Measles Elimination in Canada

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To describe the progress and challenges in achieving measles elimination in Canada, we analyzed national data on measles cases for 1998–2001. To assess the status of measles elimination in Canada, we estimated the effective reproductive number, \( R \). Measles elimination was defined as the interruption of endemic transmission and failure to reestablish endemic transmission after importation. Twelve isolated cases, 29 cases (72.4% were linked to 2 outbreaks), 199 cases (96.9% were linked to 4 outbreaks of 2, 6, 30, and 155 cases), and 34 cases (73.5% were linked to 8 outbreaks of 2, 2, 2, 3, 3, 3, and 8 cases) were reported in 1998, 1999, 2000, and 2001, respectively. \( R \) ranged from 0.58 to 0.95. Multiple chains of transmission occurred in religious communities that actively oppose or resist immunization efforts. Epidemiological and virological evidence suggests that endemic transmission of measles has been mostly interrupted since 1998.

Measles elimination has been a recommended national objective in Canada for >2 decades. In 1980, the National Advisory Committee on Immunization stated that the goal of elimination of indigenous measles was important and desirable [1]. In 1994, the Canadian Ministry of Health joined other Pan American Ministries of Health to set a target of measles elimination in the Western Hemisphere by 2000 [2]. Here we describe the progress and challenges in achieving this goal, with a focus on the period 1998–2001.

HISTORY OF MEASLES IN CANADA: 1924–1997

Measles has been a reportable disease in Canada since 1924, with the exception of a period from 1958 to 1969, during which time measles was not nationally reportable. In the prevaccine era, measles occurred in 2- to 3-year epidemic cycles (figure 1). The highest incidence was reported in 1935, with >83,000 cases (770/100,000 population). Deaths from measles complications were very common in the early 1900s; in 1926, there were 892 measles-associated deaths, the highest ever reported [3]. Live measles vaccine was licensed in Canada in 1963, and by the early 1970s, publicly funded 1-dose immunization programs, routinely given at 1 year of age, had been introduced across Canada [4]. Before 1970, killed measles vaccine was used in 2 provinces. In 1970, this practice was discontinued when it was determined that this vaccine could cause atypical measles syndrome [4]. Revaccination with the live attenuated vaccine was subsequently recommended [5].

No reliable national estimate of vaccine coverage was available until 1993. From available provincial data, it appears that measles vaccine was not used widely until the early 1970s, but national coverage was assumed to be >85% by the late 1970s [6]. In the late 1980s, after “catch-up” immunization of school entrants, immunization coverage ranged from 95% to 100% [7]. However, despite virtually 100% documented 1-dose coverage in some regions, large outbreaks of measles involving thousands of cases persisted, mostly in school-aged children [8, 9]. From 1990 to 1997, the number of cases reported annually ranged from 204 (1993) to 6178 (1991), with a median of 808 cases and an average of 1745 cases (6.1/100,000 population). An increasing proportion of cases occurred among older children or young...
Figure 1. Measles cases in Canada by year since 1924 (measles not nationally reportable 1959–1968).

adults who had received only 1 dose of measles vaccine. Clearly, because of primary vaccine failure, Canada’s 1-dose program was insufficient to interrupt endemic transmission.

In 1992, participants at a national consensus conference on measles endorsed the goal of measles elimination and set a target date of 2005. The major change in the measles elimination strategy was the recommended addition of a routine second dose of measles vaccine before school entry [10]. In 1995, Canada was the only country in the region of the Americas that had not added a second dose or catch-up program to the routine 1-dose immunization program. That year, with only 3.6% of the population of the region, Canada recorded 2362 cases of measles, which represented 40% of all reported cases in the region [10]. This discrepancy was largely due to individuals who lacked protection after 1 dose of vaccine given at 12 months of age. In 1996–1997, in response to this relatively high measles incidence, 2-dose measles vaccine schedules were adopted across the country, and catch-up campaigns involving school-aged children and adolescents were completed in most jurisdictions. Enhanced measles surveillance was introduced. A national Working Group on Measles Elimination (WGME) was established to oversee measles elimination activities, to review cases, and to recommend modifications to prevention and control strategies. These included achieving and maintaining the highest possible population immunity by providing 1 dose of measles-mumps-rubella (MMR) vaccine at 1 year of age or as soon as possible thereafter and a second dose of MMR before school entry (at age 18 months or 4–6 years); enhancing surveillance to ensure that cases are investigated thoroughly (by epidemiological, serological, and molecular methods); and promptly responding to cases and outbreaks by identifying and immunizing susceptible persons who are exposed to measles or at risk of exposure to measles.

Although the total absence of cases is the general understanding of elimination, this is not achievable in the absence of global eradication. Most importations from countries with less control over measles are not preventable, and secondary spread should be expected unless everyone is fully protected. However, if high population immunity is maintained, secondary transmission will quickly cease [11]. To assess our progress toward elimination, our working definition of elimination was the interruption of endemic measles transmission and failure to reestablish endemic transmission after importation. Here we describe the epidemiological observations between 1998 and 2001 and assess the status of measles elimination in Canada.

METHODS

We analyzed epidemiological data on individual cases and outbreaks obtained from the national Notifiable Disease Reporting System and enhanced measles surveillance system from 1998–2001. Data on all case and outbreak reports are received on a weekly basis from provincial and territorial health departments and are reviewed, collated, and analyzed by the Division of Immunization and Respiratory Diseases, Health Canada. All case and outbreak reports are reviewed annually by the WGME. Although all suspected cases of measles are investigated by local public health authorities in Canada, generally only confirmed cases are reported nationally. Confirmed cases of measles require laboratory confirmation of infection in the absence of recent immunization with measles-containing vaccine as follows: isolation or detection of measles virus from an appropriate clinical specimen, seroconversion or significant rise in measles-specific antibody titer between acute and convalescent sera, or positive results of serological testing for measles IgM antibody by means of a recommended assay [12]. In the absence of an epidemiological link or if the clinical presentation is inconsistent with a diagnosis of measles, IgM results must be confirmed by additional testing with either isolation or seroconversion from acute to convalescent sera. Measles serology is done in 17 laboratories across Canada. Measles virus genotyping is carried out at the National Microbiology Laboratory, Winnipeg [13].

For this analysis, only confirmed cases were used. Case reports include demographic and geographic data, date of onset, diagnostic status (laboratory confirmed or epidemiologically linked), outcome, immunization history, and exposure-related data. Cases are defined as imported, importation-related, or unknown-source. An imported case is one that occurs in a patient exposed outside Canada, with rash onset occurring within 7–21 days of entering Canada; illness cannot be linked to local transmission. An importation-related case is one that is linked to an imported case but acquired in Canada. An unknown-source case is a case of measles acquired in Canada, unrelated to an imported case or for which a linkage could not be established despite investigation. Data obtained from the molecular epidemiology of measles virus isolated from cases are used to provide additional information concerning the
probable source of measles importation [12, 13]. Outbreaks are defined as the occurrence of ≥2 linked cases.

To assess the status of measles elimination in Canada during 1998–2001, we estimated the effective reproduction number, \( R \). \( R \) is the average number of cases spread from an individual case and is a summary measure of the epidemic potential in a particular population [11, 14, 15]. \( R \) was estimated according to the proportion of cases imported (\( R = 1 – \) proportion of cases imported) and from the distribution of outbreak sizes [11]. The values of \( R \) were estimated by maximum likelihood based on the Borel-Tanner distribution. Approximate 95% confidence intervals were calculated by use of the profile likelihood. For the calculations based on the proportion of imported cases, the confidence intervals were truncated at a value of 1, because the method is conditional on outbreaks becoming extinct. Cases were grouped into chains of transmission on the basis of links found during the investigations. Chains in which the source of importation was identified were classified as importation-related, whereas others were of unknown source.

**RESULTS**

Since the introduction of routine 2-dose programs and catch-up campaigns in 1996–1997, the average annual incidence of measles has declined by 96% compared with 1990–1997. Multiple chains of transmission have occurred exclusively in low-coverage religious communities that either oppose or resist immunization. Cases and outbreaks are described below.

Twelve cases (0.04/100,000 population) of measles were reported in 1998; all were laboratory-confirmed and verified by the WGME. This was the lowest number of cases ever recorded in Canada and compares with 581 cases (1.9/100,000 population) in 1997. Ages of case patients ranged from 9 months to 33 years (median, 5 years). Five case patients had no history of measles vaccination, 2 were vaccinated before their first birthdays, 4 had received 1 appropriately timed dose, and 1 had received 2 doses. Five cases were found to be imported, and in the remaining 7 cases, despite investigation, the source of infection was unknown.

Twenty-nine cases (0.09/100,000 population) of measles were reported in 1999; 21 (72.4%) were associated with 2 small outbreaks (table 1). The first outbreak, involving 4 cases, began with a visitor from the Netherlands who developed measles on 30 July 1999, immediately after his arrival in Canada. Three secondary cases (his 21-year-old sister and her 2 children, aged 23 and 11 months), occurring over 2 generations, were reported. All case patients were unimmunized and belonged to a religious community that opposes immunization. It was later learned that the index case patient had visited an area of the Netherlands in which an outbreak of measles was occurring [16]. The second outbreak, involving 17 cases—3 generations—occurred in another Canadian province in the same religious community.

**Table 1. Distribution of outbreak size and estimates of the reproduction number, \( R \), for measles in Canada according to the proportion of imported cases and outbreak size.**

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<td>Total no. of cases</td>
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<td>Percentage of imported cases</td>
<td>42 (5/12)</td>
<td>28 (8/29)</td>
<td>5 (10/199)</td>
<td>3 (13/34)</td>
<td>13 (36/274)</td>
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<td>( R ) (95% CI) according to % of imported cases</td>
<td>0.58 (0.25–1)</td>
<td>0.72 (0.46–1)</td>
<td>0.95 (0.82–1)</td>
<td>0.62 (0.39–0.92)</td>
<td>0.87 (0.76–0.98)</td>
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<td>Outbreak size</td>
<td>All chains</td>
<td>0 (0–0.17)</td>
<td>0.66 (0.40–1.00)</td>
<td>0.95 (0.82–1.09)</td>
<td>0.50 (0.30–0.78)</td>
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<td>Chains with known source of importation</td>
<td>0 (0–0.39)</td>
<td>0.70 (0.43–1.07)</td>
<td>0.95 (0.82–1.09)</td>
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community that opposes immunization. This outbreak began after a mother and her 3 children returned to Canada from the Netherlands. Measles virus from this outbreak was isolated and determined to be of genotype D6 [13]. In addition to these outbreaks, 8 sporadic cases were reported, 6 in persons exposed outside Canada (India, Indonesia, Japan [2], Pakistan, and the Philippines). For the remaining 2 cases, the source of infection was unknown.

In 2000, 199 cases were reported; 4 outbreaks (2, 6, 30, and 155 cases) accounted for 96.5% of all cases reported (table 1). The 2-case outbreak involved a 7-month-old infant who had traveled to Pakistan and who was hospitalized in Canada with undiagnosed measles. The epidemiologically linked case occurred in a hospitalized 14-month-old child whose measles immunization had been delayed because of an illness. The 6-case outbreak spanned 6 weeks. All case patients were unimmunized and reported philosophical objections to immunization. The index patient, a 14-year-old girl, visited Mazatlan, a tourist area in Mexico, during 10–24 March 2000. She started to develop rash on 8 April. The family did not seek medical attention but the girl was kept home from school. The first generation of spread in Canada included 2 cases, with rash onsets on 18 and 22 April. These cases occurred in the 11-year-old sister and a 14-year-old contact of the girl. The second generation of spread resulted in a case in the index patient’s 18-year-old sibling, who lives in another town and who became ill on 1 May. In the third generation of spread, the 18-year-old’s 2 roommates (noninstitutional) became ill with rash onsets on 13 and 15 May. Both roommates were 21-year-old women. One of the roommates went to the emergency ward of a nearby hospital, which notified the local health department. This was the first patient in this cluster to receive medical attention and, thus, this was the first case to be reported to public health. Health Canada immediately notified the Pan American Health Organization (PAHO). After the chain of transmission was traced back to the index case patient who had visited Mazatlan, no measles activity potentially linked to the index case was identified in Mexico. Direct detection of measles virus in nasopharyngeal and urine specimens by reverse transcriptase–polymerase chain reaction was done, and the virus was determined to be of genotype D7 [13]. Importantly, the genotyping results indicated no genetic similarities with the D6 measles strain found in South America.

The third outbreak in 2000, involving 155 cases in a religious community that resists immunization, began in Alberta and later spread to the same religious community in British Columbia. Case patients ranged in age from <1 year to 34 years (median, 7.3 years). Children aged <10 years accounted for 59% of the cases, including 8 infants. The outbreak started on 21 May, peaked in September, and lasted until 9 October, a span of 20 weeks, ~10 generations. The index case patients were 2 unimmunized siblings, aged 2 and 3 years, with rash onsets on 21 and 25 May. The children had traveled with their parents to an affiliated religious community in Bolivia and returned to Canada on 11 May. Members of this Canadian religious community frequently travel to Bolivia to visit affiliated communities. Several closely linked families in the religious community in Canada were involved in this outbreak. Two families from the measles-affected Alberta religious community and 1 family from the affiliated Bolivian community attended a large social gathering in British Columbia on 13 June. After the gathering, 4 families in the British Columbia religious community developed measles, with subsequent spread to other families in the same community. Measles virus isolates were obtained from both the Alberta and British Columbia communities and were determined to be identical to the D6 strain circulating in South America [13]. On 1 June 2000, in the absence of preexisting measles activity in this area of Canada, Health Canada notified PAHO of the Canadian outbreak. Investigation by the Bolivian Ministry of Health, assisted by the PAHO, led to the tracing of the source of exposure to affiliated communities in the Santa Cruz area of Bolivia, where >60 cases were identified. [17].

The fourth outbreak in 2000, involving 30 cases, occurred in several families belonging to another semiclosed religious community in Quebec (population, ∼2500). Case patients ranged in age from 7 months to 33 years (median, 5.5 years). Children <10 years of age accounted for 21 cases (70%), including 3 infants. The outbreak started on 8 May and lasted until 9 August, a span of 13 weeks—6 generations. Screening of school records of 200 students in the community indicated that only ∼75% had received 1 dose of measles vaccine, whereas about half had received 2 doses of measles vaccine. Genotyping results from this community indicate that the virus was of genotype D6, a strain commonly found in Europe and South America [13]. It was reported that this community often received visitors and students from affiliated communities outside Canada, most recently from Belgium and New York. In February–March 2000, an outbreak of 8 cases in New York was linked to an outbreak in the United Kingdom [18].

Thirty-four cases (0.1/100,000 population) of measles involving 4 provinces were reported in 2001; 25 cases (73.5%) were associated with 8 small outbreaks, ranging in size from 2 to 8 cases (table 1). Case patients ranged in age from 5 months to 38 years (average, 18.5 years). Some cases in these outbreaks involved unimmunized siblings following household exposure. Seven case patients (20.6%) had a documented history of having received 1 dose of measles vaccine, and 3 (8.8%) were infants <1 year old, too young to be eligible for routine measles vaccination. At least 7 case patients required hospitalization or an emergency ward visit. The first outbreak, involving 8 cases, began with a 15-year-old unvaccinated foreign-born student
who developed measles on 15 January 2001, 6 days after returning to Canada after a holiday trip to his native country (Korea). He attended a school of ~750 students and lived in a community with a number of families who oppose immunization for philosophical reasons. This index case patient, who did not seek medical attention, was identified retrospectively after several contacts who developed measles sought medical attention. Seven secondary cases occurred, all involving school students 12–15 years of age. The outbreak lasted 24 days—2 generations. Measles virus was genotyped as H1, which is a strain found in Korea [13]. In addition, outbreaks involving 2–3 cases occurred after importations from the following countries: Singapore (3 cases in Ontario, genotype H1), Germany (3 cases in Alberta, genotype D5), New Zealand (3 cases in Alberta, genotype D5; 2 cases in British Columbia), and Pakistan (2 cases in British Columbia) [13]. For the remaining 2 outbreaks, the source was unknown (2 cases in Ontario and 2 cases in Alberta). In addition to these outbreaks, 9 sporadic cases were reported, 7 in patients exposed outside of Canada (Belgium, Germany, India, Korea or Japan, Pakistan, the Philippines, and the United States). For the remaining 2 single cases, the source of infection was unknown. Overall, 3 different genotypes of measles viruses were identified as associated with importation in Canada in 2001—H1, D3, and D5 [13].

In summary, between 1998 and 2001, Canada had a total of 36 chains of transmission with a known source of importation and 13 with no source identified (table 1). The distribution of outbreak size is bimodal, with 35 isolated cases and 3 outbreaks involving >15 cases. Although all case chains in 2000 were found to be linked to importation, the source was unknown for 7, 2, and 2 isolated cases in 1998, 1999, and 2001, respectively. The proportion of reported cases that were imported decreased from 42% to 5% between 1998 and 2000 and increased to 38% in 2001. The lower proportion of imported cases in 1999–2000 was mainly due to the 3 large outbreaks in low-coverage religious communities. R estimated for 1998–2001 from the proportion of imported cases was 0.87, whereas R was 0.82–0.86 as determined by outbreak size. In 2000, given the very large outbreak, these values were nearly 1. The distribution of outbreak size between 1998 and 2001 did not fit the theoretical distribution expected for an R of 0.85 [11] (figure 2). With this value of R, 42% of importations would lead to no secondary spread; however, this happened in 67% of chains (24/36) with a known source of importation. The lack of fit between the observed and predicted distribution of outbreak size indicates a clustering rather than homogenous distribution of susceptible persons in the population.

**DISCUSSION**

Epidemiological and virological evidence to date suggests that endemic transmission of measles has been mostly interrupted. This evidence is supported by the measles virus genotyping data, which show that a number of different genotypes have been detected in Canada since 1998. Furthermore, almost all reported cases have been imported or importation-related. Import cases have occurred in foreign visitors to Canada and Canadian residents exposed to measles while abroad. Of the 36 incidents reported in Canada during 1998–2001 for which the source of importation was known, only 6 resulted in transmission involving >4 cases. Long chains of transmission have occurred exclusively in religious communities that actively oppose or resist immunization efforts. Despite imported cases and outbreaks in certain religious communities that continued for several generations, the absence of spillover into the general population supports our belief that immunization coverage in the general population is high and that population immunity is more than adequate to prevent reestablishment of endemic transmission. However, limited interaction between these communities and the general population may also have been a factor in the limited spread. Regardless, it is recognized that measles elimination will persist only if 2-dose measles vaccine coverage is maintained at near 100% levels.

The presence of a few cases of unknown source and exclusion of unconfirmed cases illustrates that not all cases have been reported. Although it is theoretically possible that a chain of endemic transmission involving a few cases has not been identified, we believe that this can be ruled out, because cases with an unknown source were rare after 1998 and were identified throughout the country, and no single genotype is evident [13]. Furthermore, the reduction in cases of unknown source since 1998 may suggest that surveillance improved over time and that few cases were missed. Finally, a survey of all laboratories in Canada that perform measles IgM testing indicated that 6586
tests for measles IgM were done in 1998 and 1999, respectively. This approximates the total number of suspected measles cases in 1998 and 0.95 in 2000. Although this latter value would normally signal a near return to sustained transmission, this was not the case. A basic assumption of this method is the random distribution of susceptible individuals in the population. This assumption can be assessed by the distribution of outbreak sizes [11]. In contrast to the United States, where importation-related outbreaks followed the predicted outbreak size distribution with no prolonged disease transmission [15], in Canada the distribution was bimodal, with most importations followed by no transmission, a few importations leading to large outbreaks, and almost nothing in between. This and the fact that the theoretical distribution of outbreak size for an R of 0.86 does not fit the observed data indicates heterogeneity in the population, with clusters rather than an even distribution of susceptible persons, and an overestimate of R. In the general population, the immunity is very high and R very low (~0.50–0.60), but this does not prevent transmission in clusters of persons opposed to immunization. Whereas it may be tempting to discard the approach of estimating R because of this caveat, the comparison of the theoretical and actual outbreak size distribution is a robust way to determine whether the epidemiological situation is driven by clusters of susceptible persons rather than by a more generalized problem, information that is critical to designing an appropriate intervention.

Improving vaccine uptake in low-coverage religious communities in Canada has been challenging. Although some actively oppose immunization, others maintain low-level resistance or are not aware of its importance. Community leaders and members need to be advised that they often are at greater risk of importation of diseases such as measles because of frequent travel between affiliated communities in different countries. Furthermore, they are often members of large, closely knit families—an environment that facilitates measles transmission and that necessitates extremely high coverage rates. Although public health access to these communities is often limited, some have responded to special approaches, such as obtaining endorsement of immunization by religious leaders. These outbreaks remind us of the need to establish good working relationships with these communities to ensure rapid sharing of information on disease activity and acceptance of recommended public health interventions. They also remind us of the importance of prompt international dissemination of information about outbreaks of vaccine-preventable disease and of effective methods to reach special groups, such as these religious communities, to improve immunization coverage.

In 2000, Canadian residents took 4.5 million trips overseas; overseas visitors (nonresidents) made an additional 4.4 million trips into Canada (M. Campbell, Statistics Canada, 2001, personal communication). Clearly, importation of measles by susceptible Canadian residents and foreign visitors will continue to occur until global eradication has been achieved. Health Canada recommends that international travelers should have up-to-date routine immunizations. Two documented doses of measles vaccine are recommended for all international travelers aged ≥1 year who were born after 1970, unless there is serological proof of immunity or physician documentation of prior measles [2]. Monovalent measles vaccine should be given to infants ≥6 months of age when traveling abroad [2]. There are currently no vaccination requirements for immigrants, refugees, or visitors to Canada, but all Canadian residents have access to publicly funded measles vaccine.

The recent history of measles in Canada illustrates the continuing challenges of maintaining disease elimination in the absence of global eradication. Although our progress is cause for quiet celebration by Canadian parents, public health practitioners, clinicians, and policy makers, it is also cause for introspection. It reminds us of some of our challenges—conducting effective disease surveillance, mounting rapid responses to cases and outbreaks, and measuring and maintaining high, broad-based 2-dose coverage rates. Sustaining our success will require innovation and continued international cooperation and political will. All this occurs in an environment in which perceived and real vaccine safety issues are now more visible than the disease itself. Epidemics, after all, may be only a plane ride away. Elimination, unless we sustain vaccine coverage, is potentially here today and gone tomorrow.

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