Measles Eradication: Is It in Our Future?

Walter A. Orenstein, MD, Peter M. Strebel, MD, Mark Papania, MD, Roland W. Sutter, MD, MPH&TM, William J. Bellini, PhD, and Stephen L. Cochi, MD

A B S T R A C T

Measles eradication would avert the current annual 1 million deaths and save the $1.5 billion in treatment and prevention costs due to measles in perpetuity. The authors evaluate the biological feasibility of eradicating measles according to 4 criteria: (1) the role of humans in maintaining transmission, (2) the availability of accurate diagnostic tests, (3) the existence of effective vaccines, and (4) the need to demonstrate elimination of measles from a large geographic area.

Recent successes in interrupting measles transmission in the United States, most other countries in the Western Hemisphere, and selected countries in other regions provide evidence for the feasibility of global eradication. Potential impediments to eradication include (1) lack of political will in some industrialized countries, (2) transmission among adults, (3) increasing urbanization and population density, (4) the HIV epidemic, (5) waning immunity and the possibility of transmission from subclinical cases, and (6) risk of unsafe injections.

Despite these challenges, a compelling case can be made in favor of measles eradication, and the authors believe that it is in our future. The question is when. (*Am J Public Health.* 2000;90: 1521–1525)

Despite the availability of measles vaccines for more than 30 years, measles still causes almost 1 million deaths annually, primarily in the developing world.[1] The burden from measles in industrialized countries is not insignificant.[2] The estimated average cost of a case of measles in the United States in 1994 was $1000.[3] Medical care charges for patients admitted with measles to Los Angeles Children's Hospital in 1990 averaged $9264 per hospitalization.[4] During a resurgence of measles in the United States between 1989 and 1991, more than 11 000 patients were hospitalized and 123 persons died.[5]

To lessen this health burden, the United States spends at least $45 million annually for the measles component of measles-mumps-rubella vaccine.[6] Worldwide, it has been estimated that more than $1.5 billion is spent on prevention and treatment of measles each year.[7] Measles eradication with cessation of vaccination would save those lives, avert that health burden, and save those costs in perpetuity. Here we review the evidence suggesting that measles eradication is feasible and discuss some of the impediments to success. We do not deal with the pros and cons of a combined measles and rubella elimination program, although the World Health Organization (WHO) recently recommended that countries embarking on measles elimination consider such an approach, using measles-rubella or measles-mumps-rubella vaccines.[8]

Criteria for Eradication

In 1997, the Dahlem Conference on Disease Eradication established 4 criteria for a disease to be considered eradicable: (1) humans must be critical to maintaining transmission, (2) accurate diagnostic tests must be available, and (3) an effective intervention must be available. We propose as a fourth criterion that it must be possible to interrupt transmission for a prolonged period in a large geographic area.[9,10]

The Role of Humans

Humans are the only reservoir for measles virus, and virus survival in the environment is limited to several hours.[11] Measles is an acute disease with a period of infectiousness, generally, of 1 week or less. (Chronic infection with defective virions occurs rarely and manifests as subacute sclerosing panencephalitis.[12] However, subacute sclerosing panencephalitis is not contagious.) Because the infectious period is short and measles is highly contagious, a large and continuously replenished supply of persons susceptible to measles is necessary to maintain transmission. It has been estimated that sustained transmission of measles requires a threshold population of several hundred thousand.[13,14]

The cell receptor for measles virus, CD46, is found only in primate cells. Measles infections have been documented in nonhuman primates, and epizootics of measles can occur in captive colonies of monkeys.[15] However, serologic evidence of infection is uncommon among nonhuman primates who have limited contact with humans. Nonhuman primate communities do not have sufficient population size or intercommunity mixing to sustain measles virus transmission.

Diagnostic Tools

The clinical diagnosis of measles becomes unreliable when measles is a rare disease.[16] A capture enzyme-linked immunosorbent assay (ELISA) for IgM on serum developed at the Centers for Disease Control and Prevention (CDC) has specificity of 95% or higher and at least 95% sensitivity.[17–19] Commercial kits are available that have similar sensitivity and specificity, and these tests are easier to perform than the CDC assay.[20] In addition, an ELISA for use with oral fluid specimens has been developed that may be more adaptable for worldwide use.[16]

Measles virus can usually be isolated within 5 days of rash onset by means of B95A marmoset lymphocyte cells.[21] Sequencing of the nucleoprotein gene has led to the delineation of at least 15 genotypes that appear to circulate in specific geographic areas.[22] Virus isolation is useful for tracing chains of transmission and distinguishing indigenous transmission from international importations.[23] Thus, accurate diagnostic tests are available, and this criterion for measles eradication has been met.

Walter A. Orenstein, Peter M. Strebel, Mark Papania, Roland W. Sutter, and Stephen L. Cochi are with the National Immunization Program and William J. Bellini is with the National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Ga.

Requests for reprints should be sent to Peter M. Strebel, MD, Centers for Disease Control and Prevention, National Immunization Program, 1600 Clifton Road, Mailstop E-05, Atlanta, GA 30333 (pms4@cdc.gov).

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An Effective Intervention

Herd immunity threshold. As measles vaccination coverage increases, measles transmission decreases, reducing the risk of measles even among unvaccinated individuals. At some vaccine-induced immunity level lower than 100%, measles virus transmission can be interrupted.[24] Mathematical models have estimated the herd immunity threshold for measles at 93% to 95%.[25–27]

Failure to prevent transmission with a single dose. In industrialized countries, a single dose of measles vaccine administered in the second year of life induces immunity in about 95% of vaccinees.[28,29] With a 5% primary vaccine failure rate, 100% of the population would have to be vaccinated to reach a 95% immunity level with a 1-dose strategy. Approximately 95% of persons who fail to respond to the first dose respond to a second dose, and with high vaccine coverage the herd immunity target can be reached if 2 doses are administered.[30]

In developing countries, high morbidity and mortality due to measles among infants have led to a recommendation to vaccinate infants at 9 months of age, a time when maternal antibody may interfere with seroconversion.[31] A literature review of the response to standard titer Schwarz vaccine at 9 months found a median seroconversion rate of 85% (range: 70%–98%),[32] which leaves 3 times more infants susceptible (15% of vaccinees) than does a rate of 95%. After a single dose with 90% coverage and 85% seroconversion, 77% of the population would be immune. Giving a second opportunity for measles vaccination with a seroconversion rate of 95% for children aged 12 months and older can increase population immunity to more than 95%. To achieve this level of immunity, coverage at the second opportunity must be 90%, both overall and for children not reached at the first vaccination opportunity.

Elimination From a Large Geographic Area

Recent successes in measles elimination from large geographic areas provide evidence for the feasibility of global eradication.

United States. After the resurgence of measles between 1989 and 1991, an elimination initiative was launched that was based on increasing preschool immunization levels and vaccination of all schoolchildren with a second dose.[33–35] Since 1997, the annual incidence has been less than 1 case per million population, the majority of cases are internationally imported or linked to imported cases, and the number of cases not associated with importation is insufficient to represent endemic transmission.[36–38] During the measles resurgence, a single genotype was isolated from at least 8 different sites.[23] In contrast, since 1993, multiple genotypes have been isolated, and all are known to circulate in other countries. In March 2000, the CDC convened a panel of experts to review the pattern of measles transmission in the United States. Each participant concluded that measles was no longer an endemic disease in the United States.

The PAHO strategy. In 1994, the Pan American Health Organization (PAHO) established a goal of eliminating measles from the Western Hemisphere by the end of 2000.[39] The strategy consisted of 3 stages: (1) catch up—one-time mass vaccination campaigns covering all children 9 months through 14 years of age, regardless of prior disease or immunization status; (2) keep up—achievement of high levels of routine immunization coverage in each successive birth cohort; and (3) follow up—subsequent mass campaigns conducted every 3 to 5 years, covering all children, regardless of vaccination status, born since the previous campaign. The catch-up and follow-up campaigns are second opportunities for measles vaccination, at which most children receive a second dose and some receive their first dose. After the catch-up campaigns, some countries have increased the measles vaccination age to 12 months to maximize vaccine efficacy.[40]

Implementation of the PAHO strategy in the Western Hemisphere resulted in a 99% decrease in reported measles cases, from a high of almost 250 000 cases in 1990 to 3018 cases in 1999. As of June 24, 2000, only 500 cases had been reported, the lowest total ever reported for the first 25 weeks of the year.[41] Transmission was limited to 41 districts (0.3% of the more than 12 000 districts) in 5 of 47 countries or territories in the region. The pattern of measles importations into the United States confirms the success of the PAHO strategy. During 1990, 300 importations were detected in the United States, including 242 from Latin America.[42] In contrast, during 1996 no importations from Latin America were detected.

Other regions. Two other WHO regions have established measles elimination goals.[1] The European region has set a target of measles elimination by 2007, and several countries, including the United Kingdom and Finland, appear to have reached elimination.[16,43] The eastern Mediterranean region has a target of measles elimination by 2010, and Oman, Kuwait, and Bahrain appear close to achieving elimination.[44] In southern Africa, Botswana, Malawi, Namibia, South Africa, Swaziland, and Zimbabwe have conducted catch-up campaigns that have resulted in substantial decreases in reported measles morbidity and mortality.[45] In 2 provinces in South Africa, no measles deaths have been reported or identified in hospital record reviews during the 2 years after catch-up vaccination campaigns.[46]

Impediments to Measles Eradication

Political Will

Probably the greatest impediment to eradication is political will. In some industrialized countries, measles is not seen as a priority. Some of the lowest measles vaccine coverage rates are in some of the world's richest countries[47] (Table 1). Global eradication of measles will require that industrialized countries devote the resources necessary to eliminate reservoirs of measles virus in their own populations and help finance a substantial proportion of activities in developing countries. This is unlikely to occur until more industrialized countries realize that the costs of health care for measles can be high, even at low incidence levels.

Political will to control measles is high in sub-Saharan Africa and South Asia, where measles is still a major killer of children. This political will is leading to efforts to accelerate measles control in these areas.[1] However, donor support for routine immunization services de-

TABLE 1—Per Capita Gross National Product (GNP) and Reported Measles Vaccination Coverage for Selected Countries

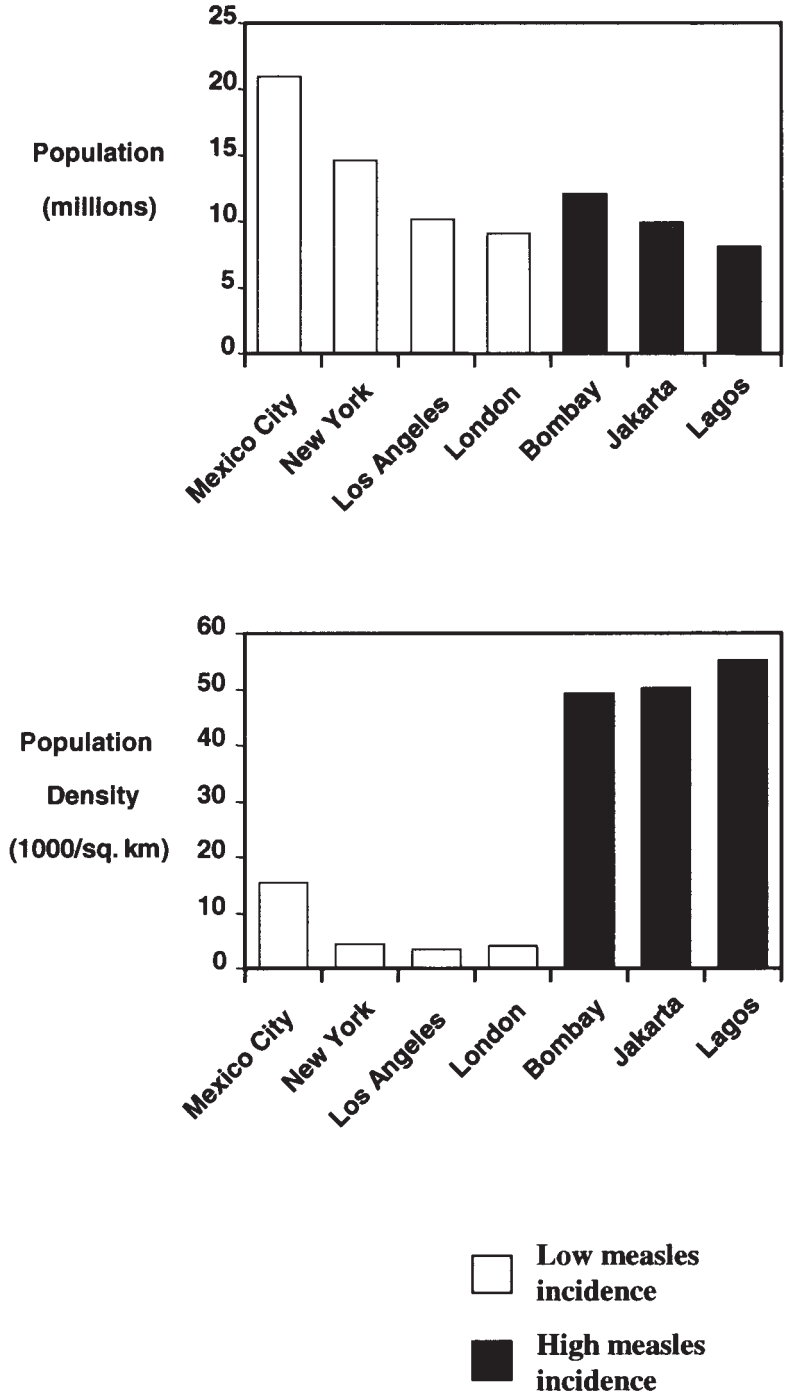
Country	GNP, US $[a]	Coverage, %[b]
Malawi	170	89
Vietnam	240	96
Tajikistan	340	80
China	620	97
Italy	19 020	50
Austria	26 890	60
Germany	27 510	75
Japan	39 640	68

Source. Data are from UNICEF.[47]
[a]Based on 1995 data.
[b]Based on reported vaccination coverage in 1995–1996.

clined during the 1990s.[48] A major new initiative, as is developing under the Global Alliance for Vaccines and Immunization, is needed to revitalize immunization infrastructure.[49] Commitment by national governments and international agencies to achieve and maintain high routine measles vaccination coverage will be critical for the success of measles eradication.

Transmission Among Adults

As vaccination programs reduce the risk of measles, susceptibility to measles can increase among adults for 3 reasons: (1) some adults have never been exposed to measles and have never been vaccinated, (2) some were vaccinated but did not respond (primary vaccine failure), and (3) vaccine-induced immunity may wane (secondary vaccine failure). In 1997, a large measles outbreak occurred in São Paulo, Brazil, among adults aged 20 to 29 years.[40] The infected adults were primarily unvaccinated, indicating that vaccine failure (primary or secondary) was not a major factor in this outbreak. Transmission among young adults in São Paulo was not sustained after 1997, suggesting that although large outbreaks may occur among adults, adult susceptibility is unlikely to sustain endemic transmission.



Source. Data are from the US Census Bureau: *Statistical Abstract of the United States, 1992*. 112th ed. Washington, DC: US Bureau of the Census; 1992.

FIGURE 1—Population size and population density of selected large cities with low or high measles incidence, 1992.

Urbanization

Densely populated urban centers are ideal settings for prolonged measles transmission, even in places with a strong immunization program.[5] It is a challenge for vaccination programs to immunize quickly enough in urban centers to prevent an accumulation of susceptible children and immigrants. Evidence that the challenge can be met comes from the success of the measles elimination program in Mexico City, the second most populous city in the world[50] (Figure 1).

Other major cities with near-zero measles incidence include New York, London, and Los Angeles. However, cities such as Bombay, Jakarta, and Lagos have population densities more than 3 times that of Mexico City. It remains to be demonstrated whether the immunity levels achieved through the PAHO-style mass campaigns using existing measles vaccines are capable of eliminating transmission in the population-dense urban areas of Africa and Asia.

The HIV Epidemic

In some areas of the world, particularly in sub-Saharan Africa, up to 30% of women are HIV positive at delivery.[51] Assuming a 33% perinatal rate of transmission, an estimated 10% of infants will become infected. HIV can cause problems for measles eradication in several ways.

First, measles vaccine immunogenicity and presumed effectiveness are substantially lower in HIV-infected persons than in the general population.[52] A review of 13 seroprevalence studies on measles antibodies in HIV-infected children living in predominantly industrialized countries found a median seroprevalence of 60% (range: 17%–100%). Nevertheless, data from South Africa, which had HIV seroprevalence of 22% among pregnant women in 1999, suggest that measles transmission can be markedly reduced and probably terminated even in places with high HIV seroprevalence.[46] Second, although this possibility has not yet been documented, there is a theoretical risk that HIV-infected persons could become chronic carriers of measles

virus and could transmit the virus years after infection. Further research is needed to evaluate these issues.

Waning Immunity

Concerns about waning of vaccine-induced immunity have been raised repeatedly.[53,54] A follow-up study of children who had seroconverted 10 years earlier found that 9 of 175 children (5%) developed measles.[55] Reports from West Africa suggest that vaccination at 6 to 9 months of age may be associated with faster waning of both antibodies and clinical protection.[56] Although seroprevalence rates tend to decrease with increasing time since vaccination, demonstration of retained immunologic memory suggests that the preponderance of persons who have lost antibody are still protected.[53]

Measles transmission in the United States has been reduced by more than 90% from the prevaccine era for almost all years since 1968. Although subclinical titer boosts following natural exposure may have played some role, the majority of the population born since then has vaccine-induced immunity. If waning of vaccine-induced immunity were a big problem, measles incidence should have increased in the adult population, but it has not. Further, attack rates for measles, even 10 or more years after vaccination, tend to be 5% or less, consistent with known primary vaccine failure rates.[57,58] While waning immunity may occur, it does not appear to be a major impediment to measles elimination in the countries in which it has been carefully evaluated.[53,54,57,58]

Vaccinees exposed to natural measles may develop subclinical infections manifested by boosts in antibody titers. This has raised concerns that measles transmission could be sustained in the absence of clinical measles cases.[59] A study of vaccinated students exposed to measles during a school outbreak found that students who were asymptomatic did not transmit measles to their unvaccinated younger siblings.[60] In addition, laboratory investigations carried out on 133 asymptomatic contacts of persons with measles found no evidence of virus shedding.[61] These data imply that persons with subclinical measles infections are unlikely to be contagious.

Risk of Unsafe Injections

Currently available measles vaccines are administered parenterally, most commonly by means of needles and syringes. In many parts of the developing world, needles and syringes are used repeatedly without intervening sterilization, potentially leading to the transmission of bloodborne pathogens.[62] If sterile procedures are not used, mass campaigns could become opportunities to spread hepatitis B virus and HIV. "Bundling," or distribution of disposable auto-disable syringes and needles along with each vaccine shipment, is strongly recommended.[63] Studies are under way to evaluate needle-less delivery modes such as aerosol and mass injection devices that prevent contamination.[64] Although measles eradication may be feasible without such devices, these tools would facilitate eradication in the safest possible manner.

Reasons for Optimism

The available information supports the technical feasibility of measles eradication. Experience from the Americas and several countries in other regions suggests that measles transmission can be interrupted, at least transiently.[40,65] If current regional and national elimination efforts are successful, and polio eradication can be achieved, considerable momentum will be built for a worldwide measles eradication program. Is measles eradication in our future? In our opinion, yes. The real question is, When? The answer to that question is less certain and will depend on experience gained in the field, new research findings, and the ability to overcome the impediments to eradication. □

Contributors

Each author contributed to the concept and content of the report and participated in drafting and revising the manuscript.

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