

Measles Outbreak Epidemiology in the United States, 1993–2001

Fuyuen Y. Yip,¹ Mark J. Papania,² and Susan B. Redd²

¹University of Michigan, School of Public Health, Ann Arbor; ²Centers for Disease Control and Prevention, National Immunization Program, Atlanta, Georgia

To evaluate the extent of measles virus circulation and populations at risk in the United States, we reviewed measles outbreaks during 1993–2001. A total of 120 measles outbreaks, constituting 1804 outbreak-related cases, were reported during this period. The maximum outbreak size decreased from 233 cases in 1993–1995 to 119 cases in 1996–1998 and 15 cases in 1999–2001. The maximum outbreak duration decreased from 127 days in 1993–1995 to 65 days in 1999–2001. The majority of outbreaks resulted from documented spread from an internationally imported case (42%) or had a strain of measles virus not endemic in the United States (12%). Outbreaks in which adults were the predominant age group affected accounted for 35% of all outbreaks, compared with 29% of outbreaks predominantly affecting preschool children, 30% predominantly affecting school-aged children and adolescents, and 6% with no predominant age group. The extremely limited size and duration of measles outbreaks indicates very high population immunity to measles and suggests that measles is no longer endemic in the United States.

When introduced into a population with enough susceptible people, measles virus spreads aggressively and rapidly in outbreaks, in which transmission from person to person can be traced both by traditional epidemiological methods and by genetic epidemiology. In the United States, local and state health departments respond to passively reported measles by actively searching for additional cases in the area, especially among contacts of the reported case [1]. Epidemiological links between cases are investigated and documented to describe the chains of transmission. In the United States, a chain of transmission consisting of ≥ 3 confirmed measles cases is considered an outbreak.

Outbreak investigations are important for measles control because studying outbreak epidemiology, in addition to studying individual measles cases, helps to understand patterns of measles virus transmission—

including who is susceptible and in which settings the disease spreads. This information is essential for refining strategies for measles prevention.

Results of outbreak epidemiology strengthen the evidence for the absence of endemic transmission of measles along 4 lines of reasoning. First, actively searching for cases in response to the report of a single case contributes to the credibility of the data on measles incidence. When small outbreaks are identified, confidence increases in the system's ability to detect large outbreaks if they occurred.

Second, tracing chains of transmission is the best method to verify measles virus circulation. Because measles is rare and laboratory tests are not 100% specific, results of tests of suspected cases will include false-positives. However, when laboratory-confirmed cases are linked epidemiologically to other laboratory-confirmed cases, the likelihood that they are misclassified because of false-positive results is diminished.

Third, outbreak epidemiology is helpful in assessing the extent of measles virus circulation following imported measles cases. Finally, when a thorough investigation of outbreaks is part of measles surveillance, the distribution of the size and duration of the measles

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Reprints or correspondence: Dr. Mark Papania, National Immunization Program, Mailstop E-61, Centers for Disease Control and Prevention, 1600 Clifton Rd., Atlanta, GA 30333 (mpapania@cdc.gov).

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outbreaks may be used to estimate the effective reproductive rate of measles, which is an indicator of the population immunity [2].

BACKGROUND

Measles outbreaks: 1985–1988. There were 16,155 cases and 276 outbreaks reported to the Centers for Disease Control and Prevention (then Centers for Disease Control [CDC]) from 1985 through 1988, with an annual median of 47 outbreaks [3, 4]. The median outbreak sizes in 1985–1986 were 10 cases for adult-related outbreaks (>50% of reported cases in persons aged ≥ 19 years), 13 cases for outbreaks among preschool-aged children (>50% of reported cases in persons aged <5 years), and 25 cases for outbreaks among school-aged children (>50% of reported cases in persons aged 5–18 years). For 1987–1988, the median outbreak size was 18 cases. The largest outbreak that concluded in 1985–1988 included 945 cases. However, an additional outbreak in Los Angeles included >10,000 cases, which began in 1987 and continued until 1990. Among the school- and college-aged case patients, most reported prior receipt of 1 dose of measles-containing vaccine, suggesting vaccine failure as a cause of outbreaks. In December 1989, as a result of the increased number of outbreaks among school-aged children who had reported receiving 1 dose of measles-containing vaccine, the US Public Health Service Advisory Committee on Immunization Practices recommended a second-dose measles vaccination policy for students [5].

Measles resurgence: 1989–1991. Between 1989 and 1991, the United States experienced a resurgence of measles, with reports of >55,000 cases and 754 outbreaks [6, 7]. The median outbreak size during the resurgence was 12 cases (range, 5–10,670). However, 70 outbreaks reported during the 3-year period involved >100 cases, and at least 11 outbreaks were reported with >1000 cases; many of these outbreaks lasted >1 year. The median age of outbreak-related case patients decreased annually throughout the resurgence, from 12 years in 1989 to 5.2 years in 1991. The majority of outbreak cases occurred in inner-city areas among unvaccinated minority preschool-aged children [3, 6, 7]. This prompted efforts to improve vaccine coverage among preschool-aged children [8].

After resurgence: 1992. By 1992, the resurgence had subsided, with only 2 large outbreaks—one in Texas and the other in Kentucky—that continued from 1991 into 1992. The number of cases decreased from 9643 in 1991 to 2237 in 1992, with 25 outbreaks reported in 1992 [9]. Of the 25 outbreaks reported in 1992, 12% were categorized as outbreaks among preschool-aged children, 64% involved school-aged children, and 20% involved persons older than school age (>18 years). More than 50% of all the outbreak-related case patients were unvaccinated. From mid-October 1992 to the beginning of January 1993, no

measles outbreaks were reported, signifying that the resurgence had truly ended [9].

To assess the changes in measles epidemiology since the measles resurgence, we review the epidemiology and characteristics of measles outbreaks occurring in the United States between 1993 and 2001.

METHODS

We reviewed the case information about all confirmed measles cases reported on a weekly basis to the CDC through the National Notifiable Disease Surveillance System for 1993–2001. The cases were reported from 52 reporting areas (including 50 states, New York City, and the District of Columbia). Additional data on the cases from state health departments and from epidemiological investigations of outbreaks, which are received by the National Immunization Program, were also reviewed. Data from these 2 sources, which include information on epidemiological linkage of a case to another case as well as whether a case was part of an outbreak, were compiled into an outbreak database that detailed each outbreak, including the size, source, setting, duration, and characteristics of the cases in the outbreak.

For the analysis of vaccination status, children <12 months of age were considered to be too young for vaccination, and case patients who received vaccine within 14 days of their rash onset were considered not appropriately vaccinated.

Before 1995, a measles outbreak was defined as ≥ 5 epidemiologically linked cases. Beginning in 1995, the outbreak definition changed to include chains of transmission with ≥ 3 epidemiologically linked cases, to track smaller chains of transmission. During the pre-resurgence and resurgence periods, outbreaks that spread across county or state lines were typically defined as multiple outbreaks. For the post-resurgence analysis, outbreaks have been traced according to spread and categorized as a single outbreak regardless of whether the outbreaks took place in multiple states [10]. As a result, a subset of post-resurgence outbreaks may have been considered multiple outbreaks according to earlier classification.

We examined trends in outbreak incidence, size, duration, setting of transmission, age distribution, and vaccination status of case patients and the source of transmission. The source of transmission was classified as follows: imported-source outbreaks—the source case (the first detected case patient in the chain of transmission) had acquired measles outside the United States; imported-virus outbreaks—the source case patient acquired measles in the United States, but an imported measles virus genotype was identified in specimens from a case in the outbreak; and unknown-source outbreaks—the source case patient acquired measles in the United States, and no imported measles virus genotype was identified. (All measles genotypes identified in the United States during the study period have been

classified as imported. Unknown-source outbreaks lack any identified measles genotype.) Both imported-source and imported-virus outbreaks are considered importation-associated.

To more clearly characterize the outbreak epidemiology since the resurgence, we further analyzed the outbreaks according to the age group in which a majority (>50%) of cases occurred: preschool-aged children (≤ 4 years of age), school-aged children (5–18 years of age), and adults (≥ 19 years of age). Outbreaks with no age majority were categorized as “other” and were not included in the additional analyses.

RESULTS

From 1 January 1993 to 31 December 2001, 120 measles outbreaks were reported, which consisted of 1804 outbreak-related measles cases, or 69% of the total 2632 measles cases reported in this period. The average number of outbreaks per year for this period was 13 (range, 6–27). Of the 120 outbreaks reported, 45 included < 5 cases and would not have been classified as outbreaks according to the earlier definition (table 1).

The median outbreak size for this period was 7 cases (range, 3–233). The numbers of outbreaks of all sizes, except outbreaks with < 5 cases, decreased over the 9-year period, with no outbreaks of > 25 cases in 1999–2001. The maximum size of outbreaks decreased from 233 cases in 1993–1995 to 119 cases in

1996–1998 and 15 cases in 1999–2001. The median outbreak duration was 42 days in 1993–1995, with the longest outbreak lasting 127 days. The duration of outbreaks decreased to a median of 18 days and a maximum of 65 days in 1999–2001 (table 1).

Thirty-one states (64%) reported the occurrence of at least 1 measles outbreak, and among them, California, Texas, and Massachusetts reported the highest percentage of outbreaks at 17%, 7%, and 7%, respectively. Among the 120 outbreaks, 64 (53%) had a predominant setting reported. Among these, the largest number of outbreaks, 24, took place in health care settings, 20 outbreaks occurred in school settings, 12 outbreaks in day care centers, and 8 outbreaks in college settings. The remaining 56 outbreaks did not have a predominant setting reported.

School-aged children and adolescents (5–18 years of age) accounted for the largest proportion (46%) of all outbreak cases (includes school-aged children involved in preschool, adult, or other outbreaks in addition to those in school outbreaks). Of all outbreak cases, 30% occurred in adults (> 18 years of age) and 28% occurred in preschool-aged children (< 5 years of age.) The median age of all outbreak-related case patients during the 9-year period was 15 years (range, 1 month to 56 years) and increased from 14 years in 1993–1995 to 15 years in 1996–1998 and 1999–2001. Among all outbreak-related case patients, 9%

Table 1. Measles outbreaks, size, duration, age distribution and type, 1993–2001.

Parameter	No. of outbreaks (no. of cases) ^a			
	1993–1995	1996–1998	1999–2001	Total, 1993–2001
Total reported cases	1584	746	302	2632
No. of outbreaks (no. of cases)	43 (1124)	46 (510)	31 (170)	120 (1804)
Median age of outbreak case patients, years	14	15	15	—
No. of cases per outbreak, median (range)	8 (4–233)	5 (3–119)	4 (3–15)	—
Outbreak size				
< 5 cases ^b	3 (12)	23 (77)	19 (66)	45 (155)
5–24 cases	26 (205)	18 (146)	12 (104)	56 (455)
25–99 cases	12 (536)	4 (168)	0	16 (704)
≥ 100 cases	2 (371)	1 (119)	0	3 (490)
Outbreak duration, days, median (range)	42 (7–127)	22 (4–131)	18 (3–65)	—
Outbreaks among				
Preschool-aged children	16 (199)	9 (70)	10 (62)	35 (331)
School-aged children	13 (664)	14 (270)	9 (53)	36 (987)
Adults	13 (250)	18 (130)	11 (52)	42 (432)
Other	1 (11)	5 (40)	1 (3)	7 (54)
Imported-source outbreaks	10 (135)	19 (141)	21 (115)	50 (391)
Imported-virus outbreaks	6 (394)	6 (245)	2 (11)	14 (650)
Unknown-source outbreaks	27 (595)	21 (124)	8 (44)	56 (763)
Outbreaks associated with groups opposed to vaccination	10 (550)	8 (69)	6 (39)	24 (658)

^a Unless indicated otherwise.

^b Beginning in 1995, the outbreak definition changed from 5 to 3 epidemiologically linked cases.

were younger than the recommended age for the first vaccination, 61% were eligible for vaccine but were unvaccinated, 20% reported receiving 1 dose of measles-containing vaccine, and 2% received 2 doses (figure 1).

From 1993 to 2001, the largest outbreak, involving 233 cases from 7 states, was associated with persons opposed to vaccination. Overall, 24 outbreaks (20%) involved at least 1 person who was philosophically or religiously opposed to vaccination. These outbreaks included 658 cases (36%). Among outbreaks associated with a person or groups opposed to vaccination, only 11% of case patients reported being vaccinated with at least 1 dose of measles-containing vaccine, compared with 29% in outbreaks not associated with these groups. The median outbreak size was 6.5. The majority of these outbreaks involved school-aged case patients (72%).

Overall, 50 outbreaks (42%) had internationally imported sources, and there were an additional 14 outbreaks (12%) from which an imported measles virus strain was isolated (table 1). The proportion of importation-associated outbreaks (imported-source or imported-virus) increased from 36% in 1993 to 100% in 2001 (figure 2). This increase in proportion of outbreaks was a result of a decrease in unknown-source outbreaks, with the number of imported-source and imported-virus outbreaks remaining fairly constant over the period.

Outbreaks among preschool-aged children. Thirty-five outbreaks (29% of all outbreaks) involved predominantly preschool-aged children, representing 18% of all outbreak-related cases reported. The median size of the outbreaks was 6 cases (range, 3–48). The median duration of outbreaks among preschool-aged children was 30 days (range, 4–131). Of the 7 outbreaks (20%) among preschool-aged children for which the transmission setting was known, 57% took place in a day care setting, and for the remaining outbreaks, transmission was reported to occur in health care settings.

The median age of case patients involved in preschool outbreaks was 1 year (includes ages 12–23 months), and the age range was 1 month to 49 years. Among case patients in preschool outbreaks, 26% were under the recommended age of vaccination of 12 months, 79% were eligible for vaccine but unvaccinated, 13% reported being vaccinated with 1 dose of measles vaccine, and <1% had received 2 doses. Three preschool outbreaks (9%), including a total of 44 cases, involved groups who were opposed to vaccination.

An imported-source case was reported for 12 (34%) of the preschool outbreaks, whereas an imported-virus case was identified from 5 additional outbreaks (14%). The source was unknown for 1 outbreak.

Outbreaks among school-aged children. Thirty-six outbreaks (30%) were among school-aged children, which represented 55% of outbreak-related cases during the 9-year period. The median outbreak size was 6 cases (range, 3–233), and the median duration was 28 days (range, 1–113). The median age among all case patients in outbreaks among school-aged children was 14 years (range, 1 month to 46 years). Transmission most often occurred in school settings (69% of outbreaks).

Of persons in outbreaks among school-aged children, 4% were too young to receive vaccination, 70% were eligible for vaccine but unvaccinated, 20% reported receiving 1 dose of measles-containing vaccine, and 1% reported having 2 doses of measles-containing vaccine. Overall, 17 school outbreaks (47%), consisting of 566 cases, involved persons who were opposed to vaccination.

With respect to the source of the school outbreaks, 14 (39%) had reported an imported source, an additional 6 outbreaks (17%) were classified as imported-virus outbreaks, and 16 (44%) had an unknown source.

Outbreaks among adults. The largest number of outbreaks (42) occurred predominantly among adults, representing 35%

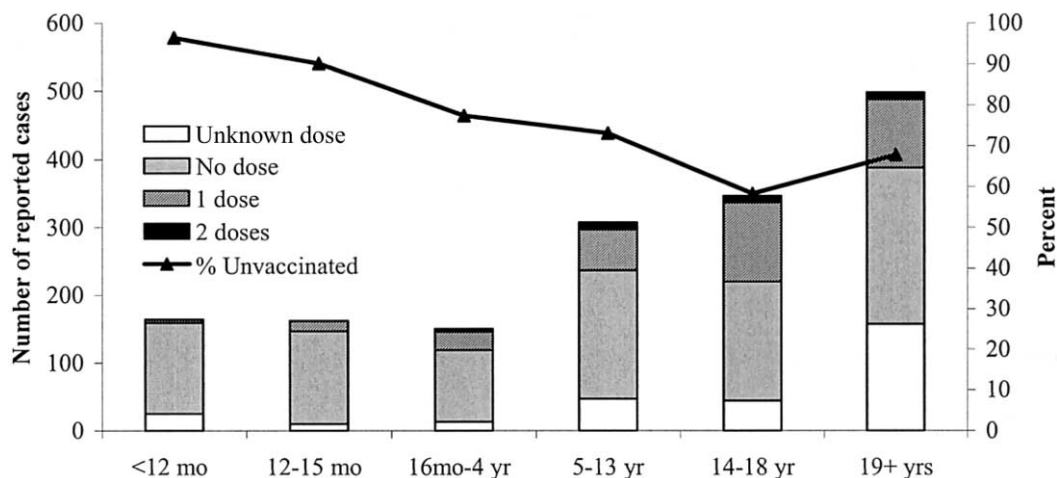


Figure 1. Number of vaccine doses among outbreak-related cases, by age group, 1993–2001. mo, months.

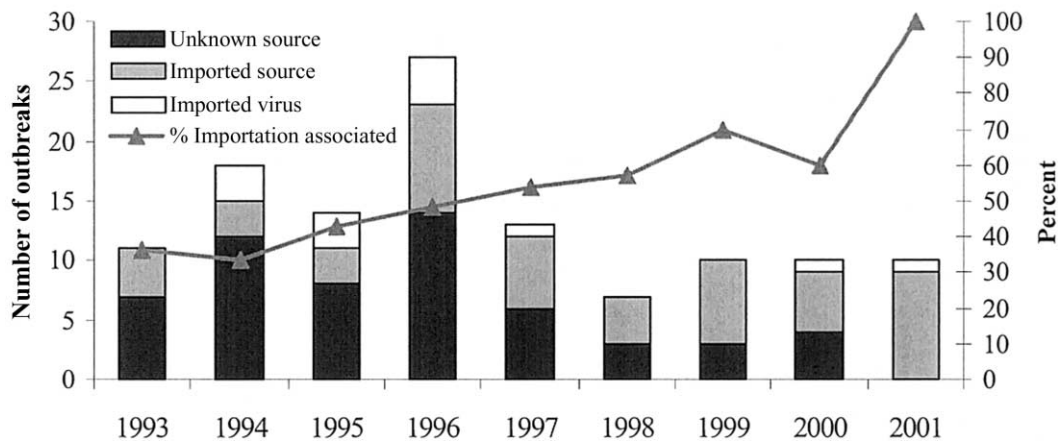


Figure 2. Importation status of measles outbreaks, United States, 1993–2001

of all outbreaks; however, because many of these outbreaks were small, they constituted only 24% of all outbreak-related cases. The median outbreak size for predominantly adult outbreaks was 5 cases (range, 3–87), with a median duration of 25.5 days (range, 3–127). The largest outbreak (87 cases) occurred in 1996, and all other adult outbreaks involved <25 cases. Among the outbreaks among adults with transmission locations reported, the majority of outbreaks were reported to take place in health care settings (61%).

The median age of the outbreak-related case patients was 22 years (range, 4 months to 56 years). Among case patients in adult outbreaks, 6% were too young to be vaccinated, 12% were born before 1957, 89% were eligible for vaccine but unvaccinated, 21% reported receiving 1 dose of measles-containing vaccine, and <2% had received 2 doses. Three adult outbreaks, including 45 cases, involved persons who were opposed to vaccination. Among adult outbreaks, 48% had imported sources, 7% had imported virus, and 7% had unknown sources.

DISCUSSION

During 1993–2001, measles outbreaks decreased in number, size, and duration. These decreases were especially marked in comparison to the resurgence period. Compared with 779 outbreaks and 57,859 outbreak-related cases reported during 1989–1992 [6, 7, 11], there were 120 outbreaks with 1804 cases reported between 1993 and 2001, and 45 (38%) of these outbreaks were so small that they would not have been classified as outbreaks before 1995.

Outbreaks in all age groups decreased in comparison with the resurgence period, but the most notable decrease was in outbreaks among preschool-aged children. During the 1989–1991 resurgence, because of low first-dose measles vaccine coverage among preschool-aged children, there were many large preschool outbreaks, with >70 outbreaks reported with >100

cases and at least 11 reported with >1000 cases [6, 7]. For the period 1993–2001, the largest preschool outbreak included 48 cases. The sustained decrease in preschool outbreaks suggests that efforts to improve preschool vaccination coverage have been effective, and this is documented with preschool coverage estimates that have been $\geq 90\%$ since 1996 [12, 13].

Outbreaks among school-aged children have also decreased substantially. Although several large outbreaks occurred in school-aged children during 1993–1998, including 3 outbreaks with >100 cases, there have been no outbreaks among school-aged children with >24 cases since 1999. The large outbreaks among school-aged children occurred in states without a second-dose measles vaccine requirement, in children in grades not covered by a second-dose requirement, or in groups opposed to vaccination [14–16]. Gradual implementation of requirements for a second dose of measles vaccine has resulted in all but 1 state requiring a second dose of measles vaccine for schoolchildren. By the fall of 2001, most (82%) school-aged children in the United States were in grades requiring a second dose of measles vaccine [17].

Measles outbreaks occurred more frequently among adults than in other groups during this period, although the adult outbreaks were small. Population immunity studies have documented lower immunity in some adult age groups compared with preschool- and school-aged children, and no specific program has targeted increasing immunity to measles among adults [18]. Because of the recognition that adults may be more likely to travel internationally or to be exposed to imported measles cases, as well as to become exposed to measles as health care workers, specific recommendations for vaccination of international travelers and health care workers have been made to address these issues [19]. However, the very small size of adult outbreaks (median, 5 cases) indicates that population immunity is sufficient among adults to minimize the spread of the measles virus and prevent endemic transmission.

Although the number and size of outbreaks decreased in all age groups, the more marked decrease in outbreaks among preschool- and school-aged children resulted in an increase in the median age of case patients. During the peak of the resurgence, the median age of case patients was 5 years [6]. In contrast, the median age of the outbreak related case patients overall during 1993–2001 was 15 years.

In addition to the decrease in numbers of outbreaks, there has also been a considerable decline in the size and duration of outbreaks. During the resurgence, it was not uncommon to observe sustained transmission over several months to >1 year as a result of the large population of susceptible persons. The median outbreak size during the resurgence was 12, and the maximum size of outbreaks exceeded 10,000 cases [6]. In contrast, after the resurgence, the median outbreak size decreased to 6 cases, and the largest outbreak involved 233 cases. Furthermore, the maximum outbreak durations during 1993–2001 were all <131 days, compared with outbreaks observed during the resurgence that persisted for several years [6].

Decreases in outbreak numbers, size, and duration are also evident across the study period 1993–2001. Decreases in the size and duration of outbreaks during this period were more pronounced than decreases in the number of outbreaks. However, this is the result of the change in definition in 1995 to count clusters of 3–4 cases as outbreaks. With the exception of these outbreaks of <5 cases, outbreaks of all sizes decreased in number from 1993 to 2001. The maximum size of outbreaks decreased from 233 cases in 1993–1995 to 119 cases in 1996–1998 and 15 cases in 1999–2001. The duration of outbreaks decreased from a median of 42 days in 1993–1995 to <25 days in 1996–2001.

The high proportion of outbreaks with transmission reported in a health care setting highlights the importance of ensuring that all health care workers are immune to measles. Measles transmission in schools and colleges reinforces the recommendation for a second dose of measles vaccine in people in these institutions [19].

In contrast to the high overall immunity to measles in the US population, the prevalence of measles immunity is lower among groups who are opposed to vaccination. A substantial proportion of the larger-sized outbreaks occurred among those opposed to vaccination, and mostly involve children of school age—a population that otherwise would be fully vaccinated according to state school immunization laws. In 1994, there was a large multistate outbreak of >200 cases among predominantly school-aged children, many of whom were members of families opposed to vaccination [16]. These groups can serve as an effective means of transmission if an imported case introduces measles virus into the population. Rigorous outbreak control measures and high vaccination coverage in the general population play an important role in minimizing the risk of

exposure to measles in groups opposing vaccination. However, the lack of exposure of members of such groups to imported measles cases is another factor that has led to relatively few outbreaks in these groups in recent years. Other countries have recently had large outbreaks associated with groups objecting to vaccination. In 2000, an outbreak of 155 cases occurred in Alberta and British Columbia, Canada, among a religious group that objects to vaccination and was linked to an outbreak of 60 cases in a similar group in the Santa Cruz area in Bolivia [20]. Exposure of a group to imported measles virus could lead to similar outbreaks in the United States. The susceptibility to measles virus among groups opposed to vaccination is increasing because of lack of exposure to endemic measles. Groups opposed to vaccination in the United States are similar to island populations in that they do not have frequent outbreaks of measles virus affecting several age cohorts but are at risk of infrequent large outbreaks affecting many age cohorts. Although the rights of groups who choose not to be vaccinated must be respected, the best means of reducing the risk of large outbreaks in these groups is to decrease the risk of introduction of measles virus through sustaining high immunity in the general population and reducing imported measles cases through improved global control of measles.

In the last 3 years of the time period we studied, most of the outbreaks observed have been importation-associated; 77% of the outbreaks had index case patients who acquired measles outside the United States or had a virus strain that was not indigenous to the United States. In fact, all of the outbreaks reported in 2001 were importation-associated. The number of importation-associated outbreaks has been fairly consistent, indicating a stable capacity to detect outbreaks, whereas unknown-source outbreaks have decreased.

Unknown-source outbreaks most likely spread from undetected links to imported cases of measles [21]. Detection of the epidemiological linkage to the imported-source case is not possible for every outbreak, because patients with imported cases may transmit measles virus and leave the country before they can be detected by public health authorities in the United States. Identifying the measles virus genotype in such outbreaks can be very useful; however, specimens for virus isolation and identification are not available from every outbreak. Increased efforts to obtain virus specimens from suspected measles cases would increase the ability to identify the source of the rare outbreaks, which cannot be linked epidemiologically to an imported case.

Other studies have demonstrated that the recent pattern in the distribution of outbreak size and duration in the United States indicates an effective reproductive rate (R) of measles of <1. This means that the average measles case results in <1 spread case and transmission cannot be sustained [2, 22, 23]. More specifically, estimation of R is based on a model of the spread

of infection—arising from an importation—that predicts the distribution of sizes and durations of chains of transmission. In this supplement, Gay et al. [23] evaluate reported measles outbreaks from 1997 to 1999 to estimate R by means of 3 different methods: methods based on the proportion of imported cases, distribution of “chain” (a series of cases that can be linked to the same source) sizes, and distribution of chain durations. The authors found that the estimates of R for all 3 years for the 3 estimation methods were very similar, with ranges from 0.63 to 0.68, suggesting that the susceptibility to measles during 1997–1999 was beneath the epidemic threshold and that endemic transmission did not occur.

The lack of sustainable transmission of measles virus demonstrated by the small size of measles outbreaks and the predominance of imported sources for outbreaks both also indicate that measles is no longer an endemic disease in the United States; rather, the infection is brought into the country and transmitted briefly among susceptible persons. The consistent detection of small outbreaks provides evidence that the measles surveillance system is adequate to detect endemic measles if it were occurring.

The lack of sustainable transmission of measles virus is a direct result of the population immunity achieved through vaccination in the United States. However, the majority of outbreak-related cases still occur in unvaccinated persons >12 months of age. To maintain the low levels of measles transmission in the United States, continued high levels of vaccine coverage are needed, including first-dose coverage among young preschool children and second-dose coverage among school-aged children. Strong surveillance must also continue to detect imported cases that may instigate a chain of transmission among those who are still susceptible. Finally, the risk of imported cases, which lead to local outbreaks, should be minimized by improved global measles control.

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