A Rare Event: A Measles Outbreak in a Population With High 2-Dose Measles Vaccine Coverage

Jane F. Seward and Walter A. Orenstein

Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, and Emory University School of Medicine, Atlanta, Georgia

Widespread global vaccination with highly effective measles vaccines, first licensed in 1963, has resulted in a decline in estimated global measles deaths, from 2.6 million in 1980 to 164,000 by 2008 [1, 2], and in measles elimination in many countries [3–6]. The World Health Organization (WHO) Region of the Americas has had no year-round endemic measles circulation since 2002 and may become the first region to achieve measles elimination [7]. Because measles is highly contagious, achieving and maintaining elimination requires extremely high population immunity through high 2-dose vaccine coverage. Measles postelimination epidemiology is characterized by importations and limited outbreaks, primarily in unvaccinated persons, provided population immunity remains high [8]. However, if population immunity declines, as occurred in the United Kingdom, when vaccination coverage declined because parents were deterred from vaccinating by misinformation about the safety of the measles, mumps, and rubella vaccine, endemic measles transmission can be rapidly reestablished, bringing with it preventable complications and deaths [9].

In this issue of the Clinical Infectious Diseases, De Serres et al discuss a rare occurrence: a measles outbreak in a school with high vaccination coverage; 92% of students were vaccinated, 85% with 2 doses [10]. Almost half the cases occurred among 2-dose vaccine recipients; however, this is not an unexpected finding in a setting with high 2-dose coverage. Despite high vaccine effectiveness, when the great majority of children have received 2 doses, such children can still compose a high proportion of remaining susceptible individuals. The outbreak occurred following an “initial superspreading event.” A teacher, susceptible after a single dose, developed measles following a trip abroad and triggered an outbreak with 4 generations of spread. Ten students were infected by the teacher, and a large second generation of >60 cases followed. Thereafter, the number of cases declined precipitously, and the outbreak ended <2 months after it began. The proportion of unvaccinated students (5%) in the school likely contributed to sustaining transmission.

The attack rates among unvaccinated and fully vaccinated students were 82% and 4.8%, respectively, so 2 doses of vaccine were 94% effective in preventing measles, which is consistent with other experience [11]. However, the major study finding was the higher attack rate (5.8%) among 2-dose recipients who received the first dose at the age of 12 months, rather than at the age of ≥15 months (2.0%). This finding is consistent with a suboptimal immune response after the first dose, possibly due to persisting maternal antibody. The optimal age for first dose vaccination is a balance between age-specific immune response, disease severity, and the risk of measles exposure. The WHO recommends receipt of the first dose of measles vaccine at the age of 9 months, when 85%–90% of healthy 9-month-olds mount a detectable antibody response to the vaccine [12]. Most developed countries deliver the first dose at age ≥12 months, when ≥95% children respond. On the basis of investigations demonstrating lower vaccine effectiveness for the first dose administered at ages 12–14 months versus ages ≥15 months [13–15], some countries recommend first-dose vaccination at the age of ≥15 months. Experience with primary vaccine failure rates of approximately 5% for children vaccinated at ≥12 months of age prompted 2-dose vaccine policies, first in developed countries and now globally [12, 16, 17]. While the second measles vaccine dose overcomes...
≥95% of primary vaccine failures for infants aged ≥12 months, if there are more susceptible children following initial vaccination at 12 months than at older ages, comparable seroconversion rates for dose 2 among susceptible children will still leave more children without immunity who were first vaccinated at 12 months, compared with older ages. Additionally, earlier first-dose vaccination may independently affect the second-dose immune response for some infants. Poland et al demonstrated a lower seroconversion rate after the second dose for younger first-dose nonresponders (<13 months vs ≥13 months at initial immunization), although after 2 doses, 98.2% of all study subjects were seropositive [18]. The students involved in the Quebec outbreak were likely born to mothers with immunity from measles disease. However, as levels of vaccine-induced antibodies are lower and persist for shorter periods than antibodies acquired from measles disease, the potential for maternal antibodies to interfere with the immune response to measles vaccine will decline in Canada and elsewhere as women of child-bearing age increasingly acquire immunity from vaccination [19].

What is the relevance of these study findings? Perhaps the most intriguing finding is the absence of widespread transmission to and in other schools in Quebec and in much of North America [8], despite many areas in which initial vaccination at 12 months occurs. In fact, measles outbreaks in settings with high 2-dose vaccine coverage are extraordinarily rare. A measles outbreak in a US boarding school totaled 9 cases; however, as in the outbreak described in this issue, it affected primarily 2-dose recipients (because vaccine coverage was high), and 2-dose vaccine effectiveness was 99% [20]. Second, an outbreak among persons who received their second dose more than a decade previously raises the question of waning immunity, although the relatively low attack rates in 2-dose vaccine recipients suggest that if waning immunity did occur, it occurred in only a small proportion of vaccine recipients. Finally, superspreaders appear to have played a special role in this outbreak, leading to an exceptionally high force of infection that overcame small differences in measles immunity that may not manifest frequently on a general population level. Therefore, as the authors caution, before making major changes in policy, such as moving the age for the first vaccination to 15 months, confirmatory studies are needed.

Postponing vaccination poses the risk of leaving children vulnerable to measles. This outbreak exposed high school students; however, importations into younger age groups may have quite different consequences. In Catalonia, where vaccine is recommended at 15 months and 4 years, an importation-induced measles outbreak affected primarily preschool-aged children. In 15 child care centers, high vaccine effectiveness for 1 (95%) and 2 (100%) doses was unable to prevent 77 measles cases, because 43% of the outbreak cases occurred among unvaccinated children aged 12–14 months [21]. On the basis of these findings, health authorities lowered the recommended age for the first dose from 15 to 12 months.

The 2-dose measles vaccine policy has been highly successful globally in controlling and eliminating measles. Countries that have sustained high population immunity through high 2-dose vaccine coverage—using various vaccine schedules—have maintained measles elimination for more than a decade despite continuous bombardments from measles importations [7, 8]. The greatest threat to maintaining global achievements in measles control and elimination and to achieving future global measles goals, including eradication, is failure to vaccinate, either because of a lack of access or because of parents’ choice not to vaccinate, a phenomenon increasingly shared across countries with developed and developing economies [22]. As De Serres et al aptly conclude, “efforts to immunize children who have not received any measles vaccine doses should continue to have the foremost priority since they remain at greatest personal risk and continue to pose the greatest public health threat.” We should also remember that monitoring immunity from vaccines delivered many decades before is also important to ensure that vaccine policies continue to protect people everywhere, throughout their lifetimes [23, 24]. The authors are to be commended for thoroughly evaluating this outbreak and for raising a concern that should be evaluated in investigations of future measles outbreaks.

**Notes**

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**References**

7. Castillo-Solorzano CC, Matus CR, Flannery B, Marsigili C, Tambini G, Andrus JK. The