Major emerging vector-borne zoonotic diseases of public health importance in Canada

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In Canada, the emergence of vector-borne diseases may occur via international movement and subsequent establishment of vectors and pathogens, or via northward spread from endemic areas in the USA. Re-emergence of endemic vector-borne diseases may occur due to climate-driven changes to their geographic range and ecology. Lyme disease, West Nile virus (WNV), and other vector-borne diseases were identified as priority emerging non-enteric zoonoses in Canada in a prioritization exercise conducted by public health stakeholders in 2013. We review and present the state of knowledge on the public health importance of these high priority emerging vector-borne diseases in Canada. Lyme disease is emerging in Canada due to range expansion of the tick vector, which also signals concern for the emergence of human granulocytic anaplasmosis, babesiosis, and Powassan virus. WNV has been established in Canada since 2001, with epidemics of varying intensity in following years linked to climatic drivers. Eastern equine encephalitis virus, Jamestown Canyon virus, snowshoe hare virus, and Cache Valley virus are other mosquito-borne viruses endemic to Canada with the potential for human health impact. Increased surveillance for emerging pathogens and vectors and coordinated efforts among sectors and jurisdictions will aid in early detection and timely public health response.

Keywords: Canada; emerging infectious disease; Lyme disease; prioritization; public health; vector-borne disease; West Nile virus; zoonosis

INTRODUCTION

Zoonoses are infections or infectious diseases transmissible under natural conditions from vertebrate animals to humans and involve a wide range of causal agents including: viruses, bacteria, parasites, fungi, and prions. Emerging zoonoses are defined as newly recognized diseases or those that have increased in incidence or expanded their geographic, host, or vector range. Zoonoses comprise approximately 60% of all known infectious diseases, while 75% of emerging infectious agents are zoonotic.1

The complex ecology of zoonotic infections poses both a challenge to, and opportunities for, surveillance and control. Transmission of zoonotic pathogens occurs through direct human–animal contact, arthropod vectors, inhalation of infectious drops or aerosolized pathogens in the environment, or through ingestion of contaminated food or water. The resulting infection in a susceptible host may be inapparent or manifest, with the latter causing disease. Enteric zoonoses are those that cause gastrointestinal illness, such as Salmonellosis, Campylobacter, and Giardia infections, and are generally transmitted through contaminated food or water, while the category of ‘non-enteric zoonoses’ is a catch-all group of diseases that can be divided generally into vector-borne diseases (such as Lyme disease, West Nile virus (WNV), plague), directly transmitted zoonoses (such as Brucellosis, rabies, influenza, and Hantaviruses), environmentally mediated zoonoses (such as Anthrax, Echinococcosis, Leptospirosis), and food-borne parasitic infections (such as Toxoplasmosis, Trichinellosis), although some may have more than one pathway of transmission.

The rate of zoonotic disease emergence has increased markedly since the 1940s as indicated by the increasing incidence of emerging infectious disease events, even after controlling for increasing infectious disease reporting effect.1 This trend is likely due to a combination of demographic changes, land-use alterations, urbanization, increased travel and trade, agricultural practices, encroachment into animal habitat, and possibly also increased awareness.1,2

Ongoing global environmental and socioeconomic changes may create favorable conditions for emergence and transmission of vector-borne diseases in Canada by: (i) the import of vectors and pathogens exotic to Canada through international movements and their subsequent establishment here as has happened in the past with malaria and WNV3 and could occur in the future with Rift Valley fever, Japanese encephalitis, and chikungunya;4,5 (ii) the northward spread of vector-borne pathogens from endemic areas in the USA as has recently happened with Lyme disease and eastern equine encephalitis; and (iii) the re-emergence or resurgence of endemic vector-borne diseases such as WNV, snowshoe hare virus (SSHV), and Jamestown Canyon virus (JCV), which may occur due to changes to...
their geographic range and ecology driven by environmental changes such as climate change.6,7

Similar environmental and socioeconomic changes (e.g. climate change, and land use changes due to urbanization and agricultural expansion) may impact on wildlife populations that serve as reservoirs of zoonotic diseases, altering the dynamics of transmission amongst natural reservoir hosts, changing the geographic footprint of endemic areas, and altering the likelihood of animal–human transmission (a.k.a. ‘spillover’).

Recognizing the potential need for multi-sector and multi-jurisdictional coordination, we review the state of knowledge on the public health importance of key emerging vector-borne zoonoses in Canada.

RATIONALE FOR THE REVIEW FOCUS

Selection of priority diseases presented in our review was based on the results of a prioritization exercise that was conducted with public health stakeholders across Canada in 2013. The prioritization exercise aimed to assess diseases of public health significance with the highest risk of emergence or re-emergence in Canada: (i) those known to be present in Canada with potential to expand in incidence, impact, or geographic range; (ii) those with potential to arrive from the USA (through range expansion); or (iii) those with potential to be introduced via international travel or trade; with an emphasis on the first group (Table 1). A detailed description of the prioritization exercise is outside of the scope of this paper, but we provide a brief summary here as context for disease selection in our review.

Technical experts from provincial and territorial ministries of health-, agriculture- and/or environment-provided professional perspectives on non-enteric zoonoses for their respective jurisdiction. Methods and criteria for the selection of zoonoses of priority were adapted from Vorou et al. (2008) and are described in detail elsewhere.8 Briefly, each participating jurisdiction (n = 10; includes nine provinces and one territory) completed a questionnaire to assess each pathogen/disease on the basis of six criteria (indices) of disease emergence. The questions asked respondents to assess a pre-defined list of pathogens (Table 1) according to three internationally accepted indicators defining disease emergence (scored as yes/no) and three indices of public health capacity (scored as high/medium/low): (i) increased incidence in humans in the last five years; (ii) increased geographic range (either newly detected in a given jurisdiction in the last five years, or an endemic agent detected in a novel geographic area in a given jurisdiction in the last two years); (iii) detection of the pathogen in novel animal species in the last two years (for endemic agents in a given jurisdiction); (iv) absence of any current animal or vector surveillance systems; (v) necessity for inter-sectoral collaboration in surveillance (between public health and animal health organizations); and (vi) necessity for inter-jurisdictional collaboration in research, surveillance, diagnostic testing, or communication/education. An overall positive index was scored when three or more jurisdictions provided a positive answer for the corresponding pathogen and index. Pathogens with three or more positive indices were identified as high priority. A series of round table discussions was held to discuss the results of the survey and to reach expert consensus on priority non-enteric zoonoses in Canada.

The prioritization exercise identified vector-borne diseases, in particular Lyme disease and other emerging tick-borne diseases, and WNV and other emerging mosquito-borne diseases, as top emerging non-enteric zoonotic disease priorities. Rabies and zoonotic influenza were also identified as high priorities in this exercise; however, these non-vector-borne pathogens are outside the scope of this paper and may be the subject of a future review.

A systematic review was conducted to determine the state of knowledge in Canada on the emerging vector-borne diseases identified as priorities by public health stakeholders. A literature search was performed in consultation with Health Canada Library services to identify published articles from five databases, including MEDLINE, CAB Abstracts, Agricola, EMBASE, and Global Health. A keyword search was performed for English or French language articles published between January 2008 and September 2013 using the following terms: disease name or pathogen name or zoonotic* and Canada or province/territory name. Titles and abstracts were reviewed and subjected to screening using pre-defined inclusion and exclusion criteria, and full article text was reviewed where necessary to confirm inclusion or exclusion. Forward and backward reference tracking approaches were applied to key documents meeting the inclusion criteria to identify additional relevant articles. Articles were included if they related to the epidemiology of the identified priority vector-borne diseases; their human health impact in Canada; geographic range; surveillance, diagnostic testing, and public health awareness/education. Articles were excluded if they related primarily to therapeutics and/or treatment, vaccine development, and/or vaccine safety. More than 450 publications were identified, including research articles, case reports, reviews, and conference proceedings. One hundred eight documents met the inclusion criteria and were retained for full review.

EMERGING VECTOR-BORNE ZOONOSES IN CANADA

Emerging vector-borne zoonoses in Canada are caused by a number of bacteria and viruses transmitted to humans by the bite of an infected tick (e.g. Lyme disease – *Borrelia burgdorferi*) or mosquito (e.g. WNV).

**Lyme disease**

Lyme disease, caused by the spirochete *B. burgdorferi*, is an emerging vector-borne disease in Canada due to the northward expansion of the geographic range of the tick vector *Ixodes scapularis* in southern Canada.9,10 Lyme disease is a multisystem disorder characterized by three clinical stages: early, disseminated, and late Lyme disease.9,11 Early diagnosis and treatment are needed to prevent more severe
disseminated and late Lyme disease, which may present with neurological, cardiac or joint involvement. The reported incidence of human Lyme disease cases in Canada is low but increasing. The range of some vector ticks is expanding faster than had been predicted and in the eastern portions of this expanding range is generally followed within three–five years by the invasion of tick-borne pathogens such as *B. burgdorferi*. Risk of exposure to infected western blacklegged ticks (*I. pacificus*) is relatively low and incidence of Lyme disease in British Columbia (BC) is stable. In contrast, significant risk exists or is emerging across the range of *I. scapularis*, with the exception, for now, of Alberta, Saskatchewan, and Prince Edward island; populations of infected ticks are established in southern parts of Manitoba, Ontario, and Quebec, and in certain locations in New Brunswick and Nova Scotia.

Climate change is anticipated to accelerate the geographic spread and intensity of transmission of Lyme disease in Canada. The progressive pattern of Lyme risk emergence is consistent with an association with warming temperatures, and *I. scapularis* tick population establishment has been shown to be driven by temperature suitability at provincial and national scales. Additionally, there is a low risk of Lyme disease being contracted almost anywhere in Canada due to the transport of infected ticks over large geographic distances by migratory birds.

Lyme disease has been nationally notifiable in Canada since 2009 and has also been nationally notifiable in the USA since 1991. Through a combination of increased transmission risk, but also possibly increased awareness, human cases of Lyme disease reported in Canada have increased dramatically, from 64 cases in 2005 to nearly 700 cases in 2013 (PHAC, unpublished data), although there may be considerable underreporting of this disease, e.g. an estimated 40% underreporting of Lyme disease cases in BC in 1997–2008. In the USA, over 30 000 probable and confirmed cases of Lyme disease are reported each year to the Center for Disease Control and Prevention, with the majority of cases in the North Central and Northeastern states. Lyme disease in Canada involves the monitoring of the tick vectors and the pathogens they carry, in addition to any reports of human infections that may arise in Canada.

Human granulocytic anaplasmosis

Due to recent establishment of the blacklegged tick, *I. scapularis*, in southeastern and south central Canada, HGA and babesiosis are of growing concern for public health. The rickettsial bacteria that cause HGA has been detected in 15% of ticks collected from hunter-caught deer in a study in Quebec in 2007 (although genotypes in deer may not be pathogenic in humans). The infection has also been found in dogs in Saskatchewan as well as in horses in Saskatchewan and Nova Scotia, while no dogs showed evidence of exposure to *A. phagocytophilum* in a study in remote communities along the Central and North coasts of BC. The seropositivity of dogs to *A. phagocytophilum* antigens was assessed in Canada in 2010, and positives were found in only four provinces: Saskatchewan, Manitoba, Ontario, and Quebec; the provinces with the highest canine seroprevalence for *A. phagocytophilum* were Manitoba and Saskatchewan.

HGA is not a nationally notifiable disease in Canada and very few human cases have been recorded in Canada, with the first locally acquired case reported in Alberta in 2009 and another in a US traveler to Manitoba in 2010. In the USA, human and canine infections with *A. phagocytophilum* have been reported in the Pacific northwest, the upper midwest, and the northeastern and mid-Atlantic USA, and most human cases occur in Minnesota, Wisconsin, New York state, New Jersey, and Connecticut, suggesting that expansion from the USA may further drive the emergence of this tick-borne disease in Canada. HGA has been a nationally notifiable disease in the USA since 1998, facilitating tracking of the expanding geographic range of this infection south of the border.

Babesiosis

Babesiosis, caused by the protozoan parasite *Babesia microti*, has recently been identified in ticks in Canada and has caused one endemic case from Manitoba. It is emerging in the USA, and there is a risk of transmission via blood transfusion. In North America, over 70 cases of transfusion-transmitted babesiosis (one from Ontario, Canada) and nine associated deaths were reported up to 2008, mostly from the USA. Risk assessment for this emerging tick-borne disease involves the monitoring of the tick vectors and the pathogens they carry, in addition to any reports of human infections that may arise in Canada.

West Nile virus

Of the five zoonotic mosquito-borne viruses currently or recently endemic to Canada, WNV is the best known. WNV is transmitted from birds to humans via the bite of an infected mosquito and is transmissible through blood transfusion and tissue and organ transplantation. In North America, mosquitoes of the genus *Culex* are the most common vectors. Most human infections cause no illness, while about 20% suffer from WN fever, and less than 1% experience severe neurological disease including meningitis and encephalitis.

Between 2002 and 2012, 5339 human WNV cases were reported in Canada, including 980 (18.4%) cases with neurological symptoms and 73 (1.4%) deaths associated with WNV infection (http://www.phac-aspc.gc.ca/wnv-wvn/), and since 1999 there have been over...
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30 000 confirmed WNV cases in the USA;61 however, these values under-represent the true infection rates as most infected individuals remain asymptomatic59 or do not seek medical attention. The long-term consequences of WNV neuroinvasive disease include acute flaccid paralysis and other neurological sequelae, often resulting in a poor physical and mental prognosis for patients,62 particularly those with comorbid conditions.63 In a study including 156 WNV patients from four Canadian provinces, physical and mental outcome measures were found to normalize within approximately one year in patients with West Nile non-neuroinvasive disease, while patients with neuroinvasive disease took slightly longer to recover.63 However, more recent studies indicate that long-term effects and chronic manifestations resulting from WNV neurological infections are significant public health issues that require increased attention.54

WNV is now endemic to southern Canada from Alberta to Quebec and has been detected in BC since 2009.65-68 Culex tarsalis, the main vector of WNV in western Canada, has been found as far north as Yellowknife, Northwest territories in 201069,70; the main vectors of WNV in eastern Canada belong to the Culex pipiens complex.71,72 While WNV is currently restricted to southern latitudes, the presence of WNV vector mosquitoes as far north as Yellowknife indicates the need for systematic surveillance of arthropod vectors, because a warming climate has the potential to favor the spread of competent vectors and pathogens further north.70

The intensity of WNV activity has varied greatly among years and appears associated with a range of ecological factors affecting mosquito and bird population parameters,4,73,74 with the first epidemic associated with the initial invasion of WNV into wild reservoir and vector populations in 2001/2002 in Ontario and Quebec, and 2002/2003 in the Prairies, and then epidemic ‘re-emergence’ events in 2007 in the Prairies and in 2012 in Ontario and Quebec. Certainly the 2007 epidemic in the prairie provinces was associated with a combination of unusual weather events (a particularly warm winter of 2006 followed by a particularly warm and wet spring of 2007) that drove unprecedented abundance of Cx. tarsalis mosquitoes.75 Increasingly variable weather, which can drive epidemic re-emergence of endemic mosquito-borne diseases, is anticipated with climate change.75 Two serological studies conducted in Canada in 2003 provide insights into the levels of population exposure following the initial WNV outbreaks in Ontario and the Prairies. A household-based seroprevalence survey in southern Ontario found 3.1% (n = 1505) of respondents tested positive for WNV IgG with confirmation by plaque reduction neutralization test; the ratio of severe illness (meningitis or encephalitis) to WNV IgG with confirmation by plaque reduction neutralization analysis and predictive modeling.92-96 Data from these studies resulted in the valence of WNV was almost 10% (n = 501), with significantly higher seropositivity in rural areas (16.8%) compared to urban areas (3.2%).78 Similarly, serological surveys conducted in areas of intense WNV transmission in the USA have reported low prevalence of antibodies to WNV in human populations, indicating that additional epidemic outbreaks of human disease from WNV can be expected in the future when the abundance of human-biting, infected mosquitoes reaches critical levels.68

In recent years, considerable research has been conducted on WNV molecular characterization,79-81 vector studies, and WNV ecology,82-88 public risk behavior and health-care provider knowledge,89-91 and risk factor analysis and predictive modeling.92-96 Data from these studies will help to inform public health action for human, vector, and animal surveillance,77,98 diagnosis,99-102 and prevention and control, including messaging.103-105 For example, public health managers could use prediction maps, which are based on animal or human information and developed from annual early season meteorological information, to guide ongoing decisions about when and where to focus intervention strategies for WNV as a complement to public health preparedness. Ongoing disease modeling research may further enable the development of weather-generated forecasting tools for WNV risk that could be used in decision support systems for interventions such as mosquito control and enhanced public awareness of imminent increased risk of WNV infection.107,108

Other mosquito-borne diseases

At least four other mosquito-borne viruses that cause human encephalitis are currently, or have been in recent years, present in Canada, including eastern equine encephalitis virus (EEEV), JCV, SSHV, and Cache Valley virus (CVV). However, the burden of illness associated with these viruses is unmeasured and unknown at present as these diseases are not nationally notifiable. Western equine encephalitis virus is also of historic importance in western Canada, with epidemics recorded every decade from the 1930s to the 1980s.43 The health consequences of human infection with these mosquito-borne viruses range from mild febrile illness to severe neurological disease; the latter may result in long-term neurological sequelae or death. As with WNV, the endemic mosquito-borne viruses in Canada differ in their geographical distribution, which is influenced by the distributions of their main mosquito vector species, animal reservoir hosts, and of environmental conditions suitable for transmission.109 Although data on incidence are not available, it is likely that the impact of many of these mosquito-borne viruses in Canada is considerably less than in the USA because of the temperature constraints that restrict transmission to limited periods of warmer months and may restrict the geographic occurrence of different vector species, particularly for EEEV. Nevertheless, sporadic arbovirus epidemics could result in severe illness in substantial numbers of persons in Canada.

California serogroup viruses

JCV and SSHV are mosquito-borne viruses belonging to the California serogroup (CSG) of bunyaviruses.14,110 JCV is widely distributed throughout North America; both SSHV and JCV were first identified as the causal agents of febrile and neurological illness in Canada during the late 1970s and 1980s; however, routine testing had not been conducted for almost 20 years.111 Recently, enhanced testing for CSG virus-associated disease has resulted in the identification of new neuroinvasive and non-neuroinvasive cases associated with these bunyaviruses111,112 (Drebot et al., unpublished data). Widespread exposure to these viruses in wildlife populations in Canada has been demonstrated,110 e.g. seroprevalence data suggest that up to 88% of deer along the south shore region of Nova Scotia have been infected by JCV.113 There have been rare reports of human SSHV and JCV infection in Canada.113,114 Studies in northern Quebec have found up to 10% seroprevalence of CSG viruses in residents of local communities.115 Analysis of sera collected from suspect WNV cases in Manitoba found that 25% of suspect WNV cases were seropositive for CSG viruses when tested for virus-specific antibody in 2010; of these a significant number of individuals also had IgM antibody to SSHV and/or JCV which correlates with possible cases of illness associated with these pathogens.112 Although persistent IgM and cross-reactivity among CSG antigens may pose a diagnostic challenge rendering attribution of acute neurological symptoms to these viruses difficult,116-118 Importantly, such studies demonstrate that infection of Canadians...
with CSG viruses may be occurring, and suggest that SSHV and JCV may be contributing to an under recognized burden of disease during the mosquito season in Canada.111

Eastern equine encephalitis virus
EEEV is found along the US gulf and Atlantic coasts, as well as in the US mid-West and in Canada, with human cases reported in at least 19 US states.109 No autochthonous human cases of EEEV have been reported in Canada to date, although the vector of EEEV, Culiseta melanura, has been reported from Quebec, Ontario, Newfoundland, and Manitoba,119 and the virus has caused periodic outbreaks in horses and exotic domestic bird populations (pheasants and emus) in Ontario and Quebec through the 2000s (e.g. http://www.omafra.gov.on.ca/english/livestock/horses/facts/09-047.htm#neurological). However, the recent increase in EEEV epizootic activity in Quebec and Nova Scotia since 2008, with an unprecedented number of equine cases (43 and 13, respectively) reported from localized regions of these provinces during the period 2008–2010, is indicative of an emerging disease.120 The emergence of EEEV in eastern Canada likely relates to a similar, more extensive, EEEV epizootic that has been occurring in the northeastern USA since 2003, which is thought to coincide with the arrival of a novel genotype of EEEV, and has recently extended in range and intensity outside its historic geographic focus in central New York state.121

Cache Valley virus
CVV has been documented to cause congenital defects in livestock but three cases of CVV-associated neurological disease in humans have been reported in the USA.122,123 While CVV, in common with CSG viruses in most jurisdictions, is not included in routine mosquito surveillance programs, CVV has been detected in mosquitoes in Alberta, Saskatchewan, Manitoba, and Ontario.124 Human CVV disease is not nationally notifiable in Canada; however, serological studies of WNV suspect cases from Manitoba and Saskatchewan in 2009 identified probable CVV infections in 5%–16% of patients.122 In 2012 and 2013, CVV infections in livestock were noted for the first time in Ontario125 and Quebec126 and were associated with lamb malformations in flocks of sheep.

CONCLUDING REMARKS
A prioritization exercise was conducted by public health stakeholders in Canada that identified vector-borne diseases, including Lyme disease and WNV, among the highest priority emerging zoonoses of public health importance. Much is known about the ecological drivers of disease emergence, including climate change, habitat disruption, and population movements; yet fragmented surveillance systems across jurisdictions and the need for inter-sectoral coordination pose a challenge to the timely detection and response to these and other emerging and re-emerging diseases. Research on the ecology and public health impact of vector-borne diseases in Canada has resulted in increased diagnostic capacity and predictive ability to identify areas at risk of disease emergence. Further research is still needed, however, to fill critical knowledge gaps on the ecology and burden of these diseases, which in turn will assist in public health decision-making.

In addition to the priority emerging diseases reviewed here, there is a need for enhanced surveillance to detect other emerging diseases and those with potential for introduction through international travel and trade. While Canada records several hundred imported cases of malaria in international travelers each year, these have not resulted in local transmission despite the presence of competent vector species; the prevailing assumption is that malaria risk will remain negligible, although climate change impacts remain unclear.3 However, several non-endemic mosquito-borne viruses may have the potential for either re-emergence or importation into Canada, including La Crosse virus and St Louis encephalitis virus which are both known in North America, and Rift Valley fever virus, Japanese encephalitis virus, Dengue virus, and Chikungunya virus, which have all recently expanded in global distribution.4,127

Given the rapid spread of tick vectors associated with the rise in tick-borne diseases such as Lyme disease in many parts of Canada, and the potential for climate-driven re-emergence of mosquito-borne diseases such as WNV, public health vigilance in Canada will benefit from a One Health approach that emphasizes multi-sectoral and multidisciplinary coordination among human and animal health stakeholders. A coordinated approach will enable the development of informed risk assessments and promote the early detection of and response to emerging infectious diseases of public health significance in Canada. Clinicians, laboratory medical practitioners, and public health officials should be aware of the risk of local infection with emerging vector-borne diseases in Canada, including those that may not be provincially or nationally notifiable.

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