Feasibility of global measles eradication after interruption of transmission in the Americas


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Measles is one of the most infectious diseases. Before the introduction of the measles vaccine, nearly all children contracted measles. By the end of the 1980s, most countries of the world had incorporated the measles vaccine into their routine vaccination programs. Globally, some 345,000 deaths due to measles still occur every year. Eradication of measles would play an important role in improving child survival. The goal to eradicate measles from the Americas was set by the Pan-American Sanitary Conference in 1994. Progress to date has been remarkable. Measles is no longer an endemic disease in the Americas and interruption of transmission has been documented in most countries. As of December 2007, 5 years have elapsed since the detection of the last endemic case in Venezuela in November 2002. This experience demonstrates that interruption of measles transmission can be achieved and sustained over a long period of time. Global eradication should be feasible if the appropriate strategies are implemented. Even in a new paradigm in which eradication is not followed by the discontinuation of vaccination, eradication of measles should be a good investment to avoid expensive epidemics and save those children that would potentially die due to infection with the measles virus. It is not only a dream to think that we will see a world free of measles by the year 2015.

KEYWORDS: Americas • eradication • measles • transmission • vaccination

Measles is one of the most infectious diseases. Before the introduction of the measles vaccine, nearly all children contracted measles. Human beings are the only reservoir of measles, although other primates, such as monkeys, can also have the infection. The most infectious phase is the prodromic one, approximately 4 days before fever and exanthema appear. The communicability diminishes rapidly after the appearance of exanthema [1].

By the end of the 1970s, an attenuated live measles virus vaccine, which was authorized for use in the USA in 1963, had been widely administered in some parts of the world. It is believed that the immunity conferred by the vaccine lasts for the entire life [2]. Its effectiveness is approximately 90–95%. Due to the interference of maternal antibodies, the effectiveness of the vaccine increases after the first 6 months of life, peaking at approximately 95% at 12–15 months of age [3]. By the end of the 1980s, most countries of the world had incorporated measles vaccines into their routine vaccination programs, and coverage with this vaccine has increased considerably. By 1990, the world reported measles vaccination coverage of children aged 2 years to be approximately 70%; by 2005 this coverage increased to an estimated 77% [101].

Data from the WHO indicate that in 1999 measles was responsible for 10% of deaths worldwide among children aged less than 5 years. At the beginning of this decade, some 40 million cases and 800,000 deaths due to measles still occurred each year; and more than half of the deaths occurred in Africa. As a result of efforts by the global coalition of partners – Ministries of Health, the WHO, UNICEF, the US CDC and the American Red Cross – measles mortality in Africa was reduced from 506,000 in 1999 to 126,000 in 2005. The strategies used were similar to those used in the Americas. Achieving zero cases of measles and, ultimately, the eradication of measles virus transmission, would play an important role in improving child survival.
globally. The purpose of this paper is to review the experience of measles eradication in the Americas to better understand whether global eradication of measles is feasible.

Measles eradication in the Western hemisphere

The goal to eradicate measles from the Western hemisphere was set by the Pan-American Sanitary Conference in 1994, at the same time that the International Commission for Certification of Poliomyelitis declared the region free from polio [4]. The rationale for the strategy used to achieve this goal was based on the epidemiology of measles before and after the vaccine was introduced. Before the vaccine was introduced, measles epidemics occurred every few years (FIGURE 1). Epidemics occurred when the pool of susceptibles provided by each birth cohort was of sufficient size to fuel transmission when the virus was introduced in a given population. After the introduction of the vaccine, and with subsequent increases in vaccination coverage, the interepidemic periods lengthened, sometimes stretching for several years between one epidemic and the next.

In the prevaccine era, measles occurred in very young children and by the age of 5 years almost all had already suffered the disease. With the introduction of the vaccine, and with increased coverage, the age-specific rate increased to older children. As a consequence, even young adults and adults began suffering measles [5].

A considerable number of children remain susceptible because they never received the vaccine. Since vaccine effectiveness is not 100%, a small proportion of those vaccinated who were primary failures also remain susceptible, adding to the accumulating total pool of susceptibles. Over time, even with a very good immunization program in place, accumulation of susceptible children will occur. Clearly, vaccine coverage does not equal population immunity.

Strategies

Given this background, the strategy recommended by the Pan American Health Organization (PAHO) called for high vaccination coverage at all times and effective surveillance to detect measles transmission and respond accordingly. The vaccination strategy is three-pronged [6]. First, a one-time-only ‘catch-up’ campaign, implemented during the low season, targets all children 1–14 years of age in an attempt to interrupt all chains of measles transmission. This age group was chosen because it was among this group where more than 90% of the cases were occurring by the time this program started in the Americas. Second, a ‘keep-up’ component, with vaccination in routine services to achieve the highest coverage possible, is sustained in the new birth cohorts in every district of every country in order to minimize and delay the accumulation of susceptibles.

However, even with high coverage in every district, susceptibles will accumulate because some children will be missed and a few that received the vaccine are primary failures, as indicated previously. With an average vaccination coverage of 80%, it is estimated that it takes approximately 4–5 years for
elimination. Now all suspected cases are tested for both measles and rubella. Performance indicators have been introduced, including:

- Percentage of sites reporting weekly;
- Percentage of suspected cases with adequate epidemiological investigation: home visit within 48 h of investigation plus completeness of relevant data (date of notification, date of investigation, date of rash onset, date sample taken, type of rash, presence of fever and dates of previous measles/rubella vaccinations); and active case-searches;
- Percentage of cases with adequate blood samples;
- Percentage of samples received by the laboratory in less than 5 days;
- Percentage of laboratory results reported in less than 4 days;
- Percentage of cases discarded by laboratory;
- Number of chains of transmission with representative samples for viral isolation.

For each outbreak, pharyngeal or urine samples are taken for virus isolation. The proportion of laboratory results available within 5 days of receipt at the laboratory serve to measure the network performance. An active search for cases is also conducted periodically in areas that have suffered recent outbreaks or have low coverage, have not reported suspected cases for some time, or where the population has low access to health services. Classification of confirmed cases is done by source of infection as imported, import-related or unknown.

All countries have conducted ‘catch-up’ campaigns with very high coverage levels and now most of them are implementing ‘follow-up’ campaigns (Figure 4). These campaigns have usually achieved very high coverage, more than 90% at the national level. Districts that are below 95% coverage are identified and additional ‘mopping-up’ campaigns are then implemented in districts at risk.

Surveillance indicators have fluctuated at the regional level and between countries (Figure 5). Laboratory response within 5 days has improved and the laboratory-discarded cases now reach over 95% [102].

**Results**

In 1990, there were more than 240,000 cases reported in the region. In 1996, only 2106 cases of measles were reported in the Western hemisphere. Of these, some 50% were laboratory confirmed. By the end of 1996, the number of measles cases in the Americas had been reduced by 99%, compared with 1990. In 1997, there was a resurgence of measles in São Paulo, Brazil, the country’s only state that did not implement a follow-up campaign due in 1996. An outbreak that started in early 1997, originating from a probable importation from Europe, spread to other states and to several other countries in the region. By the end of 1997, more than 50,000 cases were reported in the Americas, with more than 90% originating in Brazil [7,8].
In 1998, 14,000 cases were reported following the epidemic generated in Brazil in 1997, with subsequent spread to Argentina, Bolivia and, eventually, to the Dominican Republic and Haiti. In 2001, only 545 cases were reported in the entire region, with epidemic transmission at the end of 2001 only in Venezuela and importations into the northern border areas of Colombia. Transmission in the Dominican Republic and Haiti was interrupted in mid-2001. The majority of cases reported in 2002 were from Venezuela, with other countries reporting a few cases related to importations from other regions of the world [8].

The large measles epidemic that affected Venezuela between September 2001 and November 2002 is the last instance of widespread endemic transmission of the measles virus in the Americas (FIGURE 6) [8, 9]. This outbreak was caused by an importation of measles virus from Europe. It resulted in 2501 cases (109 in 2001 and 2392 in 2002) reported from 17 of the country’s 27 states. Only 18% of the confirmed cases had been vaccinated with a measles-containing vaccine. This outbreak spread to Colombia, resulting in 140 confirmed cases between January and September 2002 [10]. The Venezuela outbreak was controlled by mass vaccination campaigns targeting individuals aged 6 months to 14 years nationwide, and 15–34 years in areas considered at risk. The eradication of the clade 9 of measles virus that was imported into Venezuela has been documented [11].

Measles after the interruption of endemic virus circulation

Since 2003, measles cases in the Americas annually have been reported, following importations from other parts of the world, at historically low numbers (119 in 2003, 108 in 2004, 85 in 2005, 237 in 2006 and 165 in 2007) (FIGURE 7). Between 2003 and 2007, besides isolated cases, limited outbreaks have occurred [12–14, 103].

- In 2003–2004, Mexico reported outbreaks totaling 108 cases related to an H1 virus genotype indigenous to the Far East but not the Americas. The most affected age group was individuals aged 20–29 years (36%), followed by children less than 1 year of age;
- In 2005, Brazil reported an outbreak of six cases related to an imported case infected in South Asia related to a D5 virus genotype;
- From November 2005 to February 2006, Canada, Mexico and the USA reported cases related to a B3 virus genotype, a strain indigenous to Central and Western Africa. The 27 cases reported in Mexico were limited to Mexico City. Even though the source of the outbreak could not be identified, the index case patient was a baggage handler at the international airport;
- In May 2006, the USA reported an outbreak of 18 cases in Boston related to an imported case of likely infection in Southeast Asia. The genotype of the virus isolated was D8;

Figure 4. Measles elimination in the Americas, 1980–2007*.
*Preliminary data – 165 confirmed cases in 2007, coverage data not available.

Figure 5. Measles surveillance indicators in the Americas, 2003–2007*.
Data as of 17 January 2008.
Source: FCH-IM/Pan American Health Organization.
Between October and December 2006, 57 cases were confirmed in the state of Bahia, Brazil. Seven cases were hospitalized. The measles genotype in this outbreak was D4, genetically related to a D4 measles virus isolated from four measles cases that occurred in Canada that year. D4 circulates widely in Europe and Africa, but not in the Americas. The source of the Brazilian outbreak and the Canadian cases could not be identified.

From February 2006 to February 2007, Venezuela reported 122 cases, the primary-case patient was probably exposed to the measles virus in Spain. Three distinct foci occurred: one between February and June 2006, with 81 cases distributed in the Metropolitan District of Caracas, neighboring Carabobo, Nueva Espana and Zulia states; the second between November and December 2006, with 12 in Camaguan municipality, Guarico state; and the third between December 2006 and February 2007, with 25 cases in Puerto Ayacucho and rural areas in the Amazonas state. Active case searches for the silent period between epidemiological weeks 27 and 43 of 2006 identified 14 cases that were classified as clinical measles, which had not been reported. The virus isolated from these foci were all B3; the same genotype circulating in Spain.

Finally, between April and September 2007, an outbreak in Quebec, Canada resulted in 95 confirmed cases. Ten cases required hospitalization. The virus isolated was D4.

A common feature among all import-related outbreaks is that most cases have either been underimmunized (i.e., one dose of measles-containing vaccine) or, most frequently, not vaccinated at all. For example, only four of the 122 cases confirmed in Venezuela had a history of being vaccinated. In Quebec, most of the 78 individuals without a history of receiving a measles-containing vaccine dose opposed vaccination on philosophical grounds [103].

An accumulation of susceptibles was a contributing factor that led to the 2006–2007 outbreak in Venezuela, the largest of all the measles outbreaks occurring in the postelimination era in the Americas. In Venezuela, the age distribution of the 122 reported cases was 16% in children aged less than 1 year, 32% in individuals aged 1–4 years, 12% in individuals aged 5–17 years and 30% in individuals aged 18–39 years. The last follow-up campaign was in 2001 and vaccination coverage reached 93%. However, routine measles, mumps and rubella coverage in Venezuela had been approximately 80% and, in most of the outbreak areas, coverage had been particularly low.

Figure 6. Measles elimination in the Americas, 2001–2007.

*Provisional data as of 17 January 2008.

Canadian cases from 2007 (D4 genotype) linked to a case or transmission chain where the source of index case is unknown.

Source: Country reports to FCH/IM. Global Measles Laboratory.
The outbreak started before the follow-up campaign planned for April 2006. All measles genotypes identified from outbreaks occurring since 2003 have been nonendemic to the Americas.

**Lessons learned**

In summary, the ‘catch-up’, ‘keep-up’ and ‘follow-up’ vaccination strategies have been successful in interrupting measles transmission in the Americas. Campaigns aimed at eliminating rubella continue to strengthen measles elimination by providing an additional vaccine dose to adolescents and adults. All countries and territories have been free of indigenous measles transmission for more than 5 years.

The Americas suffered a re-emergence of measles in 2001–2002 because of failure to fully implement the recommended strategy. In that instance, most cases were seen in vaccinated preschool-aged children and in unvaccinated young adults, with health professionals playing a very important role in the chain of transmission. A similar re-emergence of measles occurred in 1997 and 1998 in Brazil for the same reason; failure to fully implement the strategy.

Although the resurgence of measles in the Americas during 1997 represented an important increase compared with the 1990. Nevertheless, important lessons can be extracted from this experience.

First, the lack of a timely ‘follow-up’ vaccination campaign in 1996 in São Paulo for children 1–4 years of age, combined with low coverage of routine vaccination (‘keep-up’) of infants with at least one dose of measles vaccine, allowed for a fast and dangerous accumulation of susceptible children. Second, the presence of young adults who were not exposed to the natural infection and had never been vaccinated exacerbated the risk of an outbreak. Third, the measles virus was most likely introduced from Europe into São Paulo. Finally, the city’s great population density facilitated contact between infected individuals and the susceptible population.

However, since 2003, importations of measles into countries that have followed the PAHO recommended strategies have not generated sustained epidemics. In most instances, the outbreaks have been quickly controlled. Surveillance data for measles, combined with the results of molecular epidemiology studies, indicate that the countries of the Americas are continually exposed to the measles virus from other regions of the world where measles continues to be endemic.

For the early detection of imported cases, recent outbreaks have illustrated that it is necessary to include private-sector health facilities that care for tourists and intercontinental travelers in the surveillance system. In addition, door-to-door and active case searches for additional cases once an importation has been identified have proven essential for defining the size and extent of the outbreak and to tailor the strategies required to control it. In the Dominican Republic and Haiti there were door-to-door vaccinations to control a vaccine-derived polio outbreak that occurred in 2000–2001. This polio outbreak was concomitant with the importation of measles into both countries; therefore, the vaccination campaigns used polio and measles vaccines. Furthermore, health workers were offered a US$100 reward if they found a case of polio or measles during the house-to-house visits. No case of either disease was found.

Measles importation should result in significant efforts to trace all contacts. For example, the initial case of a six-person outbreak reported in Brazil in 2005 was exposed to a confirmed measles outbreak in the Maldives during a surfing tournament. During the periods of incubation and communicability, this person traveled by air on international flights before arriving in Brazil and traveled on five domestic flights within Brazil. Two secondary infections among fellow passengers traveling between São Paulo and Florianópolis were confirmed by viral isolation and serology. Of the 334 passengers traveling with this index passenger during his period of communicability, 118 were contacted and investigated. No other secondary cases were identified [13]. In 2007, three examples of active international follow-up of measles contacts occurred. A student from India came down with measles during an international student fair in New Mexico. Contacts were swiftly followed in eight countries of the Americas. The second instance occurred when 14 individuals from Latin America and the Caribbean were exposed to measles in Quebec, Canada, after one of the confirmed measles cases attended an event, potentially exposing over 800 international participants. Finally, one of the participants of the ‘Little League World Series’ tournament held in Williamsport, Pennsylvania, USA, was diagnosed with measles. The infected player had traveled from Japan where he was exposed to the measles prior to his departure for the USA. Four international teams from the region were participating in the event. No secondary case resulted in the region from any of these events.
To prevent importations, the PAHO issued an epidemiological alert to individuals of the Western hemisphere attending the FIFA World Cup in Germany in 2006, where a measles outbreak was occurring at the time [14]. Similarly, the Caribbean countries hosting the Cricket World Cup in 2007 issued an alert to strengthen surveillance and advise visitors to be vaccinated [15]. Another alert was issued for those participating in the Pan-American Soccer Cup (Copa America) in Venezuela in 2007, when the measles outbreak was ongoing. Such special global alerts have helped the region of the Americas maintain its status of measles elimination.

Expert commentary & five-year view

The experience of the last 5 years with the measles eradication program in the Americas shows that measles transmission can be interrupted and interruption can be sustained over a long period if countries fully apply the appropriate strategies of vaccination and active, integrated surveillance of measles and rubella, as recommended by the PAHO for all the countries of the Americas.

The experience described indicates that the PAHO strategy can effectively achieve and sustain the interruption of epidemic transmission in a very large geographical area, such as the Western hemisphere. From this experience, we believe that global eradication is feasible if the appropriate strategies are implemented. The current measles vaccine, with 95% vaccine efficacy, has been adequate to stop endemic measles transmission when used in the recommended strategies of catch-up, keep-up and follow-up, as described previously. The eradication of measles will have a major impact in childhood morbidity and mortality. Even in a new paradigm on which eradication is not followed by the discontinuation of vaccination, eradication of measles should be a good investment to avoid expensive epidemics of measles but, most importantly, to save the almost 300,000 children who die every year due to infection with the measles virus.

However, before a global initiative on measles eradication is launched, it is necessary to demonstrate that poliomyelitis has been eradicated. There also will be programmatic, political and financial obstacles that will need to be overcome before global measles eradication is launched. Partnerships will be essential to support governments embarking on it. It is not only a dream to imagine a world free of measles by the year 2015.

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Key issues

- Measles is no longer an endemic disease in the Americas and interruption of transmission has been documented in most countries.
- As of December 2007, 5 years have elapsed since the detection of the last endemic case in Venezuela in November 2002.
- This experience demonstrates that interruption of measles transmission can be achieved and sustained over a long period of time.
- Global eradication should be feasible if the appropriate strategies are implemented.

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