

Inside this issue: Vaccine preventable diseases

This issue heralds National Immunization Awareness Week, April 26-May 3. Learn about the work needed to maintain our elimination status for measles and rubella; read a summary of recommendations of the Canadian Immunization Committee to expand human papillomavirus vaccine programs to young males and other high-risk groups and link to summaries of recommendations on pertussis vaccine by the National Advisory Committee on Immunization.

Surveillance and outbreak report

Documenting the elimination of measles, rubella and congenital rubella syndrome in Ontario: 2009-12 143

Lim GH, Deeks SL, Fediurek J, Gubbay J and Crowcroft NS

Summaries

Summary of Canadian Immunization Committee (CIC) recommendations for HPV immunization programs 152

Canadian Immunization Committee

What are the new active vaccine recommendations in the *Canadian Immunization Guide*? 154

Warshawsky B and Gemmill I on behalf of the National Advisory Committee on Immunization

Useful links

National Immunization coverage reports (NEW!)

Public Health Agency of Canada, Centre for Immunization and Infectious Respiratory Diseases

<http://webqa.phac-aspc.gc.ca/im/nics-enva/icc-cvc-eng.php>

Update on pertussis vaccination in pregnancy: summary table.

National Immunization Advisory Committee.

http://www.phac-aspc.gc.ca/naci-ccni/acs-dcc/2014/pvip-vcpg_0214-eng.php

Statement on the booster for 4-6 year-olds for protection against pertussis: summary table.

National Immunization Advisory Committee.

http://www.phac-aspc.gc.ca/naci-ccni/acs-dcc/2014/bpap-drcc_0314-eng.php

Correction



[CATMAT correction on its Statement on Pregnancy and Travel - CCDR 2010:36: ACS-2](#)

Committee to Advise on Tropical Medicine and Travel. CATMAT correction on its Statement on Pregnancy and Travel. CCDR 2010:36: ACS-2

Documenting the elimination of measles, rubella and congenital rubella syndrome in Ontario: 2009–12

Lim GH^{1*}, Deeks SL^{1,2}, Fediurek J¹, Gubbay J^{1,3,4} and Crowcroft NS^{1,2,4}

¹ Public Health Ontario, Toronto, Ontario

² Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario

³ Department of Paediatrics, University of Toronto, Toronto, Ontario

⁴ Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario

* Corresponding author: Gillian.lim@oahpp.ca

Abstract

Background: Under the guidance of the Pan American Health Organization (PAHO), countries of the Americas are currently documenting the elimination of measles, rubella, and congenital rubella syndrome.

Objective: This paper describes Ontario's progress in documenting the elimination of these conditions between 2009 and 2012.

Methods: All possible case classifications, including those that did not meet surveillance case definitions, were extracted from the provincial reportable disease database, the integrated Public Health Information System (iPHIS). Data were analyzed against select criteria specified by the PAHO, specifically with respect to epidemiology, vaccination coverage, and the quality of the surveillance system.

Results: There were no known endemic cases of measles, rubella or congenital rubella syndrome reported in Ontario during the study period. Cases were predominantly the result of importation, as these diseases remain endemic in many countries. A total of 27 confirmed cases of measles were reported over the four-year period, most of which could be verified as being directly or indirectly linked with travel outside Canada. In addition, five confirmed cases of rubella and one case of imported congenital rubella syndrome were identified. A review of immunization coverage and surveillance data quality identified gaps. The combined annual rates of suspected measles and rubella cases (between 0.7 and 1.1 cases per 100,000 population) and suspected congenital rubella syndrome cases (0.21 to 0.49 cases per 10,000 live births) were below PAHO's thresholds. Also, the frequent absence of immunization and travel histories within iPHIS was of concern (77.3% and 44.6% respectively).

Conclusion: These results support Ontario's sustained elimination status. However, in order to satisfactorily meet PAHO's requirements for documenting the elimination of these diseases, continued vigilance is required. Efforts are currently under way within Ontario to improve reporting.

Introduction

The Region of the Americas adopted the goal of eliminating measles by 2000, and rubella and congenital rubella syndrome by 2010. The interruption of endemic measles virus was achieved in the Americas in 2002 while the last confirmed endemic rubella case was reported in Argentina in February 2009 (1). The last endemic measles and rubella cases were reported in Canada in 1997 and 2005 respectively (2).

In order to achieve measles elimination two doses of measles-containing vaccine are required, whereas a single dose of rubella-containing vaccine is required for elimination of rubella and congenital rubella syndrome (3, 4). In Canada, measles and rubella vaccines are available only in combination with mumps, or with mumps and varicella vaccine (MMR and MMRV respectively). In Ontario, a single dose of the combined MMR vaccine was implemented in 1975 followed by a two-dose program in 1996. The first dose of the MMR vaccine is routinely given at 12 months of age, while the timing of the second dose has varied between 18 months and 4–6 years of age (5). Under the guidance of the Pan American Health Organization (PAHO), countries of the Americas are

currently documenting the elimination of measles, rubella, and congenital rubella syndrome. PAHO and the World Health Organization (WHO) developed a Plan of Action (6) for the documentation and verification of measles, rubella, and congenital rubella syndrome elimination (hereafter referred to as “the Plan”). The Plan provides guidance regarding the necessary evidence to verify that transmission of endemic measles and rubella viruses has been interrupted, and specifies several criteria and indicators that must be satisfied. The objective of this study was to evaluate Ontario’s progress in documenting elimination against a subset of the criteria specified by PAHO’s Plan of Action, using data that were readily available for analysis. The scope of the investigation was thus limited to an assessment of the epidemiology, vaccination coverage, and quality of surveillance for these diseases. We analyzed data between 2009 and 2012 to satisfy PAHO’s criteria that the absence of endemic transmission must be demonstrated for at least three years.

Methods

To assess the epidemiology of measles, rubella, and congenital rubella syndrome in Ontario, we extracted all reports (regardless of case classification) between 2009 and 2012 from the provincial reportable disease database, the integrated Public Health Information System (iPHIS), as of June 3, 2013. Cases were classified as confirmed using provincial case definitions specified in Appendix B of the Ontario Infectious Diseases Protocol (7). Immunization information and travel histories were based on a review of several fields in iPHIS, including free text fields. Descriptive analyses presenting temporal, geographic, and demographic trends were limited to confirmed cases. An imported case was defined as a case who had traveled outside Canada 7-21 and 14-21 days before symptom onset for measles and rubella respectively. These definitions were modified from those in the Plan to reference travel outside Canada rather than the Americas and to be consistent with the incubation periods specified in the Infectious Diseases Protocol (7). An import-related case was one that resulted from transmission by an imported case (i.e. epidemiologically linked). If a chain of transmission spanned 12 months or longer, cases would be considered endemic.

Within the context of elimination, we considered a single confirmed case as an outbreak, even in the absence of subsequent disease transmission. For measles, we applied the methodology described by De Serres et al. (8) to estimate the effective reproductive number (R_e); outbreaks with no subsequent transmission (i.e. $N=1$) were also included in this analysis. R_e was derived using maximum likelihood estimation; 95% confidence intervals were also estimated.

For the purpose of this analysis Canadian guidelines were applied, requiring immunization coverage with two doses of measles vaccine and a single dose of rubella vaccine, to satisfy PAHO criteria using 2011–12 coverage data among 7- and 17-year-olds from the provincial Immunization Record Information System (IRIS); the number of doses required for adequate coverage is not explicitly stated in the Plan.

All suspected and confirmed case classifications of measles, rubella, and congenital rubella syndrome were analyzed when assessing the quality of surveillance. **Table 1** lists the specific indicators and minimum thresholds required to satisfy PAHO criteria. Adequate investigation was determined on the basis of the data elements that were available in iPHIS; genotype information on outbreaks was sourced from the Public Health Ontario Laboratories.

Table 1: Documenting elimination in Ontario: components of PAHO's Plan of Action that were within the scope of this study

Component	Indicators and suggested analyses
Epidemiology of measles, rubella and congenital rubella syndrome (CRS)	Verify the interruption of endemic measles, rubella, and CRS cases for a period of at least 3 years from the last known endemic case, through an examination of <ul style="list-style-type: none"> • Morbidity rates • Temporal and spatial characteristics • Seasonality • Demographic characteristics • Outbreaks
Measles and rubella vaccinated population cohorts	<ul style="list-style-type: none"> • Population cohort aged less than 40 years with ideally at least 95% coverage.
Quality of measles, rubella and CRS surveillance	<p>Reporting rate</p> <ul style="list-style-type: none"> • Annual rate of suspected measles and rubella cases ≥ 2 per 100,000 population • Annual rate of suspected CRS cases ≥ 1 per 10,000 live births <p>Adequate investigation</p> <ul style="list-style-type: none"> • % suspected measles and rubella cases with the following 11 data points completed: name and/or identifier, place of residence, sex, age or date of birth, date of reporting, date of investigation, date of rash onset, date of specimen collection, presence of fever, date of prior MR vaccination, and travel history • % suspected CRS cases with the following eight data points completed: name and/or identifier, place of residence, sex, date of birth, date of reporting, date of investigation, date of specimen collection, and vaccination history of mother; also clinical examinations for deafness, blindness, and congenital cardiopathy $\geq 80\%$ <p>Viral detection</p> <ul style="list-style-type: none"> • % measles and rubella outbreaks with genotype information available from at least one viral specimen • % confirmed congenital rubella syndrome cases with adequate specimen analyzed for virus detection/isolation $\geq 80\%$

We compiled and analyzed all data in SAS version 9.2 and Microsoft Excel 2010. Incidence rates of measles and rubella were calculated using demographic data from Statistics Canada, accessed through IntelliHealth Ontario. Incidence rates of congenital rubella syndrome were determined using live births data from Statistics Canada.

Results

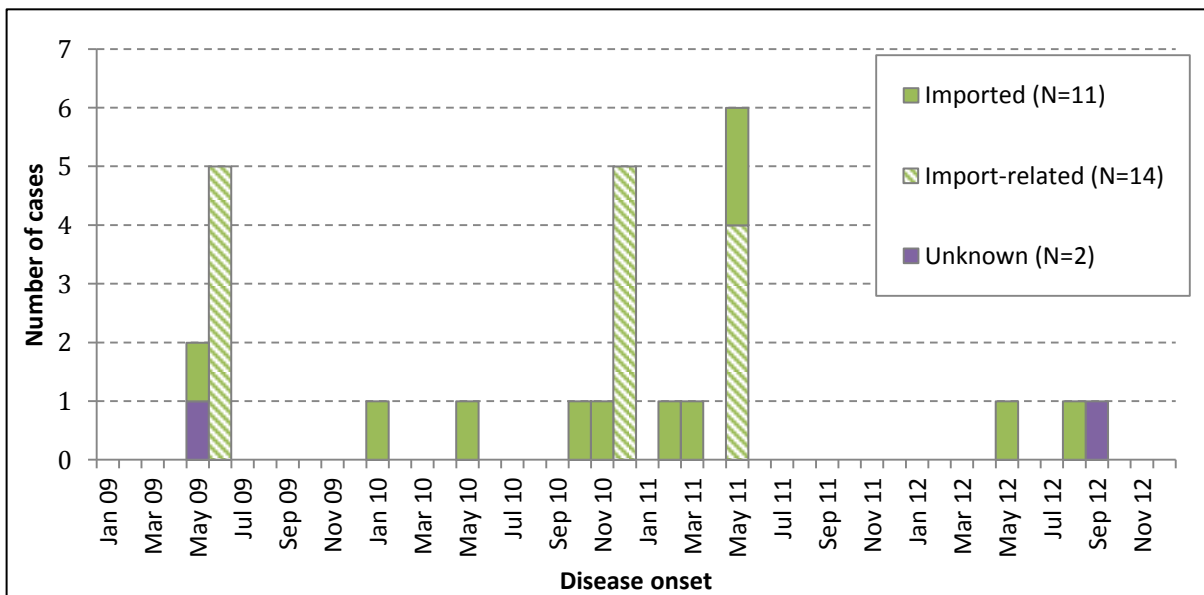
Measles epidemiology

Between 2009 and 2012, 27 confirmed and nine probable cases of measles were reported in Ontario. In addition, 316 cases were investigated but did not meet the case definition. Among confirmed cases, the annual incidence rate between 2009 and 2012 was 0.54 (2009), 0.68 (2010), 0.60 (2011), and 0.22 (2012) cases per 1,000,000 population. Two thirds of the cases were female (18/27, 66.7%). The annualized incidence rate was 0.34 and 0.67 cases per 1,000,000 among males and females respectively. The median age of cases was 13.6 years, ranging between six months and 59 years. The highest annualized age-specific incidence rate occurred among infants <1 year of age (7.0 cases per 1,000,000). Immunization status could only be assessed for 19 of the 27 cases (70.4%). Of these, 13 (68.4%) were unimmunized, three (15.8%) had had one dose, and three (15.8%) had received two doses of measles-containing vaccine (up-to-date). Three of the unimmunized cases had a history of travel, and were under one year of age and therefore too young to have received routine MMR vaccine.

During the period of investigation, three outbreaks associated with at least one chain of transmission stemming from importation resulted in a total of 17 cases of measles. An additional 10 cases were reported that did not result in further transmission. Analysis of data from these 13 outbreaks revealed an estimated R_e of 0.52 (95% confidence interval 0.29, 0.83).

Importation status could be determined for all but two cases (25/27 or 92.6%) (**Figure 1**). If importation status had been defined solely on the basis of travel outside the Americas, as per the original PAHO definition, only 66.7% of cases (18/27) would have been classified as imported or import-related.

Figure 1: Confirmed Ontario measles cases by onset date and importation status, 2009–12 (N=27)



Two distinct episodes of importation were associated each with the United Kingdom, France, and Pakistan (Table 2).

Table 2: Travel histories and genotype information for confirmed cases of measles and rubella in Ontario that were found to be imported, 2009–12 (N=15)

Imported case ID	Episode month	Country of travel	Genotype	Number of subsequent cases
MEASLES				
1	May 2009	Exposure to measles case from United Kingdom during travel in United States	D4	5
2	Jan 2010	Pakistan		
3	May 2010	Sri Lanka		
4	Oct 2010	France		
5	Nov 2010	Philippines	D9	5
6	Feb 2011	United Kingdom	D9	
7	Mar 2011	India		
8	May 2011	United States		
9	May 2011	France		4
10	May 2012	Pakistan	B3	
11	Aug 2012	Afghanistan		
RUBELLA				
1	Jan 2009	Sri Lanka and India		
2	Apr 2009	India		
3	Apr 2010	Bangladesh		
4	Jan 2012	Russia and Belarus		

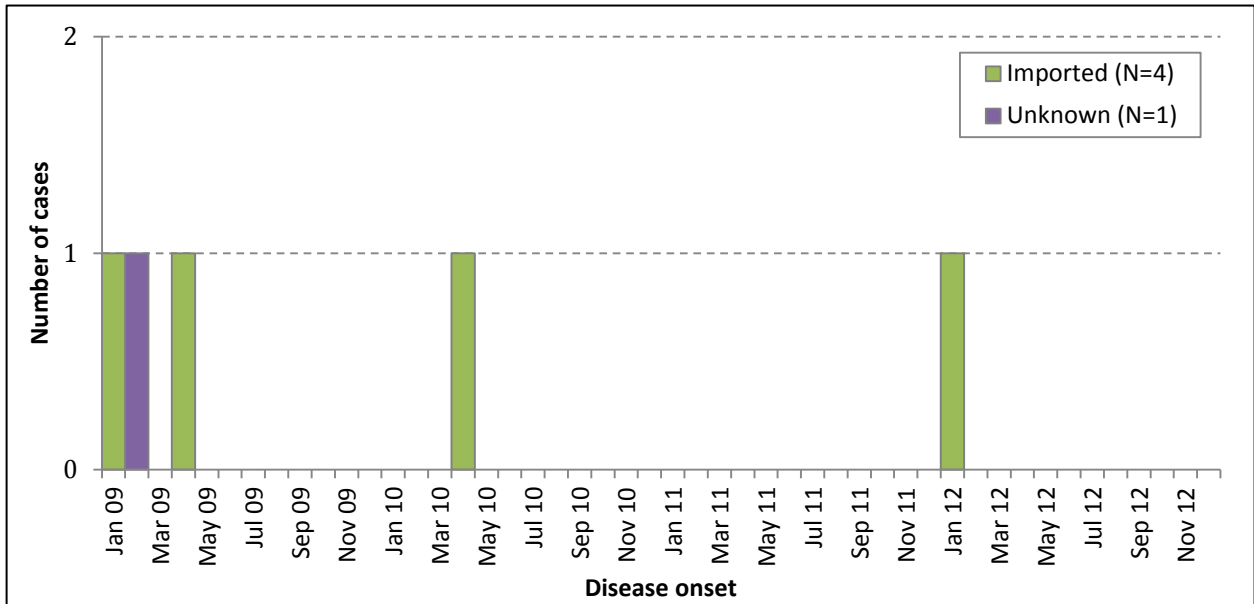
Genotype information was reported for only seven cases; of these, genotype D9 was identified in four cases (57.1%), D4 in two cases (28.6%) and genotype B3 in one case (14.3%). Overall, the genotype was known for only four of the 13 outbreaks (30.8%).

Rubella epidemiology

Between 2009 and 2012, five confirmed cases and one probable case of rubella were reported in Ontario. In addition, 139 cases were investigated but did not meet the case definition. Among confirmed cases, the annual incidence rate between 2009 and 2012 was 0.23 (2009), 0.08 (2010), 0.00 (2011) and 0.07 (2012) cases per 1,000,000. No secondary transmission occurred. There was an equal distribution of male and female rubella cases, excluding one case for which the sex was unknown. The median age of cases was 28.3 years and ranged between 22 and 54 years.

Figure 2 presents the distribution of cases by month of disease onset and importation status. Travel to Russia and Belarus, India, Sri Lanka, and Bangladesh were implicated as the source of exposure for the imported cases; genotype information was not reported for any of the cases in iPHIS (**Table 2**). For two cases, the reported country of birth was consistent with the country of travel (India and Bangladesh). Immunization status could be determined for only one case (20%), who was unimmunized.

Figure 2: Confirmed Ontario rubella cases by onset date and importation status, 2009–12 (N=5)



Congenital rubella syndrome epidemiology

Only one confirmed case of congenital rubella syndrome was reported in iPHIS during the period under surveillance, and this occurred in 2009. It was found to be an imported case, since the mother travelled outside of Canada during her pregnancy. A further 16 cases were investigated but did not meet the case definition. This equates to an incidence of 0.07 cases of congenital rubella syndrome per 10,000 live births in 2009 and an annualized incidence of 0.02 congenital rubella syndrome cases per 10,000 live births over the entire study period.

Vaccine coverage

Coverage estimates from the 2011–12 school year indicate that between the ages of seven and 17 years, two-dose measles-containing vaccine coverage ranged between 89.1% among students seven years of age and 95.0% among students 16 years of age. Single-dose rubella vaccine coverage ranged between 95.1% among seven-year-olds and 96.9% among both 15- and 16-year old students. Single-dose measles coverage was similar to that of rubella.

Quality of surveillance

The combined annual rate of suspected measles and rubella cases ranged between 0.7 and 1.1 cases per 100,000; the annual reporting rate of suspected congenital rubella syndrome cases ranged between 0.21 and 0.49 cases per 10,000 live births. Genotype information was available for only four of 18 (22.2%) measles and rubella outbreaks.

Only 2.4% (N=12) of suspected measles and rubella cases had all the required 11 data elements recorded within iPHIS. None of the suspected congenital rubella syndrome cases could be assessed, as some of the required data elements were not captured in iPHIS. **Table 3** identifies the highest proportion of missing or incompletely

recorded data elements, which included travel history (77.3%), the date on which a specimen was collected for laboratory testing (54.1%), and the presence or absence of fever (50.1%). Other data elements that tended to be incomplete included the date of rash onset (46.5%), date of prior measles-rubella-containing vaccination (44.6%), and date of investigation (30.8%).

Table 3: Data elements that were missing among suspected cases of measles and rubella in Ontario, 2009–12

Data elements	Suspected cases (N=497)	
	Number	Proportion (%)
Name	0	0.0
Place of residence	0	0.0
Sex	4	0.8
Age	3	0.6
Date of reporting	0	0.0
Date of investigation	153	30.8
Date of rash onset	231	46.5
Date of specimen collection	269	54.1
Fever	249	50.1
Date of prior measles-rubella vaccine ¹	125/280	44.6
Travel history	384	77.3

¹ **Note:** Percentages were calculated as a proportion of suspected cases when it was known that at least one dose of measles- or rubella-containing vaccine had been received.

Discussion

There were no known endemic cases of measles, rubella, or congenital rubella syndrome reported in Ontario between 2009 and 2012. During this period, 27, five and one confirmed cases of measles, rubella, and congenital rubella syndrome respectively were reported. Most imported cases resulted in no or limited onward transmission, supporting the presence of high herd immunity and suggesting effective case investigation and management by health care providers and public health. Further, the estimated effective reproduction number for measles was within the range associated with elimination (<1). Since these diseases are no longer endemic in Ontario, a travel-related exposure should be indicated for all cases. However, the source of exposure was unknown for three of the 32 cases (9.4%) of measles and rubella, suggesting that either there were data quality issues or there was unrecognized disease transmission.

The PAHO definition of an imported case was modified to reflect travel outside Canada rather than the Americas, given that Ontario is one jurisdiction within Canada. As a result, two cases of measles with travel to the United States (U.S.), as well as the ensuing five cases associated with the first case, were classified as imported and import-related respectively. In the first instance, there was documented contact with a measles case from the United Kingdom during travel to the U.S., and therefore this would have met the PAHO definition of import-related. However, on the basis of information recorded in iPHIS the lack of documented measles activity in the area of travel for the second case would have resulted in a classification of unknown under the original PAHO definition.

As Ontario does not have a comprehensive provincial immunization registry, we are not able to assess whether PAHO's criterion for vaccine coverage was met in the population aged one to 40 years. However, according to 2011–12 coverage estimates among school-aged children using data in IRIS, coverage targets were not being

met for two doses of measles vaccine but were met for a single dose of rubella vaccine. As single antigen measles and rubella vaccines are not available in Ontario, single dose measles vaccine coverage is comparable with rubella coverage (data not shown).

Of the 352 individuals who were investigated as being potentially infected with measles virus between 2009 and 2012, 27 cases were confirmed. For rubella, 145 investigations occurred, and five cases were confirmed. This suggests that the surveillance systems currently in place are sensitive at identifying potential cases and ruling out a diagnosis. However, the annual measles and rubella reporting rate did not meet PAHO's minimum threshold. Ontario may not satisfy this requirement in part because of efficient laboratory testing, which may predispose clinicians to wait for measles and rubella to be ruled out rather than report their suspicions to public health. The suitability of this benchmark in countries targeting elimination was evaluated by Tikhonova et al. (9), who modeled the impact of increasing the investigation rate in the Russian Federation and found a decline in the relative increase in measles cases detected through enhanced versus routine surveillance strategies. The authors cited the need to consider the local epidemiology and associated resource implications. Apart from the national elimination report from the Public Health Agency of Canada (2), we are unaware of studies from other Canadian jurisdictions.

These analyses demonstrate that few suspected cases had all of the required data elements entered in iPHIS, which is a major data quality deficiency. The extent to which immunization information and travel history were missing is a concern, since this information is specified as a key requirement under the Ontario Infectious Diseases Protocol. This suggests that the requisite information is not captured well in iPHIS, which may be due to incomplete data entry or inadequate system infrastructure, wherein iPHIS may not capture the requisite information. It is not known whether there is further information that has not been captured in iPHIS. Despite this, iPHIS remains a centralized data repository for the province, and the active role that the local health units play in conducting surveillance in partnership with the province is a strength of the surveillance system in Ontario.

Lastly, although all specimens that are received by the Public Health Ontario Laboratory for measles and rubella PCR (polymerase chain reaction) testing are forwarded to the National Microbiology Laboratory for genotyping, and results are disclosed to local public health agencies, this information was missing for many cases. This is likely because entry of the information is not mandatory according to current iPHIS data entry guidelines.

Since the transfer of case management responsibilities to Public Health Ontario in 2012, a concerted effort has been made to follow up with local public health units to ensure that suspected measles and rubella cases are appropriately classified as either confirmed or not meeting the definition, and that this is captured accurately in iPHIS. This additional follow-up frequently yields significantly richer information than what is entered in the database. In addition to the development of an investigation form to support local public health units in their investigation of measles and rubella cases, the results from this analysis demonstrate there is a need to improve clarity in iPHIS user guidelines so that critical information such as travel and immunization histories are recorded consistently and comprehensively. Efforts are currently under way within Ontario to address this in order to improve reporting.

Conclusion

In order for Ontario to satisfactorily demonstrate and maintain elimination of measles, rubella, and congenital rubella syndrome, continued vigilance is required. Although the number of cases identified and the size of outbreaks support sustained elimination, reported immunization coverage and surveillance data quality challenge our ability to document elimination with confidence.

References

- (1) Final report of the XIX Technical Advisory Group (TAG) Meeting on Vaccine-preventable Diseases of the Pan American Health Organization, held in Buenos Aires, Argentina, July 2011; http://www.paho.org/hq/index.php?option=com_content&view=article&id=1862&Itemid=2032
- (2) Public Health Agency of Canada. Elimination of measles, rubella and congenital rubella syndrome in Canada. Documentation and verification report. December 2011; <http://www.phac-aspc.gc.ca/im/vpd-mev/measles-rougeole-mrer-eng.php>
- (3) National Advisory Committee on Immunization. Measles vaccine. In: *Canadian Immunization Guide*. 7th ed. Ottawa: Public Health Agency of Canada; 2012; <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-meas-roug-eng.php>
- (4) National Advisory Committee on Immunization. Rubella vaccine. In: *Canadian Immunization Guide*. 7th ed. Ottawa: Public Health Agency of Canada; 2012; <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-rube-eng.php>
- (5) Ontario Ministry of Health and Long-Term Care. Publicly Funded Immunization Schedules for Ontario – August 2011; <http://www.health.gov.on.ca/en/public/programs/immunization/docs/schedule.pdf>
- (6) Pan American Health Organization. Plan of Action for the Documentation and Verification of Measles, Rubella, and Congenital Rubella Syndrome Elimination in the Region of the Americas. Washington, DC. 2011; http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=16739
- (7) Ministry of Health and Long-Term Care. Infectious Diseases Protocol. Toronto: Queen's Printer for Ontario. 2013; http://www.health.gov.on.ca/en/pro/programs/publichealth/oph_standards/docs/measles_chapter.pdf
- (8) De Serres G, Gay NJ, Farrington CP. Epidemiology of transmissible diseases after elimination. *Am J Epidemiol* 2000; 151:1039-1048; <http://aje.oxfordjournals.org/content/151/11/1039>
- (9) Tikhonova NT, Bichurina MA, Gerasimova AG, Zvirkun OV, Vladimerova NP, Mamaeva T, Lipskaya G, Elsaadany S, Spika JS. Enhanced surveillance for measles in low-incidence territories of the Russian Federation: defining a rate for suspected case investigation. *Epidemiol Infect* 2011; 139:239-246.

Conflict of interest

The authors have no conflicts of interest to declare.

Summary of Canadian Immunization Committee (CIC) Recommendations for Human Papillomavirus Immunization Programs

Canadian Immunization Committee^{1*}

*Correspondence to: CIC Secretariat (cic-cci@phac-aspc.gc.ca)

Background

There are over 100 different types of human papillomavirus (HPV), and many have been linked to cancers and benign lesions of the anogenital tract, head, and neck. In women, almost all cervical cancers can be traced to infection with oncogenic HPV types, including the high-risk types 16 and 18. Of HPV-associated cancers in men, approximately 92% of anal cancers, 63% of penile cancers, and 89% of oral cavity and oropharyngeal cancers are attributable to high-risk HPV types 16 and 18. HPV-associated anogenital warts also represent a quality-of-life and an economic burden for both males and females. Publicly funded HPV immunization programs for girls are currently in place in all provinces and territories; however, uptake ranges from 60% to 85%. On the basis of scientific evidence, the National Advisory Committee on Immunization (NACI) now recommends HPV immunization for males and females between 9 and 26 years of age for the prevention of HPV disease. In response to expanded indications for the quadrivalent HPV vaccine, as well as with the introduction of a new bivalent HPV vaccine, the Canadian Immunization Committee (CIC) considered the programmatic issues of the HPV vaccines and their appropriateness for inclusion in provincial and territorial routine immunization schedules. This document is a brief summary of the full CIC HPV recommendations (1).

Objective

To make recommendations for HPV immunization programs in light of an expanded HPV immunization program goal of reducing vaccine preventable HPV-related morbidity and mortality in the Canadian population.

Approach

A Task Group of the CIC considered the following: disease characteristics and burden of illness, vaccine safety and efficacy, feasibility and acceptability, cost-effectiveness, the ability to evaluate HPV immunization programs, research questions, and equity and ethical considerations.

Findings

There are currently two HPV vaccines approved for use in Canada: Gardasil[®] and Cervarix[™]. Gardasil[®], a quadrivalent vaccine, has been approved for females aged 9 to 45 years and males aged 9 to 26 years for the prevention of infection caused by HPV types 6, 11, 16, and 18. Cervarix[™], a bivalent vaccine, has been approved for females aged 9 to 25 years for the prevention of cervical cancer caused by oncogenic HPV types 16 and 18. The immunogenicity, efficacy, and safety of both vaccines have been clearly demonstrated; however, some studies indicate higher immunogenicity and cross-protective vaccine efficacy for Cervarix[™]. The quadrivalent vaccine's protection against anogenital warts has been shown to be economically more important than the possible advantages of the bivalent vaccine in cancer prevention; thus the quadrivalent vaccine is more cost-effective than the bivalent vaccine.

When considering the inclusion of males in HPV immunization programs in Canada, cost-effectiveness studies show that a male program is predicted to be cost-effective only when immunization coverage is lower than 50% among girls. If a male program targeted at high-risk boys and men (e.g. men who have sex with men) were initiated, the quadrivalent vaccine would be the product of choice, as it is the only one currently approved in Canada for use in males. As Canada's provinces and territories already have HPV immunization programs in

place for girls, some evaluations have been published. More data is required before an evaluation of the new HPV immunization programs can occur at the national level.

Many factors must be considered when evaluating HPV immunization programs, such as the availability of systems to 1) measure coverage and vaccine utilization, and the quality of immunization services; 2) measure the impact of HPV-related infections; and 3) link health outcomes databases, immunization registries, and population registries. Research priorities for HPV immunization have been identified by the 2005 National HPV Research Priorities Workshop, the 2012 NACI statement, and the HPV Expert Group, which met in June 2013. Indicators for evaluating the impact of HPV immunization on the population are also under development. In addition to equity and ethical considerations, the impact of HPV immunization on cervical cancer screening should be considered; an immunization program should constitute part of a comprehensive cervical cancer prevention program.

Recommendations

The goal of the HPV immunization program was expanded in June 2013 from decreasing the morbidity and mortality of cervical cancer, its precursors, and other HPV-related cancers in women in Canada to reducing vaccine preventable HPV-related morbidity and mortality in the Canadian population. The expanded national goal provides flexibility for HPV immunization to consider other aspects of HPV morbidity, as well as the inclusion of males and other population subgroups in HPV immunization programs. It also continues to allow for an emphasis on the reduction of morbidity and mortality of cervical cancer, its precursors, and other HPV-related cancers in women.

In support of the new national goal, the CIC makes the following recommendations: 1) improve national coverage rates among immunization program recipients; 2) prioritize evaluation and the setting of program indicators; 3) address new and unresolved research priorities; and 4) integrate new population groups into immunization programs with a thoughtful, risk-based approach.

Reference

- (1) Canadian Immunization Committee. Recommendations for Human Papillomavirus Immunization Programs. 2013; <http://publications.gc.ca/site/eng/464264/publication.html>

¹ **Note:** The Canadian Immunization Committee provides operational and technical advice related to immunization policies and programs in Canada. CIC consists of representatives from provincial and territorial jurisdictions, the National Advisory Committee on Immunization, the American Advisory Committee on Immunization Practices, and Health Canada's Biologics and Genetics Therapies Directorate, Marketed Health Products Directorate, and First Nations and Inuit Health Branch.

What are the new active vaccine recommendations in the *Canadian Immunization Guide*?

Warshawsky B¹ and Gemmill I²
on behalf of the National Advisory Committee on Immunization (NACI)*

¹ NACI Chair, London, Ontario

² NACI Vice-Chair, Kingston, Ontario

* Correspondence to: althea.house@phac-aspc.gc.ca

Introduction

The scientific advisory body on immunization for the Public Health Agency of Canada is the National Advisory Committee on Immunization (NACI), which develops recommendations for the use of vaccines for Canadians (1). These recommendations and other immunization information are published in the *Canadian Immunization Guide* (the *Guide*).

Since the first edition in 1979, the *Guide* has been a trusted, reader-friendly summary of information that has been used by health care providers to give advice and vaccinations to their patients, and by policy-makers for the delivery of vaccination programs. The document consists of five parts, covering key immunization information, vaccine safety, special populations, active vaccines, and passive immunization agents. Since the 2006 edition, the *Guide* has undergone extensive revisions and is now published online in an electronic format (2). The objective of this article is to provide some highlights of updates made to Part 4 on Active Vaccines up to February 28, 2014.

Approach

In revising the Active Vaccine chapters of the *Guide*, NACI reviewed literature regarding new products, changes in indication, evolving science and practices, as well as national and international recommendations released since 2006. In addition NACI consulted external expertise as necessary.

Summary of updates and additions to Part 4 (Active Vaccines)

Several new vaccines have been produced since 2006, including vaccines against herpes zoster, human papillomavirus, and rotavirus. Additionally, indications and recommendations have been revised for other vaccines.

Table 1 provides an overview of key changes and additions up to February 28, 2014. As with any therapy, it is most prudent to check the most recent prescribing information prior to use.

Table 1: Highlights of key changes to active vaccine recommendations in the Canadian Immunization Guide

Active vaccine	New NACI recommendation
BCG	Revised recommendation regarding when a TB skin test should be given before administering BCG vaccine to children < 6 months of age
<i>Haemophilus influenzae</i> type b	<p>One dose is recommended regardless of past immunization for those 5 years of age or older with the following high-risk conditions:</p> <ul style="list-style-type: none"> • Anatomic or functional asplenia (including sickle cell disease) • Cochlear implants • Congenital (primary) immunodeficiency • HIV • Malignant hematologic disorders • Transplant candidates/recipients (see <i>Guide</i> for details – three doses recommended post-hematopoietic stem cell transplant)
Hepatitis A	Vaccination recommended for family and close contacts of children adopted from hepatitis A endemic countries.
Hepatitis B	<p>Higher doses recommended for the following:</p> <ul style="list-style-type: none"> • Chronic renal failure or dialysis • Congenital immunodeficiency • Hematopoietic stem cell transplant (HSCT) • Solid organ transplant • HIV infection • Non-responder with advanced liver disease • Schedules provided for DTaP-HB-IPV-Hib (INFANRIX hexa)
Herpes zoster	<p>New chapter: Live attenuated vaccine was authorized for the prevention of shingles, August 2008.</p> <ul style="list-style-type: none"> • Recommended for individuals 60 years of age and older, and can be considered for those 50 to 59 years of age. • As it is a live vaccine, it is contraindicated in people with immunocompromising conditions and people taking immunocompromising drugs, with some exceptions as outlined in the <i>Guide</i>. • Expert opinion recommends waiting at least one year from a previous episode of shingles before receiving the herpes zoster vaccine. • Re-occurrence of herpes zoster ophthalmicus after vaccination (in persons with previous herpes zoster ophthalmicus) has been reported in several cases world-wide. The <i>Guide</i> contains management and patient counseling advice. • In contrast to previous recommendations, the herpes zoster vaccine and pneumococcal vaccines can be co-administered.
Human papillomavirus	<p>New chapter: Since 2006, two human papillomavirus (HPV) vaccines have been authorized for use that protect against four (HPV-4) and two (HPV-2) types of HPV.</p> <ul style="list-style-type: none"> • <u>Women</u>: HPV-4 or HPV-2 is recommended for 9–26-year-olds; consider in those 27 years and older with ongoing risk of exposure. • <u>Men</u>: HPV-4 is recommended for 9–26-year-olds; consider in 27 years and older with ongoing risk; strongly consider for men who have sex with men regardless of age.

Active vaccine	New NACI recommendation
Influenza	<ul style="list-style-type: none"> • Egg allergy is not a contraindication. • <u>Children</u>: 0.5 mL dose is recommended for children when the intramuscular products are used; live attenuated intranasal vaccine is preferentially recommended for some age groups; see <i>Guide</i> for details. <p>For up-to-date information on influenza immunization, please review the most recent version of the annual influenza statement.</p>
Measles mumps rubella	<ul style="list-style-type: none"> • Chapters clarify who is considered immune, including health care workers, military personnel, students in post-secondary educational settings, and travellers. • Health care workers and military personnel require two doses of measles and mumps vaccine, regardless of year of birth, to be considered immune.
Meningococcal	<ul style="list-style-type: none"> • If vaccinated as infants with meningococcal C vaccine, another dose is recommended in the second year of life (12–23 months). • The use of quadrivalent conjugate meningococcal vaccines is reviewed. <p>High risk due to medical conditions</p> <ul style="list-style-type: none"> • Expanded to include terminal complement inhibitor eculizumab (Soliris™). • Others include functional or anatomic asplenia, including that associated with sickle cell disease; congenital properdin, factor D, or primary antibody deficiencies; consider in HIV, especially if congenitally acquired. • For high-risk children < 2 years of age, Men-C-ACYW-135-CRM (Menveo) is the recommended product. For those 2 years and older, any quadrivalent conjugate meningococcal vaccine can be used. Number of doses depends on age. For those 12 months and over, two doses given 8 weeks apart is now recommended. <p>High risk due to exposures</p> <ul style="list-style-type: none"> • Travellers; laboratory workers with potential routine exposure to meningococci; military personnel during recruit training and during certain deployments. • For 2 years of age and over, one dose of any quadrivalent conjugate meningococcal vaccine. • For children < 2 years of age, Men-C-ACYW-135-CRM (Menveo) is the recommended product; two or more doses recommended depending on age. <p>Boosters</p> <p>If at ongoing high risk because of medical condition or exposure, a booster is recommended:</p> <ul style="list-style-type: none"> • Every 3–5 years, if < 7 years old at last vaccination • Every 5 years, if 7 years or over at last vaccination <p>Recommendations are provided for post-exposure revaccination of those previously vaccinated.</p>

Active vaccine	New NACI recommendation
Pertussis	<p>Preschool booster at 4–6 years of age</p> <ul style="list-style-type: none"> • Either DTaP-IPV or Tdap-IPV can be used. <p>Adult dose</p> <ul style="list-style-type: none"> • One dose of pertussis-containing vaccine (Tdap) if not previously vaccinated in adulthood. • Tdap can be given after previous Td without delay. <p>Pregnancy</p> <ul style="list-style-type: none"> • One dose of Tdap can be offered to pregnant women (26 weeks' gestation or over) who have not previously been vaccinated against pertussis in adulthood. • In special circumstances, e.g. regional outbreaks, Tdap may be offered to pregnant women (26 weeks' gestation or over) irrespective of previous immunization.
Pneumococcal	<p>Chapter includes updated vaccination schedules and recommendations for the use of Pneu-C-13 (Pneumovax[®]13).</p> <p>Pneu-C-13 is recommended for the following:</p> <ul style="list-style-type: none"> • Children < 59 months of age who have never received conjugate pneumococcal vaccine • High-risk children < 18 years of age who have never received Pneu-C-13 • Adults with immunocompromising conditions <p>Number of doses is dependent on age; those 2 years and over receive only one dose, except for those who are post-HSCT, for whom a three-dose schedule is recommended. Polysaccharide vaccine is also recommended for high-risk children 2 years of age and over after receipt of PCV 13.</p> <p>Definitions of high-risk and immunocompromising conditions are provided in the <i>Guide</i>. Catch-up schedules for those < 59 months of age who have received another conjugate pneumococcal vaccine, but not Pnevax 13, are provided in the <i>Guide</i>.</p>
Poliomyelitis	<ul style="list-style-type: none"> • Adults should be vaccinated if not previously vaccinated. • Priority for people at risk, such as travellers possibly exposed to someone excreting polio virus; others should be vaccinated when they need a primary tetanus series or tetanus booster.
Rabies	<ul style="list-style-type: none"> • A four-dose schedule (instead of five) is recommended for post-exposure management for those who are not immunocompromised and not taking anti-malarial prophylaxis. Give on day 0 (first dose), 3, 7, and 14. • If immunocompromised or taking anti-malarial prophylaxis, give five doses on day 0 (first dose), 3, 7, 14, and 28. • Post-exposure management based on risk assessment. Factors to consider provided in the <i>Guide</i>.

Active vaccine	New NACI recommendation
Rotavirus	<p>New chapter: Since mid-2006, two live, oral rotavirus vaccines have been authorized for use; one requires three doses and the other requires two doses.</p> <ul style="list-style-type: none"> For both products, the first dose should be given before 14 weeks and 6 days of age and the last dose before 8 months of age. Intussusception is recognized as a rare adverse event following rotavirus vaccination.
Travel vaccines	<p>Japanese encephalitis vaccine</p> <ul style="list-style-type: none"> New inactivated vaccine (Ixiaro) for 18 years and over. <p>Yellow fever</p> <ul style="list-style-type: none"> Classification of countries into risk levels. Probable transmission during breastfeeding reported. <p>Tick-borne encephalitis</p> <ul style="list-style-type: none"> New chapter has been added to the <i>Guide</i>.
Varicella	<ul style="list-style-type: none"> Two doses recommended for susceptible individuals of all ages. Use of MMRV vaccine outlined in the chapter. Chapter outlines who is considered immune. Adults 50 years of age and older can be considered immune unless known to be susceptible on the basis of previous laboratory testing; health care providers and those born in or after 2004 require a health care provider diagnosis of chickenpox, two documented doses of varicella vaccine or laboratory-confirmed disease, or immunity (this is currently under review by NACI). Minimum intervals between varicella-containing vaccines identified.

Conclusion

The *Canadian Immunization Guide* is a trusted and reliable resource for immunizers in Canada. Part 4 of the *Guide* on active vaccines has been updated to incorporate new science and practices and reflects recent recommendations by NACI. NACI and the Public Health Agency of Canada are committed to providing this information in an easily accessible, reader-friendly format through timely and ongoing updates of the on-line version.

References

- (1) National Advisory Committee on Immunization. 2014; <http://www.phac-aspc.gc.ca/naci-ccni>
- (2) National Advisory Committee on Immunization. Part 4: Active vaccines. In: *Canadian Immunization Guide*. 2014; <http://www.phac-aspc.gc.ca/publicat/cig-gci/>

Acknowledgements

The authors would like to thank the extremely dedicated members of NACI who devoted considerable time and effort to revising the *Guide* as well as the excellent Public Health Agency of Canada staff who have supported the revision process.

Conflict of Interest

No conflicts of interest to declare.

CATMAT correction on its *Statement on Pregnancy and Travel*. CCDR 2010:36:ACS-2

Correction

The *Statement on Pregnancy and Travel* by the Committee to Advise on Tropical Medicine and Travel (CATMAT) (1) published in March 2010, contained incorrect information. It suggested in the text that Diclectin – a doxylamine-pyridoxine delayed release combination pill – had been studied in over 200,000 pregnant women and, in Table 4, indicated there was good evidence to support its use for motion sickness in pregnant women.

In the text under the sub-heading of Motion Sickness, it should have noted: “Diclectin has not been shown to increase the risk of teratogenicity. Its use for motion sickness is off-label and based on expert opinion.” Likewise in Table 4, the recommendation “Diclectin can be used during pregnancy to prevent and treat motion sickness.” should be given a Category C for strength of evidence (i.e. poor evidence to support a recommendation for or against use) and a Grade III for quality of evidence (i.e. Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees).

In a further paragraph in the motion sickness section, a statement regarding the lack of teratogenicity of various H1 antagonists and phenothiazines was incorrectly attributed to the Motherisk Program at the Hospital for Sick Children in Toronto and an incorrect reference was used. The attribution should be removed and the correct reference for this sentence is Mazzotta P, & Magee LA. A risk-benefit assessment of pharmacological and nonpharmacological treatments for nausea and vomiting of Pregnancy. *Drugs*. 2000;59 (4): 781-800.

Reference

(1) Committee to Advise on Tropical Medicine and Travel. *Statement on Pregnancy and Travel*. *Can Comm Dis Rep* 2010:36:ACS-2.

<http://www.publications.gc.ca/site/eng/367605/publication.html>

Citation

Committee to Advise on Tropical Medicine and Travel. CATMAT correction on its *Statement on Pregnancy and Travel*. *CCDR* 2010:36: ACS-2. *CCDR* 2014; 9:159.