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Measles and Rubella Eradication in the Americas

Seasoned Strategies for Sustained Success

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Abstract

This chapter reports on the measles and rubella eradication initiatives in the Americas, where initiatives demonstrate feasibility. Excellent, cost-effective interventions and the lack of an animal reservoir have made it possible to eradicate measles and rubella in the Americas. The driving force behind the eradication of measles, and more recently rubella and congenital rubella syndrome, has been to strengthen national capacity to conduct effective routine national immunization programs. High population immunity through vaccination coverage and high-quality surveillance are necessary, and the benefits of vaccination for measles prevention and control are substantial. This chapter details the progress achieved and the implications for future benefits in both developed and developing countries.

Introduction

Among other factors, disease eradication is possible if there is no animal reservoir and excellent, cost-effective interventions like vaccination exist. Certainly, that is the case for both measles and rubella viruses (CDC 1999b). The benefits of vaccination for measles prevention and control have been substantial, since measles traditionally has caused significant childhood mortality and disabilities. In the case of rubella, morbidity associated with congenital rubella syndrome has also been a huge burden on society, particularly in developing countries (Andrus et al. 2006).

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Four of the WHO regions (American, European, Western Pacific, and the Eastern Mediterranean regions) have regional measles eradication targets (WHO 2009), and the African region recently established an elimination goal for 2020. Measles eradication is feasible and practical (de Quadros et al. 2008). The challenge for regions embarking on measles eradication will be to maintain high population immunity with excellent vaccination coverage and high-quality surveillance (Andrus et al. 2011a). As long as the virus is circulating anywhere in the world, meeting this challenge means confronting the possible importation of the measles virus.

Some experts believe that a global measles eradication initiative could impede or prevent the eradication of polio. This opinion is contrary to the experience of the Americas. In addition, in the Americas, rubella eradication sustained the polio and measles achievements. How was this done?

Countries of Latin America and the Caribbean (LAC) prioritized long-term strengthening of their country routine national immunization programs despite having short-term, targeted disease-specific goals. In so doing, they encountered new opportunities to expand the benefits of disease control and elimination activities to other aspects of public health, most importantly toward improving health care for women and newborns and reducing inequities in health in the region's poorest communities. Implementation of similar strategies could lead to the global eradication of measles, rubella, and congenital rubella syndrome early this century, while strengthening routine immunization programs and developing the capacity to introduce new and underutilized vaccines.

This chapter describes the historical perspective of measles and rubella eradication, the progress that has been achieved, and the implications for future benefits in both developed and developing countries. In this chapter, the term "eradication" will be used instead of "elimination" (cf. Cochi and Dowdle, this volume).

Routine Immunization

Strengthening national capacity to conduct effective routine national immunization programs was, and remains, the predominant driving force behind the eradication of polio, measles, and, more recently, rubella and congenital rubella syndrome. In 1993, in a review of cost-effective health measures, the World Bank concluded that measles vaccination was one of the most cost-effective public health interventions currently available (World Bank 1993). This report was very timely, coming on the heels of polio eradication in the Americas. Although measles vaccine coverage through strengthened routine immunization programs markedly increased in the 1990s in the Americas, measles outbreaks continued to occur. Typically, several years of low measles incidence culminated in the occurrence of a large measles outbreak. Even in

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areas where high coverage rates had been achieved and maintained, outbreaks were reported (Bloch et al. 1985).

In addition, both in countries of LAC and elsewhere, large measles outbreaks were reported where programs failed to achieve and maintain high levels of vaccination coverage (Clements and Cutts 1995). Moreover, some outbreaks were reported from countries that had developed strong systems for vaccine delivery and had achieved high measles vaccination coverage (Cutts and Markowitz 1994). Factors that have been implicated in these outbreaks include the occurrence of primary vaccination failure (the failure to seroconvert following vaccination) in 5% to 10% of vaccinated children and the accumulation of susceptible children over time.

Efforts to control measles transmission, once an outbreak has started, have proved to be frustratingly difficult. Because of the very high communicability of measles, many susceptible people usually have already been infected before the outbreak is recognized and control activities implemented. Given the difficulties in controlling measles outbreaks, accelerated efforts are essential to prevent them. What other strategies are required?

Evolving Strategies for Eradication

An early success in interrupting measles transmission occurred in The Gambia, a country of approximately 1 million people located on the Atlantic coast of West Africa. Transmission was reestablished when the strategies were no longer supported. The Gambia was the first developing country to interrupt measles transmission and to demonstrate that measles eradication was technically feasible (Foege 1971).

In 1986, Cuba developed a new national measles vaccination strategy based on the measles elimination experience of The Gambia, as well as its own successful experience with polio eradication. All Cuban children aged 1 to 14 years, regardless of measles disease history or vaccination status, were targeted in a mass measles vaccination campaign. Because of the accumulation of susceptible preschool-age children since the prior campaign, another mass measles vaccination campaign was conducted in 1993 targeting all children 2 to 6 years of age, regardless of prior vaccination or measles disease history. The last serologically confirmed measles case in Cuba occurred in June 1993 (Galindo et al. 1998). Many countries in the region embarked on accelerated strategies intended to eliminate measles long before the regional initiative to eradicate polio was achieved.

Given the measles eradication experiences of several countries, but particularly in The Gambia and Cuba, the Pan American Health Organization (PAHO) developed in 1994 a regional measles elimination strategy that continues to evolve as additional experience accumulates (de Quadros et al. 1996). Basically, the strategy aims to interrupt measles transmission rapidly and to

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maintain the interruption in measles virus circulation by sustaining high population immunity. Measles case surveillance and measles virus surveillance are key elements of the strategy (de Quadros et al. 1996).

The PAHO measles eradication strategy has three main vaccination components. First, a one-time-only "catch-up" measles vaccination is conducted. Attempts are made to vaccinate all children 9 months to 14 years of age, regardless of measles disease history or vaccination status. The goal is to interrupt measles virus circulation rapidly through the achievement of high levels of measles immunity across a wide age cohort where most measles transmission is occurring (de Quadros et al. 1996).

Following the catch-up campaign, efforts are directed at strengthening childhood immunization through routine vaccination services to slow down the accumulation of susceptible children and to help maintain the interruption of measles virus circulation. This component of the strategy is referred to as "keep-up" vaccination. Since the risk of an infant being exposed to circulating measles virus is low, the age of routine measles vaccination can be safely increased from 9 months to 12 months of age, thus providing an increase in measles vaccine effectiveness. Efforts are made to achieve 90% coverage in each successive birth cohort in every district (Andrus et al. 2011a).

Since measles vaccine is less than 100% effective and universal vaccination coverage is rarely achieved, by definition there will be an accumulation of susceptible infants and children over time, thus steadily increasing the risk of a measles outbreak should the virus be reintroduced. To reduce the number of susceptible preschool-age children to low levels, periodic "follow-up" vaccination campaigns are conducted targeting all children 1 through 4 years of age born since the "catch-up" campaign, regardless of vaccination status or disease history. In addition to raising the level of measles immunity among previously immunized children, these campaigns provide measles vaccination to previously unvaccinated children as well as to those children who were vaccinated but who, for some reason, failed to respond to the vaccine. Through these periodic vaccination campaigns, which supplement vaccination coverage obtained through routine vaccination services, the strategy aims to achieve and maintain high measles population immunity in preschool-age and school-age children (Andrus et al. 2011a, b).

The interval between follow-up campaigns is determined by the vaccination coverage obtained through routine vaccination services. Campaigns are conducted when the estimated number of accumulated susceptible preschool-age children approaches the number of infants in an average birth cohort. In practice, these campaigns will need to be conducted every three to five years (Andrus et al. 2011a). Most countries conduct them every four years.

By the end of 1995, all countries of Latin America and the English-speaking Caribbean had conducted catch-up measles vaccination campaigns. The combined regional 1- to 14-year-old measles vaccination coverage was estimated to be 93%. The catch-up measles vaccination campaigns had an immediate

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impact in reducing measles incidence in the region (Figure 3.1). Following the catch-up campaign in the English-speaking Caribbean in 1991, it has been more than 14 years since the last indigenous laboratory-confirmed case was reported from those countries. Similarly, it has been more than 17 years since the last laboratory-confirmed measles case was detected in Cuba (Andrus et al. 2011a). As a direct result of these successes, as well as the eradication of poliomyelitis from the Americas, in September 1994 the Ministers of Health of the Region of the Americas unanimously established the goal of measles eradication from the Western Hemisphere by 2000.

Nearly all countries had eliminated endemic measles disease by the target date of 2000. However, in 2001–2002 a huge measles outbreak occurred in Colombia and Venezuela, resulting from a measles virus importation from Europe. Transmission of the imported virus D9 genotype was stopped with supplemental immunization campaigns in November 2002. This outbreak most likely represents the last endemic transmission in the region. The damage caused by the outbreak was substantial. During this outbreak, Colombia and Venezuela reported 139 and 2501 measles cases, respectively (Andrus et al. 2010).

Beginning in 2003, Mexico experienced an outbreak that resulted from an importation of measles virus H1 genotype. This particular genotype had never been previously isolated in the Americas, but is quite common in the Far East. Because population immunity was high, the outbreak remained relatively small and contained. From April 2003 to July 2004, a total of 108 measles cases were reported with all but two cases occurring in the contiguous two states and Federal District of Mexico City (Andrus et al. 2011a).

From February 2006 to February 2007, Venezuela reported 122 cases following an importation, which quickly became the largest of all measles

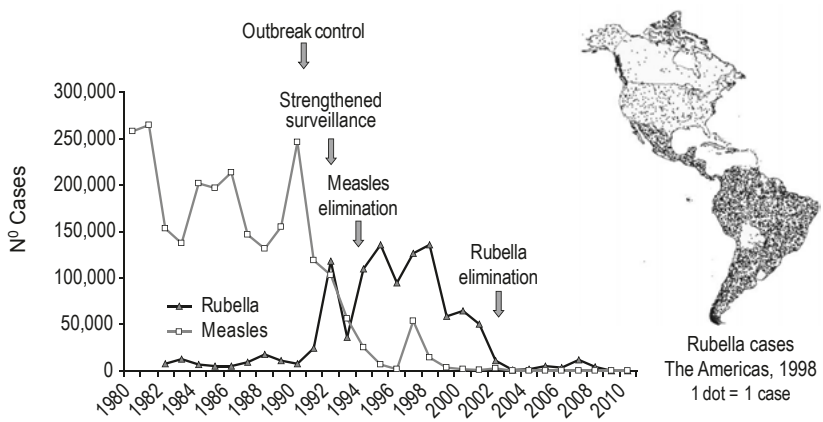

Figure 3.1 Reported measles and rubella cases in the Americas from 1980–2010. Source: EPI tables (1999–2003) and country reports to PAHO/WHO (since 2004).

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outbreaks in the post-elimination era. Three distinct foci occurred in the outbreak. Active case searches conducted during a previously silent period of zero reporting of cases (between epidemiological weeks 27 and 43, 2006) identified 14 cases that had not been previously reported. The viruses identified for all three foci were all genotype B3 (de Quadros et al. 2008).

Importations are to be expected to be the norm if endemic transmission is still occurring in other parts of the world. The PAHO strategy has clearly demonstrated that regional measles eradication is indeed possible, particularly when the strategies are implemented well. But can it be sustained?

Fortunately, PAHO advised countries early on to incorporate rubella vaccine into their routine immunization programs. This action provided a foundation of population immunity through the use of measles–rubella (MR) or measles–mumps–rubella (MMR) vaccines, upon which additional tactics could be constructed to achieve the eradication of rubella and congenital rubella syndrome (Andrus et al. 2006).

Rubella and Congenital Rubella Syndrome Eradication Sustains Measles Eradication

Active measles surveillance unveiled the hidden disease burden of rubella and congenital rubella syndrome in the Americas (Figure 3.1). In September 2003, PAHO adopted a target for rubella elimination by 2010 (PAHO 2003). Prior to 2003, PAHO recommended that vaccines used in all measles vaccination strategies contain rubella as a component either as MR or MMR. The aim was to avoid missing an opportunity to control another serious public health threat and to provide support for other essential health services (Andrus and Roses Periago 2004; Castillo-Solórzano and Andrus 2004). As a result of accelerated integrated measles and rubella surveillance, experts estimated that approximately 20,000 congenital rubella syndrome cases (CRS) were occurring annually in the countries of Latin America and the Caribbean (Andrus et al. 2006) prior to the large-scale introduction of rubella-containing vaccine. The magnitude of the CRS problem prior to measles eradication had been largely unknown.

The eradication of rubella and CRS requires the thorough and rapid vaccination of adults to reduce the numbers of susceptibles in older populations and thereby, the continuing circulation of the virus (Andrus et al. 2006). Therefore, large, one-time "speed-up" mass rubella vaccination campaigns were implemented in all countries, targeting both women and men age <40 years using MR vaccine. In most countries the target group represented approximately 45% of the nation's population. These efforts were a huge undertaking, but experience demonstrated that if done well, only one campaign was required to interrupt endemic rubella transmission (Castillo-Solórzano and de Quadros 2002). The added benefit of using MR vaccine is that it boosted measles

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population immunity and so protected the country from both measles and rubella importations and their spread. Rigorous analysis of the surveillance and vaccination coverage data determined within each country the effectiveness of the campaign.

The molecular epidemiology data indicate that the last endemic case of measles in the region was in November 2002 (Figure 3.2). All other virus isolates in subsequent years are a result of importations from the rest of the world. To support country commitment to maintain their measles and rubella eradication status, PAHO has mandated that transmission occurring in a LAC country as a result of virus importation that lasts more than a year should be considered endemic transmission, and that such a country would no longer be considered as having eradicated these diseases (PAHO 2004).

Critical to maintaining the achievement of measles and rubella elimination has been sustaining high-quality surveillance, and maintaining high levels of population immunity with high routine measles coverage and the continued implementation of "follow-up" campaigns with MR vaccine every four years. In so doing, importations, once they occur, are contained much more effectively with rapid interruption of transmission (Castillo-Solórzano et al. 2008). Cumulative global knowledge regarding the molecular epidemiology of rubella virus transmission is increasing rapidly, enabling the region of the Americas to more readily determine which virus isolates are endemic and which are imported. In particular, a substantial number of rubella virus genotypes have been detected throughout the Americas, with the most common ones including 1 B, 1C, 1E, and 2B genotypes. These virologic data are critical evidence to document that measles and rubella eradication are being sustained.

Lessons Learned and Implications for the Future

The routine national immunization programs in the Americas spearheaded the eradication of polio, measles, rubella, and congenital rubella syndrome. The strengthened routine immunization program served all in the public sector and permitted the initiation and expansion of other programs to control vaccine-preventable diseases. The prime objective has always been to target the most vulnerable populations using the data from coverage performance and surveillance. One important by-product of this approach has been the strengthened capacity for countries to introduce new life-saving vaccines, as well as respond to emergencies (Andrus et al. 2010). In 2004, only 13 countries had introduced seasonal influenza vaccination. Today, more than 35 countries have introduced seasonal influenza vaccination (Ropero-Alvarez et al. 2009). In addition, the number of LAC countries that have introduced pneumococcal conjugate, rotavirus, and HPV vaccines are 16, 16, and 6, respectively. Countries have been able to reduce the time lag between the development of new vaccines and their introduction into use in the developing countries.

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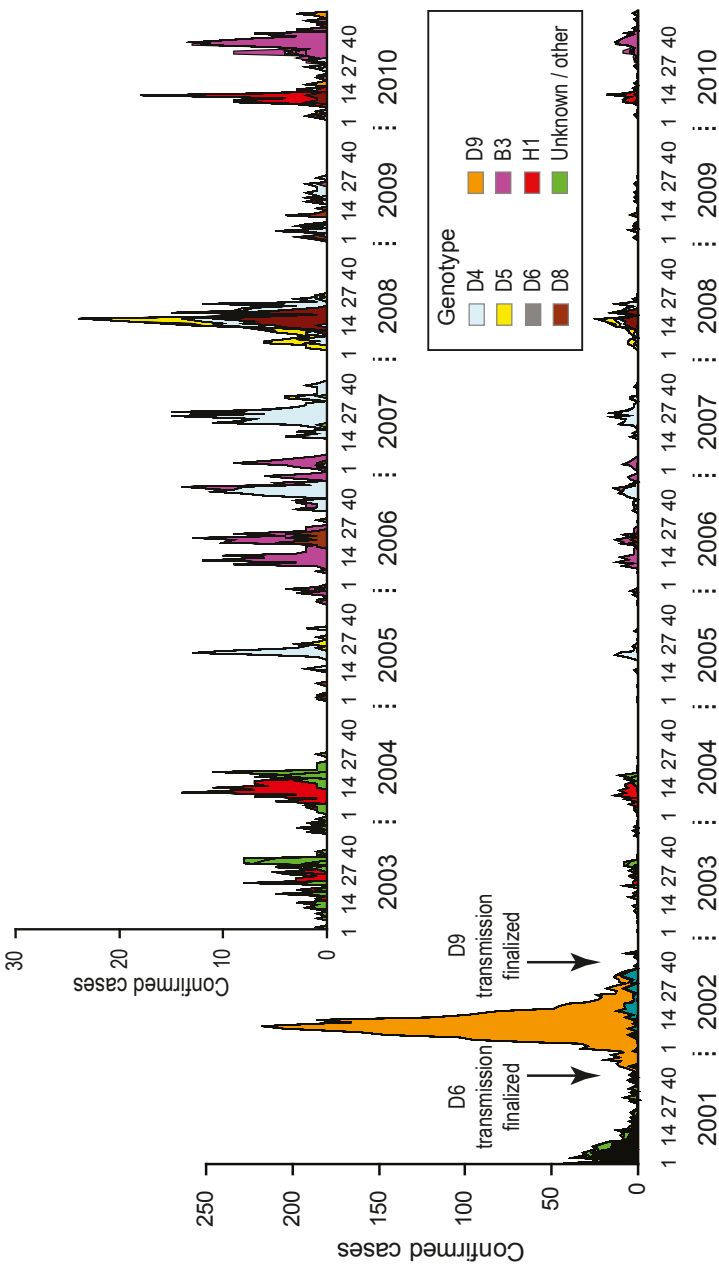

Figure 3.2 Reported measles cases in the Americas from 2001–2010 (bottom), with magnification of confirmed cases from 2003–2010 shown in the top panel. Source: Country reports to FCH/IM Global Measles Laboratory. Note: Canadian cases from 2008 (D8 genotype) were linked to a case or transmission chain where the source of index case is unknown.

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Evidence from Uruguay and Chile suggests that these countries may have eliminated invasive *Haemophilus influenzae* type b (Hib) disease (Danovaro-Holiday et al. 2008). Coverage for this vaccine is generally >90% in all countries throughout the region. Experience in the United States and Canada suggests that when such coverage is achieved, the disease disappears. To that end, PAHO is mobilizing resources to better document this achievement. One important by-product will be strengthened surveillance. This experience and the data should help countries in other regions with their policy decisions on the potential introduction of Hib vaccine.

The accelerated introduction and deployment of new vaccines, and the potential elimination of invasive Hib disease, would not have been possible if routine immunization had not been prioritized as a critical public health function in the developing countries of the Americas, taking precedence over the short-term disease eradication initiatives. However, the short-term eradication initiatives served to provide a special influx of enthusiasm, commitment, and solidarity for national immunization programs.

Conclusions

The challenge for regions embarking on strategies similar to PAHO's strategy will be to maintain high population immunity with excellent immunization coverage and high-quality surveillance, especially to deal with importations. In addition, implementation of measles eradication strategies uncovered the "hidden" disease burden of rubella and CRS.

The last endemic case of measles in the Americas was reported in 2002, and the last endemic case of rubella in 2009. Meanwhile, substantial progress has been achieved in accelerating introduction and deployment of new vaccines in populations who need them most (Andrus et al. 2009). Integrating the eradication of measles with the eradication of rubella has greatly enhanced the capacity of countries to sustain progress. Such efforts have fostered a culture of prevention among adult men and women and have served as a springboard for the transition from child to family immunization programs (Tambini et al. 2006). In addition, countries are encountering new opportunities to expand the benefits of disease control and elimination activities to other aspects of public health, most importantly in improving health care for women and reducing inequities in health care in the poorest countries (Andrus and Roses Periago 2004; Castillo-Solórzano and Andrus 2004; Andrus et al. 2009). It is expected that the adoption of similar strategies in countries worldwide would achieve global eradication of measles in the next decade of the twenty-first century (Andrus et al. 2011b).

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