (12,13). When persistent over a prolonged period of time (ie, six months), this self-reported symptom complex is referred to as post-treatment Lyme disease syndrome (14). It is important to recognize that post-treatment Lyme disease syndrome occurs in the absence of compelling evidence of ongoing or chronic infection due to *B. burgdorferi* (12,15). However, patients remain at risk for reinfection and development of second and further incident episodes of Lyme disease (16).

Lyme disease is an important and emerging infection in Canada that warrants our attention. The Public Health Agency of Canada has developed an action plan (initiated March 2014) that includes the three pillars of: engagement, education and awareness; surveillance, prevention and control; and research and diagnosis (17). Bill C-442 aims to provide further federal support for a Lyme disease strategy. While we support an enhanced strategy for Lyme disease surveillance and management in Canada, Bill C-442 raises several important points worthy of discussion.

First, while we recognize its present and potential future importance, we must consider the burden of Lyme disease in context with other community-onset bacterial diseases in Canada. The most recent estimates of the number of Lyme diseases cases in Canada is approximately 500; considering a national population of 35.2 million residents, this translates to an annual incidence rate of approximately 1.4 per 100,000 population (2,18). Death from Lyme disease is uncommon. As an example to place this rate in context, community-onset bloodstream infection occurs at a rate of approximately 100 per 100,000 per year and is associated with a case-fatality rate of approximately 12% (19). In other words, the current rate of deaths associated with community-onset bloodstream infection is 10-fold higher than the overall incidence of Lyme disease in Canada. Furthermore, the emergence of antimicrobial-resistant pathogens poses a far greater threat to the present and future health of Canadians (20). While in general we welcome any enhanced support for infectious diseases surveillance, management and research, we do question prioritization of limited resources in preference to other infections that have an objectively far greater burden of disease in Canada.

Second, the bill preamble states that diagnostics for Lyme disease are inadequate and it proposes to correct this problem. The present diagnostic approach in Canada generally involves clinical assessment (including exposure risk and clinical features) and use of a two-step enzyme immunoassay and confirmatory Western blot serological testing strategy (21). Serological testing is known to have a low sensitivity early in disease (ie, <1 month) and diagnosis and treatment based on clinical features alone (ie, presence of erythema migrans) is recommended. Later in the disease, the enzyme immunoassay is highly sensitive but risks false positives, such that confirmatory Western blot with interpretation according to standardized criteria is used (21). As with all infectious diseases, diagnostic tests alone are never perfect and false positives and negatives may occur. There are ≥70 available serological tests that have been approved for diagnosing Lyme disease in North

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America (22). In addition, there is extensive ongoing research investigating Lyme disease diagnosis and there is significant financial reward and incentive for industry to develop new and improved tests. We are, therefore, skeptical that Bill C-442 will afford the vast research and development resources required for development and implementation of a notably improved diagnostic testing strategy in Canada.

Third, the bill aims to improve treatment of patients with Lyme disease in Canada. It appears reasonable that Bill C-442 may lead to earlier treatment of infected patients as a result of improved vector and disease surveillance and by increasing awareness and education among health care providers. However, we doubt that implementation of Bill C-442 will lead to treatment of a significant cohort of "abandoned patients with continuing infection", as noted in the bill preamble (1). Implicit within this statement in the preamble is the assumption that there is some sizable patient population with "chronic Lyme disease" existing in Canada that is failing to receive adequate diagnosis and therapy. Indeed, in the Member of Parliament discussion area associated with the bill, there are numerous comments suggesting the frequent failure of Lyme diagnosis in Canada and the availability of better tests and treatments in the United States (23). Anecdotally, we are aware of a sizable cohort of patients in Canada who have nonspecific chronic 'Lyme-like' syndrome who are not deemed to have Lyme disease based on clinical

assessment and negativity on approved diagnostic tests. While the possibility exists that some small proportion of these patients could truly have Lyme disease (and benefit from therapy), most will not. Some of these patients will seek private testing with unapproved, nonvalidated tests with potentially dubious results and inappropriate recommendations for therapy. If falsely positively diagnosed, these patients may be subjected to potentially costly and toxic therapies, and delays in diagnosing the true underlying disease. To this end, any federal strategy must utilize the best clinical and scientific evidence possible to guide management of patients with Lyme disease (24,25).

SUMMARY

While we have some reservations surrounding the potential relative resource allocation implications and clinical objectives, we in principal generally support Bill C-442 and its goals to reduce the adverse impact of Lyme disease on the health of Canadians. While we will hope for improvements in the diagnosis of Lyme disease, we are skeptical that major advances will arise as a result of Bill C-442. Accordingly, we believe that a sizable cohort of patients with chronic Lyme-like disease will remain. It is our opinion that any strategy aimed at improving Lyme disease diagnosis and management must also include a provision for developing a registry, and enhanced clinical and research efforts aimed at elucidating the causes and treatments of Lyme-like syndrome.

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