Measles: The Need for 2 Opportunities for Prevention

Walter A. Orenstein,1 Alan R. Hinman,2 and Peter J. Strebel3

1Emory Vaccine Center, Atlanta, and 2Task Force for Child Survival and Development, Decatur, Georgia; and 3Expanded Programme on Immunization, World Health Organization, Geneva, Switzerland

(See the article by Marin et al. on pages 315–9)

Measles is one of the greatest vaccine-preventable killers of children in the world today. Despite the availability of safe and effective vaccines since 1963, the World Health Organization (WHO) estimates that 530,000 children aged <15 years died of measles and its complications in 2003 [1]. Since the 1960s, public health officials have been intrigued with the potential to eradicate measles through vaccination [2]. Three major factors suggest the scientific feasibility of eradicating an infectious disease: (1) humans are essential to maintain transmission, (2) accurate methods are available to diagnose cases, and (3) effective interventions exist [3]. Although measles can be transmitted among nonhuman primates in captivity, the preponderance of data support human-to-human transmission as essential for maintaining the virus. The clinical diagnosis of measles may be inaccurate, particularly as the disease becomes rare. However, serologic tests—particularly IgM assays, now widely available—have allowed accurate differentiation of cases caused by the measles virus from cases of other clinically compatible illnesses [4].

A major question has been whether the immunity induced by live, further-attenuated measles vaccines is sufficient to terminate transmission. Measles is one of the most contagious infectious diseases. Mathematical modelers have estimated that, in the industrialized world, the average number of secondary infections that follow a single introduction of measles into a fully susceptible population (R0) ranges from 12 to 18 [5]. By contrast, the R0 for smallpox is generally 5–7. Thus, it has been thought that high levels of population immunity, on the order of 92% or higher, are needed to induce adequate herd immunity to interrupt measles transmission. Initial strategies to eliminate measles focused on the administration of a single dose of vaccine, which generally induces 100% immunity when administered at age 12–15 months or older [6]. Experience in the United States indicated that measles in school settings was sufficiently contagious to overcome the immunity barrier induced by a single vaccine dose. Thus, in 1989, the United States adopted a 2-dose strategy [2]. During the 1990s, extensive efforts were made to eliminate endemic measles transmission through increasing immunization coverage with the first dose among young preschool-age children while maintaining very high coverage with the second dose among school-age children. In 2000, measles was assessed to be no longer a disease endemic to the United States [7].

The conditions in the developing world make measles transmission even more difficult to interrupt there than in the United States. Crowding in urban areas is associated with greater forces of infection leading to higher infection rates among young children, compared with those in industrialized countries [3].

The experience in the Republic of the Marshall Islands (RMI) provides further evidence that a single dose of measles vaccine, despite its high effectiveness and despite the fact that it was administered to a high proportion of the population, is not adequate to prevent a major outbreak of measles in densely crowded populations [8]. The levels of crowding in the RMI are some of the highest in the world. As Marin et al. [8] report, the population density on the island is similar to that of Chicago, and the 5.5 persons per room in the average household give ample opportunity for intrafamilial and extrafamilial transmission. Vaccine coverage was estimated to be close to 90%, and the point estimate of the effectiveness of a single dose was 92%. This translates to ~17% of each cohort remaining susceptible (100% – (0.9 × 0.92 × 100%)). Because of poor implementation, susceptibility was not substantially reduced by a second dose of measles vaccine. Nor was susceptibility reduced by circulating natural measles. There were no
reported cases of measles in the RMI between 1989 and the recent outbreak in 2003. Thus, there was ample time for accumulation of enough susceptible persons in the population to fuel a large outbreak. The absence of measles may give a false sense of security that a population is protected when, in fact, each successive year builds the susceptible pool so that, when measles is finally introduced, the epidemic can be quite large.

The point estimate of vaccine effectiveness among children aged 6–14 years in the RMI (92%) is consistent with estimates of seroconversion rates against measles in children aged 12–15 months in the United States but is higher than is commonly encountered in younger children in the developing world [9]. The reasons for this are unclear. Regardless, these data are consistent with other information that 1 dose will not be adequate to sustain interruption of measles transmission. A 1-dose strategy is not an effective strategy to eradicate measles.

To overcome the susceptibility remaining after a single dose of vaccine, much of the industrialized world has implemented a 2-dose schedule, which has led to the elimination of endemic measles in countries such as the United States. The Pan American Health Organization (PAHO) has pioneered a slightly different strategy that appears to have eliminated indigenous transmission of measles in Latin America and that has had substantial impact when applied in many African countries. This strategy, termed a “2-opportunity strategy,” consists of routine immunization with a first dose of vaccine at age 9 months or, preferably, at age 12 months and mass campaigns initially targeting all children aged 9–14 years, regardless of prior vaccination status [10]. Subsequently, mass campaigns every 3–5 years offer the vaccine to all children at least 1 year of age born since the prior campaign, regardless of vaccination status. As well as delivering a second dose to most children, through the mass campaign approach, the second opportunity reaches many previously unvaccinated children who did not have access to routine immunization services.

The PAHO strategy has been adopted by the Expanded Programme on Immunization of the WHO in its accelerated effort to reduce measles mortality by 50% by the end of 2005, compared with 1999 levels [1]. Preliminary information suggests that this effort is on target to meet the goal. Substantial logistic, financial, and scientific barriers remain before a goal of measles eradication can be established and achieved, including demonstration that the PAHO strategy can eliminate transmission in densely crowded urban areas of Africa and Asia. However, the available information suggests that eradication is scientifically feasible. Whether or not eradication is the target, there must be increased efforts to incorporate 2-dose or 2-opportunity schedules into all countries’ immunization programs to make significant progress against the burden of measles.

Acknowledgments

Potential conflicts of interest. W.A.O. has received clinical trials support from Merck and MedImmune, has received grants from Chiron Foundation, and has been a consultant for Data Safety Monitoring Board–Dynport. A.R.H. and F.J.S.: no conflicts.

References