

EMERGING INFECTIONS



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CCDR CANADA COMMUNICABLE DISEASE REPORT

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EMERGING INFECTIONS

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Surveillance for Lyme disease in Canada: 2009–2015

S Gasmi¹, NH Ogden^{2*}, LR Lindsay³, S Burns⁴, S Fleming⁵, J Badcock⁶, S Hanan⁶, C Gaulin⁷, MA Leblanc⁷, C Russell⁸, M Nelder⁸, L Hobbs⁸, S Graham-Derham⁹, L Lachance¹⁰, AN Scott^{11,12}, E Galanis¹³, JK Koffi^{1*}

Abstract

Objective: To summarize seven years of surveillance data for Lyme disease cases reported in Canada from 2009 to 2015.

Methods: We describe the incidence over time, seasonal and geographic distribution, demographic and clinical characteristics of reported Lyme disease cases. Logistic regression was used to explore differences between age groups, sex and year to better understand potential demographic risk factors for the occurrence of Lyme disease.

Results: The number of reported Lyme disease cases increased more than six-fold, from 144 in 2009 to 917 in 2015, mainly due to an increase in infections acquired in Canada. Most locally acquired cases were reported between May and November. An increase in incidence of Lyme disease was observed in provinces from Manitoba eastwards. This is consistent with our knowledge of range expansion of the tick vectors in this region. In the western provinces the incidence has remained low and stable. All cases reported by Alberta, Saskatchewan and Newfoundland and Labrador were acquired outside of the province, either elsewhere in Canada or abroad. There was a bimodal distribution for Lyme disease by age with peaks at 5–9 and 45–74 years of age. The most common presenting symptom was a single erythema migrans rash (74.2%) and arthritis (35.7%). Variations in the frequency of reported clinical manifestations were observed among age groups and years of study.

Conclusion: Lyme disease incidence continues to increase in Canada as does the geographic range of ticks that carry the Lyme disease bacteria. Ongoing surveillance, preventive strategies as well as early disease recognition and treatment will continue to minimize the impact of Lyme disease in Canada.

Suggested citation: Gasmi S, Ogden NH, Lindsay LR, Burns S, Fleming S, Badcock J, Hanan S, Gaulin C, Leblanc MA, Russell C, Nelder M, Hobbs L, Graham-Derham S, Lachance L, Scott AN, Galanis E, Koffi JK. Surveillance for Lyme disease in Canada: 2009–2015. Can Commun Dis Rep. 2017;43(10):194-9. https://doi.org/10.14745/ccdr.v43i10a01

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Introduction

Lyme disease, caused by the spirochete *Borrelia burgdorferi* sensu stricto, is the most commonly reported vector-borne disease in North America. Lyme disease is transmitted by blacklegged ticks, *Ixodes scapularis*, in central and eastern Canada and *Ixodes pacificus* in western Canada (1). Lyme disease is a multisystem infection that is manifested by progressive stages (2). In the early stage, the cutaneous erythema migrans rash appears within 30 days of infection at the site of the infective tick bite in approximately 70% of infected individuals (3). The rash can be accompanied by flu-like symptoms such as fever, fatigue, headache, myalgia or arthralgia. If left untreated,

B. burgdorferi can disseminate hematogenously within three months of infection (2). Manifestations of early disseminated Lyme disease include multiple secondary erythema migrans lesions, neurologic manifestations (e.g., facial palsy and meningitis) and cardiac symptoms (e.g., heart block), which may on rare occasions be fatal (4). Over months or years, untreated early disseminated Lyme disease can progress to the late disseminated stage, when arthritis is the most common manifestation (3).

In 2004, approximately 40 human cases of Lyme disease were reported in Canada (1). In 2009, Lyme disease became nationally notifiable, with provincial and territorial health departments reporting clinician-diagnosed cases to the Canadian Notifiable

Disease Surveillance System (CNDSS) of the Public Health Agency of Canada (PHAC) (5). In 2010, the Lyme Disease Enhanced Surveillance (LDES) system, designed by a working group of the Pan-Canadian Public Health Network, was implemented. This system aims to improve identification of Canadians at risk by analyzing information beyond that normally transferred to the CNDSS (6). This study aligns with the three pillars of the Federal Framework on Lyme Disease, one of which aims for "the establishment of a national medical surveillance program to use data collected by Public Health Agency of Canada to properly track incidence rates and the associated economic costs of Lyme disease" (7).

The objective of this study is to summarize seven years of surveillance data for Lyme disease cases reported in Canada from 2009 to 2015 in order to identify incidence over time, geographic and seasonal distribution, and demographic and clinical characteristics of Lyme disease cases.

Methods

Case definition

Confirmed case

The 2009 national Lyme disease case definition during the study period (8) is shown in **Table 1**.

Probable case

Table 1: 2009 national Lyme disease case definition

Clinical evidence of illness with Clinical evidence of illness laboratory confirmation: without a history of residence in or visit to an endemic area but isolation of with laboratory evidence of Borrelia burgdorferi from an infection: appropriate clinical specimen OR positive serologic test using the two-tier ELISA and Western detection Blot criteria of B. burgdorferi DNA by PCR • clinician-observed erythema clinical evidence of illness with migrans without laboratory a history of residence in, or evidence but with history visit to, an endemic area and of residence in or visit to an with laboratory evidence of endemic area infection, i.e., positive serologic test using the two-tier ELISA and Western Blot criteria

Abbreviations: DNA, deoxyribonucleic acid; ELISA, enzyme-linked immunosorbent assay; PCR, polymerase chain reaction

Data sources

Information on reported Lyme disease cases from 2009 to 2015 was obtained from the CNDSS and LDES system. The CNDSS collects only demographic data (age and sex), episode date and case classification. The LDES system captures additional data, including:

- possible geographic location of infection, including both locally acquired and travel-related cases;
- clinical manifestations; and
- results of laboratory testing.

By 2015, eight provinces were participating in the LDES system: British Columbia, Alberta, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island and Newfoundland and Labrador. British Columbia did not provide data on location. Quebec and Saskatchewan provided data only through the CNDSS.

Analysis

Incidence over time

Incidence of reported Lyme disease cases in Canada was calculated by year, province, age group and sex per 100,000 population. The denominators were census population estimates for July 1 of each year of the study period (2009–2015) based on Statistics Canada data (9).

Seasonal and geographic distribution

The seasonal occurrence of cases (by month) was obtained from the reported month of onset for Lyme disease signs or symptoms in the LDES system. The most likely geographic location for acquisition of Lyme disease infection was the centroid of the census subdivision (CSD) or the municipality in which the patient was exposed to Lyme disease risk. Any cases for which there was a history of travel (within or outside of Canada) within 30 days of reporting were not included in geographic analyses. Geographic analysis of cases acquired in BC was not possible as the location of acquisition was not reported to PHAC.

Demographic and clinical characteristics

Variations among age groups, sex and years of reporting clinical manifestations were explored by logistic regression using IBM SPSS Statistics version 24 (IBM, Chicago, IL, USA). In separate models, the outcomes were absence or presence of:

- erythema migrans (early Lyme disease);
- neurologic and cardiac symptoms and multiple erythema migrans (early disseminated Lyme disease); and
- arthritis (late disseminated Lyme disease).

For each model, explanatory variables were age group, sex and year. For the variable "age group," two age intervals, 10 years and 15 years, were explored in each model, and the reference group were 0–9 years and 0–14 years, respectively. The variable "province" was included in the analysis to account for possible variability in reporting between provinces. The significance level for explanatory variables retained in the multivariable model was less than 0.1. The most parsimonious multivariate models were sought by backward elimination of nonsignificant variables until all factors in the model were significant (P<0.05).

Results

Incidence over time

From 2009 to 2015, a total of 3,012 Lyme disease cases were reported in Canada. The number of reported cases increased more than six-fold, from 144 in 2009 to 917 in 2015. The national incidence per 100,000 population increased from 0.4 to 2.6 (Table 2).



Table 2: Lyme disease cases per 100,000 population reported by province and year in Canada, 2009–2015

Province	2009	2010	2011	2012	2013	2014	2015		
Lyme disease cases reported in Canada (n=3,012)									
British Columbia	0.2	0.2	0.4	0.4	0.1	0.1	0.4		
Alberta*	0	0.0	0.2	0.2	0.5	0.2	0.3		
Saskatchewan*	0	0.0	0.1	0.0	0.1	0.0	0.0		
Manitoba	0.4	1.0	1.0	1.5	2.3	2.7	2.4		
Ontario	0.8	0.7	1.0	1.4	2.4	1.7	3.1		
Quebec	0.2	0.1	0.4	0.5	1.7	1.5	1.9		
New Brunswick	0	0.3	0.7	0.9	0.7	0.7	1.7		
Nova Scotia	1.7	1.8	5.7	5.4	16.2	12.1	26.1		
Prince Edward Island	0.0	0.0	0.7	1.4	0.0	0.0	2.7		
Newfoundland & Labrador*	0.0	0.2	0.0	0.0	0.0	0.0	0.4		
Canada	0.4	0.4	0.8	1.0	1.9	1.5	2.6		
Lyme disease cases acquired in Canada [†] (n=2,004)									
Manitoba	0.3	0.6	0.6	1.0	2.0	2.4	2.3		
Ontario	0.5	0.5	0.8	0.8	2.1	1.3	2.7		
New Brunswick	0.0	0.3	0.4	0.7	0.7	0.5	1.5		
Nova Scotia	1.5	1.5	5.2	5.3	16.1	12.1	26.1		
Prince Edward Island	0.0	0.0	0.0	0.7	0.0	0.0	0.0		

 $^{^{\}star}$ All cases reported from Alberta, Saskatchewan and Newfoundland and Labrador were travel-related

Among the cases acquired in Canada, 63.9% were confirmed cases and 36.1% were probable cases (**Table 3**).

Table 3: Classification (confirmed and probable) of all reported Lyme disease cases and cases acquired in Canada*, 2009–2015

Classification	Number (percentage of cases)								
Year	2009	2010	2011	2012	2013	2014	2015	Total	
Lyme disease cases reported in Canada (n=3,012)									
Confirmed	115 (79.9%)	109 (76.2%)	195 (73.3%)	232 (68.6%)	485 (71.1%)	334 (64.0%)	651 (71.0%)	2,121 (70.4%)	
Probable	29 (20.1%)	34 (23.8%)	71 (26.7%)	106 (31.4%)	197 (28.9%)	188 (36.0%)	266 (29.0%)	891 (29.6%)	
Total	144	143	266	338	682	522	917	3,012	
Lyme disease cases acquired in Canada (n=2,015)									
Confirmed	56 (70.9%)	56 (65.1%)	96 (60.0%)	129 (58.1%)	286 (61.1%)	198 (59.5%)	467 (70.0%)	1,288 (63.9%)	
Probable	23 (29.1%)	30 (34.9%)	64 (40.0%)	93 (41.9%)	182 (38.9%)	135 (40.5%)	200 (30.0%)	727 (36.1%)	
Total	79	86	160	222	468	333	667	2,015	

^{*} The information on Lyme disease cases acquired in Canada (number and percentage) is provided by provinces participating in the LDES system (Alberta, Manitoba, Ontario, New Brunswick, Nova Scotia and Prince Edward Island). For clarification, all cases reported to be acquired in Canada within or outside the province are included

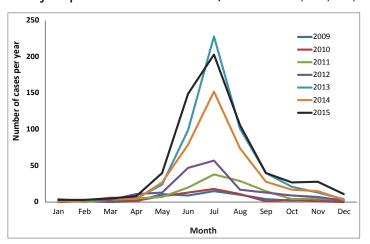
The increased incidence of Lyme disease in Canada was mainly due to an increase in the number of locally acquired infections—79 in 2009 and 667 in 2015.

Over the study period, information on the country of exposure was available for 1,950 cases. Of those, 1,709 (87.6%) were acquired in Canada. Of those cases for which information on location of acquisition was available, the majority were reported as being acquired in known risk areas. However, some cases were reported as having been acquired in Canada, but outside known risk locations. The rest of these cases, 241 (12.4%), were acquired abroad; more than half of these travel-related cases were reported as being acquired in the United States.

Seasonal distribution

For the provinces participating in the LDES system, the month of illness onset for Lyme disease cases acquired in Canada was available for 2010 cases. Of these, 96% were reported between May and November, with a consistent peak in case numbers in July. Most cases were reported during the summer months of June (20.7%), July (35.4%) and August (17.3%) (Figure 1). In 2015, a greater number of cases were reported with illness onset in November and December, suggesting that the ticks may have been active later in the season that year than in other years.

Figure 1: Month of Lyme disease illness onset for locally-acquired infection: Canada, 2009–2015 (n=2,010)



Geographic distribution

Between 2009 and 2015, provinces from Manitoba eastwards had an increase in incidence of Lyme disease, with the largest increase in Nova Scotia. In the western provinces, the incidence has remained low and stable. All cases reported by Alberta, Saskatchewan and Newfoundland and Labrador were acquired outside of the province, either elsewhere in Canada or abroad. The year 2014 saw a decrease in incidence in most provinces, followed by an increase in 2015.

For the provinces participating in the LDES system, the number of municipalities with acquisition of Lyme disease cases in Canada increased more than five-fold over the study period, from 21 in 2009 to 109 in 2015 (Table 4).

[†] The information about whether Lyme disease cases were acquired in Canada was provided by some of the provinces participating in the LDES system (Alberta, Manitoba, Ontario, New Brunswick, Nova Scotia and Prince Edward Island). However, only Lyme disease cases acquired in the province of origin are included

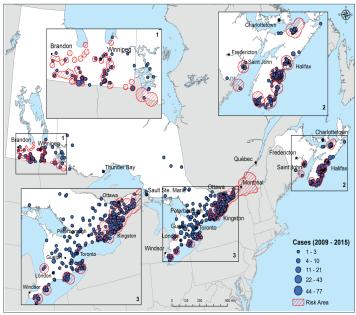
Table 4: Annual number of cases and municipalities of disease acquisition reported by provinces participating in the Lyme Disease Enhanced Surveillance system, Canada, 2009–2015

Pro	vince	2009	2010	2011	2012	2013	2014	2015
British Columbia*	Cases (N)	NA						
	Municipalities (N)	NA						
Alberta	Cases (N)	0	0	0	0	0	0	0
	Municipalities (N)	0	0	0	0	0	0	0
Manitoba	Cases (N)	0	4	7	12	19	28	22
IVIATIILODA	Municipalities (N)	0	2	4	3	9	17	12
Ontario	Cases (N)	37	38	85	92	184	144	323
	Municipalities (N)	18	18	31	37	54	45	74
New Brunswick*	Cases (N)	NA	0	3	5	1	3	7
	Municipalities (N)	NA	0	1	1	1	2	2
Nova Scotia	Cases (N)	13	17	50	50	151	114	239
	Municipalities (N)	3	5	10	7	13	15	21
Prince Edward Island*	Cases (N)	NA	NA	NA	1	0	0	0
	Municipalities (N)	NA	NA	NA	1	0	0	0
Newfoundland & Labrador	Cases (N)	0	0	0	0	0	0	0
	Municipalities (N)	0	0	0	0	0	0	0
Total	Cases (N)	50	59	145	160	355	289	591
	Municipalities (N)	21	25	46	49	77	79	109

Abbreviations: N, number; NA, not available

The reported locations of where Lyme disease was acquired in Canada are shown in **Figure 2**. Lyme disease risk areas have increased over time for Manitoba, Ontario, Quebec, New Brunswick and Nova Scotia (1).

Figure 2: Reported locations of Lyme disease acquisition, Canada, 2009–2015

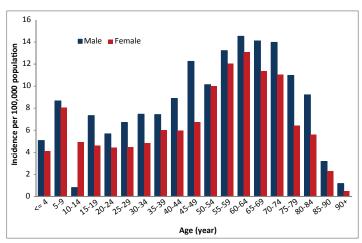


Legend: The size of each circle represents the number of cases acquired in a given municipality. The centre of each circle is the centroid of the probable municipality of acquisition. The data on location of acquisition are not available for cases reported in British Columbia, Saskatchewan and Quebec. Furthermore, cases reported in Alberta and Newfoundland and Labrador are travel-related cases only. Hatched areas indicate Lyme disease risk areas. These are locations where field surveillance suggests that populations of the Lyme disease vector *Ixodes scapularis* have begun to become established (1)

Demographic and clinical characteristics

Over the study period, slightly more cases of Lyme disease were reported among men (n=1,688, 56% of cases) than women (n=1,316, 44% of cases). The mean age of all reported cases was 45 years (95% CI: 44.3–45.8). The incidence per 100,000 population showed a bimodal pattern with high incidence in adults aged 45–74 years and children aged 5–9 years. In all age groups, incidence was higher among males than females, except for the 10–14 age group (**Figure 3**).

Figure 3: Incidence of Lyme disease by age group and sex, Canada 2009–2015 (n=3,004)



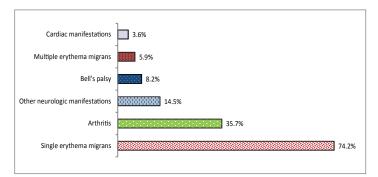
Clinical information on those affected by Lyme disease acquired in Canada was available in 1,657 (55%) of reported cases. A single erythema migrans rash (74.2%) and arthritis (35.7%)

New Brunswick, Prince Edward Island and British Columbia started participating to the Lyme Disease Enhanced Surveillance (LDES) system in 2010, 2012 and 2015, respectively. British Columbia does not provide information on location of acquisition of disease. Cases reported in Alberta and Newfoundland and Labrador are travel-related cases only



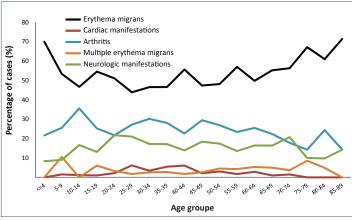
were the most common manifestations, and multiple erythema migrans lesions (5.9%) and cardiac symptoms (3.6%) were the least common (**Figure 4**). Multiple clinical manifestations were reported in 33.2% of cases.

Figure 4: Percentage of clinical manifestations for Lyme disease infections acquired in Canada, 2009–2015 (n=1,657)



The relative proportions of the different clinical manifestations were somewhat different for cases reported in children younger than 15 years of age than in other age groups. In this age group, erythema migrans lesions were more commonly reported, whereas neurologic and cardiac manifestations were less frequently reported than for older age groups (**Figure 5**). Cardiac manifestations were more frequently reported for adults of 20–44 years of age than for other age groups.

Figure 5: Percentage of reported Lyme disease cases by clinical manifestation and age group, Canada, 2009–2015 (n=1,657)



Reported in the Lyme Disease Enhanced Surveillance System

In the multivariate analysis for clinical manifestations, children aged 0–9 years had a greater number of cases reported as early Lyme disease (erythema migrans only) than patients aged 10–19 and 30–39 years (P<0.05) (**Table 5**). For early disseminated manifestations, young adults 20–29 years of age reported more neurologic manifestations, cardiac manifestations or multiple erythema migrans than the reference age group of 0–9 years (P<0.05). For late disseminated manifestations, children under 15 years of age were more frequently reported as having arthritis than other age groups.

Table 5: Final multivariate logistic regression models predicting occurrence of Lyme disease clinical manifestations in patients, Canada, 2009–2015 (n=1,657)

Explanatory variables	Estimate	Odds ratio	CI at 95%	Wald test	P value				
Early Lyme disease (erythema migrans)									
10–19 years vs 0–9 years	-0.490	0.613	0.378-0.994	3.932	0.047				
30–39 years vs 0–9 years	-0.513	0.599	0.378-0.950	4.753	0.029				
Early disseminated (neurologic and cardiac symptoms; multiple erythema migrans)									
Male vs female	-0.272	0.762	0.585-0.992	4.083	0.043				
20–29 years vs 0–9 years	0.678	1.969	1.071-3.623	4.751	0.029				
Year 2010 vs 2015	-0.555	0.574	0.392-0.841	8.137	0.004				
Late disseminated (arthritis)									
Male vs female	0.246	1.279	1.031–1.586	5.012	0.025				
75+ years vs 0–14 years	-0.691	0.501	0.283-0.888	5.604	0.018				
Year 2011 vs 2015	0.565	1.759	1.221–2.533	9.200	0.002				
Year 2010 vs 2015	0.774	2.168	1.630-2.883	28.777	0.000				
Year 2009 vs 2015	0.472	1.603	1.168–2.199	8.554	0.003				

Abbreviations: CI, confidence interval; vs, versus

Cases reported as being in the late disseminated phase were significantly higher in 2009–2011 than in 2015 (P<0.01). Consistent with this was the observation that there were more cases reported as being in the early disseminated phase in 2015 than in 2010 (P<0.01).

Discussion

Since Lyme disease became nationally notifiable in Canada in 2009, the number of reported Lyme disease cases has continued to increase from 0.4 to 2.6 per 100,000 population. Over the seven-year period, most of the cases were reported from three provinces, Ontario, Quebec and Nova Scotia; and most were locally acquired. The increase in geographic distribution of Lyme disease cases is consistent with the ongoing range expansion of blacklegged ticks, which is likely associated in part with effects of a warming climate on range spread of the tick vector I. scapularis in eastern and central Canada (10). However the incidence remains low and stable in western provinces of British Columbia, Alberta and Saskatchewan. This is due to the fact that in BC, fewer western blacklegged ticks, the Lyme disease vector in this area, are being infected with the Lyme disease bacterium than blacklegged ticks found in central and eastern Canada. In Alberta and Saskatchewan despite an increased effort, no known black-legged tick populations have been detected.

Reported illness onset was greater during the summer months which corresponds with the activity period of *I. scapularis* ticks seeking hosts (11) and overlaps with the period when most Canadians engage in outdoor activities.

Among adults, the highest incidence was between 55–74 years. Among children, the highest incidence was between 5–9 years. This is consistent with demographic trends seen in the United States (3,6) and may be useful when targeting awareness messaging (12,13). Fewer late disseminated Lyme disease cases were reported in 2015 compared with the years from 2009 to 2011, which could suggest increased awareness and earlier diagnosis and reporting of Lyme disease cases over time.



Strengths and limitations

This study summarizes data from the Canadian Notifiable Diseases Surveillance System, supplemented in most provinces with information from the Lyme Disease Enhanced Surveillance system. Using these data, we are able to follow spatial and temporal trends in the evolution of Lyme disease incidence in Canada and observe the geographic spread of Lyme disease risk and effectiveness of public health actions.

There are three main limitations to the interpretation of these findings. First, it is likely that the incidences over time are conservative estimates as some Lyme disease cases may be undiagnosed and probable cases may be underreported. Second, information on whether the Lyme disease infection was locally acquired or travel-related is an estimate because not all provinces provided this data. Finally, because of limited resources, field tick surveillance to detect expanding Lyme disease risk areas may not be up to date in many locations, which would affect classification of cases.

Conclusion

The number of reported Lyme disease cases has continued to increase in Canada over recent years, as is the geographic range of ticks that carry the Lyme disease bacteria. Continued surveillance, preventive strategies as well as early disease recognition and treatment will continue to minimize the impact of Lyme disease in Canada.

Authors' statement

SG, JKK – Data collection and curation, Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review and editing

LRL, NO – Conceptualization, Methodology, Writing – review and editing

JP, SF, JB, SH, CG, MAL, CR, LH, SG-D, LL, ANS, EG – Writing – review and editing

Conflict of interest

None.

Acknowledgements

The authors thank all the provincial and regional public health workers who collect and report data to the CNDSS, and Yann Pelcat of the Public Health Agency of Canada for preparing Figure 5.

Funding

This study was supported by the Public Health Agency of Canada and all the provincial public health organizations that contributed to the data.

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Blastomycosis hospitalizations in northwestern Ontario: 2006–2015

S Litvinjenko^{1*}, D Lunny²

Abstract

Background: Blastomycosis, caused by the organism *Blastomyces dermatitidis*, is an invasive fungal disease found in Central Canada and Central and Midwestern United States.

Objective: To describe trends in and epidemiology of hospitalized cases of blastomycosis reported among northwestern Ontario residents between 2006 and 2015.

Methods: Blastomycosis hospitalization data were extracted from the Discharge Abstract Database (DAD), accessed through IntelliHEALTH Ontario. The DAD includes administrative, clinical and demographic information on hospital discharges provided by the Canadian Institute for Health Information (CIHI). Blastomycosis records were identified using ICD-10 codes B40.0 to B40.9. Hospitalization rates were calculated for all of Ontario, and age-specific hospitalization rates were calculated for northwestern Ontario and analyzed by local health region, time and seasonality as well as presenting symptoms.

Results: There were 581 hospitalizations for blastomycosis reported in Ontario over this 10-year period. Of these, 245 (42%) were from northwestern Ontario, although this region accounts for only 0.6% of the Ontario population. The average hospitalization rate for blastomycosis in northwestern Ontario was 35.0 per 100,000 per year. This rate varied from 1.7 in the Red Lake region to 57.9 in the Kenora region. The most common presentation was acute pulmonary symptoms. Men were 1.36 times more likely to be hospitalized for blastomycosis than were women (95% confidence interval [CI]: 1.06-1.75, P<0.05). Most hospitalizations were registered in the late fall months, suggesting blastomycosis exposure in the spring/summer season followed by a lengthy incubation period.

Conclusion: Areas of northwestern Ontario have high reported rates of blastomycosis. It is not known to what extent there are regional differences in other states and provinces. Interregional differences may warrant prioritizing strategies for blastomycosis prevention and control as well as additional research and surveillance.

Suggested citation: Litvinjenko S, Lunny D. Blastomycosis hospitalizations in northwestern Ontario: 2006–2015. Can Commun Dis Rep. 2017;43(10):200-5. https://doi.org/10.14745/ccdr.v43i10a02

Introduction

Blastomycosis, caused by the organism *Blastomyces dermatitidis*, is an invasive fungal disease whose only known natural reservoir is in soil. Cases of blastomycosis have occurred mainly across the eastern areas of North America, in the provinces and states that border the Great Lakes (i.e., Ontario, Michigan, Wisconsin, Minnesota), but some have also been found in the midwestern United States and central Canada (1). Rarely have cases been reported outside North America.

Symptomatic disease is thought to occur in approximately 50% of cases (2), suggesting that healthy individuals are fairly resistant to the harmful progression of the invasive fungus. It is estimated that 70% of cases can be attributed to pulmonary blastomycosis, which usually presents as flu-like illness; the symptoms may be commonly misdiagnosed as other morbidities, for example, tuberculosis. Extrapulmonary disease most commonly manifests as cutaneous blastomycosis, but it can also occur in the skeletal, urogenital and central nervous systems. With appropriate antifungal and/or surgical treatment, the mortality rate of blastomycosis is between 5 to 10% (2).

Affiliations

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The average incubation period of blastomycosis is generally accepted to be 30 to 45 days, although the range can be anywhere from 13 to 106 days, depending on inoculum size (3) and the form of the disease (4). Although blastomycosis infection occurs primarily through the inhalation of airborne spores, it can also occur, though rarely, through a puncture in the skin with infected material. Exposure to the fungal spores may increase during excavation and construction operations as well as during recreational activities that involve contact with soil near waterways as the moist and acidic soil environment is favourable to B. dermatitidis growth (2,5). Aerosolization of spores occurs more readily from dry soil that is disturbed (2). Due to changing climatic conditions (i.e., rainfall, temperature and humidity) and the effects on soil composition (i.e., pH and organic content), isolating B. dermatitidis from the environment can be challenging (2,3,6).

In Ontario, blastomycosis has not been on the list of reportable diseases since 1989 (due to limited transmissibility and few cases being reported), although the disease remains notifiable in the

province of Manitoba (7). Blastomycosis is common in the central and midwestern United States (8) and remains a reportable illness in Arkansas, Louisiana, Michigan, Minnesota and Wisconsin (9). According to Health Canada, the annual incidence rate of blastomycosis across Ontario, Quebec, Manitoba and Saskatchewan is 0.62 cases per 100,000 population, with areas that have hospitalization rates of 0.3 to 0.6 cases per 100,000 population (10).

A 2005 study on blastomycosis in northwestern Ontario identified a high annual incidence rate of 17.0 cases per 100,000 population in 1989–2005 (Mann V, Limerick B, Wiebe L. Northwestern Health Unit blastomycosis cases, 1989 to 2005: preliminary analysis. 2005; Unpublished data). An earlier study over a shorter period (1997–1999) calculated an annual blastomycosis rate of 117.2 cases per 100,000 at the time of an outbreak in Kenora (11). Along with the rate of 404.9 per 100,000 people living on reserve, these rates are considered exceptionally high (11).

The objective of this study is to utilize hospitalization data from the past decade (2006–2015) to describe recent trends in the epidemiology of blastomycosis hospitalization in northwestern Ontario.

Methods

This analysis focuses on hospitalized cases of blastomycosis in northwestern Ontario. For the purposes of this report, the term "northwestern Ontario" refers to the Northwestern Health Unit (NWHU) catchment area. The NWHU catchment area is one of the 36 public health unit regions in Ontario. It serves a population of just under 82,000 across an area of 171,288 square kilometres (roughly one-fifth the size of the province). The area contains part of the Kenora District and all of the Rainy River District, and this analysis includes Kenora, Dryden, Red Lake, Sioux Lookout, Rainy River, Emo, Fort Frances and Atikokan. These regions include the named municipalities as well as any nearby smaller communities and First Nations reserves. There are 39 recognized First Nations in the NWHU catchment area; some are located around the main municipalities while others are more northern and less easily accessible.

Inclusion criteria

The study sample included hospitalization records for any form of blastomycosis diagnosed in Ontario residents between 2006 and 2015 using ICD-10 codes B40.0 to B40.9 as the primary diagnosis (12).

Location of hospitalizations were based on patients' residence rather than where they were hospitalized. For example, if a patient from northwestern Ontario was hospitalized in Toronto, the hospitalization would be classified as northwestern Ontario. Hospitalizations that occurred outside of Ontario, however, were not captured in the data and could not be assessed.

Data sources

Blastomycosis hospitalization data were extracted on January 20, 2017 from the Discharge Abstract Database (DAD). The DAD was accessed through IntelliHEALTH Ontario, a knowledge repository operated by the Ministry of Health and Long-Term Care. The DAD includes administrative, clinical and demographic information on hospital discharges provided by the Canadian

Institute for Health Information (CIHI). IntelliHEALTH Ontario is operated by the Ontario Ministry of Health and Long-Term Care.

Population estimates for the NWHU catchment area came from Statistics Canada and were accessed through IntelliHEALTH Optario

Hospitalization counts and rates

Counts of blastomycosis hospitalizations for each of Ontario's 36 public health units were tabulated. From these, hospitalization rates were derived for residents of northwestern Ontario as well as from smaller geographical regions within this area.

Crude and age-specific hospitalization rates were calculated by dividing the number of hospitalizations occurring over the time period by the total person-years at risk, and multiplying the result by 100,000 person-years. A rate displayed in 100,000 person-years indicates the number of hospitalizations that occur in a population of 100,000 people over the course of one year.

Age-standardized hospitalization rates were calculated using the 2011 Canadian Census population as the reference population. All analyses were conducted using Microsoft Excel, Open Epi and Epilnfo7.

Northwestern Ontario rates

Age-standardized hospitalization rates for the population within the NWHU catchment and the subregions within it as well as the corresponding 95% confidence intervals (CIs) were calculated using the Poisson approximation of the normal distribution. Rate ratios were calculated and used to identify any statistical differences in hospitalization rates between the subregions. Results were considered statistically significant if the 95% CI around the rate ratio did not contain one.

Rates by age and sex

Age- and sex-specific hospitalization rates and 95% CIs were calculated using the Mid-P Exact method. Ten-year age groups were used for the analysis (0–9, 10–19, etc.). Tests for statistical differences in rates between age and sex strata were carried out by calculating the rate ratios. Results were considered statistically significant if the 95% CI around the rate ratio did not contain one.

Counts by diagnosis code

Counts of hospitalizations categorized by type of blastomycosis were tabulated for northwestern Ontario. Counts for each type of blastomycosis were based on ICD-10 diagnosis codes, which ranged from B40.0 to B40.9 (12).

Counts by year and month

Counts of hospitalizations were examined by year and month of occurrence. Cumulative month totals over the 10-year study period were calculated to determine when in the year hospitalizations were the most common.

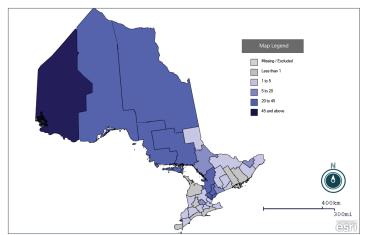
Results

Blastomycosis hospitalizations in Ontario

Between 2006 and 2015, a total of 581 blastomycosis hospitalizations were recorded by 29 of Ontario's 36 public

health units (the remaining seven health units registered no cases). Notably, 245 blastomycosis hospitalizations (42%) were attributed to residents of northwestern Ontario alone (i.e., in the NWHU) (Figure 1).

Figure 1: Number of blastomycosis hospitalizations by public health unit, Ontario, 2006–2015 (n=581)

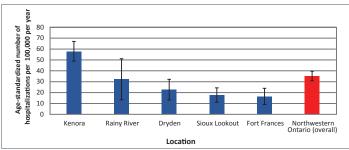


Source: Inpatient Discharges 2006-2015. Ontario Ministry of Health and Long-Term Care. IntelliHEALTH Ontario. Date Extracted: January 10, 2017

Hospitalizations in northwestern Ontario by region

In northwestern Ontario, the hospitalization rate for blastomycosis was 35.0 per 100,000 per year between 2006 and 2015. Kenora had the highest rate of hospitalizations, at 57.9 per 100,000 per year, and a statistically significant rate ratio of 3.13 (95% CI: 2.42–4.09; P<0.01) compared with the rest of northwestern Ontario. Due to small counts, hospitalizations in the Atikokan, Emo and Red Lake subregions have been suppressed and are not reported on. Other regions in the area had hospitalizations rates that ranged from 16 to 32 per 100,000 per year (**Figure 2**).

Figure 2: Blastomycosis hospitalizations* by northwestern Ontario region[†], 2006–2015



* Rates per 100,000 per year age standardized, with 95% confidence intervals

Note: Results from Red Lake, Emo and Atikokan were omitted due to small counts Source: Inpatient Discharges 2006–2015. Ontario Ministry of Health and Long-Term Care. IntelliHEALTH Ontario. Date Extracted: January 10, 2017

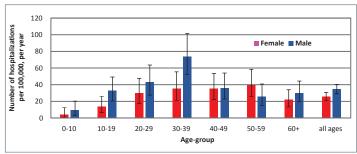
Hospitalizations in northwestern Ontario by age and sex

Males, who represented 50.3% of the population in the NWHU catchment area between 2006 and 2015, accounted for 58%

(n=142) of all blastomycosis hospitalizations (compared with n=103 for females). The rate of blastomycosis hospitalizations for males of all ages was 34.4 per 100,000 per year, compared with 25.3 per 100,000 per year for females. This equals a statistically significant rate ratio of 1.36 (95% CI: 1.06-1.76; P<0.05).

Blastomycosis hospitalizations were lowest among children aged less than 10 years and adults aged 60 years and older. Rates were generally highest among adults in their twenties to their fifties (**Figure 3**). People in the 30- to 39-year age category had a statistically significant rate ratio of 2.04 (95% CI: 1.49–2.76; *P*<0.01) compared with the other age categories. However, examination of the data showed that overrepresentation of males inflated this overall estimate; the rate ratio among men aged 30–39 years was 2.51 (95% CI: 1.70–3.66; *P*<0.01) compared with females in this age group, among whom rates were insignificant.

Figure 3: Blastomycosis hospitalization rates* by age and sex, northwestern Ontario, 2006–2015

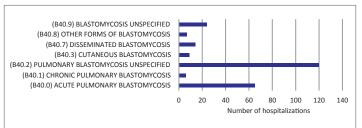


*Rates per 100,000 per year with 95% confidence intervals Source: Inpatient Discharges 2006–2015. Ministry of Health and Long-Term Care. IntelliHEALTH Ontario. Date Extracted: January 10, 2017

Hospitalizations in northwestern Ontario by ICD-10 diagnosis code

The majority of blastomycosis hospitalizations between 2006 and 2015 (75% of total cases), were due to pulmonary illness (**Figure 4**). While the nature of some cases (~10%) is unspecified, it can be assumed that most would also have been attributed to acute pulmonary infection indicative of temporary infection. This differs from the more infectious relapsing chronic condition, which accounts for 2.5% of known hospitalizations. Other manifestations of blastomycosis disease, including cutaneous and disseminated varieties, accounted for less than 5% of known hospitalizations.

Figure 4: Blastomycosis hospitalizations by ICD-10 diagnosis code, northwestern Ontario, 2006–2015



Source: Inpatient Discharges 2006–2015. Ontario Ministry of Health and Long-Term Care. IntelliHEALTH Ontario. Date Extracted: January 10, 2017

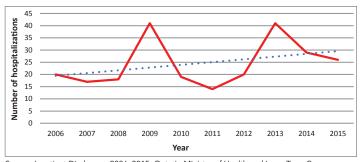
[†] Regions include the named municipality in addition to smaller nearby communities and First Nation reserves



Hospitalizations in northwestern Ontario by year and month

There was a slight increase in the number of blastomycosis hospitalizations in northwestern Ontario between 2006 and 2015 (**Figure 5**). Aside from the general increasing trend in hospitalization counts, 2009 and 2013 were noted as peak years, both with 41 hospitalizations.

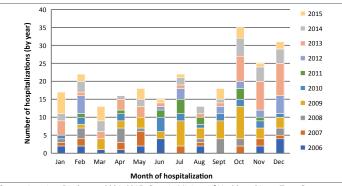
Figure 5: Blastomycosis hospitalizations in northwestern Ontario by year, 2006–2015



Source: Inpatient Discharges 2006–2015. Ontario Ministry of Health and Long-Term Care. IntelliHEALTH Ontario. Date Extracted: January 10, 2017

Between 2006 and 2015, there were more hospitalizations in the late fall to early winter months, on average, than during any other time of the year (**Figure 6**).

Figure 6: Blastomycosis hospitalizations in northwestern Ontario by month, 2006–2015 (n=245)



Source: Inpatient Discharges 2006–2015. Ontario Ministry of Health and Long-Term Care. IntelliHEALTH Ontario. Date Extracted: January 10, 2017

Discussion

Between 2006 and 2015, almost 600 hospitalizations for blastomycosis were reported in Ontario. Based on 2015 population estimates, northwestern Ontario accounts for only 0.6% of the provincial population and yet over 40% of total hospitalizations over the period of the study. These rates are likely to be an underestimate of the true incidence of blastomycosis, as the literature suggests that only about 50% of people with blastomycosis present clinical symptoms for hospitalization (13). There appeared to be a lot of regional variation even within northwestern Ontario, with certain health regions reporting zero cases over this 10-year period, while the Kenora region consistently demonstrated one of the highest hospitalization rates for blastomycosis in the province, driving regional/provincial estimates of morbidity. Coupled with previously identified estimates from the literature, high rates

in the Kenora region may be due to geological differences compared to eastern and southern parts of northwestern Ontario, which may result in better soil conditions for blastomycosis, although soil types were not tested as part of this study. It is not known whether such regional variations are also characteristic of other Canadian provinces or the United States (US).

Furthermore, our finding of 35.0 per 100,000 per year hospitalization rate for northwestern Ontario remain well above the highest average annual rate reported in any US state but overlaps with some regional data in the US. In Wisconsin, for example, although there was an age-adjusted rate of 2.9 hospitalizations per 100,000 reported for the state (16), there were reports of 10–40 cases per 100,000 in certain Wisconsin counties (17). It should be noted that average annual increases in blastomycosis rates in the northwestern Ontario might be indicative of genuine increases of incidence of the disease, or reflect improved clinical awareness and testing from physicians (12).

That the majority of blastomycosis cases in Ontario in 2006–2015 were male (58%) is consistent with data from other studies. This finding can be attributed to men dominating the types of labour (such as excavation or construction) common in these areas. More men than women may also prefer recreational activities near waterways that favour growth of *B. dermatitidis* (5). The exception was in the 50- to 59-year age group, where 59% of cases were female and 41% male.

Most blastomycosis hospitalizations were in the 30- to 39-year age group. This is in contrast to Manitoba where 50- to 69-year-olds shared the highest incidence rate (2). Similarly, an older report from northwestern Ontario found the highest hospitalization rates among people in the 40- to 59-year age group (Mann V et al unpublished data). Irrespective of age and sex, seasonality trends are consistent with exposure in the spring/summer season and an incubation period that would lead to diagnosis in the late fall.

Strengths and limitations

A strength of this study was the quality of the CIHI data in its capacity to detect regional differences in disease and to provide a comprehensive hospitalization-based sample population (a large proportion of blastomycosis literature is based on outbreak-specific reporting). In terms of validity, Public Health Ontario supplied the NWHU with count data of laboratory-confirmed positive cultures of *B. dermatitidis* for the years 2010–2015, which in theory would be a more representative measure of blastomycosis incidence in the region. However, as the hospitalization data yielded numbers comparable to the laboratory-confirmed count data, the hospitalization data were considered an adequate proxy measure for blastomycosis-associated hospitalization in northwestern Ontario.

A limitation of the study is the use of hospitalization records to assess blastomycosis, which can only serve as a proxy for true incidence, given that not everyone can be expected to seek and/or have access to care or be hospitalized if they do seek medical care. In addition, some cases, particularly severe cases, are referred to Winnipeg, Manitoba; as a result they would not be captured as an Ontario case, and may potentially confound incidence rates in Manitoba between locally attributed exposures, and out of province visitations (14). Moreover, while other studies found significantly higher rates of blastomycosis in Indigenous populations (11,14,15), information



on the Indigenous status of the cases was not available in our study population. Future studies assessing individualized case-record data, the monitoring of relevant risk factors (e.g., socio-demographic factors), isolating probable sources of infection, and determining overall rates of incidence would help address some of the limitations of the current study and increase our understanding of this disease.

Conclusion

Areas of northwestern Ontario have high reported rates of blastomycosis. It is not known to what extent there are regional differences in other states and provinces. Interregional differences may warrant prioritizing strategies for blastomycosis surveillance, prevention and control, as well as additional research.

Authors' statement

SL – Conceptualization, Methodology, Formal Analysis, Investigation, Visualization, Writing – original draft, Writing – review and editing, Project administration

DL – Conceptualization, Methodology, Validation, Resources, Data Collection, Writing – review and editing, Supervision, Project administration

Conflict of interest

None.

Acknowledgements

We would like to thank Dr. Kit Young-Hoon, Medical Officer of Health for the Northwestern Health Unit, for her supervision, expertise and validation of this report. An additional thank you to all of those in the field who helped collect these data and who provide care to those with infectious diseases.

Funding

This research was supported by the Northwestern Health Unit.

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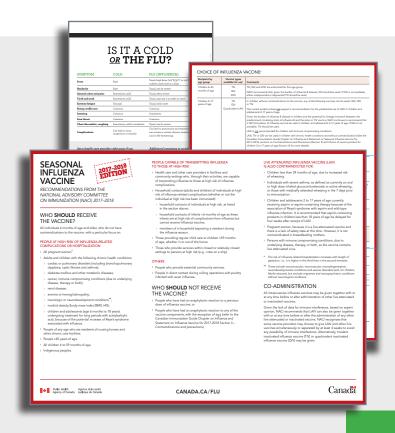
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Emerging infectious diseases: prediction and detection

NH Ogden¹, P AbdelMalik², JRC Pulliam³

Abstract

Emerging infectious diseases (EIDs), including West Nile virus, severe acute respiratory syndrome (SARS) and Lyme disease, have had a direct effect within Canada, while many more EIDs such as Zika, chikungunya and Ebola are a threat to Canadians while travelling. Over 75% of EIDs affecting humans are, or were originally, zoonoses (infectious diseases transmitted from animals to humans). There are two main ways by which infectious diseases can emerge: by changes in their geographical ranges and by adaptive emergence, a genetic change in a microorganism that results in it becoming capable of invading a new niche, often by jumping to a new host species such as humans. Diseases can appear to emerge simply because we become capable of detecting and diagnosing them. Management of EID events is a key role of public health globally and a considerable challenge for clinical care. Increasingly, emphasis is being placed on predicting EID occurrence to "get ahead of the curve" - that is, allowing health systems to be poised to respond to them, and public health to be ready to prevent them. Predictive models estimate where and when EIDs may occur and the levels of risk they pose. Evaluation of the internal and external drivers that trigger emergence events is increasingly considered in predicting EID events. Currently, global changes are driving increasing occurrence of EIDs, but our capacity to prevent and deal with them is also increasing. Web-based scanning and analysis methods are increasingly allowing us to detect EID outbreaks, modern genomics and bioinformatics are increasing our ability to identify their genetic and geographical origins, while developments in geomatics and earth observation will enable more real-time tracking of outbreaks. EIDs will, however, remain a key, global public health challenge in a globalized world where demographic, climatic, and other environmental changes are altering the interactions between hosts and pathogen in ways that increase spillover from animals to humans and global spread.

Suggested citation: Ogden NH, AbdelMalik P, Pulliam JRC. Emerging infectious diseases: prediction and detection. Can Commun Dis Rep. 2017;43(10):206-11. https://doi.org/10.14745/ccdr.v43i10a03

Introduction

The World Health Organization (WHO) defines an emerging infectious disease (EID) as "one that has appeared in a population for the first time, or that may have existed previously but is rapidly increasing in incidence or geographic range" (1). EIDs that have directly affected Canada include West Nile virus, severe acute respiratory syndrome (SARS) and Lyme disease, while many more EIDs such as Zika, chikungunya and Ebola have been a potential threat to Canadians travelling abroad. A particular feature of many EIDs is their capacity to spread internationally and impact global health. Consequently, the capacity to predict, identify and respond to them is a key preoccupation of public health.

Over 75% of EIDs affecting humans (2) are, or were originally, zoonoses (infectious diseases transmitted from animals to humans), particularly those maintained by wild animals. They are transmitted by various routes including via direct contact, food, drinking water, recreational water and arthropod vectors (3). Many zoonoses (like West Nile virus and Lyme disease) are only transmissible from animal reservoir hosts to humans without (under normal circumstances) human-to-human transmission.

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Some zoonoses are transmissible from humans infected by animals to another human but with an efficiency of transmission too low for sustained human-to-human transmission in the absence of animal reservoir hosts (4). An example is the recently discovered Middle East respiratory syndrome (MERS) caused by a coronavirus (MERS-CoV), which is transmitted from putative bat reservoir hosts (5), via domesticated animals (camels) to humans (6). Transmission from infected people to other people in close contact (particularly health care workers) can also occur, but to date human-to-human transmission has been in the form of "stuttering chains" that eventually die out (4,7). Some zoonoses are intrinsically highly transmissible from human-to-human; once they infect a human, an epidemic can occur in the human population as seen during the outbreak of Ebola in West Africa in 2013–2016 (8).

In this article, we briefly review how diseases emerge, discuss the drivers for their emergence and spread and present what advances are underway to improve the prediction and detection of EIDs.



How do infectious diseases emerge?

Infectious diseases can appear to "emerge" because we develop the capacity to identify a new endemic pathogen and subsequently begin to detect infections in humans. Recently, a number of tick-borne pathogens, including *Borrelia mayonii* and Heartland virus, have been detected in North America through careful re-examination of samples from those patients who exhibited clinical manifestations consistent with an infectious disease but who tested negative for known pathogens (9,10). However, there are two ways by which infectious diseases can truly emerge: by changes in their geographical range and by adaptive emergence.

Emergence by changes in geographical range

Many disease emergence events are associated with changes in the geographical footprint of pathogens or parasites. This may be due to changes in the natural geographical ranges of animal hosts of zoonoses and vectors and/or via dispersal of pathogens in infected humans, animal reservoirs or vectors. Dispersal may be long-distance—even global—via infected travellers; trade (legal and illicit) that may carry infected animals, animal products or vectors; and natural animal migrations. Examples of long-distance dispersal include the introduction of SARS into Canada by infected travellers from the Far East (11); the introduction of West Nile virus into North America, likely via an infected mosquito carried in an aircraft into New York (12): and the introduction of Zika virus into the Americas from Asia via Micronesia (13). Dispersal may be more local due to local movements of infected people or due to changing geographical footprints of wild animal hosts and vectors, usually due to changing environmental conditions that render new ecosystems/ regions suitable for the invading species (see "Predicting infectious disease emergence" section below). Examples of EIDs that have emerged by local geographical spread include the recent expansion of Lyme disease into Canada due to the northward spread of the tick vector Ixodes scapularis from the United States (US) (14), and the local spread of Zika virus within south and central America (15).

Adaptive emergence

Adaptive emergence is the genetic change of a microorganism that results in a phenotype that is capable of invading a new ecosystem, particularly via jumping to a new host species, including humans (16). For example, the emergence of SARS and MERS-CoV is thought to have been facilitated by genetic changes enhancing transmissibility between different species and, perhaps, pathogenicity (5,16), while a single mutation of chikungunya virus is thought to have facilitated its transmission by *Aedes albopictus* mosquitoes and its emergence in more temperate regions of the world (17). Both mutation and reassortment of genes from viruses that infect different animal species are considered key to the development of novel pandemic influenza virus strains such as pH1N1 (18).

What are we doing about EIDs?

Our response to EIDs comprises a range of activities from outbreak management, disease surveillance following

emergence, and scanning for EID events. Increasingly, research aims to improve our capacity to predict EID outbreaks.

Management of outbreaks

The efforts to ensure local, national and international capacity to respond to infectious disease outbreaks, including EIDs, are beyond the scope of this review. The capacity to respond has underpinned the creation and/or design of many international (e.g., WHO) and national (e.g., Public Health Agency of Canada) public health organizations and the development of management plans for local and pandemic infectious diseases (19). To further facilitate the detection, communication and management of health threats, the international community agreed to the International Health Regulations. This legally binding instrument came into force in June 2007 with the aim of helping "...the international community prevent and respond to acute public health risks that have the potential to cross borders and threaten people worldwide" (20). How this works is described next.

Surveillance for EID events

Surveillance for EIDs is an ongoing public health activity around the world and takes many forms. As a core capacity requirement of the International Health Regulations, all WHO member states are obligated to have the capacity for both indicator- and event-based surveillance. Member states are also required to report "unusual or unexpected" events (human cases, contaminated produce or infected vectors) to WHO in a timely manner (20). Several types of and approaches to surveillance have been implemented over the years to help identify EIDs, and development efforts in this area continue. For example, the Global Early Warning System (GLEWS) is a warning system for health threats and emerging risks at the human-animal-ecosystems interface that recognizes the zoonotic nature of many EIDs (21). This warning system is run jointly by Food and Agriculture Organization (FAO), World Organisation for Animal Health (OIE) and WHO. A number of "passive" surveillance programs that operate internationally, such as the GeoSentinel Surveillance Network, an international network of voluntarily participating medical clinics (22) and laboratory-based surveillance (23), use more traditional indicator-based approaches. Changes in technology and the availability of data have also led to the development of event-based surveillance systems, many of which scrutinize publicly available content on the Web in search of valid signals of potential emerging threats. Examples include the Program for Monitoring Emerging Diseases (ProMed) (24), HealthMap (25) and MediSys (26). One of the earliest of these is Canada's Global Public Health Intelligence Network (GPHIN), currently maintained and operated by the Public Health Agency of Canada. GPHIN is particularly active in EID surveillance through its ongoing technical development and team of multilingual and multidisciplinary human analysts (27).

Predicting infectious disease emergence

Emphasis is being increasingly placed on predicting occurrence of EIDs. The idea is to "get ahead of the curve" so that public health actors can be poised to respond to them, or even prevent them. Assessing risk involves focusing on a number of key criteria for the level of threat that a pathogen or event poses and considering the sensitivity of pathogens to internal and



external drivers that may trigger emergence. The key criteria include the pathogenicity of the micro-organism (i.e., the severity of the disease it causes), the potential for the pathogen to spread locally or internationally and become established in a new environment, as well as our existing capacity to control it. These different criteria can be synthesized using multi-criteria decision analysis (MCDA) in order to decide whether to act or for purposes of prioritization (28). Studies, both anticipatory and in response to ongoing EID events, are used to quantify these criteria. Examples include assessment of the capacity for international spread of infections (29) and the suitability of local environments for their invasion (30).

Assessments of risk of disease emergence that are even more anticipatory in nature involve understanding the impact of external drivers. Examples include assessment of effects of climate change and extreme weather events as actual or potential future drivers of emergence of climate-sensitive diseases such Lyme disease in Canada (31) and West Nile virus in the US (32). Other external drivers under study include levels of biodiversity; changes in biodiversity and in agriculture and land use (which may drive emergence of zoonoses as threats for the human population) (3,33,34); and social changes induced by, for example, conflict that may enhance disease emergence or re-emergence by impacting public health programs (35) or by increasing international spread (36).

Another approach to getting even more "upstream" in predicting EID events is identifying animal or pathogen traits that increase the potential of microorganisms to emerge as human pathogens in terms of their capacity to spill over from animals to humans and then be transmissible from human to human (37). In general, viruses are more likely to emerge as human pathogens than other disease-causing microorganisms, as are microorganisms that are host generalists; that is, they can already infect a range of different animal species (37-40). Characteristics of the viral genome may determine the potential of viruses to emerge and spillover into humans (41). Some host species such as bats and rodents also have a particularly high potential to be reservoirs of pathogens that can spill over and emerge into humans (40,42).

EIDs and public health in the future

EIDs will continue to be at the forefront of global challenges to public health. Increasing climate, biodiversity, social and land use changes, combined with a world increasingly connected by travel and trade, mean that opportunities for pathogens to emerge in animals, spillover into humans and spread rapidly and globally are increasing. Public health will need to continue to focus on three elements:

- capacity and preparedness for EID outbreak management;
- surveillance for EID events; and
- upstream assessment of the risk of infectious disease emergence.

Currently, the risks of EIDs are increasing, but so is our technological capacity to deal with them. The development of modern genomics and bioinformatics is increasing our ability to detect EID outbreaks, locate their sources (43), and identify genetic changes that can be predicted to drive emergence (16).

Technologies to capture EID events by web-based scanning and analysis for signals in social media are increasing (44). At the same time, developments in the field of earth observation (by satellites) are increasing the spatio-temporal precision of the data, and their capacity to identify changes in climate, weather, habitats and socioeconomics that may drive disease emergence (45). Increasingly then, the focus is shifting to surveillance for changes in drivers of EIDs, rather than the EIDs themselves. Thus the potential to respond preventatively to EIDs is becoming a reality.

There is a growing recognition that EIDs are equivalent to those invasive species that may be important to conservation biology and natural resource management (46). Therefore, a "One Health" approach that employs knowledge of the interconnectivity of animal, environmental and human health enhances risk assessments, predictive modelling and detection of EIDs (47). Ultimately, both indicator-based and event-based surveillance fall along a surveillance continuum, providing different but valuable data for analysis, interpretation and action. Efforts to link the different approaches into comprehensive systems that capitalize on available historical and contextual data would further strengthen the ability to detect, prepare for and respond to EIDs.

Conclusion

We continue to make great strides in our capacity to predict, detect, prepare for and manage EIDs. However, EIDs will remain a key, global public health challenge in a world where demographic, climatic and other environmental changes, including globalization, are enhancing the emergence of new pathogens, their spillover from animals to humans and their global spread.

Authors' statement

NHO, JRCP – Conceptualization; NHO, PA and JCRP, Writing original draft

Conflict of interest

None.

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Synopsis: Lyme Disease in Canada – A Federal Framework

Centre for Food-borne, Environmental and Zoonotic Infectious Diseases^{1*}

Abstract

The Federal Framework on Lyme Disease Act required the federal government to develop a Federal Framework on Lyme Disease. To do this, the Public Health Agency of Canada held a conference with a wide variety of stakeholders who shared their experiences with Lyme disease, and discussed current knowledge and research. A draft version of the Framework was publicly posted on Canada.ca for a 30-day public consultation period. The final report, Lyme Disease in Canada: A Federal Framework was released in May 2017. The Framework includes the three pillars of surveillance; education and awareness; and guidelines and best practices. Implementation will require the involvement and collaboration of all stakeholders and all levels of government, with the Government of Canada committed to collaborating with domestic and international partners to exchange best practices in the prevention, diagnosis and treatment of Lyme disease.

Suggested citation: Centre for Food-borne, Environmental and Zoonotic Infectious Diseases, Public Health Agency of Canada. Synopsis: Lyme Disease in Canada – A Federal Framework. Can Commun Dis Rep. 2017;42(10):212-4. https://doi.org/10.14745/ccdr.v43i10a04

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Introduction

The Federal Framework on Lyme Disease Act, which received Royal Assent on December 16, 2014, required the federal government to develop a Federal Framework on Lyme Disease that would bring a sense of cohesiveness to surveillance, education and awareness, and guidelines and best practices efforts. To inform the development of this Framework, the Public Health Agency of Canada, on behalf of the Minister of Health, held a conference with over 500 participants. Lyme disease patients, their families and others shared their experiences with Lyme disease, while Lyme disease experts provided information on current knowledge and research related to Lyme disease treatment, prevention, diagnosis and management. Additionally, to allow for further feedback and refinement, a draft version of the Framework was publicly posted on Canada.ca for 30 days. The full report, Lyme Disease in Canada – A Federal Framework, was released on May 30, 2017 and is available online (1). It is intended to be a first step in guiding concrete action in areas where the federal government has a role. This is a synopsis of the full report.

Background

Canada has approximately 40 species of ticks. Of these, only a few are capable of transmitting pathogens, including bacteria and viruses, which have the potential to cause human illness.

Lyme disease, the most common tick-borne illness in Canada, is caused by the bacterium *Borrelia burgdorferi*. This bacterium is transmitted to people through the bite of blacklegged ticks and western blacklegged ticks.

Lyme disease occurs mainly in or near areas where infected tick populations are established. Adult ticks are about the size of a sesame seed, and nymphal (immature) ticks are about the size of a poppy seed. This means that people may not even know that they have a tick attached to them. People engaging in occupational or leisure activities, such as camping and hiking near or in forested or semi-forested areas where infected ticks are found, are at a higher risk of bite transmission. Exposure to ticks can occur in other circumstances, such as gardening, golfing or dog walking, if these activities occur in locations where ticks are found. It should be noted that ticks carrying Lyme disease are active through much of the year; however, bites leading to human infection are much more common during the spring and summer months.

In 2016, 987 Canadians were newly confirmed to have Lyme disease (2). These cases have been steadily growing since Lyme disease became nationally notifiable in 2009 and, while advances in knowledge and diagnostics have occurred over time, there is likely some degree of underreporting. The federal government and provinces and territories continue to work together to identify where Lyme disease cases are occurring in Canada.

Responsibility

The Government of Canada plays a national leadership role in preventing and controlling the spread of disease by helping to reduce the risk to Canadians posed by infectious diseases. It fulfills this role by tracking and monitoring infectious disease threats, undertaking research, promoting healthy behaviours,

brokering knowledge transfer, and facilitating research and innovation.

Several federal government departments and agencies are involved in addressing Lyme disease in Canada:

- Public Health Agency of Canada
- Canadian Institutes of Health Research
- Health Canada
- Department of National Defence / Canadian Armed Forces
- Parks Canada

In Canada, prevention and control of Lyme disease requires collaboration among all levels of government and non-governmental organizations. As guided by the provisions of the Canada Health Act, provinces and territories are primarily responsible for the delivery of both direct health care services and public health activities. Provincial and territorial public health authorities, and Indigenous public health authorities, undertake prevention and control activities specific to their own jurisdictions. This work is conducted, in some jurisdictions, in collaboration with universities and other professional and non-governmental organizations.

Public health actions

All stakeholders, including patients and their advocates, health care providers, and public health authorities, recognize the importance of evidence-based approaches to both public health and the practice of medicine. Similarly, many agree that additional research is needed to fill in evidence gaps that exist for Lyme disease prevention and control, diagnosis and treatment.

As a first step to addressing evidence gaps, the Government of Canada will allocate new funding to address research gaps for Lyme disease, and will continue to collaborate with domestic and international partners to exchange best practices in the prevention, diagnosis and treatment of Lyme disease.

Other new actions under the Framework align with the federal role as they relate to surveillance; education and awareness; and guidelines and best practices. Implementation will require the involvement and collaboration of Lyme disease patients, patient groups, health care providers, public health authorities, expert researchers, and federal, provincial and territorial governments.

Surveillance

Surveillance is essential to understanding the risk posed to Canadians and is the foundation of the public health approach. Surveillance for Lyme disease includes monitoring both the distribution and spread of ticks that carry the pathogen *B. burgdorferi*, and tracking human cases of the disease across the country.

Federal and provincial public health authorities will continue to build on surveillance activities through integration and dissemination of innovative methods and best practices for human surveillance.

In addition, collection of human surveillance data in Canada on people who do not meet the case definition for probable or

confirmed Lyme disease, but who experience various symptoms consistent with Lyme disease or similar ailments, will be initiated.

The increase in the distribution and number of individuals affected by Lyme disease in Canada is having a financial impact on the health care system. An analysis of the costs associated with Lyme disease will be undertaken, including both direct and indirect costs, where possible. Additionally, a national tick-borne surveillance system will be developed that includes Lyme disease and other possible tick-borne infections.

Education and awareness

Efforts need to be strengthened to enhance Lyme disease educational efforts so that they are more effective and available to Canadians and front-line health professionals, in support of provincial and territorial governments and other efforts.

Strengthening stakeholder engagement and partnerships will be critical to successful education and awareness campaigns. The development of early detection/early diagnosis educational materials, with a focus on high risk groups, will be supported to assist front-line health professionals and public health authorities in the prevention and timely diagnosis of Lyme disease using an evidence-based and patient-centered approach. Given that prevention is key in the public health approach for infectious diseases, a national tick and Lyme disease education and awareness campaign will be developed, in collaboration with partners, to complement existing outreach efforts aimed at reducing the risk of contracting Lyme disease and inform early intervention, diagnosis and treatment.

Guidelines and best practices

Guidelines and best practices that are evidence-based and effectively targeted to reach specific groups will be critical to address Lyme disease. Elements of consideration include prevention, diagnostics, treatment and research.

Currently, the best way to protect against Lyme disease is to prevent tick bites, or if bitten, to minimize the likelihood of infection by removing the tick in a timely, effective manner (3). Prevention and awareness programs are implemented by local public health authorities and other health care/veterinary providers to raise awareness of the risks of Lyme disease and measures to protect against tick bites.

The diagnosis of early Lyme disease infection by a physician or nurse practitioner is primarily a clinical one, based on symptoms and supported by a history of possible tick exposure, including travel history. Diagnosis is limited by the fact that not all patients will present with symptoms in the early stages. Current laboratory tests, which look for antibodies, perform better for untreated, later-stage Lyme disease, after the patient has developed an immune response. Concerns about false negative tests results have led some patients to seek private testing. The development and availability of improved laboratory testing options may reduce the current practice where some patients seek laboratory testing in private, for-profit laboratories that may not be using standardized testing. It is recognized that specific and more sensitive tests for Lyme disease are needed.

There remain evidence gaps which can be informed through further research on treatment options. For example, some people experience symptoms that continue more than six months following treatment, described by some physicians as post-treatment Lyme disease syndrome or post Lyme disease syndrome. Other patients experience various chronic symptoms consistent with Lyme disease or similar ailments, sometimes referred to as chronic Lyme disease, which is not recognized by the majority of the medical community in Canada. Adding to the confusion is that current treatment guidelines for Lyme disease, developed by medical and scientific professional organizations and based on the best available evidence known worldwide, are not uniform. In Canada, the Association of Medical Microbiology and Infectious Diseases Canada (AMMI Canada) has endorsed and promoted the use of the Lyme disease treatment guidelines developed by the Infectious Diseases Society of America (IDSA), which represents physicians, scientists and other health care professionals who specialize in infectious disease (4). As such, the IDSA guidelines are used by the broader medical community. However, there are a small number of front-line health professionals who follow guidelines developed by the International Lyme and Associated Disease Society (ILADS), a multidisciplinary medical society dedicated to the diagnosis and treatment of Lyme and its associated diseases. The treatment recommendations in the ILADS guideline are different from those in the IDSA, particularly with regards to antibiotic use. Further research on best treatment approaches is required.

Moving forward, the Government of Canada will work with international public health partners to share best practices, which in turn, will be shared with all stakeholders. Front-line health professionals and provincial laboratories will continue to be supported in the laboratory diagnosis of Lyme disease. Partners, including provincial and territorial health care regulatory authorities, will be consulted on innovative, evidence-based approaches to address the needs of patients and a Lyme disease research network will be established to build on existing research to fill in evidence gaps and engage with clinical experts, researchers, and patient groups.

Conclusion

To ensure ongoing efforts to address Lyme disease are evidence-based and that the Government of Canada continues making inroads at preventing and controlling the spread of Lyme disease, the Public Health Agency of Canada will review this Framework within five years of its publication.

Acknowledgements

The Public Health Agency of Canada would like to thank all those who contributed their time and expertise during the development of the Federal Framework on Lyme Disease.

Funding

The development of the Federal Framework on Lyme Disease was paid for by the Government of Canada.

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Measuring health burden and climate change

Source: Ebi KL, Ogden NH, Semenza JC, Woodward A. Detecting and Attributing Health Burdens to Climate Change. Environ Health Perspect. 2017 Aug 7;125(8):085004. https://www.ncbi.nlm.nih.gov/pubmed/28796635

BACKGROUND: Detection and attribution of health impacts caused by climate change uses formal methods to determine a) whether the occurrence of adverse health outcomes has changed, and b) the extent to which that change could be attributed to climate change. There have been limited efforts to undertake detection and attribution analyses in health.

OBJECTIVE: Our goal was to show a range of approaches for conducting detection and attribution analyses.

RESULTS: Case studies for heatwaves, Lyme disease in Canada, and Vibrio emergence in northern Europe highlight evidence that climate change is adversely affecting human health. Changes in rates and geographic distribution of adverse health outcomes were detected, and, in each instance, a proportion of the observed changes could, in our judgment, be attributed to changes in weather patterns associated with climate change.

CONCLUSIONS: The results of detection and attribution studies can inform evidence-based risk management to reduce current, and plan for future, changes in health risks associated with climate change. Gaining a better understanding of the size, timing, and distribution of the climate change burden of disease and injury requires reliable long-term data sets, more knowledge about the factors that confound and modify the effects of climate on health, and refinement of analytic techniques for detection and attribution. At the same time, significant advances are possible in the absence of complete data and statistical certainty: there is a place for well-informed judgments, based on understanding of underlying processes and matching of patterns of health, climate, and other determinants of human well-being.

Emerging issues with fungal disease outbreaks

Source: Benedict K, Richardson M, Vallabhaneni S, Jackson BR, Chiller T. Emerging issues, challenges, and changing epidemiology of fungal disease outbreaks. Lancet Infect Dis. 2017 Jul 31. http://dx.doi.org/10.1016/S1473-3099(17)30443-7 [Epub ahead of print].

Several high-profile outbreaks have drawn attention to invasive fungal infections (IFIs) as an increasingly important public health problem. IFI outbreaks are caused by many different fungal pathogens and are associated with numerous settings and sources. In the community, IFI outbreaks often occur among people without predisposing medical conditions and are frequently precipitated by environmental disruption. Health-care-associated IFI outbreaks have been linked to suboptimal hospital environmental conditions, transmission via health-care workers' hands, contaminated medical products, and transplantation of infected organs. Outbreak investigations provide important insights into the epidemiology of IFIs, uncover risk factors for infection, and identify opportunities for preventing similar events in the future. Well recognised challenges with IFI outbreak recognition, response, and prevention include the need for improved rapid diagnostic methods, the absence of routine surveillance for most IFIs, adherence to infection control practices, and health-care provider awareness. Additionally, IFI outbreak investigations have revealed several emerging issues, including new populations at risk because of travel or relocation, occupation, or immunosuppression; fungal pathogens appearing in geographical areas in which they have not been previously recognised; and contaminated compounded medications. This report highlights notable IFI outbreaks in the past decade, with an emphasis on these emerging challenges in the USA.



How close are we to a Zika vaccine?

Source: Thomas SJ. Zika Virus Vaccines — A Full Field and Looking for the Closers. N Engl J Med 2017; 376:1883-1886 May 11, 2017. https://doi.org/10.1056/NEJMcibr1701402. (summary).

There are no licensed antiviral drugs to prevent or treat Zika virus (ZIKV) infection or disease. Caring for patients with severe ZIKV disease manifestations, especially patients who were exposed in utero, is challenging for all involved. Because of these challenges, the WHO has called for development of a ZIKV vaccine, with an initial focus on protecting women of childbearing age. Two recent reports describing the successful testing of experimental ZIKV vaccines in animal models — one by Pardi et al. and another by Richner et al. — are welcome news. Both groups engineered messenger RNAs (mRNAs) with sequences encoding the ZIKV precursor membrane (prM) glycoprotein and envelope (E) glycoprotein.

Data from studies in animals have now been described for numerous ZIKV vaccine candidates. The candidates produced no acute safety signals, induced ZIKV-specific humoral or cellular immune responses, and conferred at least some protection against live virus challenge. The mRNA vaccine constructs reviewed here offer numerous potential advantages, including ease and cost of manufacturing, applicability across diverse pathogens, and a favorable safety profile. Vaccinology, however, constantly warns against extrapolating conclusions from animal experiments to humans. In the case of ZIKV vaccines, most of the available data have been generated with the use of animals that have had no previous exposure to flaviviruses. Will preexisting immunity to flaviviruses (such as the dengue, yellow fever, West Nile, and Japanese encephalitis viruses) affect the safety or immunogenicity of a ZIKV vaccine? Demonstrating safety in a small number of volunteers appears feasible; demonstrating that vaccine-induced immune responses are associated with clinical efficacy will be a much more formidable task.

Despite the challenges, the pace of ZIKV vaccine research and development has been impressive. However, history has shown that the race for a vaccine typically begins with many contenders at the start, of whom very few finish the race. This observation notwithstanding, the recently published data from Pardi et al. and Richner et al. represent an important step toward the goal of protecting people from ZIKV through active immunization.

Correction for Can Commun Dis Rep. Supplement 2008;34(S2)

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Suggested citation: Canada Communicable Disease Report Editorial Team. Correction for Can Commun Dis Rep. 2008;34(S2). Can Commun Dis Rep. 2017;43(10):217.

In the Final Report to Outcomes from the National Consensus Conference for Vaccine-Preventable Diseases in Canada, June 12-14, 2005 – Quebec City, Quebec published in March, 2008, the citation on the inner cover of the PDF had the incorrect year of publication and supplement number.

Was:

Suggested citation: Public Health Agency of Canada. Final Report of Outcomes from the National Consensus Conference for Vaccine-Preventable Diseases in Canada. CCDR 2007;33S3:1-56.

Correction October 5, 2017:

Suggested citation: Public Health Agency of Canada. Final Report of Outcomes from the National Consensus Conference for Vaccine-Preventable Diseases in Canada. CCDR 2008;34S2:1-64.

TACKLING LYME * DISEASE IN CANADA

We are focusing our actions in 3 AREAS:



SURVELLANCE

- Strengthen current efforts and create a national tick surveillance system
- Expand data collection to include people who may not meet the formal case definition for Lyme disease
- Conduct analysis of the costs associated with Lyme disease
- Continue to assess the current and future risk of Ly me disease in Canada and work with our partners on innovative methods on surveillance



EDUCATION AND AWARENESS

- Support health professionals by developing education materials in prevention and diagnosis
- Enhance national awareness about Lyme disease through education and awareness campaigns



GUIDELINES AND Best practices

- Inform guidelines and best practices through the creation of a Lyme disease research network
- Support laboratory diagnostic testing
- Work with international partners to share best practices
- Consult on innovative and evidence-based ways to address patients needs

For more information on Lyme Disease: Canada.ca/Lyme Disease

Canada



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To promote and protect the health of Canadians through leadership, partnership, innovation and action in public health.

Public Health Agency of Canada

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This publication is also available online at

http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/17vol43/index-eng.php

Également disponible en français sous le titre : Relevé des maladies transmissibles au Canada