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Pertussis is one of the most common vaccine preventable diseases in Canada. Many have assumed we have conquered this disease with pertussis vaccine. Not yet. Find out what has happened recently with pertussis outbreaks in two provinces in Canada, how Canadian disease trends compare to global trends, and what recommendations are in place to control this re-emerging disease.

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Useful links

Public Health Agency of Canada: Canadian Immunization Guide (Pertussis)
http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pert-coqu-eng.php

Public Health Agency of Canada: Pertussis
http://www.phac-aspc.gc.ca/im/vpd-mev/pertussis-eng.php

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Pertussis Surveillance in Canada: Trends to 2012

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Abstract

Objective: The purpose of this report is to provide a summary of the pertussis activity in Canada.

Methods: A descriptive analysis of pertussis incidence by year, age group, gender and province/territory was conducted using national surveillance data, clinical administrative data and vital statistics data.

Results: Pertussis is an endemic cyclical disease in Canada with peaks in activity occurring every 2 to 5 years. Canada has experienced a decline in pertussis activity following the introduction of routine pertussis immunization programs. The incidence of pertussis is highest in infants and children. Hospitalization and mortality are more common among infants, particularly those less than three months of age. Trends in pertussis vary by province and territory. Canada experienced a notable increase in incidence in 2012. Reasons for this increase are unknown.

Conclusion: Our understanding of the epidemiology of pertussis in Canada could be enhanced by improved approaches for monitoring the disease. Although the peak in activity observed in 2012 could be an isolated event, further work to support outbreak response in provinces and territories, including rapid research tools and resources, should be considered.

Introduction

In Canada, pertussis has been under national surveillance since 1924 and a target of childhood immunization programs since 1943. Infant, child, adolescent, and adult routine immunization programs exist across Canada, with notable differences in the vaccine product used and schedule of immunization, depending on the province/territory[1]. The introduction of childhood immunization programs contributed to a significant reduction in disease; however, pertussis remains one of the most commonly reported vaccine preventable diseases in Canada. In early 2012, the Public Health Agency of Canada (the Agency) received reports of increased pertussis activity in multiple jurisdictions which prompted a review of Canadian pertussis data. The purpose of this report is to provide a summary of pertussis activity in Canada since it became notifiable with an emphasis on more recent activity.

Methods

DATA SOURCES

National Case Reports

Nationally reported confirmed cases of pertussis from 1924 to 2011 were extracted from the Canadian Notifiable Diseases Surveillance System (CNDSS) database in March 2013[2]. National pertussis case definitions were published in 1991[3], 2000[4] and 2009[5]. Prior to 2000, a confirmed case of pertussis required isolation of *Bordetella pertussis* and presence of clinically compatible symptoms. Between 2000 and 2008 the case definition required laboratory confirmation (via culture from an appropriate clinical specimen or detection of DNA) or an epidemiological link to a laboratory confirmed cases and one of a list of clinical symptoms. In 2009, the case definition was further refined to require those cases in which *B. pertussis* DNA was detected to also have clinically compatible symptoms. Confirmed pertussis cases for 2012 were obtained directly from the provinces and territories in March 2013 by the Agency's Centre for Immunization and Respiratory Infectious Diseases, and are preliminary.

Hospitalizations

Pertussis cases reported through the Canadian Immunization Monitoring Program Active (IMPACT) from 1991 to 2012 were extracted from the IMPACT database in April 2013[6]. Data for 2012 are preliminary. IMPACT has provided enhanced data on pediatric pertussis cases treated at tertiary care centres in Canada to the Agency since 1991, initially from 5 centers and then expanded to 10 centers in 1993, 11 centers in 1995 and 12 centers in 1999.

Data on pertussis-related acute care hospitalizations from 1995 to 2010 were extracted from the Canadian Institute for Health Information's (CIHI) Hospital Morbidity Database (HMD) in June 2013.These dates were selected as the data sets were complete for each year. Pertussis hospitalizations were defined as those with the International Classification of Diseases (ICD) version 9 or 10 discharge diagnoses (all diagnosis levels) corresponding to pertussis (0330, 0339, 4843, A370 or A379). Exclusion criteria included hospital transfers and readmissions, with readmissions defined as hospitalizations which occurred <1 year apart.

Vital Statistics

Mortality data were obtained from the Death Database, a national mortality database which includes demographic and medical (underlying cause of death) information collected annually from all provincial and territorial vital statistics registries on all deaths in Canada[7]. Deaths with an underlying cause of pertussis were identified using the same ICD codes listed above.

Analysis

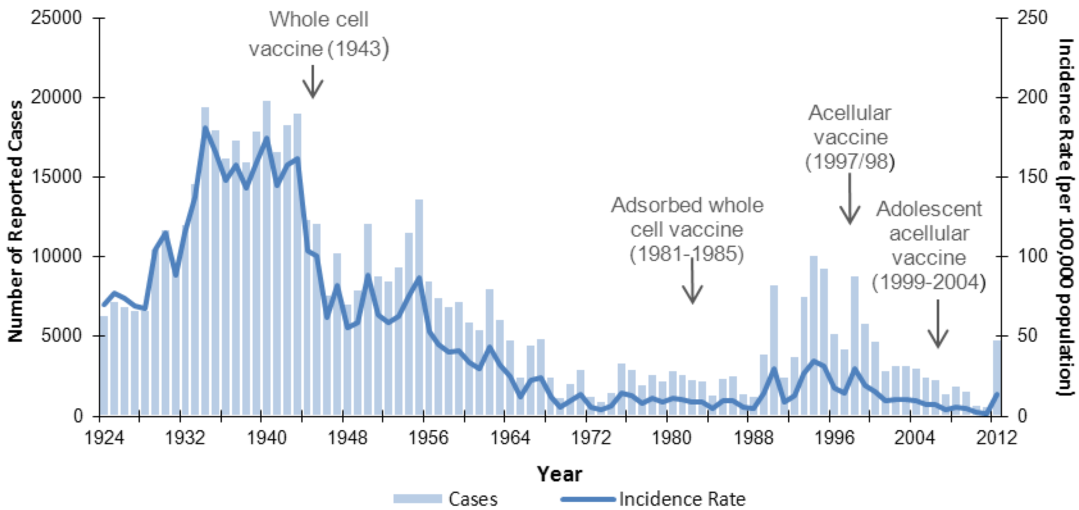
A descriptive analysis of pertussis incidence by year, age group, gender and province/territory was conducted. Population data for the calculation of rates was obtained from Statistics Canada[8]. Data sent to CNDSS are aggregated by age group, therefore the calculation of age-specific rates were limited to the following age groups in years <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-39, 40-59, and 60 and over. Confirmed case rates are given per 100,000 population. Provinces/territories that were not able to report case counts were removed from the denominator for the corresponding year. Annual percent change was used to describe changes in reporting rates over time. Incidence rate ratios were calculated to examine gender differences.

Results

Annual Incidence

In the five years prior to vaccine introduction, the average incidence of pertussis was 156 cases per 100,000 population. After vaccine introduction, the incidence decreased to a mean annual low of 7 cases per 100,000 population from 1984 to 1988 (Figure 1). A resurgence of pertussis was observed beginning in 1989/90 which peaked at 34.9 cases per 100,000 in 1994. After 1998, incidence declined to the lowest incidence recorded in Canada at 2 cases per 100 000 in 2011. A seven-fold increase in national incidence to 13.9 per 100,000 was observed in 2012. Observing trends over time, peaks in activity occurred every 2 to 5 years. These peaks have become less obvious as incidence of disease has decreased.

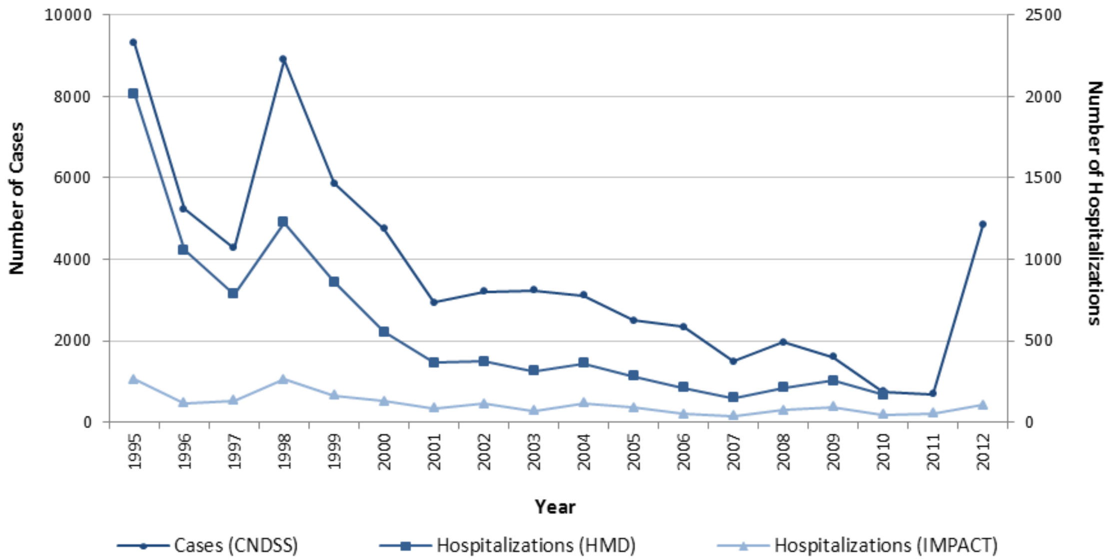
Figure 1. Reported cases and incidence rate (per 100,000 population) of Pertussis in Canada by year, 1924 to 2012*



*Case data from 1924 to 2011 were obtained from the Canadian Notifiable Diseases Surveillance System. Case data for 2012 were obtained directly from provinces and territories by CIRID and are preliminary. PEI did not report 1924-1928; Newfoundland did not report until 1949; Yukon did not report 1924-1955; Northwest Territories did not report 1924-1958; Nunavut data for 1999 are only partial, for 2007 & 2009 are missing, and for 2008, 2010-2011 are preliminary. Population data (July 1st annual estimates) were obtained from Statistics Canada.

In general, trends in pertussis hospitalization data were similar to those observed in notifiable disease reports (Figure 2). National case reports and acute care hospitalizations decreased by 92% from 1995 to 2010; case reports from 9308 (31.8 per 100,000) in 1995 to 748 (2.2 per 100,000) in 2010, and HMD hospitalizations from 2,016 (6.8 per 100,000) in 1995 to 168 (0.5 per 100,000) in 2010. In this same time frame, IMPACT hospitalizations decreased by 82% from 264 in 1995 to 48 in 2010. Peaks in activity in 1998 and minor increases in 2002 and 2008 were observed across all data sources. However, minor increases in hospital admissions were also observed in 2004 (HMD: 16%; IMPACT: 65%) and 2009 (HMD: 20%; IMPACT: 26%) while case reports declined in these years from the preceding year by 4% and 18% respectively. As with national case reports, cases reported through IMPACT hospitals increased in 2012, but not as dramatically as the national incidence rate of disease (2-fold increase).

Figure 2. Number of reported cases and hospitalizations for pertussis in Canada by year, 1995 to 2012*



*Case data from 1995 to 2011 were obtained from the Canadian Notifiable Diseases Surveillance System. Case data for 2012 were obtained directly from provinces and territories by CIRID and are preliminary. Nunavut data for 1999 are only partial, for 2007 & 2009 are missing, and for 2008, 2010-2011 are preliminary; IMPACT data for 2012 are preliminary.

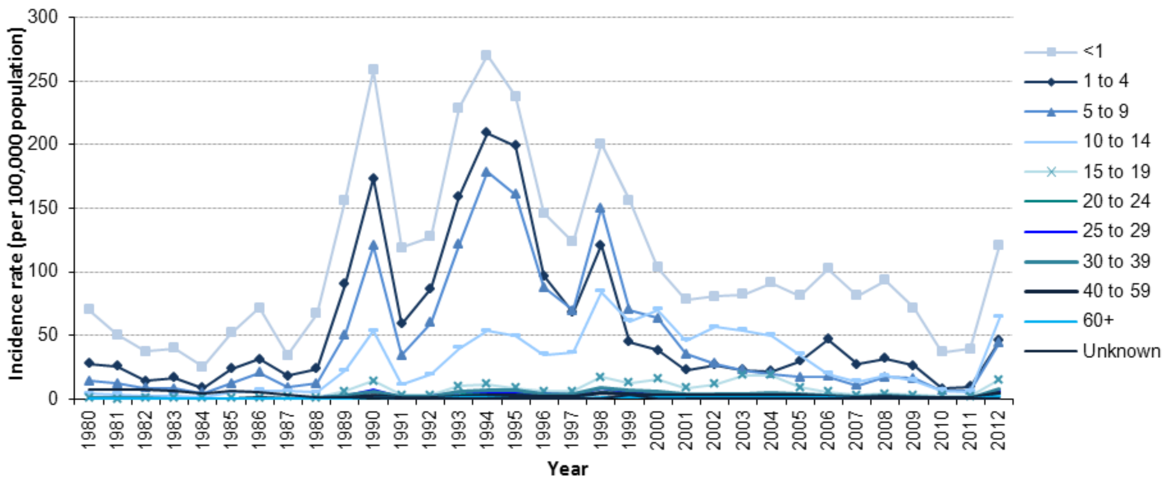
Age Distribution

The incidence of pertussis is highest in infants and children, and decreases sharply in those older than 14 years (Figure 3). The highest mean incidence rates from 2005 to 2011 were 72.2 cases per 100,000 population among infants less than 1 year of age (mean: 261 cases per year), 25.6 cases per 100,000 population among 1 to 4 year olds (mean: 362 cases per year), and 16.0 cases per 100,000 population among 10 to 14 year olds (mean: 328 cases per year). Comparatively, the mean incidence of pertussis among all individuals 15 years and greater from 2005 to 2011 was 1.6 cases per 100,000 population (mean: 428 cases per year).

Between 2005 and 2011, the incidence of pertussis decreased in all age groups, most notably among those aged 10 to14 years (84% decrease) and those aged 15 to 19 years of age (81% decrease). In 2012, increases in incidence were observed across all age groups nationally with the highest incidence rates in those less than one year (120.8 per 100,000; n=460) and those 10-14 years of age (64.1 per 100,000; n=1203). The highest incidence rates in the majority of provinces/territories were within age groups below 15 years of age.

Figure 3. Incidence rate (per 100,000 population) of pertussis reports in Canada by age group (in years) and year, 1980 to 2012*****

*Case data from 1980 to 2011 were obtained from the Canadian Notifiable Diseases Surveillance System. Case data for

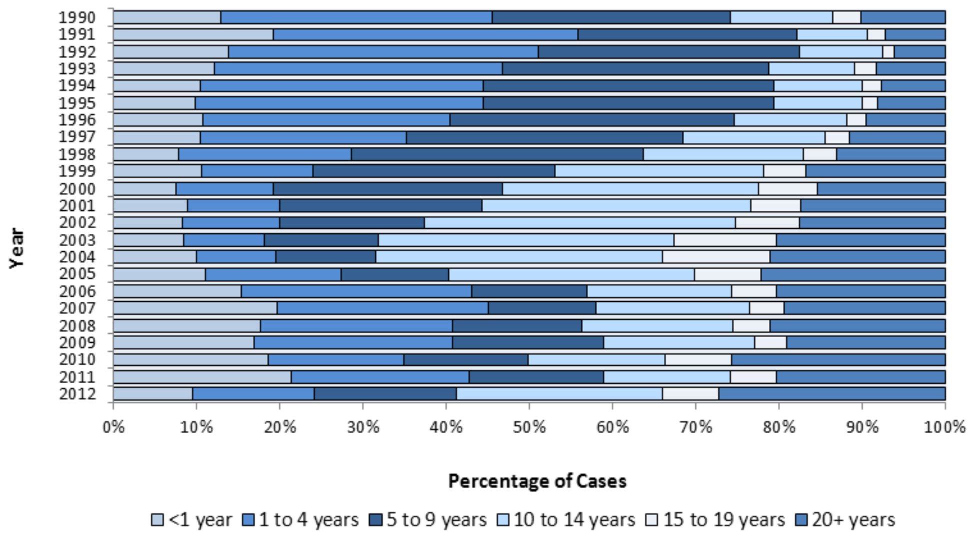


2012 were obtained directly from provinces and territories by CIRID and are preliminary. Nunavut data for 1999 are only partial, for 2007 & 2009 are missing, and for 2008, 2010-2011 are preliminary. Population data (July 1st annual estimates) was obtained from Statistics Canada and uses.

Fluctuations in the proportion of pertussis cases by age group have occurred in the last twenty years, particularly among children aged 1 to 9 years and adolescents aged 10 to 19 years (Figure 4). During the 1990s, the highest proportion of cases occurred in the 1 to 9 year age groups (mean: 62% per year). Between 2000 and 2005, the proportion of cases in adolescent age groups (i.e. 10 to 19 years) increased and was on average 42% of cases per year, while the proportion of cases among those 1 to 9 decreased to an average of 30% per year. Between 2006 and 2011, cases 10 to 19 years of age decreased (mean: 23% per year), while the number of cases 1 to 9 years increased marginally (mean: 38% per year). As these larger shifts occurred, minor increases occurred in infants (<1 year) and adults (20 years and older) from respective annual means of 12% and 10% of cases in the 1990s, to 18% and 21% of cases between 2006 and 2011. In 2012, 10% of cases were less than one, 32% were between 1 to 9 years, 31% were between 10 and 19 years and 27% were 20 years or older.

In contrast, the age distribution of acute care hospitalized cases has not varied considerably over time with the proportion of hospitalizations consistently highest among children less than one. Between 1995 and 2010, on average each year, a total of 69% of pertussis-related admissions were among those less than 1 (range: 59 to 78%). Of those less than one, the majority of admissions occurred in young infants with an annual mean of 62% cases under the age of 3 months (range: 49 to 71%).

Figure 4. Age distribution of pertussis cases in Canada, 1990 to 2012*****



*Case data from 1990 to 2011 were obtained from the Canadian Notifiable Diseases Surveillance System. Case data for 2012 were obtained directly from provinces and territories by CIRID and are preliminary. Nunavut data for 1999 are only partial, for 2007 & 2009 are missing, and for 2008, 2010-2011 are preliminary.

Gender Distribution

From 1990 to 2012, the number of nationally reported pertussis cases and incidence rate has been consistently higher among females in all age groups. During this time period, the annual median male to female ratio in incidence rate was 0.87:1 (range: 0.81:1 to 0.96:1). Females made up on average 54.0% of cases, males 45.8% of cases, and 0.2% had an unknown gender each year. Similarly, between 1995 and 2010, the median male to female ratio in the incidence rate of hospitalization was 0.89:1 (range: 0.73:1 to 1.05:1) and on average, each year, females made up 53.5% of cases.

Geographic Distribution

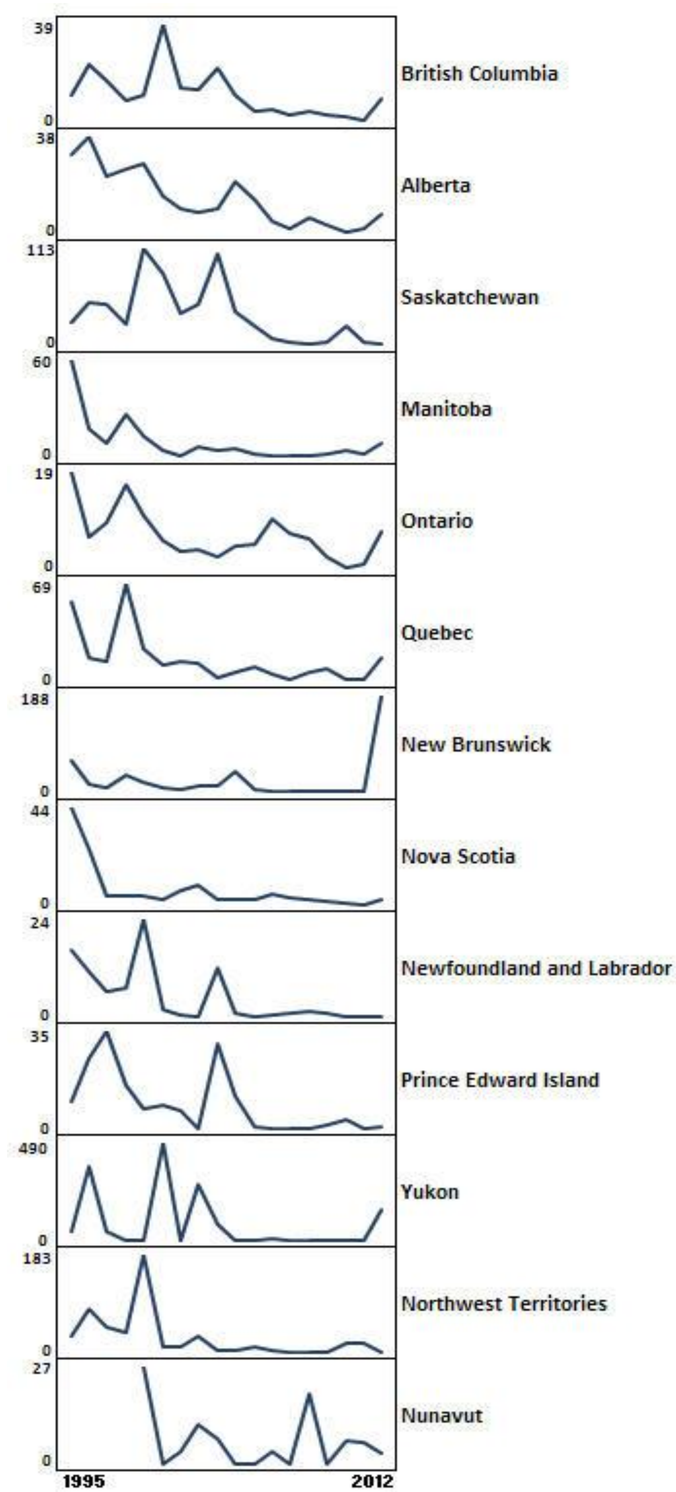
Asynchrony in the timing and geographic focus of 2-5 year cyclical pertussis peaks is expected. Although Canada experienced an overall decline in pertussis incidence from the late 1990s to 2011, the timing, magnitude and overall trend in decreased activity varied across the provinces and territories (Figure 5). From 1995 to 2011, peaks in laboratory-confirmed pertussis notifications were observed, with the highest incidence by province across this period variously occurring in 1995 (Manitoba, Ontario, New Brunswick and Nova Scotia), 1996 (Alberta), 1997 (Prince Edward Island), 1998 (Quebec), 1999 (Saskatchewan, Newfoundland, Northwest Territories and Nunavut) or 2000 (British Columbia and Yukon). The absolute difference between the highest and lowest incidence rates within a province/territory during this time, ranged from 18 cases per 100,000 to a much larger difference of 489 cases per 100,000, with large fluctuations more common in jurisdictions with smaller populations. From provincial-/territorial-specific peaks to 2011, each province and territory experienced a decline of more than 75% in incidence with the vast majority seeing decreases exceeding 90%.

National increases in incidence are typically the result of peaks observed in multiple jurisdictions. The national increase observed in 1998 was due to increased activity experienced in Manitoba, Ontario, Quebec and New Brunswick. This was also the case in 2012, when increases in incidence relative to 2011 were observed in 9 of the 13 provinces and territories. At the provincial/territorial level, these increases ranged from a negligible 0.7 cases per 100,000 to a more substantial 152 cases per 100,000. Within jurisdictions that experienced substantial increases, causes varied from province-wide outbreaks, to regional outbreaks, to localized outbreaks. The most notable increase in activity was observed in New Brunswick, due to a province-wide outbreak that accounted for approximately one-third of the national case count in 2012.

Mortality

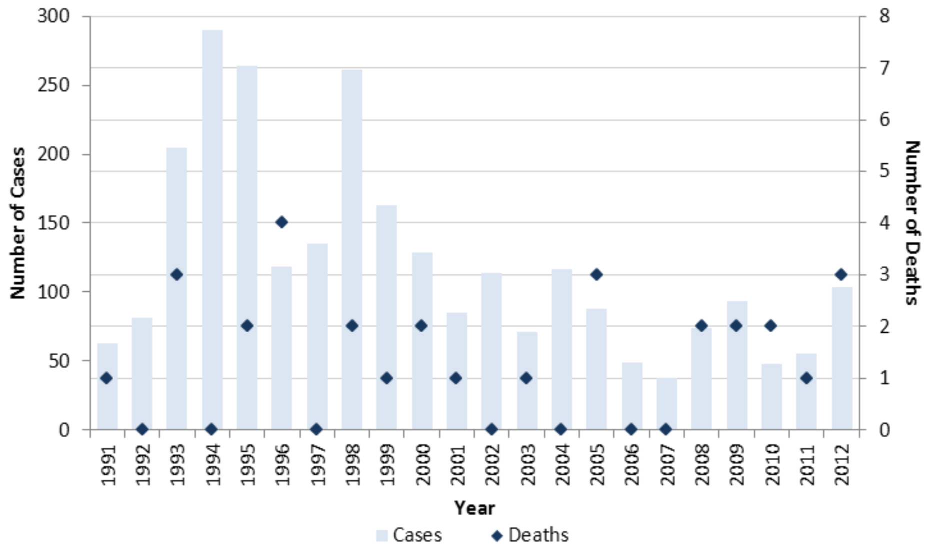
From 2000 to 2009, Statistics Canada reported a total of six deaths with pertussis listed as the underlying cause of death. Between zero and two deaths occurred each year and all deaths were reported in infants less than one year of age. However, this is likely an underestimation of the total deaths associated with pertussis in Canada. According to data from IMPACT, from 2000 to 2009, 11 of the 858 reported pertussis cases identified through IMPACT died (1.2%). From 1991 to 2012, 30 deaths have been reported through IMPACT, with the number ranging from zero to four per year (Figure 6). The majority of deaths occurred in infants less than 2 month of age (78%). All deaths, except for one, occurred in infants with no previous pertussis immunizations and 78% of deaths were in children considered previously healthy. Causes of death included respiratory distress/failure, pneumonia, hypoxia, pulmonary hypertension, pulmonary hemorrhage, fulminant septic shock, cardiovascular failure, and acute arrhythmia.

Figure 5. Trends in annual incidence of pertussis (per 100,000 population) by province/territory, 1995 to 2012



*Case data from 1995 to 2011 were obtained from the Canadian Notifiable Diseases Surveillance System. Case data for 2012 were obtained directly from provinces and territories by CIRID and are preliminary. Nunavut data for 1999 are only partial, for 2007 & 2009 are missing, and for 2008, 2010-2011 are preliminary; Population data (July 1st annual estimates) were obtained from Statistics Canada.

Figure 6. The number of pertussis cases and deaths, IMPACT, 1991 to 2012*****



*Data for 2012 are preliminary.

Discussion

Pertussis is an endemic cyclical disease in Canada with peaks in activity occurring every 2 to 5 years. Although resurgence was observed in the 1990s, overall, Canada has experienced a decline in pertussis activity following the introduction of routine pertussis immunization programs. This was first observed with the introduction of the whole cell vaccine in 1943, followed by the introduction of the acellular vaccine in 1997/98 and lastly, between 2005 and 2011 after the introduction of adolescent immunization programs across the country[9]. As previously noted, the resurgence observed in the 1990s was likely due to a combination of factors, including the low efficacy of the whole-cell vaccine introduced between 1981 and 1985, as well as increased physician awareness and improved diagnostics and reporting of pertussis infection[10]. From a geographic perspective, all provinces and territories experienced a decline in the incidence in pertussis in the seven years prior to 2012; however, trends in disease were unique to each jurisdiction in terms of timing and magnitude of cyclical peaks.

The incidence of pertussis is consistently highest among infants, as are hospitalization and death, particularly among those 3 months of age or less. This group is of particular interest as they are too young to benefit directly from immunizations. Different approaches have been tried which include cocooning and immunization of pregnant women to allow for passive immunity to the infant[11,12,13]. Canada's National Advisory Committee on Immunization has recommended immunization in pregnancy if there is a regional outbreak of pertussis[14].

The increase in incidence observed in 2012 was due to outbreaks in several jurisdictions across the country. Increases in incidence were observed across all age groups nationally with the highest incidence rates in those less than one. However, age groups most affected varied by province/territory. As with national case reports, cases reported through IMPACT hospitals increased in 2012, but not as dramatically which could suggest that the increase in cases was not associated with increasing severity.

Increases in pertussis activity have also recently occurred in other countries with several reasons for increases proposed in the literature, including waning immunity[15], reduced natural immune boosting[16], higher rates of detection[17], genetic changes in the bacteria[18], as well as clustering of unvaccinated individuals[19]. Based on nationally available data, it's difficult to determine the contributing factors for the increases observed in Canada in 2012. At present, data collected at the national level is minimal, often in an aggregate format that does not include the immunization history of cases. The National Microbiology Laboratory does not currently conduct routine surveillance of circulating pertussis strains. According to the validated results of the 2009 childhood National Immunization Coverage Surveys, immunization coverage is high; 98% for four or more doses in two year olds and

89% for five or more doses among seven year olds[20]. However, evaluations of specific immunization programs and coverage within populations and sub-populations in Canada have yet to be done in a systematic way.

Limitations

Due to the passive nature of CNDSS, reported cases are expected to be underestimates of the true burden of disease, particularly among adolescents and adults. It is likely that the incidence of pertussis is actually higher among adults than reported, as symptoms are generally milder, and testing for *B. pertussis* among adults with persistent cough is infrequent. In addition, the pertussis-related hospitalizations identified in the HMD are coded based on the physician's diagnosis as it appears in the medical chart and do not necessarily match the national case definition (e.g. may not be based on laboratory results). As a result, the number of pertussis-related acute care hospitalizations featured in this report could be an overestimate of the actual burden.

Conclusion

In conclusion, our understanding of the epidemiology of pertussis in Canada could be enhanced by improved approaches for monitoring the disease. National pertussis surveillance that also captures vaccine history, microbiological characteristics and indication of outbreaks, may yield answers that can inform public health action. Although the peak in activity observed in 2012 could be an isolated event, further work to support outbreak response in provinces and territories, including rapid research tools and resources, should be considered.

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Notes and Acknowledgements

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Conflict of interest

No conflicts of interests to declare.

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Pertussis Surveillance Trends in British Columbia, Canada, over a 20-year Period: 1993-2013

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Abstract

Objective: To provide a surveillance update on overall and age-related pertussis trends in British Columbia (BC), Canada, spanning the 20-year period from 1993-2013.

Methods: Provincial surveillance data for confirmed pertussis cases were extracted from January 1, 1993 to October 31, 2013. Annual and age-specific incidence rates were derived using provincial and regional population estimates.

Results: BC experienced substantial pertussis epidemics in the late 1990s and early 2000s with incidence ranging from 20 to 40 per 100,000 overall and peaking in pre-teens aged 10-13 years at >200 per 100,000 during the epidemic of 2000. Overall incidence dropped to historical lows ranging from 1 to 6 per 100,000 between 2005 and 2011. This low-level activity was followed by resurgence in 2012 driven by outbreaks in Lower Mainland regions of BC with overall provincial incidence reaching 10 per 100,000. Age-specific incidence in 2012 was highest among infants <1 year old (64 per 100,000) and children 12-13 years old (56-57 per 100,000), with a shift in the age distribution away from preschool-aged children toward pre-teens and young teens evident since 2000. Adult incidence remained <10 per 100,000 throughout the study period and was 5 per 100,000 in 2012. Year-to-date provincial incidence rates overall for 2013 are 6 per 100,000, with ongoing asynchronous activity observed primarily on Vancouver Island.

Conclusions: Pertussis activity in BC showed expected cyclical fluctuations, with a peak incidence observed in 2012, mostly affecting infants and pre-teens/teens but at lower levels than prior peaks. Following substantial epidemics in the 1990s and early 2000s and the incorporation of acellular pertussis vaccine into the routine immunization program, the immuno-epidemiology of pertussis may still be in transition. Further monitoring and evaluation are needed to guide possible program changes for BC.

Introduction

Pertussis (“whooping cough”) remains an endemic disease in Canada, as elsewhere, with cyclical peaks occurring every 2-5 years.[1] Infants <1 year old are at higher risk for severe disease, including hospitalization, intensive care unit (ICU) admission and death, with the highest risk occurring in very young infants <3 months old.[2;3]

Following the introduction of a routine paediatric immunization program using whole-cell pertussis formulation in Canada in 1943, pertussis incidence dropped by >90%, from an average of 165 cases per 100,000 in 1935-1939 to ≤10 cases per 100,000 during the late 1980s, and a historical low of 4 cases per 100,000 recorded in 1988.[4-6] However, despite universal paediatric immunization programs, pertussis incidence increased dramatically in Canada during the 1990s and early 2000s accompanied by a shift toward greater rates of infection in older children.[4] In the westernmost province of British Columbia (BC), Canada, age-specific incidence during cyclical peaks in 2000 and 2003 were for the first time notably highest among pre-teens and young teens, with peak incidences of 150-300 cases per 100,000 in these age groups, and even surpassing rates reported among infants.[7] This resurgent activity, and accompanying shift in the age profile, was largely attributed to advancing cohort effects stemming from the suboptimal effectiveness (20-60%) of the adsorbed whole-cell vaccine product that was used in Canada from 1980 to 1997,[7-12] but also to waning immunity, increased awareness among clinicians, and improvements in diagnostic testing to include a more sensitive polymerase chain reaction (PCR) assay.[4;5;7-9;12]

In response to these changing pertussis trends, most Canadian provinces and territories, including BC, switched to a more efficacious (>85% efficacy after 3 doses) and less reactogenic 5-component acellular vaccine beginning in 1997.[10;13] Since then, acellular pertussis vaccine has been used for the routine paediatric immunization program in BC at 2, 4, 6 and 18 months of age and for the kindergarten booster dose at 4-6 years. A further adolescent booster dose in Grade 9 (14-15 years of age) was introduced in BC in 2004.[4;14]

Following the substantial outbreaks of pertussis in the late 1990s and early 2000s, when provincial incidence peaked at 20-40 per 100,000 overall in BC, pertussis activity declined to lows of 1-6 per 100,000 between 2005 and 2011. [3,] This historically low activity in BC, however, was concurrent with widespread reporting of resurgent pertussis activity in the United States,[15] notably in the corresponding west coast state of California in 2010 where overall incidence of ~25 cases per 100,000 was the highest reported in more than 50 years.[16]

In 2012 and 2013, BC experienced further cyclical peaks in pertussis activity affecting certain regions of the province. This surveillance update describes overall and age-related pertussis trends in BC spanning the 20-year period from 1993 to 2013. This perspective captures the population-level immuno-epidemiologic impact of previous epidemics and immunization program variations that may have potentially contributed to recent pertussis disease patterns

Methods

Surveillance dataset

Pertussis is a notifiable disease in BC. Cases of pertussis are reported to the BC Centre for Disease Control through the integrated Public Health Information System (iPHIS; all health authorities, with the exception of the Vancouver Coastal Health Authority (VCHA)) or the Primary Access Regional Information System (PARIS; VCHA only). Consistent with national notification requirements, this report describes epidemiologic trends based on confirmed case reporting only. Confirmed cases are those with a laboratory-confirmed (culture or PCR) infection with *Bordetella pertussis* or an epidemiological link to a laboratory-confirmed case with symptoms consistent with *B. pertussis* infection.[17]

PCR was introduced in April 1998 as a routine diagnostic test along with culture for pertussis by the BC Public Health Microbiology and Reference Laboratory (PHMRL), which provides the majority of pertussis testing in BC and contributes ≥85% of all confirmed cases detected in BC historically and during recent outbreaks.[7] PCR has been accepted nationally alongside culture as evidence of laboratory confirmation since May 2000. All laboratory-confirmed cases of pertussis, regardless of testing laboratory, are notifiable to provincial public health and are reported in iPHIS/PARIS by health authorities.

Provincial surveillance data (age, sex, and geographic locators) were extracted from iPHIS/PARIS from January 1, 1993 to October 31, 2013 for all confirmed (laboratory-diagnosed or epidemiologically-linked) cases of pertussis reported in BC. Enhanced surveillance information pertaining to the 2012 outbreak was summarized locally within affected health authorities (Fraser Health Authority (FHA) and VCHA), including details such as immunization status and severe outcomes (e.g. hospitalizations and deaths). Cases were assigned to a regional health authority according to the local health unit that reported the case to provincial public health. Analysis of the monthly number of test requests to the PHMRL and pertussis test-positivity rates was based on data extracted from the Sunquest laboratory information system from January 1, 2011 to September 30, 2013.

As data were collected for the purposes of public health surveillance, they are exempt from research ethics board approval.

Statistical analysis

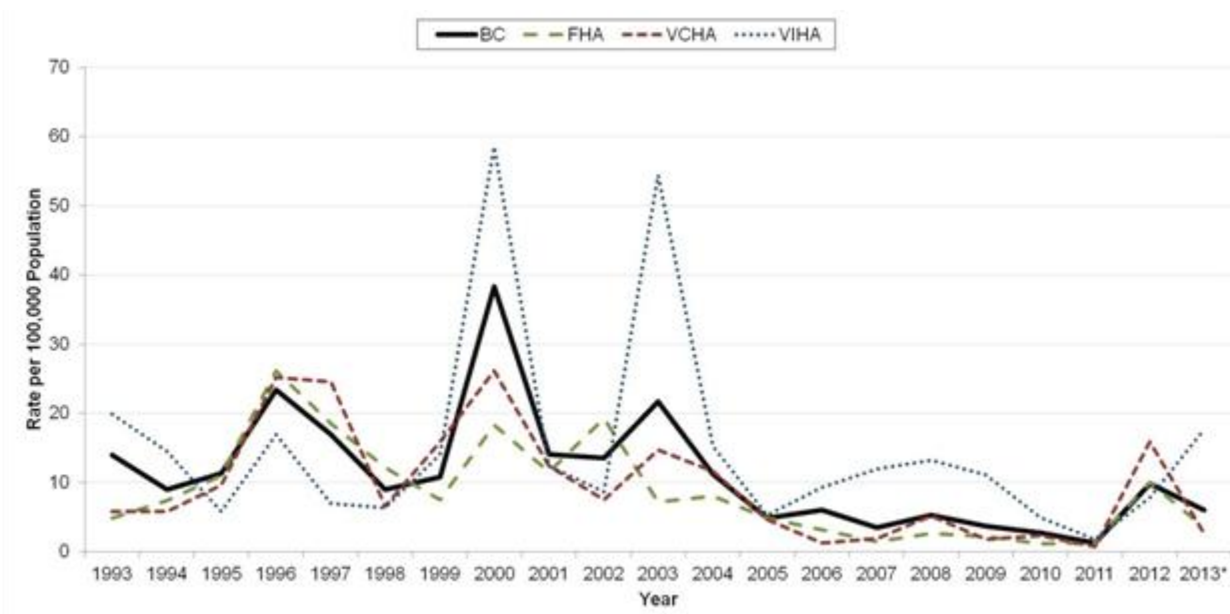
Annual and age-specific incidence rates were calculated using provincial and regional population estimates from BC Stats (http://www.bcstats.gov.bc.ca/Home.aspx). Analyses were conducted using SAS version 9.3 (SAS Inc., Cary, NC).

Results

Overall incidence trends, provincial

Following peak epidemic periods in 1996, 2000 and 2003, pertussis incidence decreased to low-level endemic activity in BC, with only minor periodic activity observed in limited geographic regions (e.g. Interior Health Authority (IHA) in 2006 and 2010 and Northern Health Authority and Vancouver Island Health Authority (VIHA) in 2008) (Figure 1). Overall provincial incidence reached historical lows of 3 per 100,000 in 2010 and one per 100,000 in 2011, followed by a cyclical resurgence in 2012, during which provincial incidence reached 10 per 100,000 overall. The 2012 peak incidence, however, remained substantially lower (less than half) compared to historical peaks observed in 1996 (23 per 100,000), 2000 (38 per 100,000) and 2003 (22 per 100,000) (Figure 1).

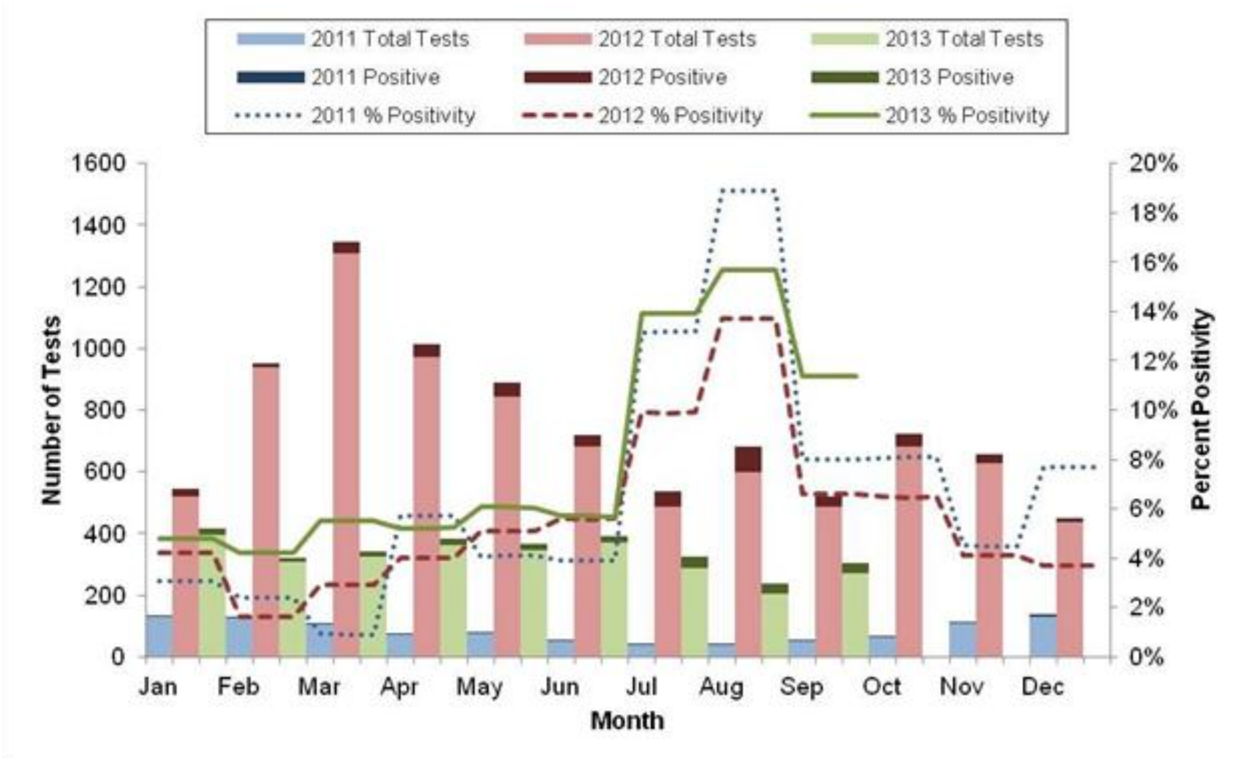
Figure 1. Annual incidence of confirmed pertussis cases in BC for the entire province and select health authorities, 1993 to 2013*



* Year-to-date (October 31, 2013); BC=British Columbia, FHA=Fraser Health Authority, VCHA=Vancouver Coastal Health Authority, VIHA=Vancouver Island Health Authority

Compared to 2011, the PHMRL received an almost 9-fold increase in pertussis test requests in 2012, averaging >700 tests per month in 2012 compared to ~80 per month in 2011; on average, 320 tests were requested per month in 2013. However, the percent of tests positive for pertussis were comparable across all years and remained below 5% during heightened test volumes from February to April 2012, consistent with other causes of respiratory illness predominating during these winter months. Pertussis test-positivity rates peaked during July and August, concurrent with lower test volumes, in all three years (Figure 2).

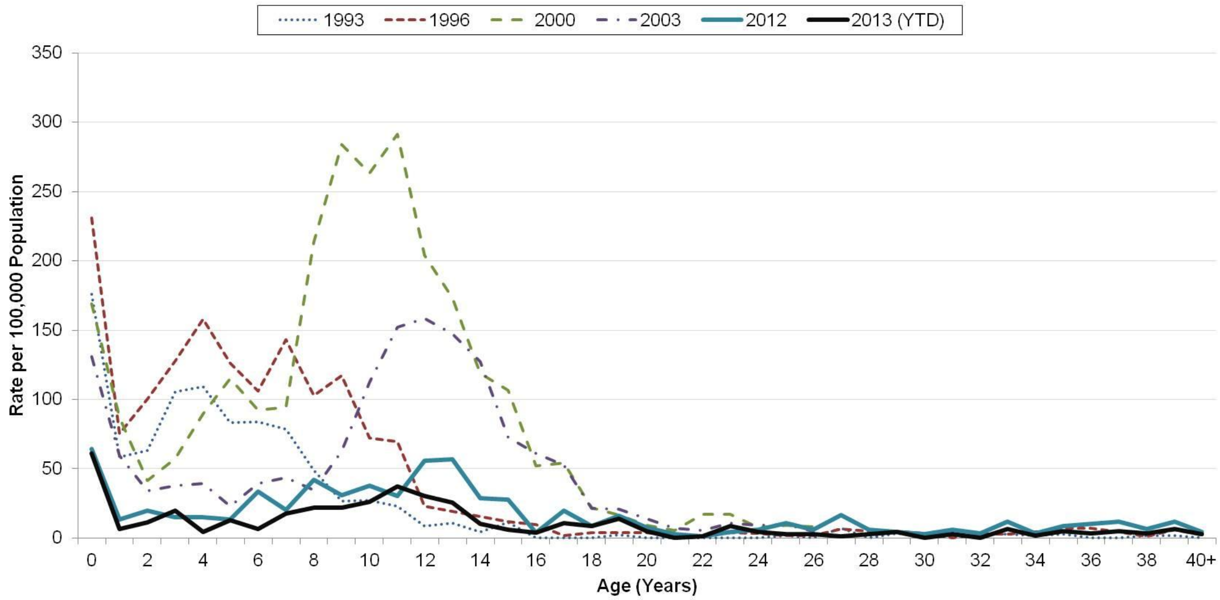
Figure 2. BC Public Health Microbiology and Reference Laboratory pertussis test requests and percent positive for pertussis by month and year, January 2011 to September 2013



Age-specific incidence trends, provincial

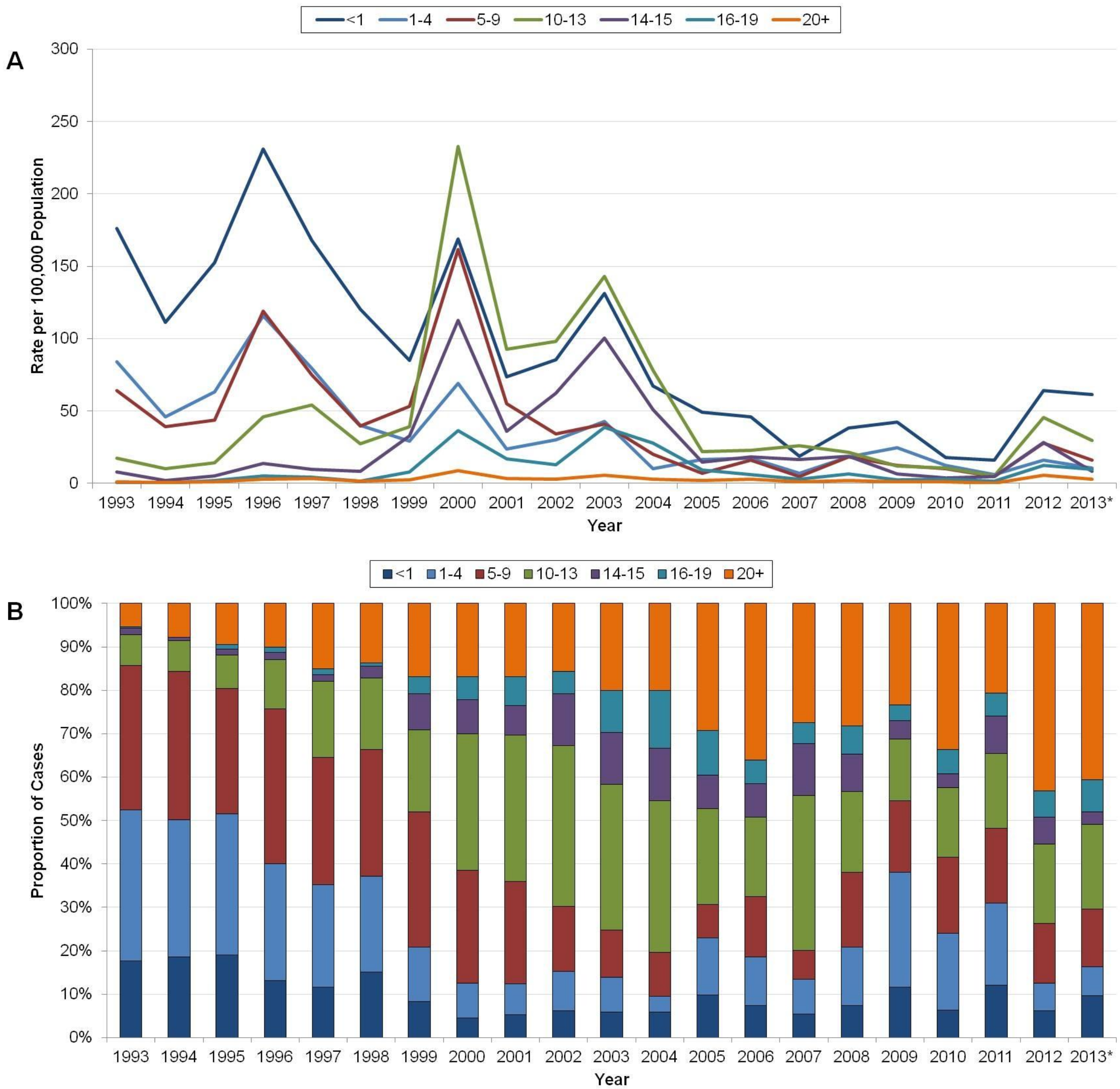
Age-specific incidence rates in 2012 were highest among infants <1 year old (64 per 100,000) and children 12-13 years old (56-57 per 100,000) (Figure 3). Incidence rates were lowest in paediatric age groups immediately following the age of scheduled immunization booster doses: 16 per 100,000 in preschool-aged children 1-4 years and 12 per 100,000 in older teens aged 16-19 years (Figure 4A). Slightly higher incidence rates were observed in younger school-aged children 5-9 years at 28 per 100,000 (Figure 4A), with age-specific incidence gradually increasing with each additional year of age since the scheduled kindergarten booster dose (Figure 3). Similarly, incidence in teens aged 14-15 years around the timing of the scheduled Grade 9 booster dose was 28 per 100,000 (Figure 4A). Overall, incidence in 2012 was lowest among adults aged ≥20 years at 5 per 100,000.

Figure 3. Age-specific incidence of confirmed pertussis cases in BC for cyclical peak years, 1993, 1996, 2000, 2003, 2012 and 2013 (year-to-date)*



* Year-to-date (October 31, 2013)

Figure 4. (A) Incidence rate and (B) proportion of confirmed pertussis cases in BC, by age group, 1993 to 2013*



* Year-to-date (October 31, 2013)

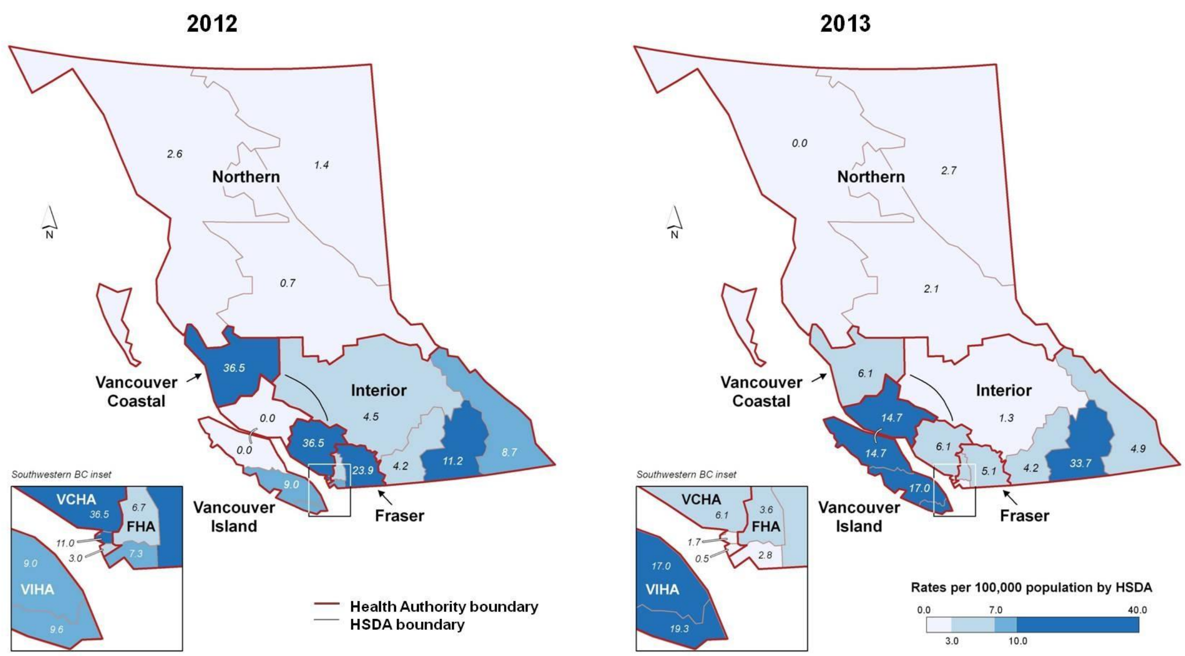
Of note, the higher incidence among pre-teens aged 10-13 years relative to infants <1 year old, first noted during the outbreak in 2000[7], persisted in BC until 2005, after which rates were higher in infants. This difference is exemplified by incidence of 64 per 100,000 for infants and 46 per 100,000 for pre-teens observed during the 2012 peak (Figure 4A). The lower incidence among teens aged 16-19 years (12 per 100,000) and 14-15 years (28 per 100,000) relative to pre-teens aged 10-13 years (46 per 100,000) in 2012 was already evident during prior non-epidemic and epidemic years of 1996 (5, 14, 46 per 100,000 respectively); 2000 (36, 113, 233 per 100,000 respectively); and 2003 (39, 100, 143 per 100,000 respectively), a pattern that notably preceded the introduction of the Grade 9 adolescent booster dose in 2004.

In all paediatric age groups, incidence during the cyclical peak in 2012 was 3-6-fold lower compared to peak activity during the prior 20-year period. Conversely, incidence in adults aged ≥20 years has remained at more stable low levels, reported at 5 per 100,000 in 2012, less than a two-fold decrease compared to historical peak activity of 9 per 100,000 in 2000. However, as a result of the dramatically declining incidence in all pediatric age groups, individuals aged ≥20 years comprise a steadily increasing proportion of cases overall (Figure 4B).

Regional outbreaks, 2012 and 2013

The 2012 outbreak in BC was largely concentrated in the Lower Mainland region, with an overall incidence of 10 cases per 100,000 reported in FHA and 16 per 100,000 reported in VCHA, rates lower than prior cyclical peaks in these regions (Figure 1). Localized clusters of more intense activity contributed significantly to regional variation in rates. In the Fraser East area of FHA, pertussis incidence reached 24 per 100,000, and in VCHA, incidence in North Shore/Coast Garibaldi areas reached 36 per 100,000 (Figure 5).

Figure 5. Incidence of confirmed pertussis cases in BC, by Health Service Delivery Area (HSDA), 2012 and 2013*



* Year-to-date (October 31, 2013)

More intense activity was associated with localized outbreaks at schools and other social gatherings, as well as pockets of low immunization coverage.

Since January 2013, incidence rates in FHA and VCHA have returned to expected endemic levels. Year-to-date incidence rates for 2013 are ≤5 per 100,000 overall in each of these health authorities and are comparable to rates observed in prior non-epidemic years and overall in BC (Figure 1). In contrast, an asynchronous peak in pertussis activity was observed in VIHA in 2013. Year-to-date incidence rates in this region of 18 per 100,000 slightly exceed full-year rates observed during recent peak periods from 2007-2009 (ranging from 11-13 per 100,000), but are about three-fold lower than historical peaks observed in 2000 (59 per 100,000) and 2003 (54 per 100,000) (Figure 1). Activity in VIHA in 2013 has also been driven by local clusters of more substantial pertussis intensity. Localized outbreaks in the Kootenay Boundary area of IHA in 2013, with incidence reaching 34 per 1000,000 in this area, were also reported (Figure 5).

During the 2012 outbreaks in VCHA and FHA, less than half of paediatric cases aged 2 months to 20 years were up-to-date for immunization by age overall; a substantial proportion was either partially immunized or unimmunized (~25% each) or had unknown immunization status (4%). There were six hospitalizations among notified cases from these regions, including two patients who were admitted to ICU. All but one hospitalization occurred in infants <3 months old. An additional three hospitalizations were reported elsewhere in the province during 2012: two infants <1 year old and one infant <3 months old who was admitted to ICU. The confirmed pertussis infant hospitalization rate in 2012 both in outbreak regions and overall provincially in 2012 was 18 per 100,000. There were no deaths notified in 2012; however, in 2013, a death in an immunized child <3 months old was reported. This is the first death due to pertussis to be identified in BC since 2005.

Discussion

This surveillance summary highlights trends in confirmed pertussis cases in BC over a 20-year period spanning 1993-2013. Over this period, pertussis activity showed expected 2-5 year cyclical fluctuations. Confirmed pertussis notifications increased throughout the 1990s, reaching an apex in 2000, followed by a diminution in notifications across the subsequent decade. Following historical lows in 2010 and 2011, another cyclical, but less substantial, peak was observed in 2012. The shift in age distribution toward greater incidence in pre-teens than preschool-aged children, first highlighted during the 2000 outbreak in BC,[7] has persisted through to the most recent period of peak activity.

In the pre-vaccine era, peak incidence was observed in pre-school-aged children and less than 20% of cases occurred in infants.[7] In the post-vaccine era, peak incidence shifted downward to infants <1 year old, followed by a secondary peak in preschool-aged children, and accompanied by a decline in overall incidence. Since 2000, a further age-related shift is evident: infants <1 year old remain at high risk, but the secondary peak has shifted away from preschool-aged children toward pre-teens and young teens. During the most recent peaks in 2012 and 2013, this age-related pattern remains evident. However, the steep rise in incidence observed in pre-teens during the 2000 and 2003 outbreaks has been replaced by a more gradual relative incline from younger to older school-aged children concurrent with lower-level activity overall.

Introduction of PCR diagnostic tests may have contributed to the dramatic increase in pertussis notifications during the late 1990s and into the early 2000s in BC. PCR is considered more sensitive than culture-based diagnosis, extending the period of detection to six weeks or more following cough onset, although sensitivity is optimal within 2 weeks of cough onset.[18-20] In particular, PCR may have increased detection among older children and adults who may have previously been missed by standard culture techniques due to delays in consultation for nonspecific, prolonged cough illness symptoms. The decline in pertussis notifications overall and across all age groups since 2000, despite ongoing availability of PCR diagnosis, requires alternative explanation.

Epidemics in 2000 and 2003, accompanied by a shift in the age distribution toward older children, were previously explained by a cohort effect of accumulated initial susceptibility and subsequent waning immunity among prior recipients of the less-efficacious adsorbed whole-cell pertussis vaccine.[5;7;12] In the 15 years since acellular vaccine was introduced into the routine pediatric immunization program, an increasing proportion of children comprise birth cohorts that received only acellular vaccine for all five of their prime-boost doses. In 2012 and 2013, individuals aged 14-15 years and younger would have been among the first cohorts of children to be fully immunized with only acellular vaccine. While pertussis overall remains well controlled in BC compared to historical activity, it is too early to assess the possible long-term impact of these changes to the routine pediatric immunization program on pertussis disease burden.

In addition to changes to the immunization program, low-level pertussis activity in BC may also reflect changes in population immuno-epidemiology resulting from the substantial provincial epidemics in 1996, 2000 and 2003. During the pre-vaccine era, almost all children would have been exposed to pertussis by their 12th birthday.[7]

Whether acellular vaccine can sustain protection in the absence of widespread immune boosting from natural infection, which is thought to provide more durable protection than vaccine-induced immunity, remains to be seen. Recent observational studies conducted during outbreaks in the United States highlight rapid waning of protection from acellular vaccine within 2-5 years of the fifth booster dose.[21-24] The age-related pattern of risk evident in our surveillance data, with gradually increasing incidence from 5 to13 years of age, is consistent with short-lived protection due to waning immunity. However, whether introduction of the adolescent booster to the provincial immunization program in 2004 attenuated the advancing cohort effect evident in pre-teens and teens cannot be resolved based on these data. Others have suggested that differences in contact networks and social mixing patterns by age may instead explain shifts in age-stratified incidence.[25] The persistent pattern of reduced incidence in older teens, pre-dating recent immunization program changes, may support that assertion, although other factors, such as age-related differences in disease severity or health care-seeking behaviour, could also explain this finding. Given current pertussis activity levels in BC, and the increasing evidence of rapid waning of immunity following receipt of acellular vaccine booster doses, the value of additional doses and their optimal timing within the routine immunization schedule requires further evaluation.

Limitation

Limitations of pertussis surveillance in BC, as elsewhere, include reporting and misclassification biases. Only confirmed cases identified through routine passive surveillance were included in this summary; as such, true incidence is under-estimated. Because more sensitive PCR testing has been routinely implemented in BC since 1998, the incidence patterns observed over time since its implementation, notably a substantial decline in rates, likely reflect accurate trends, if not absolute risk. Within individual age-groups, decreasing incidence over time is also likely to be robust; however, comparisons across age-groups may be less reliable. Young infants present with more classical and severe illness and clinicians may be more likely to test, diagnose and/or report pertussis in very young infants. Atypical disease presentation in immunized children, older teens and adults may have contributed, in part, to their low observed incidence. Hospitalizations were based on confirmed pertussis cases specially notified as part of enhanced surveillance established during the outbreak in 2012. The hospitalization rate of 18 per 100,000 is lower than estimates based on clinical diagnosis extracted from administrative hospital discharge records during previous peaks in BC (ranging from 50 to 70 per 100,000).[3] These data were not readily accessible for the current analysis. While the former may under-estimate, the latter is more likely to over-estimate pertussis hospitalization rates. Finally, asynchrony in the timing and geographic focus of cyclical peaks is not unexpected. Aggregation of surveillance data to health authority and provincial levels may obscure more intense or discrete activity at the local level.

Conclusions

Following substantial epidemics in 1996, 2000 and 2003, BC experienced historically low pertussis activity in 2010 and 2011, followed by regional outbreaks in 2012 that were concentrated in the Lower Mainland regions of the province. In 2013, pertussis activity has returned to endemic levels in these areas but with ongoing asynchronous activity localized within Vancouver Island and parts of the Interior. During cyclical peaks since 2000, reported pertussis incidence has been highest in infants and pre-teens and lowest in adults. Recent epidemics and changes to the provincial immunization program may have altered age-related immunity patterns, while differences in social contact networks may affect exposure risks, together reflected in current surveillance trends. Despite recognized surveillance limitations, ongoing monitoring as well as active studies of age-related risk and vaccine effectiveness are needed and should be encouraged to inform possible changes to provincial programs and policies.

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Conflict of interest

No conflicts of interests to declare.

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Prolonged Pertussis Outbreak in Ontario Originating in an Under-immunized Religious Community

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Abstract

Background: A prolonged pertussis outbreak began in Ontario in November 2011 in an under-immunized religious community and subsequently spread to the general population and a second religious community in the same region of the province.

Objective: To compare the epidemiology in the religious communities to that of the general population within the affected jurisdictions.

Methods: The analysis includes cases reported through the integrated Public Health Information System (iPHIS) between November 1, 2011 and April 15, 2013 that met the outbreak case definition. Health unit staff assessed whether cases were members of religious communities through case investigations and collected information on immunization status, treatment and outcomes.

Results: A total of 443 confirmed and probable outbreak cases were reported in 7 health units. The outbreak began in one religious community (138 cases), before spreading to the general population in the region (273 cases). A second under-immunized community within the region experienced 32 cases. Thirteen cases were hospitalized and no deaths were reported. Disease peaked earlier in the religious community; cases were significantly younger, more likely to be at high risk for pertussis and more likely to be unimmunized. Among the fully immunized general population, 51% of cases were between 10-14 years and with a median of 5.6 years since their last immunization.

Conclusion: The epidemiology of pertussis in the under-immunized community is distinct from the general population. Transmission of pertussis to the general community is not unexpected during an outbreak; however, the proportion of cases up to date with immunization warrants further investigation.

Introduction

Between 2010 and 2012, a number of jurisdictions throughout North America were experiencing pertussis outbreaks. [1-5] Pertussis is a highly communicable respiratory infection caused by *Bordetella pertussis*, which is most dangerous in infants under one year of age; particularly those under four months. [6,7] Disease control is challenging due to the long period of communicability, the disease's atypical presentation among adults and immunized children and the fact that it can be difficult to diagnose. [8,9,10]

Pertussis vaccines have been available in Ontario since 1943. In 1984, a combination adsorbed whole cell pertussis vaccine was used in the province's universal publicly-funded immunization program. In 1997, acellular pertussis vaccine replaced the whole cell vaccine and was delivered as part of a combination product (diphtheria [D], tetanus [T], acellular pertussis [aP], inactivated polio vaccine [IPV] and *Haemophilus influenzae* type b [Hib]) at 2, 4, 6 months of age, with a pentavalent (DTaP-IPV-Hib) booster dose at 18 months and a quadrivalent booster dose (DTaP-IPV) at 4-6 years of age. In 2003, an adolescent dose was publicly-funded using dTap at 14-16 years of age. Finally, in 2011, a single dose adult pertussis immunization program was introduced.[11]

On January 25, 2012 a provincial outbreak of pertussis was declared after a cluster of cases was detected in an under-immunized religious community (religious community A) in southwestern Ontario, Canada. The outbreak was initially limited to three health units (HUs) and one religious community (A) but subsequently spread to the general community and a second under-immunized religious community (B) in 7 HUs in the province.

Our objective is to report on the outbreak investigation, comparing the epidemiology in the religious communities to that of the general population, including demographics, immunization status, treatment and outcomes.

Methods

Surveillance

Pertussis is a legally reportable disease in Ontario (population 13.5 million in 2012).[12] Cases are identified passively and case information is entered into a provincial reportable diseases registry, the integrated Public Health Information System (iPHIS). Pertussis outbreak case definitions which included a geographic component were established and modified three times throughout the course of the outbreak to reflect the evolving situation. The outbreak period was between November 1, 2011 and April 15, 2013. We extracted data entered into iPHIS meeting the confirmed and probable pertussis outbreak case definitions on August 22, 2013. Extracted data included demographic information, laboratory results, hospitalization status, outcome, and immunization history, although completeness varied by field. We determined episode date for each case using a standardized hierarchy: symptom onset date was preferentially selected, specimen collection date if symptom onset was unavailable, and case reported date if both were unavailable.

Early in the outbreak, we supplemented iPHIS data with additional case note data using an enhanced case report form to gather information on whether the case was at high risk for pertussis, as well as health seeking behavior and treatment. A manual case record review was undertaken on cases reported between November 1, 2011 and August 15, 2012. We classified persons as high risk for pertussis if they were pregnant or under 1 year of age, and assessed whether cases obtained laboratory testing, initiated antibiotic therapy and the time interval to seek treatment.

HUs were requested to identify connection(s) to under-immunized communities within iPHIS. We classified cases as being from one of two under-immunized religious communities, A and B, using specific exposure identifiers. For some analyses, religious communities A and B were combined. We assumed cases not assigned to either exposure identifier originated from the remaining HU population, (the general population).

As accurately assessing immunization status from a single field in iPHIS was problematic, we reviewed the following fields for all cases: immunization agent, immunization administration dates, relevant immunizations up-to-date (RI), and risk factor (RF). The number of doses of pertussis-containing vaccine received was established based on the number of administration dates reported for each case. We determined the validity of doses by considering minimum age and minimum interval requirements between doses, as per the Ontario publicly funded schedule.[13] An interval of at least 14 days prior to disease onset was required for a dose to be considered valid. We assessed cases without any valid doses (i.e., no administration dates) as *unimmunized* if RI=No or RF=unimmunized; otherwise we assessed these cases as having *unknown* immunization status. We assessed cases with at least one valid dose as being *complete for age* (i.e., up to date) or *partially immunized* in accordance with the provincial immunization schedule and guidelines established by the National Advisory Committee on Immunization.[11,14]

Statistical analysis

We calculated incidence rates per 100,000 population using demographic data from Statistics Canada obtained through IntelliHealth Ontario. Population data by HU were unavailable at the time of analysis for 2013; 2012 population data were substituted. Descriptive analyses and statistical tests were performed using SPSS version

19 (IBM, Armonk, NY, USA) and SAS version 9.2. We compared median age and time intervals for selected outcomes between communities using the Kruskal-Wallis test; statistical significance was declared at $p<0.05$. Where appropriate, we excluded missing data from analyses.

Results

Descriptive epidemiology

A total of 443 pertussis cases were reported by 7 outbreak-affected HUs during the outbreak period. Of these, 344 cases (77.7%) were classified as confirmed based on laboratory confirmation of pertussis or an epidemiologic link to a laboratory-confirmed case and the remaining 99 were classified as probable based on symptomatology. Cases ranged in age from 14 days to 68 years, with a median age of 9.4 years (age was missing for 6 cases). Females accounted for 56.0% of cases. The annualized incidence rate during the outbreak was 25.7 cases per 100,000 population (2012 population of 7 HUs was 1.2 million people). The overall provincial rate during the same time period was 6.1 pertussis cases per 100,000 population. Thirteen cases (2.9%) were hospitalized and there were no deaths. All hospitalized cases were children and 8 were under one year of age.

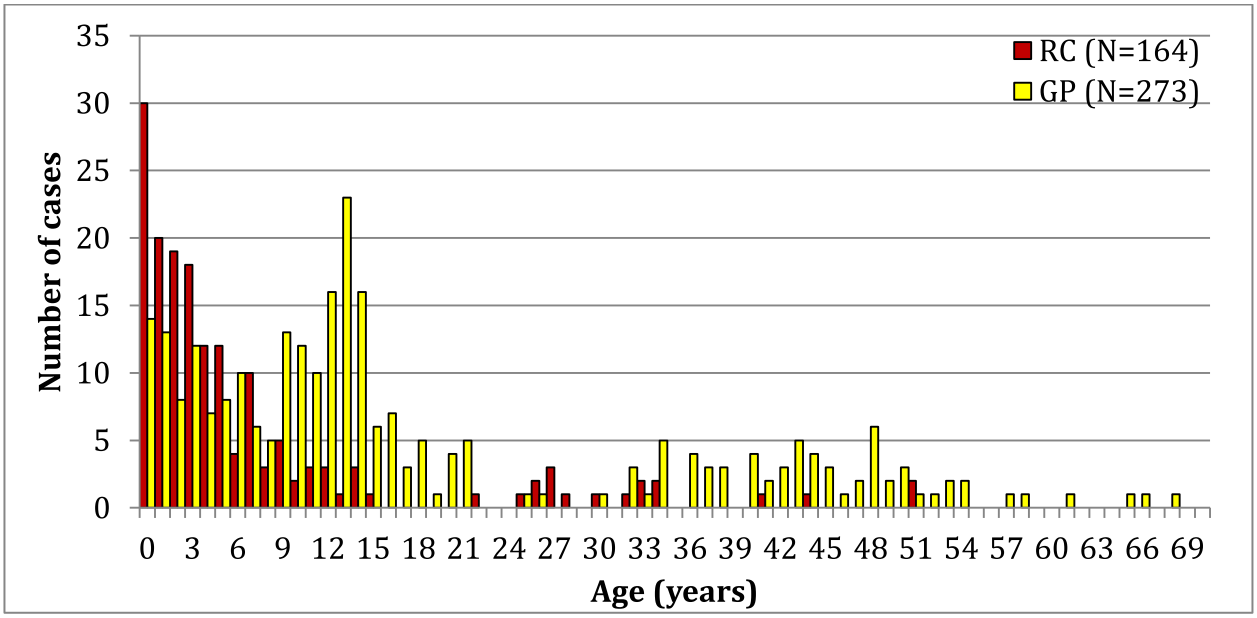
Of the 443 cases, 31.2% originated in religious community A, 7.2% in religious community B and 61.6% in the general population (Table 1). The age distribution of cases from the two religious communities was distinct from that of the general population (Figure 1). The median age of cases from the general population was approximately 10 years older and significantly higher than the median age of cases from either of the two religious communities ($p < 0.001$). While over half of the cases from religious community A and B were under 5 years of age, only 19.8% of the general population cases occurred in this age group ($p<0.0001$). Among the general population, the highest proportion of cases (28.2%) occurred in the 10-14 year age group. The probability of hospitalization did not vary by community.

Table 1: Comparison of selected outcomes among cases from religious community A, B and the general population using iPHIS and case report form data

	Religious community A	General population	Religious community B
iPHIS Data (n=443)			
Number of cases (%)	138 (31.2%)	273 (61.6%)	32 (7.2%)
Median age (years)	3.7	13.2	3.9
Proportion less than 5 years old	60.6%	19.8%	59.4%
Case Report Form Data (n=303)			
Number of forms completed	115	188	0
% high risk	22.6%	5.3%	N/A
% obtaining laboratory tests	50.9%	81.3%	N/A

N/A = not applicable

Figure 1: Pertussis Cases by Age and Community Status: Ontario, November 1, 2011 to April 15, 2013 (n=437*)

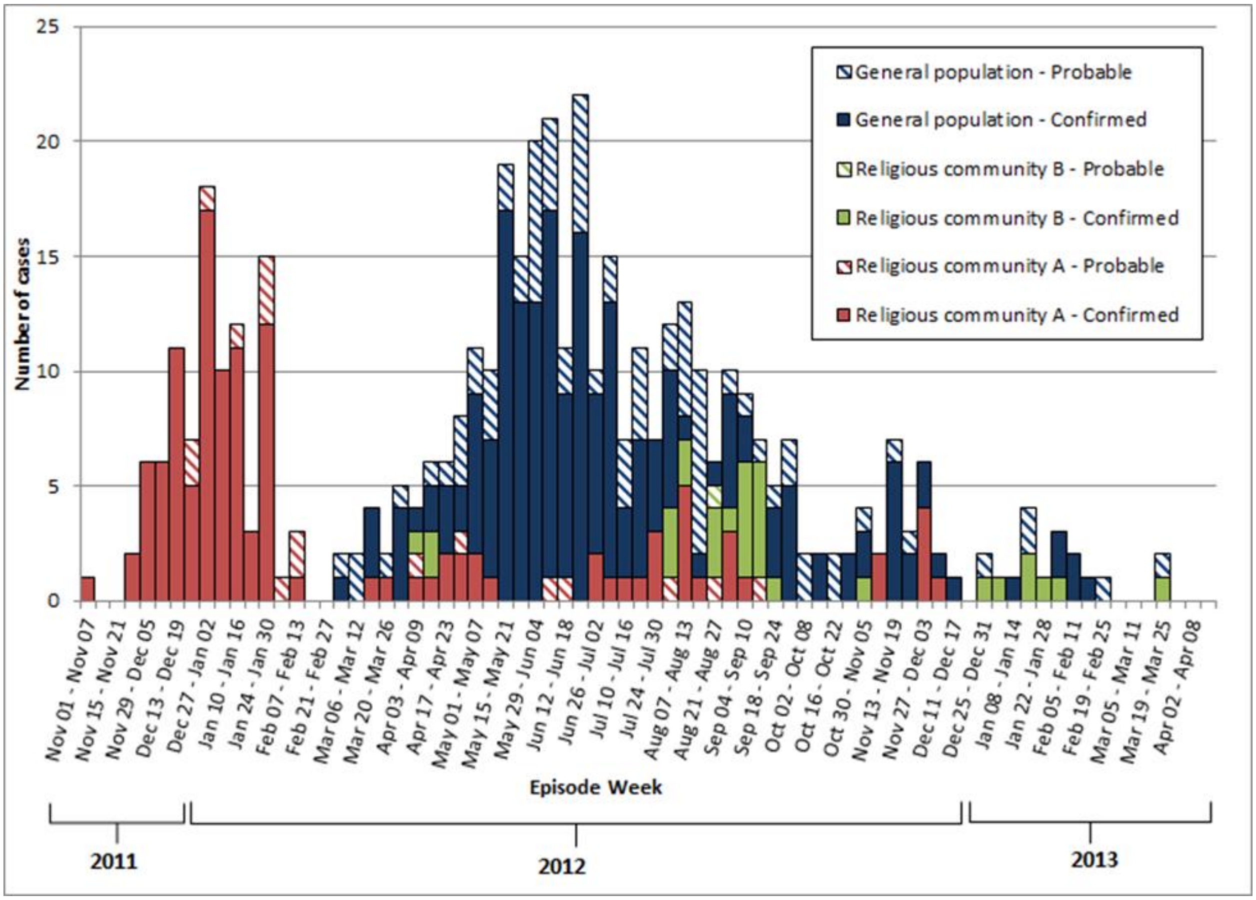


RC=religious communities A and B; GP = general population
*excludes 6 cases for whom age was unknown.

Enhanced case report forms were available for 68.4% of cases; 115 from religious community A and 188 from the general population (no cases from religious community B had enhanced case report forms as they occurred later in the outbreak). As seen in Table 1, religious community A cases were more likely than general population cases to be high risk (p <0.0001), and were less likely to obtain the recommended laboratory testing for pertussis (p<0.0001), as well as initiate antibiotic therapy (p<0.01). Religious community A cases also had a longer time period between symptom onset and initiation of treatment compared to the general population cases (p<0.005).

The temporal distribution of cases showed a bimodal pattern over the course of the outbreak (Figure 2). The first wave peaked in January 2012 and was limited almost exclusively to cases from religious community A. The second wave peaked in June 2012 and was comprised primarily of cases from the general population, although the tail of the epidemic curve was mixed and involved religious community B cases.

Figure 2: Confirmed and probable outbreak cases (n=443) by onset date, case classification and community, southwestern Ontario: November 1, 2011 to April 15, 2013



Immunization status

We could determine immunization status for 85.1% (n=377) of cases. Of these, 34.5% were complete-for age, 11.9% were partially immunized, and 53.6% were unimmunized. Immunization status was similar between the two religious communities and we therefore combined their data for this analysis. We found a significant difference in proportion immunized and complete-for-age between the religious communities and the general population ($p < 0.01$). While 86.6% of cases in the two religious communities with known status were unimmunized, only 32.0% of cases in the general population were unimmunized. The age distribution of unimmunized cases varied by community. Unimmunized cases were younger in the religious communities compared to the general population (median age of 3.0 versus 8.4 years, respectively, $p<.0001$). Conversely, 6.0% (n=9) of cases with known immunization status were complete for age in the religious communities compared to 53.1% (n=121) among the general population ($p<.0001$). The median age of cases in the general population who were complete for age was 11.7 years (range 2 months to 43 years) and over half (51.2%) were between 10- 14 years. The median number of years since their last immunization was 5.6 (range 15 days to 9.9 years).

Discussion

Ontario experienced an outbreak of pertussis that lasted more than 17 months. We found that the epidemiology of pertussis in the under-immunized community was distinct from that of the general population, with a younger age distribution, a larger proportion of cases with no immunization and a larger proportion of high risk cases. The pertussis epidemiology in the under-immunized community is more consistent with that found in the developing world and similar to that seen prior to immunization programs in North America.[15,16] Despite the younger age distribution, the disease did not appear to be more severe in the under-immunized communities. Although 86.6% of the religious community cases were unimmunized, some community members were willing to receive immunizations during specific outreach clinics held by the HUs, where testing and chemoprophylaxis were also offered.

One concern raised by public health staff arose from the observation that some religious community members declined follow-up for confirmatory laboratory testing. While cases from the religious community were less likely to have laboratory testing than cases from the general population, it was somewhat reassuring that almost half sought testing. It was also encouraging that the majority of individuals from all communities obtained treatment once they were identified as cases, although religious community cases obtained this less often. The delay in receipt of treatment by the religious community may be amenable to public health interventions.

Transmission to the general community is not unexpected during a pertussis outbreak, especially considering the infectiousness of the organism. Ontario does not have a comprehensive immunization registry, so we cannot determine immunization coverage in the general population or vaccine effectiveness. The lack of denominator information for the religious communities also precludes assessment of vaccine effectiveness using the screening method. However, Ontario has a school-based immunization information system and in 2011/2012 school year, the proportion of 7 and 17 year old Ontario students who were up to date with their pertussis immunizations was 76.0% and 67.7%, respectively.[17] This coverage is not high enough to prevent transmission of pertussis within communities, especially in regions where coverage is even lower as a result of religious or conscientious objection to immunization.

The proportion of general population cases who were fully immunized in this outbreak was concerning and has also been seen in other recent outbreaks in North America.[1,4] In Ontario, acellular pertussis vaccine was implemented in 1997, and therefore the oldest cohort of children vaccinated solely with acellular vaccine would have been between approximately 14 and 15 years of age during this outbreak. Although children 10-14 years of age account for 5.7% of Ontario's population, they accounted for 20.4% of outbreak cases overall, 28.2% of the general population cases and 51.2% of the general population cases who were up to date with their immunizations. This warrants further investigation and is suggestive of waning immunity associated with acelluar pertussis vaccine, which has also been demonstrated in the United States.[1]

Our analysis has a number of limitations. Accurately assessing immunization status within iPHIS is challenging for diseases such as pertussis with a complex immunization schedule. Records were frequently missing clinical information and immunization status was unknown for 14.9% of cases, despite extensive follow-up by health unit staff. These limitations were somewhat offset through the use of enhanced case report forms at the beginning of the outbreak. Given the prolonged nature of the outbreak and the human resources required to complete the report forms, they were only completed on cases occurring during the first nine and a half months of the outbreak, which may impact their representativeness. Finally, as noted above, we were not able to calculate vaccine effectiveness as we do not have a comprehensive provincial immunization registry.

Conclusion

This outbreak provided the opportunity to contrast pertussis epidemiology in distinct communities within one geographic area. Transmission from under-immunized communities to the general community is not unexpected, however the number of adolescent cases who were up to date with immunization suggests waning vaccine immunity.

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A Survey of Pertussis Surveillance and Immunization Practices in Canada, 2012

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Abstract

Background: In 2012 there was an increase in the incidence of pertussis in the Americas. The Pan American Health Organization (PAHO) made a number of recommendations to strengthen surveillance, investigate outbreaks, to measure adequacy and timeliness of immunizations within the population and monitor policies related to high risk individuals such as health care workers and pregnant women.

Objective: To review measures taken in Canada by provinces and territories to control and prevent pertussis spread.

Methods: A survey was developed based on PAHO recommendations and distributed through the Council of Chief Medical Officers of Health to all provinces and territories.

Results: All provinces participated in the survey. Strong surveillance is aided by consistent use of case definitions; most provinces use the national case definition. Outbreaks are investigated at the local/provincial level. Immunization coverage is not well captured but efforts are underway to improve monitoring through surveys and immunization registries. Policies have been implemented related to high risk individuals but evaluations of these policies have not been undertaken as of yet.

Conclusion: Based on the PAHO recommendations, Canada is well poised to provide surveillance data on pertussis. There are gaps in surveillance, in standardization among jurisdictions and in immunization coverage data which may need to be addressed to gain a better understanding of the impact of pertussis in Canada.

Introduction

Pertussis is a vaccine preventable disease caused by the bacterium *Bordetella pertussis*. Pertussis epidemiology is marked by a cyclical pattern of disease with cycles occurring approximately every 2-5 years. Canada has had a vaccine program in place since 1943. Since that time there has been a dramatic reduction in the incidence of disease. In the pre-vaccine era incidence rates peaked at 181 cases per 100,000[1] and have since declined with the lowest incidence on record reported in 2011 at 2.0 cases per 100,000[2]. In 2012, a 7 fold increase in disease incidence as compared to the previous year was noted within Canada. Additionally, the Region of the Americas also experienced an increase in the activity of pertussis. As a result of this increase, the Pan-American Health Organization (PAHO) announced recommendations for pertussis surveillance and immunization.(**Table 1**).

PAHO recommendations for pertussis surveillance and immunization [3]

1. Strengthen surveillance in order to monitor the disease burden, to evaluate the impact of immunization through vaccination and to identify outbreaks. Every pertussis outbreak should be thoroughly investigated to improve the understanding of the current epidemiology of the disease in the Region of the Americas.

2. Analyze the vaccination coverage of one year old infants and children under five years old, special emphasis on identifying groups without vaccination coverage.

3. Countries should ensure vaccination coverage ≥95% with 3 doses of pertussis-containing vaccines in children aged <1 year; and encourage timely vaccination and completion of the schedule. The 4th dose of the DPT vaccine should be incorporated into the regular vaccination program in every country, and the coverage attained with this dose (as with all vaccine doses) should be the object of careful recording, monitoring, reporting and evaluation.

4. Vaccinate health workers to prevent hospital transmission to infants under six months old and to people with compromised immune systems.

5. Immunize pregnant women in the case of an outbreak, for optimal protection of newborns.

The purpose of this article is to review activities undertaken by jurisdictions in Canada related to the increase in pertussis activity and to assess Canadian strengths and challenges as they relate to the PAHO recommendations.

Methods

Using Fluid Surveys, an electronic survey was created and administered by the Public Health Agency of Canada, in collaboration with public health officials in Ontario. The survey was assessed by 3 reviewers for face validity and content validity. The survey consisted of 35 questions related to the priorities for pertussis surveillance outlined by PAHO. Part one (16 questions) focused on disease surveillance, case definitions and reporting practices. Part two (19 questions) focused on immunization practices, immunization coverage and evaluation of programs. Each Province and Territory, through their Chief Medical Officer of Health, was asked to complete the survey. The survey is available upon request from the corresponding author.

Completed surveys were collated and analyzed based on common themes. A descriptive analysis of the responses was done.

Results

There was a 100% response rate to the survey with a 92% completion rate. One territory was not able to complete the entire survey.

Surveillance

The national case definition is used by all but three jurisdictions; two jurisdictions in Canada use a less specific definition in that they do not require clinical symptoms following detection of *B. pertussis* DNA from a clinical specimen. One province requires clinical symptoms along with laboratory confirmation regardless of confirmation method (i.e. B. pertussis isolation versus DNA detection); therefore, their case definition is more specific than the national definition.

Reporting occurs within each jurisdiction at varying time cycles. One province receives reports near real time with probable as well as confirmed cases being reported every hour, while other jurisdictions have daily, weekly, monthly reporting schedules. Data collected within each jurisdiction is also variable. All the Provinces and Territories collect information on the age, gender, place of residence as well as laboratory testing method and result of test. Many jurisdictions have the capacity to obtain further information by case investigation at the local level; two jurisdictions are also able to obtain information on immunization history from data sources separate from surveillance data, such as immunization registries or public health immunization databases. Interestingly, not all the Provinces and Territories routinely collect information on immunization history, when doing so would contribute to understanding if there were a possible vaccine failure or failure to vaccinate. Additional information that isn't consistently collected by the Provinces and Territories includes, symptoms, complications, duration of hospital stay and outcomes.

Outbreak Investigation

In the setting of an outbreak, pertussis monitoring is enhanced in most jurisdictions to include a change in case definition, the types of variables collected and how data is collected. Changes in case definition are dependent on the characteristics of the outbreak. In some Provinces and Territories, enhanced data is collected during outbreaks to include data on transmission setting, contacts, risk factors, preventative treatment and more detailed laboratory data.

In light of outbreaks, many Provinces and Territories have recently, modified their surveillance of pertussis to improve their understanding of disease burden and/or assess the impact of their immunization programs. These changes included additional laboratory testing, adding in variables to look at transmission especially among infants and their family members, increased emphasis on immunization history to determine effectiveness of immunization programs, the use of additional software to understand the changes in incidence, and improved communication with frontline providers. Some provinces have also increased the frequency with which they analyse their routine surveillance data to improve their ability to respond to increased disease activity.

Immunization Coverage

Childhood

All the Provinces and Territories include pertussis containing vaccine in their childhood routine immunization schedule. Immunization coverage targets have been defined nationally [4]. Of those jurisdictions who responded to questions concerning immunization targets, 4 Provinces and Territories use national targets to evaluate their immunization programs, three other jurisdictions have province-specific targets and 5 jurisdictions indicated they do not have targets in place. Despite this lack of uniformity in targets, all Provinces and Territories have methods of trying to improve immunization coverage. Only one province has automated computer generated reports that are sent directly to families when a child is 7 years of age. Coverage assessments are done by surveys, immunization registry data, or school records, although many jurisdictions rely on immunization providers to assist with timeliness and completion of immunization records.

Given the pivotal role that frontline providers have in immunization coverage, all Provinces and Territories use a variety of methods to communicate and disseminate information that would assist providers, including routine publication of reports on coverage and directly posting estimates of immunization coverage to the Provinces and Territories public health web page.

Adult immunizations and high risk individuals

Adult pertussis immunization programs are publically funded in seven jurisdictions, but most require proof of no previous vaccination in adulthood to be eligible for the dose. Immunization of health care workers is recommended for most jurisdictions.

Immunization of pregnant women has been recommended in three jurisdictions due to the increase in pertussis activity. Most other jurisdictions recommend maternal immunization based on local epidemiology and consultation with a health care provider. Immunization of close contacts of a newborn, or cocooning, has been used as an intervention in a few jurisdictions. Maternal immunization and cocooning have not been formally evaluated in Canada.

Discussion

PAHO presented each member state with a list of five recommendations in the face of an increased activity of pertussis. Reviewing this list and the activities that have been undertaken within different jurisdictions within Canada, our system for surveillance and response provides many of the attributes PAHO recommends, but additional steps can be taken to improve our ability to describe disease activity and outbreaks, to improve our understanding of immunization coverage and to protect vulnerable groups.

PAHO has recommended strengthening surveillance in order to monitor disease burden, to detect outbreaks and to assess impact of immunization programs. In Canada, pertussis is nationally notifiable but our ability to evaluate the impact of immunization and identify outbreaks is limited by the current national reporting schedule (once yearly) and format (aggregate only) in which the data is received. At the Provincial and Territorial level, pertussis is monitored routinely with many more details. The system within Provinces and Territories has allowed the detection of outbreaks. Routine monitoring varies from jurisdiction to jurisdiction not only in terms of timelines but also in terms of data collected. If additional information is required at a national level, it is possible to request data from Provinces and Territories. Methods to strengthen our current system include more detailed and timely reporting to the national level and an improved ability to capture immunization history for individual cases as well as the population at large.

The ability to thoroughly investigate an outbreak does not exist within the national surveillance program. Thorough investigation does occur at the Provincial, Territorial and local level throughout Canada. Assistance with outbreak investigation can be sought from national programs such as the Canadian Field Epidemiology Program. As an outbreak is occurring there are multiple methods through which jurisdictions can communicate, for example postings of public health alerts via the Canadian Network for Public Health Intelligence (CNPHI), community of expert groups in the Public Health Network such at the Canadian Immunization Committee (CIC) as well as more senior level tables such as Council of Chief Medical Officers of Health (CCMOH). The ability to disseminate findings from outbreaks is limited by resources. A number of jurisdictions have written up and widely disseminated their outbreak experiences but not all jurisdictions have this capacity. This poses challenges to learning from our collective experiences.

Although Canada has a national immunization survey that occurs every two years, it typically does not have the sample size to determine jurisdictional variation, or investigate specific groups who may be under or unimmunized. Many jurisdictions are moving towards immunization registries and have (or will have) the ability to analyze immunization coverage and to generate reminders for those who are not up to date. The challenges of immunization coverage include ensuring all Provinces and Territories in Canada have this capability and ensuring that estimates are comparable in terms of the methods used to derive immunization estimates.

PAHO has also recommended that all health care workers be immunized against pertussis, as well as pregnant women in the case of an outbreak. Jurisdictions in Canada are supported by The National Advisory Committee on Immunization (NACI) recommendations that include immunization of health care providers [1]. NACI also supports immunization of pregnant women in outbreak situations [5].

Based on the PAHO recommendations and the obligation that Canada bears as a member of the international community, there are important practice implications from this survey. For a frontline provider, ongoing vigilance, appropriate testing and reporting of individuals with illnesses compatible with pertussis remains of utmost importance. These case notifications are the basis of accurate surveillance and enable identification of outbreaks that require the type of detailed investigations that can improve our understanding of the disease. Since each level of government plays a role in surveillance, immunization coverage and protecting vulnerable groups, this survey also highlights opportunities for improvement from a broader public health perspective. For example, understanding the type of data collected at the provincial/territorial level and how this varies across the country will inform national deliberations on the future of pertussis surveillance. In addition, further discussion and evaluation of changes in surveillance and public health measures various jurisdictions have made can provide evidence based determination of best practices in the control of pertussis in Canada.

Conclusions

Canada routinely monitors pertussis and is able to provide a national perspective on disease incidence and more detailed epidemiologic picture via Provincial and Territorial surveillance data when necessary. Canada maintains national immunization targets in-line with the PAHO recommendations, routinely assesses general immunization coverage via population-based surveys, and has national recommendations for the immunization of health care workers and pregnant women in outbreak situations. Current gaps in Canadian surveillance and immunization practices include the availability of detailed information on pertussis activity at the national level. In addition, the absence of readily available immunization data on cases and the population in general limits our understanding of the impact of immunization on disease burden and prevents a meaningful evaluation of immunization programs in Canada. These issues have previously been identified and are currently being discussed in the context of data sharing agreements with their Provincial and Territorial partners, and the renewal of the National Immunization Strategy.

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Conflict of Interest

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Pertussis: A Global Perspective

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Over the past several years, outbreaks of pertussis have been reported from a number of jurisdictions including the United States [1-4], Australia [5], the United Kingdom [6] and Canada. In the United States, over 9000 cases were reported in California in 2010 [7]. In 2012, large outbreaks were reported in the states of Washington, Minnesota, and Wisconsin. Indeed, 49 of 50 states reported increases in pertussis in 2012 compared to 2011; only California which had its outbreak in 2010, reported a decrease in incidence [8]. In Australia, the overall incidence of pertussis in 2009 rose to >140/100,000, exceeding rates in most other industrialized countries [9]. In the UK, increased numbers of infant deaths were observed in association with an increase in the incidence of pertussis in adolescents and adults [6]. Other countries have not seen increases in the incidence of pertussis; France, Denmark, Sweden, and some other European countries continue to report low levels of pertussis. As highlighted in this issue, In Canada, increased pertussis activity has been reported in some provinces or regions [10, 11].

Has pertussis "re-emerged"? Pertussis is a cyclical disease with peaks occurring every 2 to 5 years; is this simply an expected cyclical peak? Has surveillance improved or have there been changes to diagnostic testing? Has the organism become more virulent? Has the vaccine become less effective? How does this affect the Canadian situation?

The epidemiology of pertussis around the world may be the result of multiple different factors which with varying relevance in each country. In the United States, the California outbreak in 2010 which led to 10 infant deaths was notable for its involvement of school aged children in the 7 to 10 year age group; increased time since the preschool pertussis vaccine dose was a risk factor suggesting waning of vaccine induced immunity. A sizeable number of unimmunized children may also have contributed to the outbreak [2]. Duration of protection was significantly shorter in children who had received all of their pertussis vaccines with an acellular pertussis vaccine.[1, 4] In 2012, in Washington, Wisconsin, and Minnesota, the peak incidence of pertussis was also in school-aged children. In Washington, a short duration of protection following the pre-adolescent reduced content acellular pertussis vaccine (Tdap) was also a factor [12]. Thus, the US outbreaks appear to be related to shorter than expected duration of protection associated with acellular pertussis containing vaccines, receipt of all pertussis vaccines as acellular vaccine, and pockets of completely unimmunized children. In Australia, an increase in cases was reported in preschool-aged children which was attributed to the elimination of the booster dose of DTaP in the second year of life [5, 9]. High rates of pertussis have also been reported in adults in Australia, perhaps related to the wide availability and utilization of a serological test for pertussis since the 1990s [9]. In England, an outbreak of pertussis was associated with an increased number of infant deaths. The outbreak may be related to the lack of booster dose in adolescents [6, 13].

In considering the recent data that a single dose of whole-cell pertussis vaccine is associated with improved duration of protection, one assumes that the dose or doses of whole cell pertussis vaccine preceded the doses of acellular vaccine, since the use of acellular pertussis vaccines completely replaced whole cell vaccines in the US. It is difficult to imagine that there remains any direct protection from that initial dose or doses. Instead, it may be that protection is best when the initial dose of vaccine directs the immune system toward a Th1 type response [14]. Acellular pertussis vaccine, with its alum adjuvant, skews the immune system toward a Th2 biased response. In contrast, although also adjuvanted with alum, whole cell vaccine produces a Th1 biased response, similar to natural infection, perhaps related to residual presence of *B. pertussis* lipo-oligosaccharide (endotoxin), a potent Th1 adjuvant. Despite these immunological reasons why whole cell pertussis vaccines may be superior to acellular vaccines, there have also been increased reports of pertussis activity in countries using whole cell pertussis vaccine such as Brazil and Chile [15]. However, there is not one, single whole-cell pertussis vaccine; rather, there are multiple whole-cell pertussis vaccines and there is no correlation between their relative efficacy and the mouse intracerebral assay used as a regulatory requirement for their approval. Although data from the large acellular pertussis vaccine clinical trials in the 1990s suggested that the efficacy of a “good” whole cell vaccine is superior to that of the acellular pertussis vaccines, the whole cell pertussis vaccine used in two of the largest randomized controlled trials was far inferior to all of the acellular pertussis vaccines tested [16]. Additional information is needed about whether there are other jurisdictions using the same whole cell vaccines without these observed increases.

Concerns have also been raised that changes in *Bordetella pertussis* may also be contributing to the increased number of cases. Strains that have increased production of pertussis toxin have been isolated and strains that express an altered pertactin and even pertactin negative strains are becoming more common [17, 18]. Some have suggested that these strains are emerging under immunological pressure from the current acellular pertussis vaccines. Despite the increasing isolation of these strains, there has been no clear demonstration that they are associated with increased clinical virulence or are the cause of the increased pertussis activity [19].

Outbreaks have also been reported in a number of Canadian provinces. In Saskatchewan in 2010, the incidence of pertussis in children under 1 year of age rose dramatically and 6 deaths were reported; rates that exceeded those reported from California that same year. Under-immunization, particularly amongst some First Nations communities may have contributed to the increase in pertussis rates. In 2012, New Brunswick reported over 1400 cases of pertussis accounting for almost one third of the cases reported in Canada [10], with an incidence that exceeded the rates reported in Washington, Wisconsin and Minnesota. In contrast to what had occurred in Saskatchewan, cases in New Brunswick were primarily focused in school-aged children and there were very few hospitalizations and no deaths amongst infants. Although a full analysis of the New Brunswick outbreak has yet to be reported, decreased duration of protection after the pre-school pertussis vaccine dose (but not the adolescent Tdap dose) as was reported in the US may have been a factor. In British Columbia, increased reports of pertussis were also received in the Fraser and Coastal health districts (Vancouver area); no increase was reported from the rest of the province. The cause for the localized resurgence of pertussis in BC is not clear; further evaluation of rates of vaccine refusal in the Vancouver area compared to other areas of the province might be worthwhile. In Ontario, a localized outbreak in the southwestern part of the province was clearly linked to a community that refuses childhood immunization [11].

As observed elsewhere in the world, the epidemiology of pertussis in Canada appears to be a result of a combination of factors including the natural 2 to 5 year cycles, failure to vaccinate, and vaccine failure (both primary failure related to lower vaccine efficacy post-immunization and secondary as a result of waning immunity). What are the implications for Canada? Although to date there is no definitive demonstration that changes in the organism are leading to a resurgence of disease, it will be important to continue to monitor for this in Canada and worldwide. The shift away from culture diagnosis to PCR-based diagnosis means that monitoring of changes in the organism will be more difficult. In order for strain surveillance to continue, diagnostic laboratories need to cooperate to either culture some proportion of nasopharyngeal swabs submitted for pertussis diagnosis or to save residual secretions for later isolation of organisms for microbiological surveillance purposes. Continued surveillance of Canadian cohorts who received all of their doses with acellular vaccine is also important to further explore the duration of protection from acellular pertussis vaccine. More accurate data are required on vaccine coverage at both the local and provincial level to identify pockets of under immunization. Development of new vaccines that are more effective with a longer duration of protection is essential. Novel technologies such as live attenuated pertussis vaccines [20], and vaccines with novel adjuvants that direct the immune system to a Th1 response [21] may provide the solution, but are many years away. Until better vaccines are available, it will be important to make the optimal use of the vaccines currently available. High on-time vaccine coverage is still the best method we have of controlling pertussis in Canada.

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