MAJOR ARTICLE

Largest Measles Epidemic in North America in a Decade—Quebec, Canada, 2011: Contribution of Susceptibility, Serendipity, and Superspreading Events

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Background. The largest measles epidemic in North America in the last decade, occurred in 2011 in Quebec, Canada, where rates of 1- and 2-dose vaccine coverage among children 3 years of age were 95%–97% and 90%, respectively, with 3%–5% unvaccinated.

Methods. Case patients identified through passive surveillance and outbreak investigation were contacted to determine clinical course, vaccination status, and possible source of infection.

Results. There were 21 measles importations and 725 cases. A superspreading event triggered by 1 importation resulted in sustained transmission and 678 cases. The overall incidence was 9.1 per 100 000; the highest incidence was in adolescents 12–17 years old (75.6 per 100 000), who comprised 56% of case patients. Among adolescents, 22% had received 2 vaccine doses. Outbreak investigation showed this proportion to have been an underestimate; active case finding identified 130% more cases among 2-dose recipients. Two-dose recipients had milder illness and a significantly lower risk of hospitalization than those who were unvaccinated or single-dose recipients.

Conclusions. A chance superspreading event revealed an overall level of immunity barely above the elimination threshold when unexpected vulnerability in 2-dose recipients was taken into account. Unvaccinated individuals remain the immunization priority, but a better understanding of susceptibility in 2-dose recipients is needed to define effective interventions if elimination is to be achieved.

Keywords. measles; epidemic; underreporting; surveillance; outbreak; elimination.

In 1995, Canada and other countries of the Americas adopted a measles elimination goal [1, 2]. Toward this goal, mass immunization campaigns targeting children aged 1–17 years old were conducted in Canada in 1996–1997 to provide a second dose of a measles-containing vaccine. A routine pediatric 2-dose measles-mumps-rubella (MMR) schedule was also introduced at that time [1, 2]. The incidence of measles per 100 000 rapidly declined in Canada, from 8.03 in 1995 to 0.65 in 2000 [3]. Between 2001 and the end of 2010, 360 cases were reported, with an annual incidence varying between 0.02 and 0.31 per 100 000 [4]. Three outbreaks involving ≥10 cases were reported during that period: 2007 (Quebec 94 cases), 2008 (Ontario 56 cases), and 2010 (British Columbia 82 cases) [3–5].

In 2011, Canada experienced several measles importations—mostly from Europe, where >30 000 cases had been reported [6]. Although these imported cases were generally followed by limited or no secondary transmission, 1 triggered the largest epidemic in North America since 2001. This epidemic occurred in

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the province of Quebec (total population 7.9 million) where the last major outbreak (>10 000 cases) had occurred in 1989 when the program included only 1 dose of vaccine administered at 12 months of age [7]. In 1996, a school-based mass immunization campaign was conducted during which 89% of children 5–17 years old received a second measles dose. That same year, a routine 2-dose program was introduced with a schedule of administration at 12 and 18 months of age. Although immunization is voluntary and there are no vaccine requirements for school enrolment in Quebec, provincial vaccine coverage surveys conducted in 2006, 2008, and 2010 consistently showed that by 24 months of age, approximately 96% of children had received 1 dose and approximately 85% had received 2 doses of measles vaccine, increasing to 97% and 90%, respectively, by 28 months of age [8–10]. With additional first and second doses administered between 28 and 59 months of age, population measles vaccine coverage is even higher by school entry. Against this background of high immunization coverage, we describe key epidemiological features of the 2011 epidemic in Quebec and highlight observations that may be applicable in the broad context of measles elimination.

METHODS

Setting

Measles is notifiable by Quebec physicians and laboratories. According to the national surveillance case definition, measles cases are either laboratory confirmed or epidemiologically linked [11]. Laboratory confirmation is defined virologically by culture or polymerase chain reaction or serologically by measles-specific immunoglobulin M (IgM). Cases in patients with fever ≥38.3°C (101°F) *and* cough or coryza or conjunctivitis *and* a generalized maculopapular rash for ≥3 days with an epidemiological link to a laboratory-confirmed case are considered epidemiologically linked. Reported cases were investigated by a public health practitioner for information on the clinical course of disease, vaccination status, and possible source of infection.

Since vaccine coverage rates were thought to be high enough to block sustained transmission [12], public health interventions in this outbreak focused on administering immunoglobulin to persons at higher risk of measles complications (unprotected pregnant women, infants, and immunocompromised patients). Unvaccinated contacts were offered immunization but large-scale supplementary vaccination efforts were not deployed, and there was no school exclusion policy for incompletely immunized children.

Vaccination

Case vaccination status was determined by written record. Products and schedules were per the provincially determined Quebec program for which MMR II (Merck Canada) was the only vaccine used from 1996–2008, replaced in 2008 by the GSK vaccines Priorix (MMR) and Priorix Tetra (MMR-varicella). A monovalent measles vaccine (Connaught Laboratories) was used in the 1996 school-based, second-dose campaign.

Underreporting

Underreporting was estimated in the school at the origin of this epidemic by dividing the number of cases determined by active investigation by the number previously reported by passive surveillance alone. Active investigation included a questionnaire that was distributed and answered by students in school in a single day regarding prior measles symptoms, review of the school absenteeism registry for potential measles attribution, calls to parents to confirm student information, and serological testing of potential case patients whose symptoms did not meet national case criteria.

Statistical Analysis

Proportions were compared statistically using the χ^2 test and means by Student's *t* test.

RESULTS

Surveillance Summary

In 2011, 776 measles cases were passively reported in Quebec: 295 (38%) were laboratory confirmed, 430 (55%) were epidemiologically linked cases and 51 (7%) were clinical cases without an epidemiological link. These latter cases were excluded, leaving 725 that met the national measles case definition (including those subsequently identified through active investigation). Of these 725 confirmed cases, 678 were the result of sustained transmission after a superspreading event; the remaining 47 cases occurred as a result of importations and/or discrete, limited clusters. Among the 118 strains characterized, 116 were genotype D4, and 2 were genotype B3.

Initial Importations and Ensuing Outbreaks

There were 22 documented measles imported cases in 2011 corresponding to 19 episodes of importation; 5 cases belonged to 2 families whose members had traveled together in France and developed symptoms within 14 days upon returning. Among these episodes, 12 occurred between January and June and 7 between July and December. Measles was imported after travel to France (12 episodes), other European countries (4 episodes, including 2 where travelers transited through Paris airports), and Pakistan (1 case). As described below, the imported case at the origin of the small cluster detected in September was never identified. The index case patient for the superspreading event had traveled to the Caribbean, but, as described below, had most likely acquired measles at a Canadian airport.

Only 4 of the 21 importations resulted in outbreaks, defined as ≥2 confirmed cases, linked epidemiologically, virologically, or both. The first outbreak occurred after an affected traveler returned from France on 2 February and developed rash on 5 February. This case triggered an outbreak of 20 secondary cases with protracted transmission over 11 weeks (≥6 generations). The second importation in April caused the large outbreak (678 cases), described below. The third importation in September caused only 1 secondary case. The fourth importation occurred in late September, causing 4 secondary cases. It involved a B3 genotype virus, isolated in an adolescent from a region unaffected by the large outbreak thus distinguishing it as a separate cluster from the larger epidemic. This patient's rash began on 24 September, and the patient had neither a travel history nor reported contact with a traveler. That B3 virus was also found in another adolescent from the same school, whose rash began 6 days later. These 2 patients infected 1 schoolmate and 2 household contacts, but no further transmission was detected.

The index patient for the large outbreak was a 30–39-year-old adult who became feverish on 2 April, 9 days after returning to Canada from a 1-week holiday in the Caribbean [13]. When returning to Canada on 24 March, this individual spent several hours at the Montreal airport with thousands of fellow travelers returning from spring break. Because of the 9-day interval between the return flight and the patient's fever onset and the absence of a recognized measles contact while the patient was abroad, the Montreal airport was considered the most likely source of infection. However, no other measles cases associated with this airport were identified, and this attribution is speculative; unrecognized exposure in the Caribbean remains possible. This index case patient had received 1 dose of measles vaccine in childhood and was employed in a high school. This patient remained in contact with several groups of students for 3 days after developing nonspecific symptoms but stopped working when rash appeared (7 April). The patient sought care that day, and measles was confirmed by polymerase chain reaction. The virus was isolated from secondary cases only and identified as genotype D4. Between 17 and 23 April, 10 secondary case patients became sick in this high school, followed 7–14 days later by 61 additional cases (Figure 1). Although this school outbreak, affecting 110 students and 4 other staff members, was almost over by 20 May, further substantial transmission then ensued in the adjacent rural town (approximately 70 000 inhabitants) and surrounding area. High transmission continued until the summer recess (23 June) and decreased thereafter.

Ultimately this outbreak included 678 cases and lasted 26 weeks (7 April to 4 October). The region of the "index" high school accounted for 72% of all cases (499 of 678), the neighboring region reported 20% (135 of 678 cases), and 6 other regions in the province reported the remaining cases. Montreal was almost entirely spared, with only 4 cases linked to this outbreak.

Epidemic Features

For 2011, the overall Quebec measles incidence was 9.1 per 100 000 population. The mean age of case patients was 15 years (range, 3 months to 53 years). The incidence was highest

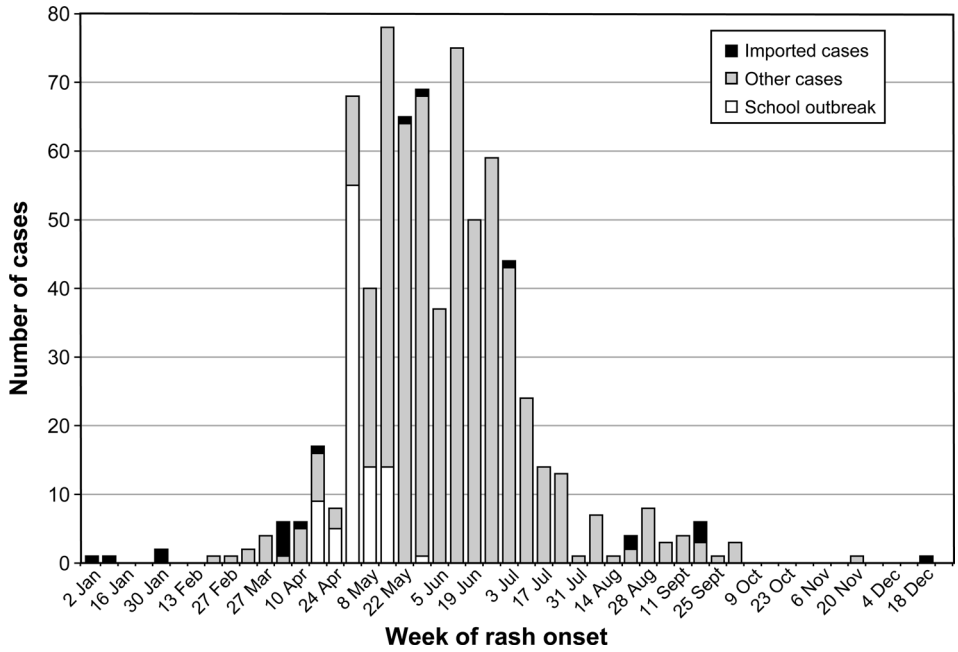

Figure 1. Numbers of all measles cases, imported cases, and cases associated with the initial school outbreak, by week of rash onset in 2011.

Table 1. Hospitalization by Age and Vaccination Status

Age, y	Cases, No.	Incidence per 100 000	Hospitalizations/Cases by Vaccination Status, No. (%)				
			Unvaccinated	1 Dose	≥2 Doses	Unknown or No Proof[a]	Total
<1	21	24.1	4/21 (19)	0	0	0	4/21 (19)
1–4	62	17.7	6/40 (15)	3/13 (23)	0/3 (0)	1/6 (17)	10/62 (16)
5–9	60	15.3	3/52 (5)	1/4 (25)	1/2 (50)	1/2 (50)	6/60 (10)
10–14	253	61.9	14/178 (8)	0/6 (0)	1/42 (2)	1/27 (4)	16/253 (6)
12–17	404	75.6	30/266 (11)	1/12 (8)	2/89 (2)	1/37(3)	34/404 (8)
15–19	223	45.6	20/128 (16)	1/9 (11)	1/51 (2)	3/35 (9)	25/223 (11)
20–29	37	3.6	4/26 (15)	3/4 (75)	0/4(0)	0/3 (0)	7/37 (19)
30–39	56	5.2	3/8 (38)	5/27 (19)	0	5/21 (24)	13/56 (23)
≥40	13	0.7	5/12 (42)	0	0	0/1 (0)	5/13 (38)
Total	725	9.1	59/465 (13)	13/63 (21)	3/102 (3)	11/95 (12)	86/725 (12)

[a] Unknown vaccination status or no written proof of vaccination.

in adolescents 12–17 years (75.6 per 100 000), and this age band comprised 56% of all case patients (Table 1; Figure 2). The incidence was 3 times lower in infants <12 months old (24.1 per 100 000) and in that same range for children up to 12 years old. Case distribution by vaccination status varied by age (Figure 3). Although only 4.1% of case patients aged 1–9 years had received 2 doses, in case patients aged 10–19 and 20–29 years, the proportions of 2-dose recipients were significantly higher, at 20% and 11%, respectively ($P < .001$). Among the 56 case patients aged 30–39 years, 48% had written proof of 1 dose (Table 1; Figure 3). All but 1 of the 13 case patients ≥40 years old were unvaccinated. According to the Canada's National Advisory Committee on Immunization, individuals born before 1970 are considered naturally immune and therefore not vaccine eligible.

Hospitalizations

Among the 21 infant case patients, 4 (19%) were hospitalized, but none had pneumonia or serious complications (Table 1). Among the 598 pediatric case patients 1–19 years old, 57 (9.5%) were hospitalized. The risk was 3% in 2-dose recipients (3 of 98 patients) but significantly higher in both unvaccinated children (10.8%; 43 of 398; $P = .02$) and 1-dose recipients (15.6%; 5 of 32; $P = .01$). In adults (≥20 years old), the overall risk of

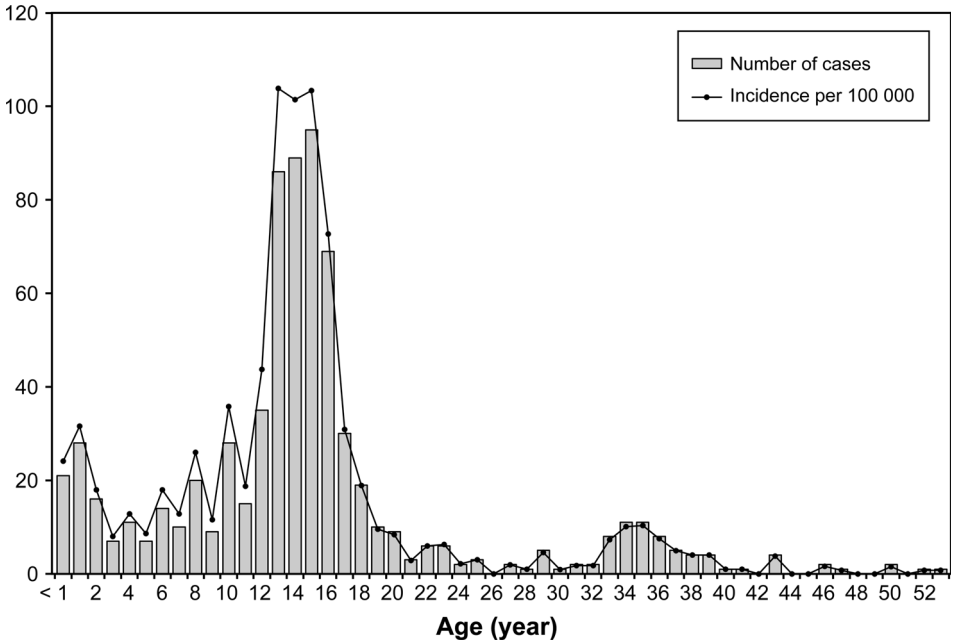

Figure 2. Number and incidence of measles cases by patient age.

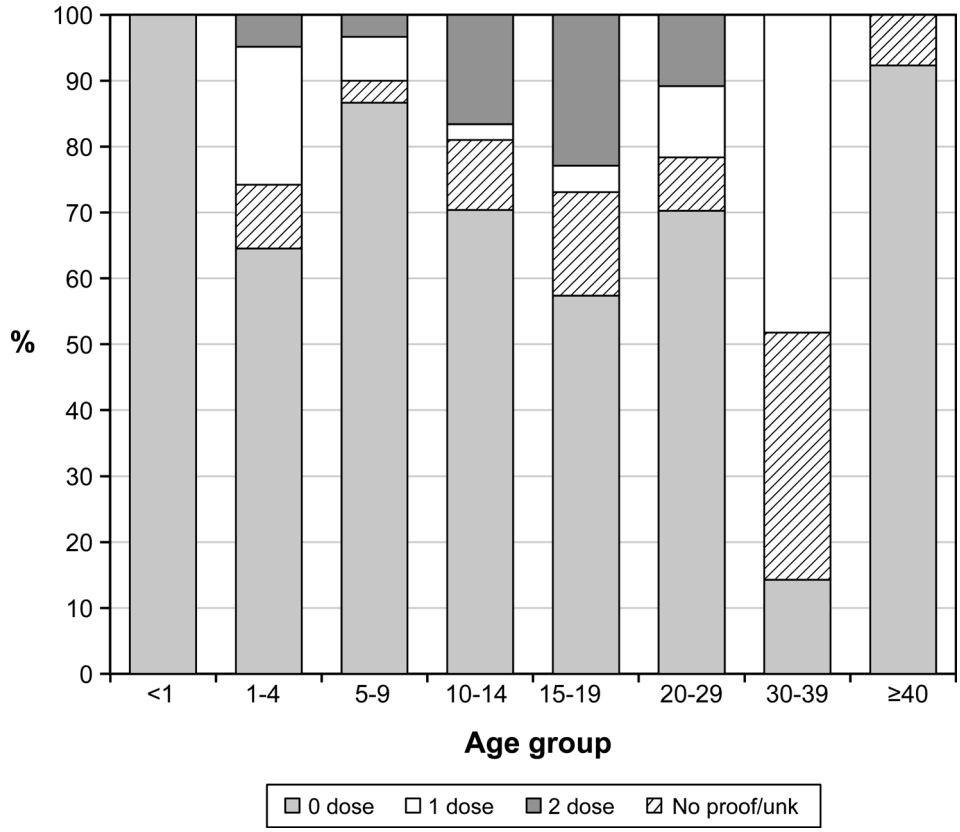

Figure 3. Vaccination status of case patients, by age group. Unknown/no proof indicates unknown vaccination status or no written proof of vaccination.

hospitalization was 24%, similar to that in unvaccinated patients (26%; 12 of 46) and single-dose recipients (26%; 8 of 31).

Exposures and Sources of Infection

Among the 725 case patients overall for the province, 84% (611 patients) reported a known source of infection; daycare or school was the most frequent source (48%), followed by household exposure (19%).(Table 2) In children <1 year old, community and daycare centers were the main sources of infection (in 29% and 24%, respectively), and household exposures accounted for only 14%. Household exposure was reported by 20% of the 106 adult case patients aged ≥20 years. Exposure in healthcare settings was reported by 3% (16 patients and 3 healthcare workers). Eight additional healthcare workers were infected; no source could be identified in 5, and 3 had community exposure.

Estimation of Underreporting

Because of documented transmission in healthcare settings, case patients in the neighboring rural town and surrounding area were instructed as of 6 May to consult a physician only if their condition was deteriorating and otherwise to avoid emergency rooms or medical clinics. This strategy resulted in underreporting, which was assessed in the outbreak school. In that school before the investigation, 77 cases had been reported through passive surveillance (Table 3). The investigation identified 21 more cases meeting the national surveillance case definition and 12 additional attenuated cases [13]. The patients with attenuated cases had symptoms of measles but did not fully meet the national case definition: blood samples collected 8 weeks after symptom onset showed no detectable IgM but immunoglobulin G (IgG) levels too high to be attributed to childhood immunization. As a result of active case finding and ascertainment of vaccination status, the number of unvaccinated case patients increased by 21% but more than doubled (130% increase) in 2-dose recipients ($P < .001$). The proportion of cases with written proof of 2-dose measles immunization shifted from 30% before the investigation (similar to the 22% observed among the 404 cases reported provincially in the 12–17-year age group) to 48%.

DISCUSSION

Given the large epidemic in Europe and the popularity of travel between Quebec and France, multiple measles importations to

Table 2. Reported Source of Infection by Age Group

Age, y	Cases, No.	Cases by Infection Source, No. (%)					
		Household	Daycare or School	Community	Healthcare Setting	Travel	Unknown
<1	21	3 (14)	5 (24)	6 (29)	2 (10)	3 (14)	2 (10)
1–4	62	19 (31)	12 (19)	10 (16)	7 (11)	0	14 (23)
5–9	60	23 (38)	17 (28)	9 (15)	0	1 (2)	10 (17)
10–14	253	38 (15)	163 (64)	27 (11)	0	1 (1)	24 (9)
12–17	404	42 (10)	287 (71)	40 (10)	0	1 (0)	34 (8)
15–19	223	31 (14)	138 (32)	25 (11)	0	2 (1)	27 (12)
20–29	37	10 (27)	2 (5)	7 (19)	3 (8)	7 (19)	8 (22)
30–39	56	8 (14)	9 (16)	11 (20)	7 (13)	4 (7)	17 (30)
≥40	13	3 (23)	3 (23)	1 (8)	0	2 (15)	4 (31)
Total	725	135 (19)	349 (48)	96 (13)	19 (3)	20 (3)	106 (15)

Quebec in 2011 were to be expected. However, the explosive school outbreak, followed by intense transmission that culminated in the largest epidemic in North America since 2001, was unexpected given the province's documented immunization coverage. Based on Pan American Health Organization criteria for elimination, defined as the absence of continuous transmission for 12 months, this epidemic is not considered evidence of reestablished endemic transmission [14]. The outbreak did eventually cease without aggressive interventions aimed at halting transmission. However, the substantial community spillover and sustained spread through the summer months revealed a population susceptibility precariously close to the epidemic threshold. Immunization coverage in Quebec is similar to that reported in other North American jurisdictions. As such, the Quebec experience raises critical questions related to measles surveillance, vaccination strategies, and the combined roles of susceptibility, serendipity, and superspreading events in determining the success of measles elimination efforts.

Surveillance of measles was enhanced in the outbreak context but this report probably underestimates the number of measles cases. The proportion of hospitalized case patients (11%) was lower than those reported in 2011 in the United States (30%) and Europe (28%) or in 2012 in the United Kingdom (18%) [15–17]. Although this may be partly attributed to healthcare system differences, patient age, or vaccination status, it also suggests greater sensitivity in the detection of milder cases and a lower level of underreporting in Quebec than elsewhere. We also excluded 51 clinical cases that occurred during the epidemic period but lacked a recognized epidemiological link. A proportion of these clinical cases would also have been confirmed had the patients' physicians requested laboratory testing. Even if vaccinated case patients are recognized by clinicians and notified, they may not meet all clinical or serological (IgM-based) surveillance criteria [18–20]. Although paired IgG testing on acute and convalescent samples could contribute to confirmation, it is infrequently requested and cumbersome. Thus, passive surveillance approaches based on classic clinical case definitions or detection of IgM may systematically exclude 2-dose recipients from official tallies [11]. If >90% of adolescents have received 2 MMR/measles vaccine doses, <5% are unvaccinated, and the

Table 3. Student Cases in Outbreak School Reported to Public Health Before Active Investigation, Cases Identified With Active Surveillance, and Percentage Increase

Identification of Cases[a]	Cases by Vaccination Status, No. (% Increase)				
	Unvaccinated	1 Dose	2 Doses	Unknown Status or No Proof	Total
Before active investigation					
Notifiable cases	43	4	23	7	77
After active investigation					
Notifiable cases	52 (21)	3 (–25)	41 (78)	2 (–71)	98 (27)
Notifiable plus attenuated cases	52 (21)	3 (–25)	53 (130)	2 (–71)	110 (43)

[a] Nonstudent cases were not included because active surveillance investigation was conducted only in students. Notifiable cases met the national surveillance case definition. Attenuated cases included symptoms of measles but did not meet the national surveillance case definition; serum samples collected from these patients 8 weeks after symptom onset showed no detectable immunoglobulin M but immunoglobulin G levels too high to be attributed to childhood immunization, most likely confirming a recent infection.

2-dose vaccine effectiveness is approximately 95%, we would expect about 50% of the case patients to have received 2 doses, if all cases were reported. However, underreporting was much greater among 2-dose recipients than among unvaccinated case patients in our study. Active surveillance in the most affected high school detected more than twice (130% increase) the number of cases in 2-dose recipients than initially reported, increasing their contribution to the total from 30% to 48% (Table 1). Milder illness in 2-dose recipients (ie, lower hospitalization rates and attenuated presentation) in combination with advice to avoid physician consultation for mild illness probably led to a disproportionate reduction in notification by passive surveillance and overestimation of the contribution of unvaccinated individuals. Although this underestimation may have been greatest in the most affected school, a significant level of underreporting probably also pertains outside this setting. The significance of attenuated cases in vaccinated patients to the overall goal of elimination is unknown but will depend on the extent to which they contribute to total transmission; this contribution is limited now relative to that of unvaccinated case patients but may become more relevant as the elimination target is approached.

This outbreak raises other important questions concerning the relative contributions of vaccine failure versus failure to vaccinate. As previously reported for the high school where the large epidemic started, the vaccine effectiveness in 2-dose recipients was 95.5% (95% confidence interval, 93.8%–96.7%) without attenuated cases and 94.2% (95% confidence interval, 92.9%–95.6%) when attenuated cases were included [13]. This estimate is similar to the median value (94.1%) reported in a synthesis of 2-dose vaccine effectiveness studies [21]. In the initial Quebec outbreak school, protection in 2-dose recipients did not change with greater intervals between the first and the second doses but increased from 93% to 97.5% when the first dose was administered at ≥15 months of age rather than at 12 months [13]. A follow-up study including Quebec cases in 2-dose recipients outside this outbreak school confirmed the greater risk of measles when the first dose was administered at 12–13 months vs ≥15 months of age [22]. These finding are consistent with results from a large serological study of twice-vaccinated German children aged 1–17 years (approximately 7000 children) in which the proportion lacking measles antibody decreased with older age at first vaccination up to 17 months of age. [23]. Two long-term prospective serological studies have shown persistence of measles antibodies in twice-vaccinated children, but these studies included mostly [24] or exclusively [25] children whose first dose was administered at ≥14 months of age. Findings from our epidemiological study [12, 22] and the German serological study [23] pertain mostly to children born to previously infected mothers. Caution is required in extrapolating to children born to vaccinated mothers, who are expected to have less maternal antibody to interfere with vaccines [26].

No extensive vaccine coverage data were available for our analysis among adolescents (aged 12–17 years), who comprised 56% of the cases and were the driving force of this epidemic. Indeed, the high school at the center of this epidemic, which contributed nearly one-quarter of all cases in this age group, probably represents the "worst-case scenario," with 4.7% of students unvaccinated. However, nearly half (48%) of the cases in this school outbreak were due to vaccine failures in 2-dose recipients. Overall, 85% of the students in this school had written proof of receiving 2 doses, slightly less than the 91%–92% reported provincially in 14–15-year-old students after the routine grade 9 immunization update (Ministère de la santé et des Services Sociaux du Québec unpublished data). In the surrounding region, where several hundreds of cases occurred, a 2008 vaccine coverage survey in 28-month-old children found that 5.4% were unvaccinated and 94.6% and 89.1% had received 1 or 2 doses, respectively, marginally less than the provincial estimates cited above (97% and 90%) [8–10]. With the addition of children receiving their first measles dose between age 28 months and school entry, the proportion of school-age children unvaccinated in that region was probably <4%. Although some heterogeneity in vaccine coverage may exist, this region is not known for clustered vaccine opposition. Whereas a school outbreak may reflect local conditions, sustained transmission involving an entire region probably provides a robust and widely applicable signal. It suggests that with 3%–5% of the population unvaccinated, the additional susceptibility in 1- and 2-dose vaccine recipients can push the population toward a critical tipping point for epidemic risk.

Several other jurisdictions in North America have similar immunization coverage, with approximately 90% 2-dose vaccinated and ≥3% unvaccinated [27–30]. In Canada, 5%–8% of children have not yet received a first dose of measles vaccine by 24 months [27, 28], compared with 7.7%–10% by 19–35 months in the United States [29] In kindergarten, rates of exemptions, including medical, religious, and philosophical exemptions, range from <1% to 6.2%, with a total exemption rate of ≥3.0% in 15 of 48 US jurisdictions [30]. In US adolescents, about 90% have received 2 MMR doses [31]. The absence of measles in jurisdictions with the highest proportion unvaccinated is unlikely to be due to a greater level of population immunity. It more likely reflects variability in the chance occurrence of superspreading opportunities. Serendipity probably played a role in the 2011 Quebec outbreak through the index case, including initial acquisition (chance exposure at an airport) and a social context (school worker) favoring broad and swift transmission. The initial superspread happened in the context of accumulated susceptibility in students who themselves had ample transmission possibilities through their own rich social networks. Absent this combination of propitious conditions, there may have been no onward or sustained

transmission. Montreal, the largest city in the province, is located just100 km from the most-affected region, has comparable immunization coverage, but was mostly unaffected (4 cases), probably reflecting a combination of luck, seasonality, and social networking. Had this outbreak begun in early winter rather than spring, it could have been much greater in intensity and geographic involvement.

The susceptibility targets of the WHO European Region for measles elimination—<15% in children aged 2–4 years, <10% in those aged 5–9 years, and <5% in those aged ≥10 years—are based on deterministic models, assuming homogeneous distribution of susceptibility [32, 33]. With the typical clustering of unvaccinated individuals because of shared socioeconomic conditions, religious, or philosophical beliefs, the true level of compensatory immunity required among the vaccinated may be higher. Models with heterogeneity in transmission (some superspreaders and many low transmitters) have shown that measles has difficulty penetrating when the population is under the elimination threshold, but epidemics can happen if initial circumstances (randomness) are favorable [34]. If, as our data suggest, 5%–6% of 2-dose recipients become or remain susceptible in adolescence, even 100% 2-dose coverage would barely meet the level of immunity required for elimination. The large proportion of cases in adolescents and the small proportion in preschoolers and elementary school children suggest a problem of waning immunity. Although the German seroprevalence study suggests increasing vulnerability with time since the second dose [22], US data suggest that the proportion of children potentially susceptible 10 years after the second MMR vaccine, is not significantly different from that before the second dose [24]. On balance, secondary vaccine failure seems the most plausible explanation for adolescent susceptibility, but this warrants further evaluation. Our findings underscore the importance of incorporating residual susceptibility among twice-vaccinated individuals into the assessment of elimination targets and feasibility. In outbreaks, aggressive public health control measures can be effective in limiting spread. Ultimately, however, if immunization programs cannot induce the required level of population immunity to stay below the epidemic threshold, then elimination will not be achievable.

In conclusion, the 2011 Quebec epidemic provides an opportunity for jurisdictions with a stated goal of measles elimination to reflect both on the very tight levels of population immunity required and on how tenuous these levels may be. Our data suggest that even with 3%–5% of children unvaccinated, the residual vulnerability in 2-dose recipients can lead to a precarious balance with respect to the epidemic threshold, exposed only through chance superspreading events. Although such events may be infrequent, they signal the challenge that may lie ahead for elimination. In this regard, unvaccinated individuals remain the top priority for immunization programs, but elimination goals require that we also anticipate, assess, and address residual vulnerability in 2-dose vaccine recipients.

Notes

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