Global Measles Elimination Efforts: The Significance of Measles Elimination in the United States

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Lessons learned from the successful end of endemic measles virus transmission (i.e., elimination) in the United States include the critical roles of strong political commitment, a regionwide initiative, adequate funding, and a broad coalition of partners. Implications of measles elimination in the United States for global measles control and regional elimination efforts include demonstration of the high vaccination coverage and, in turn, population immunity needed for elimination; the importance of accurate monitoring of vaccination coverage at local, state, and national levels; a vaccination strategy that includes at least 2 opportunities for measles immunization; and the essential role of integrated epidemiological and laboratory surveillance. The United States, with a population of 288 million, is, to our knowledge, the largest country to have ended endemic measles transmission. This experience provides evidence that sustained interruption of transmission can be achieved in large geographic areas, suggesting the feasibility of global eradication of measles.

Remarkable progress has been made in controlling measles through vaccination. Worldwide, measles vaccine prevents an estimated 80 million measles cases and >1 million measles deaths annually; however, in 2000, 30–40 million cases and ~777,000 deaths were estimated to occur every year [1]. This represents 46% of the estimated 1.7 million deaths among children each year due to diseases that are currently vaccine-preventable [2]. In 2000, measles was the fifth leading cause of mortality among children aged <5 years worldwide [3].

Measles has been proposed as a candidate for global eradication because it meets the following criteria: measles vaccination is highly effective and leads to long-lasting immunity; sensitive and specific assays are available for reliable diagnosis; and humans are the only reservoir for measles virus. In addition, it is necessary to demonstrate that endemic transmission of measles can be interrupted and maintained in large geographic areas [4]. Here we provide an update on global measles control, describe the lessons learned in the United States regarding measles elimination, and discuss the implications of measles elimination in the United States for global control and regional elimination efforts.

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STATUS OF GLOBAL MEASLES CONTROL

The World Health Assembly in 1989 and the World Summit for Children in 1990 set goals for reductions in measles morbidity and mortality of 90% and 95%, respectively, compared with prevaccine-era levels [5]. Since then, regional measles elimination goals have been established in 3 World Health Organization (WHO) regions—the region of the Americas, the European region, and the Eastern Mediterranean region—by 2000, 2007, and 2010, respectively.

In 2000, global reported vaccination coverage with 1 dose of measles vaccine among infants was 80% (figure 1) [6]. Most countries report measles vaccination coverage on the basis of the administrative method, calculated as the number of doses of measles vaccine administered during 1 year divided by the birth cohort from the previous year. In many countries, this method

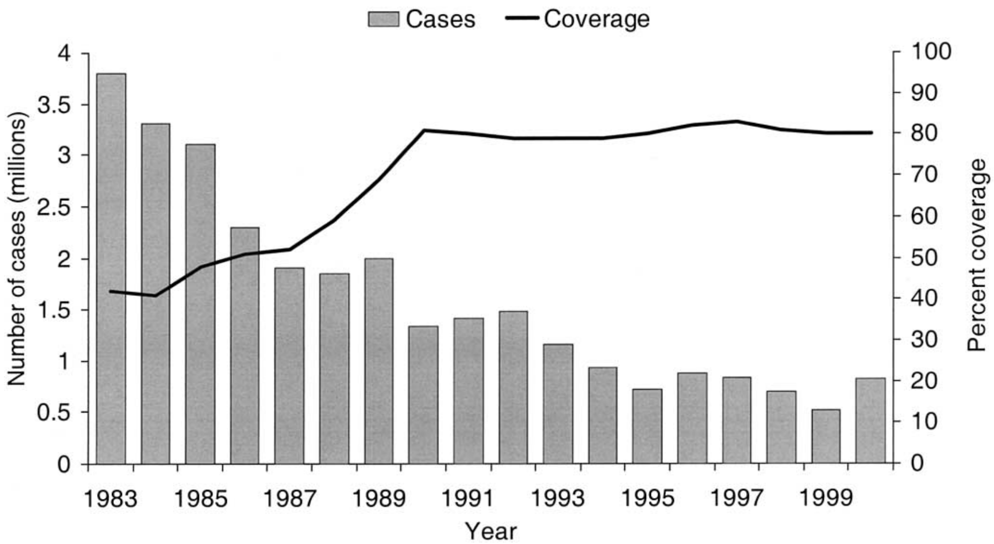

Figure 1. Reported number of measles cases and reported vaccination coverage with 1 dose of measles vaccine by 1 year of age, worldwide, 1983–2000.

tends to overestimate true coverage. In 2000, 13 of 16 countries that reported routine measles vaccination coverage of <50% were in Africa (figure 2) [6]. In 2000, with a global birth cohort of 132 million, an estimated 105 million doses of measles vaccine were administered through routine immunization services, and an additional 35 million doses were administered in supplementary campaigns aimed at either reducing mortality or interrupting transmission.

Globally, 817,161 measles cases were reported in 2000 (figure 1) [6]; however, substantial underreporting exists, and disease surveillance remains weak and underfunded in many countries.

As of December 2000, all countries in the Americas, and selected countries in Europe, the Middle East, southern Africa, Oceania, and Asia, have adopted immunization strategies aimed at measles elimination. Substantial progress in interrupting measles transmission has been achieved in these countries [7–11]. In the Americas, countries that have adequately implemented all of the Pan American Health Organization–recommended strategies have successfully interrupted measles transmission [12].

In 2000, 52 (24%) of 214 countries or territories still had a routine measles vaccination schedule consisting of a single dose at 9 months of age [2]. All remaining countries had either provided a second opportunity for measles vaccination through supplementary nationwide campaigns during the preceding 3 years or introduced a routine 2-dose schedule.

During 11–12 May 2000, participants at a WHO technical working group meeting concluded that very high immunization coverage is required to provide the population immunity level necessary for good measles control. The ongoing measles disease burden is primarily the result of low first-dose coverage among infants and absence of a second opportunity for measles vaccination in affected countries [13]. Therefore, meeting participants recommended that, in addition to the first dose at 9 months of age or shortly thereafter, a second opportunity for measles immunization should be provided either through routine services, repeated supplemental campaigns, or a combination of these strategies. To be effective, the second opportunity for measles immunization should be provided before the average age of contracting measles. A strategic plan for global measles control for 2001–2005 that includes this recommendation was published by WHO and the United Nations Children's Fund (UNICEF) in 2001 [14]. In addition, this plan includes a recommendation to integrate rubella vaccine and rubella surveillance with measles vaccination and surveillance activities, when appropriate [14, 15].

IMPLICATIONS FOR THE UNITED STATES

In March 2000, the Centers for Disease Control and Prevention convened a panel of experts to review the pattern of measles transmission in the United States. Each participant concluded that measles was no longer endemic in the United States [16]. To prevent reestablishment of endemic measles transmission, the experts also recommended the following: maintaining the highest possible vaccination coverage (>90% among preschool-aged children and >98% among children aged 4–6 years); maintaining and improving epidemiological and laboratory surveillance to detect and respond to new importations of measles virus; and advocacy and provision of resources and technical support for measles control and elimination efforts in other countries, to reduce the risk of future measles importations.

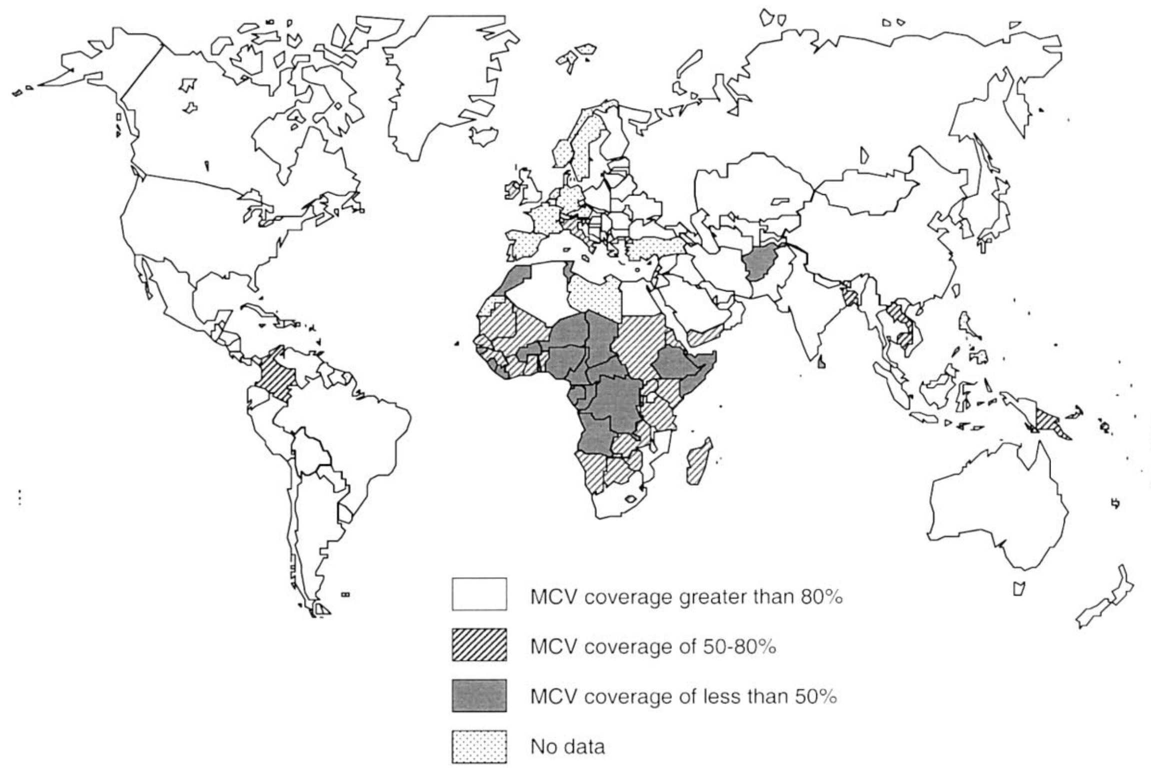

Figure 2. Reported vaccination coverage with 1 dose of measles vaccine by 1 year of age, by country, 2000. If coverage was not reported in 2000, data for 1999 were used; if 1999 data were missing, the coverage reported for 1998 was accepted. If no coverage data were reported during 1998–2000, the country was labeled as "no data." Source: [6].

The potential benefits to the United States of global measles eradication are absence of future cases, deaths, and costs related to these cases and the savings in perpetuity from discontinuing, at a minimum, 1 dose of measles vaccine, estimated at US$45 million annually [17]. Given the possibility of the use of measles virus as a bioterrorist threat after global eradication of measles has been achieved, it is unlikely that the United States would stop measles vaccination altogether.

LESSONS LEARNED THAT MAY BE APPLICABLE TO OTHER COUNTRIES

In the United States, strong political commitment to improving childhood immunization arose out of the experience with the 1989–1991 measles epidemic, when >11,000 measles hospitalizations and 123 deaths occurred [18]. In 1992, President Clinton launched the Childhood Immunization Initiative, which aimed to increase vaccination coverage for all recommended vaccines to >90% among preschool-aged children [19].

In 1994, the Ministers of Health of all member countries in the Americas set the goal of regionwide measles elimination by 2000. Under the leadership of the Pan American Health Organization, aggressive vaccination activities have been undertaken in all countries of the region [20]. Importations of measles cases from Latin America into the United States decreased from 242 in 1990 to 0 in 2000 and 2001, reducing the potential for reestablishment of measles transmission.

Adequate funding through the congressional appropriation for implementing Childhood Immunization Initiative increased the immunization budget from an average of US$233 million in 1990–1992 to US$984 million in 2000. The Vaccines for Children Program was implemented in 1995, removing cost as a barrier for poor and uninsured children in the United States.

A broad coalition of partners was formed to promote childhood immunization, including professional organizations (the American Academy of Pediatrics, the American Academy of Family Physicians), community-based organizations (Every Child by Two; Healthy Mothers, Healthy Babies; the Immunization Action Coalition), and state and local governments [19].

High vaccination coverage and a 2-dose vaccination schedule were required to end endemic measles transmission in the United States. Between 1963 and 1988, the United States had a single-dose measles vaccination policy, and the elimination efforts launched in 1966 and 1978 were unsuccessful despite reaching >95% coverage with 1 dose by school entry. Increased vaccination coverage among preschool-aged children, introduction of a second dose in 1989, and gradual implementation of catch-up vaccination of school-aged children with the second dose resulted in elimination of measles in the late 1990s. Nationwide in 1999, vaccination coverage with 1 dose of measles-containing vaccine by 2 years of age and at school entry was 92% and 98%, respectively [21]. Among school-aged children in 1998, it was estimated that at least 70% had received a second dose of measles vaccine [22].

Waning vaccine-induced immunity has not been an important factor in the United States [23, 24]. Although subclinical titer boosts following natural infection may have played some role in maintaining population immunity, the majority of the population born since 1968 in the United States has vaccine-induced immunity. If waning of vaccine-induced immunity were epidemiologically important, measles incidence should have increased in the young adult population and prevented elimination, but it has not. Ongoing monitoring and surveillance are needed to determine whether vaccine-induced immunity will wane in the absence of boosting through exposure to wild measles virus.

IMPLICATIONS FOR GLOBAL ERADICATION

Measles eradication can be defined as the sum of successful measles elimination efforts (interruption of endemic transmission) in every country. The experience in the United States demonstrates the feasibility of measles elimination in a large geographic area with a diverse population of 288 million and in the presence of ongoing importations over a period of >3 years. Sustaining the interruption of endemic measles transmission in the United States and other countries (e.g., England, Wales, Finland, Oman, Malawi) and achieving elimination in the whole of the Western Hemisphere is a critical test of the feasibility of global eradication [9–25].

To achieve elimination within a country or region, measles control must be a political and public health priority. Documentation of the measles disease burden is needed to obtain this commitment. In developing countries with high measles mortality, there is strong political pressure to prevent measles; however, the financial and logistical support for vaccination may be lacking. In industrialized countries with poor measles control (e.g., Japan, Germany, France, and Italy), it is likely that the risks of patients with measles having severe complications or dying are similar to those observed in the United States, Netherlands, and Ireland during recent outbreaks (i.e., encephalopathy, 1:1000 cases; death, 1–3:1000 cases) [26, 27]. During the 1989–1991 resurgence of measles in the United States, a total of 123 measles-associated deaths were reported, the average cost of hospitalization for a patient with measles in Los Angeles Children's Hospital was US$9264, and the estimated average cost of a measles case was US$1000 [28–30]. In addition, the costs of outbreak control can be substantial [31]. When countries with poor measles control begin to assess the human and financial cost of measles, they may develop the political support necessary to stop endemic transmission within their own borders and join the expanding partnership to reduce measles mortality worldwide.

The US experience provides evidence of the high level of population immunity required to interrupt transmission. Mathematical modelers have estimated that population immunity of at least 93%–95% is needed to eliminate measles [32, 33]. Given available coverage and seroprevalence information, the age-specific susceptibility to measles in the United States in 1999 has been estimated at 19%, 8%, 5%, 5%, and 7% among persons aged 0–4 years, 5–9 years, 10–14 years, 15–19 years, and ⩾20 years, respectively [34]. The overall proportion of the US population immune to measles was calculated to be 93%, suggesting that the mathematical predictions of the threshold for herd immunity are accurate for the United States. Higher population immunity may be necessary to interrupt measles transmission is densely populated urban areas of Africa and Asia [4].

Accurate monitoring of vaccination coverage among preschool-aged children is essential for achieving on-time vaccination coverage of >95%. In most settings, risk of measles is highest among preschool-aged children. At the time of the 1989–1991 resurgence of measles, the United States did not have a national system for monitoring preschool vaccination coverage. Since 1995 in the United States, the National Immunization Survey conducted on an ongoing basis among children aged 19–35 months has documented coverage yearly at the national, state, and major-urban-area levels and thereby promoted on-time immunization [21].

The vaccination strategy needed to eliminate measles requires at least 2 opportunities for measles immunization. In the United States, interruption of endemic measles transmission was associated with increasing preschool vaccination levels to >90%, strict enforcement of school entry requirements for 2 doses of measles vaccine, and providing a second dose of measles vaccine to a high proportion of all school-aged children. In developing countries, a dose of measles vaccine administered at age 9 months induces immunity in ~85% of vaccinees (range, 70%–98%) [35]. Because vaccination at age >12 months results in protection of >95% of recipients (both first-time vaccinees and persons who did not respond to vaccination at 9 months), a second opportunity for immunization before the average age of contracting measles can substantially increase population immunity against measles. If high coverage is achieved with the second opportunity and children who missed the first dose are reached, the herd immunity threshold for measles can be exceeded (table 1).

Increased production of measles-containing vaccines (i.e., measles vaccine, combined measles-rubella vaccine [MR], or

Table 1. Proportion of a hypothetical cohort with immunity against measles by level of vaccination coverage achieved at the first opportunity and the second opportunity.

Coverage at first opportunity, %[a]	Immunity, %	Coverage at second opportunity, %[b]	Immunity, %	
			Dependent probability[c]	Independent probability[d]
50	43	50	46	70
		80	77	86
		90	87	92
		100	97	97
80	68	50	74	83
		80	77	92
		90	88	95
		100	98	98
90	77	50	83	88
		80	87	94
		90	88	97
		100	99	99
100	85	50	92	92
		80	96	96
		90	98	98
		100	99	99

[a] Assuming 85% seroconversion.
[b] Assuming 95% seroconversion.
[c] Assuming same children get vaccinated at first and second opportunity (dependent probability).
[d] Assuming independent probability for receipt of vaccine at first and second opportunity.

combined measles-mumps-rubella vaccine [MMR]) will be needed to allow for a second opportunity for measles vaccination for all children. In the United States, the average annual number of doses of measles vaccine distributed increased from 5 million in the 1980s to 14 million in the 1990s. Preliminary global forecasts indicate that, averaged over the next 5 years, an additional 250 million doses of measles vaccine will be needed annually to cover expanding global needs for measles vaccine [36]. At current costs for a bundled dose of measles vaccine (US$0.25) and additional program costs per recipient (about US$0.71 [37]), the donor cost of providing a second opportunity for measles immunization to children in less industrialized countries is about US$1 per child.

Integrated epidemiological and laboratory surveillance for measles cases and circulation of measles virus is required for directing program activities and documenting interruption of indigenous transmission [38]. The key components of this surveillance system are as follows: collaboration between clinicians and local public health departments to ensure detection and reporting of suspected measles cases; local capacity to investigate individual cases and conduct case finding and outbreak investigations; a nationwide system for surveillance and reporting with regular analysis and feedback; availability of a diagnostic test (measles IgM ELISA) that can be done when the patient first presents for health care [39]; capacity at public health and/or private laboratories to perform diagnostic assays; a national or regional reference laboratory for virus isolation and quality control of assays; and access to a global reference laboratory for genomic sequencing and a measles virus strain bank. Improved measles control requires ongoing investment and training to develop a well-functioning local, national, and global surveillance system and laboratory network.

THE NEXT 5 YEARS

The WHO/UNICEF Strategic Plan for 2001–2005 sets out to achieve a 50% reduction in mortality compared with 1999 levels and measles elimination in the Western Hemisphere, as well as substantial progress toward elimination goals in Europe and the Eastern Mediterranean [14]. This acceleration of activities is needed to prevent the ongoing burden of measles cases and deaths and curtail the circulation of measles virus. In addition, the plan proposes a global consultation with major partners by 2005 to assess the feasibility of measles eradication, thereby deferring discussion of the establishment of a target date for global measles eradication and allowing more time to gain experience with measles control strategies.

Developments in global immunization offer new opportunities to improve measles control. As countries and regions become polio-free, resources can be redirected against measles, as was done in the Americas. New resources totaling $20 million in 2001 have been mobilized for measles mortality reduction in Africa by a partnership coordinated by the American Red Cross [40]. The Global Alliance for Vaccines and Immunization (GAVI) is attracting new financial (e.g., from the Bill and Melinda Gates Foundation/Vaccine Fund and the United Nations Foundation) and political support for immunization. GAVI support for immunization infrastructure aimed at achieving at least 80% vaccination coverage with the third dose of combined diphtheria-tetanus-pertussis vaccine in all districts should lead to increases in measles vaccination coverage and, in turn, improved measles control [41].

Use of MR or MMR vaccine for routine vaccination of children and in catch-up vaccination campaigns aimed at measles elimination offers the opportunity of combining prevention of congenital rubella syndrome and rubella control with measles initiatives in countries with strong routine immunization programs (e.g., in the Americas and some countries in the European and Western Pacific Regions). Combining rubella and measles prevention activities (both vaccination and surveillance) will increase their cost-effectiveness [15].

Ongoing research and development are needed to overcome the barriers to improve measles control and assess the feasibility of eventual global eradication [42]. This includes elucidation of the interaction between HIV and measles, effective strategies for interrupting transmission in densely populated urban centers in Asia and Africa, and easier and safer delivery of measles vaccine.

The US experience with measles elimination demonstrates that endemic transmission can be interrupted in a large population and geographic area for a period of several years. This experience provides a well-documented example for countries striving to improve their control of measles and is evidence of the feasibility of global measles eradication.

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