SUPPLEMENT ARTICLE

Interruption of Measles Transmission in Brazil, 2000–2001

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In 1992, Brazil adopted the goal of measles elimination by the year 2000; however, in 1997, after a 4-year period of good control, there was a resurgence of measles in Brazil. In 1999, to achieve the elimination goal, Brazil implemented the Supplementary Emergency Measles Action plan, with one measles surveillance technician designated to each state. Of 10,007 suspected measles cases reported during 1999, 908 (9.1%) were confirmed, and of them 378 (42%) were confirmed by laboratory analysis. Of 8358 suspected measles cases reported in 2000, 36 (0.4%) were confirmed (30 [83%] by laboratory); 92% of the discarded cases were classified on the basis of laboratory testing. In 2001, only 1 of 5599 suspected measles cases was confirmed, and it was an imported case from Japan. The last outbreak occurred in February 2000, with 15 cases. Current data suggest interruption of indigenous measles transmission in Brazil.

Brazil, the largest country in Latin America and the fifth largest country in the world, has tremendous geographic and socioeconomic diversity. The population of 169.6 million (2000 census) is distributed in 26 states and one federal district, with 81.7% living in urban areas and 17.4% in poverty [1].

In 1992 Brazil adopted the goal of measles elimination by the end of the year 2000. The success of measles elimination in a heterogeneous country such as Brazil may be instructive for other countries or regions with measles control or elimination goals. In this article, we review the history of measles control and elimination in Brazil, discuss recent strategies adopted to achieve this goal, and present evidence for the interruption of measles transmission in Brazil.

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The Journal of Infectious Diseases 2003;187(Suppl 1):S111–20

0022-1899/2003/18710S-0018

HISTORY OF AND STRATEGIES USED FOR MEASLES CONTROL AND ELIMINATION IN BRAZIL

Vaccination schedule. Measles vaccine was first used in Brazil in the late 1960s through sporadic importation of measles vaccine available on the international market. Following creation of the National Immunization Program in 1973, measles mass campaigns were conducted in urban areas of selected states during 1973 and 1974. Routine national measles vaccination was subsequently introduced as part of the development and expansion of a primary health care system. On the basis of the success of state mass immunization campaigns and on the occurrence of localized measles outbreaks during the late 1970s, national measles control was intensified in 1980 and 1981 (figure 1), with campaigns focused in areas of low coverage [2].

From 1973 through 1992 the national recommended routine schedule consisted of a single dose of monovalent measles vaccine. The minimum recommended age for measles vaccination was changed from 8 months in 1973 to 7 months in 1976 [2]. In 1982, on the basis of results from a World Health Organization multisite

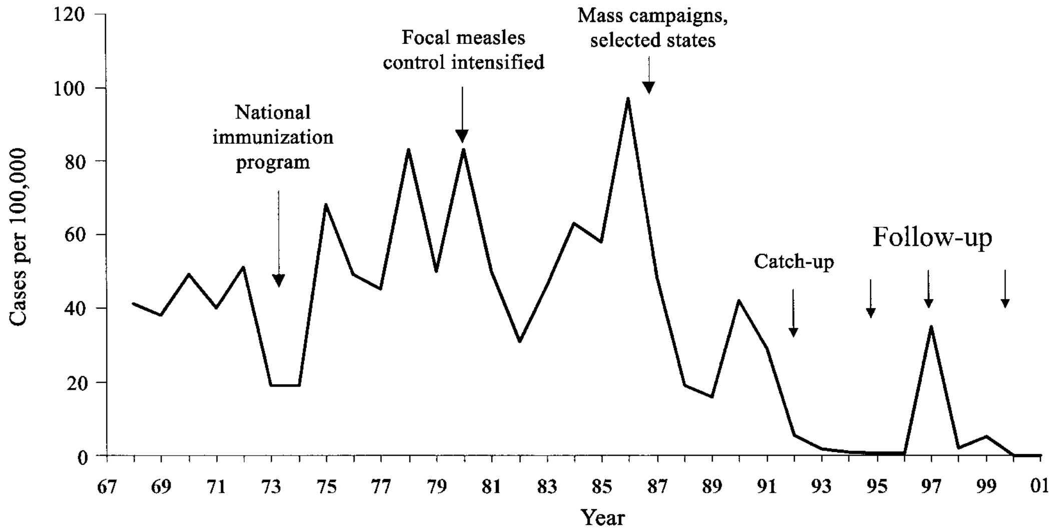

Figure 1. Measles incidence and measles control strategies, Brazil—1968–2001

study of measles vaccine immunogenicity, the age was changed to 9 months [2, 3]. In 1992, a second dose of measles vaccine, administered at 12–15 months, was recommended nationwide. For vaccination conducted during outbreaks, vaccine is recommended beginning at age 6 months [4]. The type of measles vaccine used for the second dose (monovalent measles or measles combined with mumps and rubella [MMR]) has varied by state: Introduction of the second dose of measles vaccine as a combination MMR vaccine was progressive by state between 1992 and 2000, beginning in São Paulo in 1992. As of September 2000, all states had the second routine dose of measles combined with rubella and mumps incorporated into their routine childhood vaccination schedule.

Vaccination coverage is monitored by the administrative method (doses administered divided by the estimated population, which is based on the most recent census). Coverage estimates for monovalent measles (M) at 9 months use the <1-year-old population as a denominator, and estimates for second-dose coverage (MMR or M) use the population aged 12–23 months as a denominator. Measles vaccination coverage among children <1 year of age has been estimated since 1976 [2], and increases in coverage to levels >50% have been observed since 1980. From 1980 through 1990, measles coverage varied from 56% to 78%, with a median of 66% (figure 2). Beginning in 1991, sustained increases in routine measles vaccination coverage were observed. Coverage remained at ⩾80%, with the exception of 1994, when it dropped to 78%. Median coverage from 1991 through 2000 was 91%. However, since 1997, coverage has been ⩾95% (figure 2). Measles vaccine coverage at age 12 months has been monitored nationally since 2001. On the basis of data for doses administered through August 2001, coverage for measles administered at age 12–23 months was 91%.

Measles vaccine production and supply. The monovalent measles vaccine strain has been produced in Brazil since 1984. The strain used for production in Brazil is the CAM-70 (produced by the BioManguinhos Institute, Fundação Oswaldo Cruz [FIOCRUZ], Rio de Janeiro). The immunogenicity of this strain is comparable to that for the Moraten and Schwarz strains [5]. MMR vaccine used in Brazil for routine vaccination is imported from a variety of manufacturers. All domestically produced and imported vaccines are licensed by the national regulatory authority and undergo lot quality testing prior to use in the National Immunization Program.

Measles elimination goal and mass vaccination campaigns. The success of measles mass vaccination campaigns in selected states during the 1980s in reducing measles incidence was key to adopting such campaigns as a measles elimination strategy. In addition, the experience gained with advocacy, planning, and logistics related to the twice yearly polio National Immunization Days for poliomyelitis eradication, which have been held since 1980, were critical to adapting this strategy for measles elimination. Two statewide indiscriminate measles mass vaccination campaigns were conducted in 1987 in Paraná and São Paulo and targeted children 9 months to 14 years of age. The goal of these campaigns was to rapidly interrupt transmission. In Paraná, the incidence declined from 122/100,000 in 1987 to 6.5/100,000 in 1988, and the average incidence over the next 5 years (1988–1992) was 9.4/100,000.

The experience of São Paulo is particularly instructive. São Paulo is the largest state in Brazil, with a population of 29.2 million people in 1987. The greater metropolitan area of São Paulo is the largest urban center in Brazil, and with 15.9 million

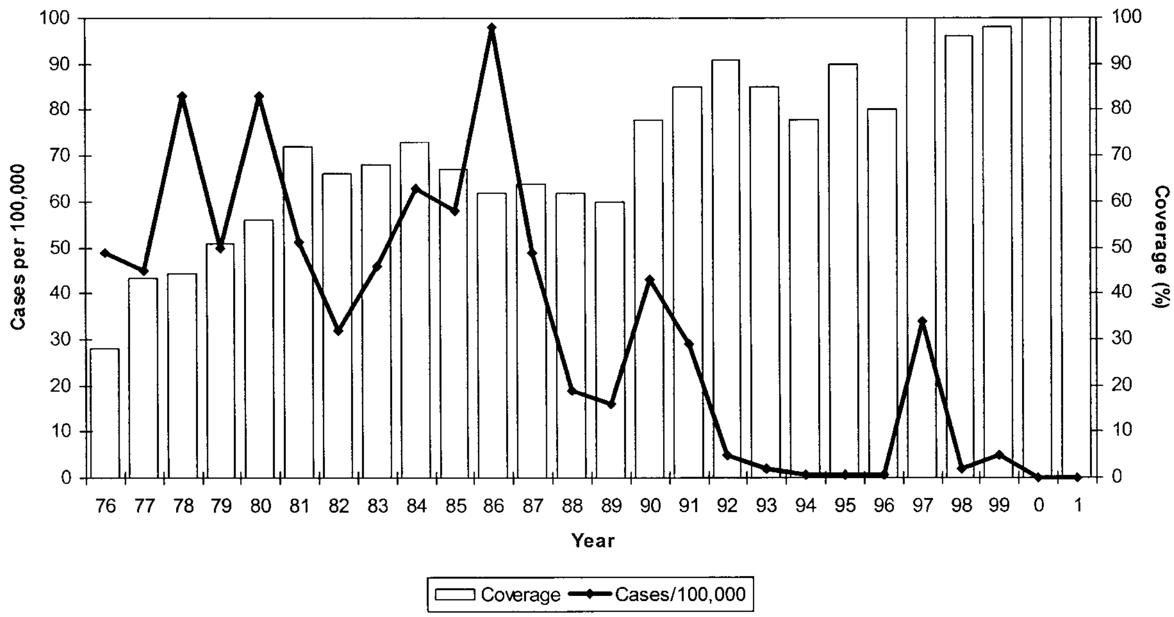

Figure 2. Measles cases and measles vaccination coverage among children <1 year of age, Brazil—1976–2001

inhabitants in 1987, it contains over half the state's population [6]. From 11 to 22 May 1987, 4.1 million doses of measles vaccine were administered to children aged 9 months to 14 years, for an estimated coverage of 86%. Following the campaign, the incidence in the targeted age group declined from 222/100,000 in 1987 to 2.7/100.000 in 1988. Seroprevalence following the campaign was 97% among children 1–14 years of age [6]. Measles surveillance was intensified following the campaign, with mandatory notification and serologic confirmation of all clinically suspected cases [7]. Following the campaign, the average annual number of cases declined by 85%, from 5516/year (1982–1986) to 823/year (1988–1992).

In 1992, due to the success of the two state campaigns and of other experiences in measles control in the Americas, particularly Cuba and the Caribbean, Brazil adopted the goal of measles elimination by the end of the year 2000 [8, 9]. The National Measles Elimination Plan was developed to meet this goal and included the measles elimination strategies recommended by the Pan American Health Organization (PAHO) for measles elimination in the Americas [10, 11].

The first National Measles Immunization Campaign ("catch-up") was held from 22 April to 25 May 1992 (figure 1). In total, 48,023,657 doses were administered to children aged 9 months to 14 years, for a coverage of 96%. In São Paulo, the target age group was children aged 9 months to 10 years. Following the campaign, measles surveillance was intensified, emphasizing case reporting and investigation with laboratory confirmation of suspected cases. In addition, resources were allocated to training and communication in order to raise awareness among the public, health care professionals, and political leaders about the importance of the measles elimination plan and the need for reporting suspected measles cases [8, 9].

The first national "follow-up" campaign was conducted in 1995 and targeted children 1–3 years of age (figure 1). The state of São Paulo did not participate in the follow-up campaign. An overall national coverage of 77% was achieved.

The resurgence of measles in 1997 led to supplementary immunization activities as part of outbreak control. The second national follow-up campaign, held in 1997, targeted children aged 6 months to 4 years and achieved 66% coverage. The third national follow-up campaign in 2000 was targeted to children aged 1–4 years and achieved 100% coverage.

Measles surveillance. Measles has been a legally notifiable disease since 1968. With the adoption of the Measles Elimination Plan in 1992, case-based surveillance was introduced, with immediate reporting of all suspected measles cases and a target of investigation within 48 h. A suspected case-patient is defined as someone with fever and rash with cough, coryza, and/or conjunctivitis, independent of age and vaccination status or any patient in whom a health care provider suspects measles. Case investigation includes collection of epidemiologic and clinical data, using a standardized case-investigation form, with collection of a blood sample for detection of measles-specific IgM antibodies. Active case-finding is conducted to detect secondary cases and potential sources of infection. For suspected measles cases, vaccination within 72 h of close contacts aged 6 months to 39 years without documentation of prior vaccination is recommended. If the suspected case is IgM positive, then more extensive vaccination is conducted, including vaccination of all susceptible contacts in the community, day care centers, school, and/or workplace [4]. Since July 2000, following a 3-month period with no measles transmission detected, additional recommendations for case investigation were introduced. For all reported IgM-positive suspected measles cases, a follow-up visit that includes state and/or national measles surveillance staff is conducted with exhaustive investigation in the area to detect or verify the absence of transmission. As part of this follow-up visit, a second blood sample is collected for paired measles IgG testing to identify seroconversion and/or dengue or rubella.

Laboratory testing. Blood samples from suspected cases are tested for measles-specific IgM antibodies by a commercially available indirect EIA assay that is highly sensitive and specific [11]. Beginning in 1996 when measles transmission had declined to low levels, additional laboratory testing was introduced to increase the specificity of measles laboratory confirmation. All samples that are initially positive are retested at the national reference laboratory (FIOCRUZ) by use of the indirect assay (Behring) and by an IgM capture EIA that has been developed and provided by the Centers for Disease Control and Prevention. IgM-positive samples from São Paulo are tested at the Instituto Adolfo Lutz, São Paulo, the reference laboratory for the state of São Paulo, using the same assays. These retesting procedures were suspended during the epidemic period in 1997–1998 and resumed in June 1999, a period of low measles transmission. All IgM-positive samples are also tested for rubella-specific IgM antibodies and, depending on local epidemiology, may also be tested for dengue-specific antibodies. Samples that are repeatedly reactive by both the indirect and the IgM capture EIA tests are considered positive. However, local epidemiology (known laboratory-confirmed epidemics of rubella or dengue) is considered in case classification if samples are positive for both measles and rubella or dengue. As an additional strategy to increase specificity of measles laboratory confirmation, since July 2000, national surveillance guidelines include collection of a second blood sample from an initially IgM-positive suspected measles case for paired IgG testing to identify seroconversion for measles, rubella, and/or dengue. Surveillance guidelines also include collection of urine and/or nasopharyngeal swab samples from all suspected measles cases for measles virus isolation.

As part of rubella surveillance, since 1992, all suspected measles case-patients who tested IgM negative for measles have been tested for rubella-specific IgM antibodies by EIA. In 1997, an integrated measles and rubella surveillance case-investigation form was introduced. Beginning in 1999, most state laboratories test a subsample of rubella IgM-negative samples for the presence of measles antibodies. In addition, depending on local epidemiology, dengue-negative samples may also be tested for measles.

Laboratory network and integration of laboratory with surveillance training. In 1992, a network of eight state laboratories was formed to support surveillance activities [12]. This network was expanded to 12 laboratories in 1995 and to 20 in 1997. By 1999, this network was expanded to at least one laboratory in each of 27 states. Prior to inclusion in the national laboratory network, all laboratory personnel receive standardized training at the national reference laboratory (FIOCRUZ). To improve surveillance by ensuring integration of laboratory and surveillance activities, all national meetings and periodic subregional meetings are held jointly with state laboratory and surveillance personnel. In 2000, a standardized database was introduced nationwide for management of laboratory results from suspected measles and rubella cases.

Measles case data. Information on measles cases is obtained through two sources: the integrated national notifiable disease surveillance system and a measles-specific weekly bulletin sent from the states to the national level. The national notifiable disease surveillance system, "Sistema de Informações de Agravos de Notificação" (SINAN), includes biweekly electronic transmission of data to the state and national level for all 30 legally notifiable diseases. This system was introduced into Brazil in 1993, but implementation was intensified beginning in 1995 and completed in 2000 [13]. Data from individual measles case-investigation forms are entered at the municipal or regional level, transferred to the next reporting level, and ultimately transferred to the National Epidemiology Center (CENEPI) in the Ministry of Health. Information on measles deaths is available through SINAN and through the national mortality system (SIM; Sistema de Informaçào de Mortalidade).

To provide immediate information on cases and outbreaks, the weekly measles-rubella-specific bulletin was implemented in 1997. Aggregate numbers of suspected, confirmed, and discarded measles cases are reported weekly through each reporting level to the state and then to the national level. This information is in turn summarized (total numbers of confirmed, suspected, and discarded cases) and is disseminated from the national level to state surveillance units, PAHO, and other key partners. This weekly bulletin is posted on the Web site of the National Health Foundation (FUNASA)/CENEPI, Ministry of Health (http://www.funasa.gov.br), and the information is also available each week on the PAHO Web site (http://www.paho.org).

In 1997, the surveillance system was evaluated in two states, São Paulo and Bahia This evaluation identified key barriers to timely measles surveillance. First, it identified a high turnover in local surveillance staff and the lack of staff with exclusive responsibility for measles surveillance at the state and local levels. Second, it identified difficulty in sustaining political will for measles-specific activities during times of low-level or absent measles virus transmission. Last, a key recommendation was to designate 1 staff person in each state to provide full-time and exclusive support for measles activities [14].

IMPACT OF MEASLES ELIMINATION STRATEGIES IN BRAZIL

Measles morbidity and mortality, 1980–2000. Prior to initiation of routine measles vaccination in Brazil, measles was a leading cause of childhood morbidity and mortality, accounting for 26% of all deaths among children 1–4 years of age [2, 15]. Between 1968 and 1980, measles epidemics were observed every 2–3 years. Intensified measles control in 1980 led to a marked reduction in incidence; nonetheless, following a 4-year period of control, a resurgence occurred in 1986 with 129,942 cases, for an incidence of 98/100,000 (figure 1) [2, 9].

Reductions in measles mortality paralleled the declines in measles incidence. Measles mortality declined from 2.7/100,000 in 1980 to 0.33/100,000 in 1990 (figure 3). The average annual number of reported measles deaths declined from 2271 during 1980–1984 to 851 in 1985–1989 and 148 during 1990–1994. The measles case-fatality ratio declined from 5.6% in 1977 to 0.78% by 1990 (figure 3).

Following the first national measles catch-up campaign in 1992, measles incidence declined dramatically. The number of reported measles cases declined by 99%, from 42,934 cases in 1991 to 2396 in 1993, and reached an historic record low in 1995, with 967 cases (0.6/100,000) (figure 1).

Measles resurgence in Brazil. In 1997, after a 4-year period of measles control, Brazil experienced a measles resurgence, with 53,335 confirmed cases and 61 deaths reported. Initial outbreaks were detected in the states of Santa Catarina and São Paulo in the second half of 1996. During the first half of 1996, three imported cases were reported. These included 2 brothers who returned from Italy to Rio de Janeiro with rash onset in June 1996. The third imported case occurred in a traveler from Japan who arrived in April in São Paulo, traveled to the state of Mato Grosso, and had rash onset in May 1996 [9]. By April 1997, the number of cases in São Paulo was increasing exponentially [7, 9].

Of the 53,335 confirmed cases in Brazil in 1997, 42,055 (79%) were reported from the state of São Paulo, and of them, 23,907 (57%) were laboratory confirmed or epidemiologically linked to a laboratory-confirmed case. Transmission was concentrated in the São Paulo metropolitan area, which had 36,803 (88%) of the state's cases and the highest geographic incidence (246/100,000) in Brazil. Overall, 71% of cases in São Paulo State occurred among persons ⩾20 years of age. The highest age-specific incidence rates were among children aged <1 year (1577/100,000), young adults aged 20–29 years (539/100,000), and children aged 1–4 years (205/100,000) [11]. The outbreak in São Paulo spread throughout Brazil. The epidemic characteristics were similar across the different states, with 55% of cases overall occurring among young adults aged 20–29 years, a cohort born between 1968 and 1977 when vaccination programs were being initiated.

A case-control study identified a number of risk factors for measles, including lack of measles vaccination, having been born outside of São Paulo or in a rural area, being employed, and spending time in a semiclosed institution, such as a nursery, day care center, or school. Specific risk factors for measles

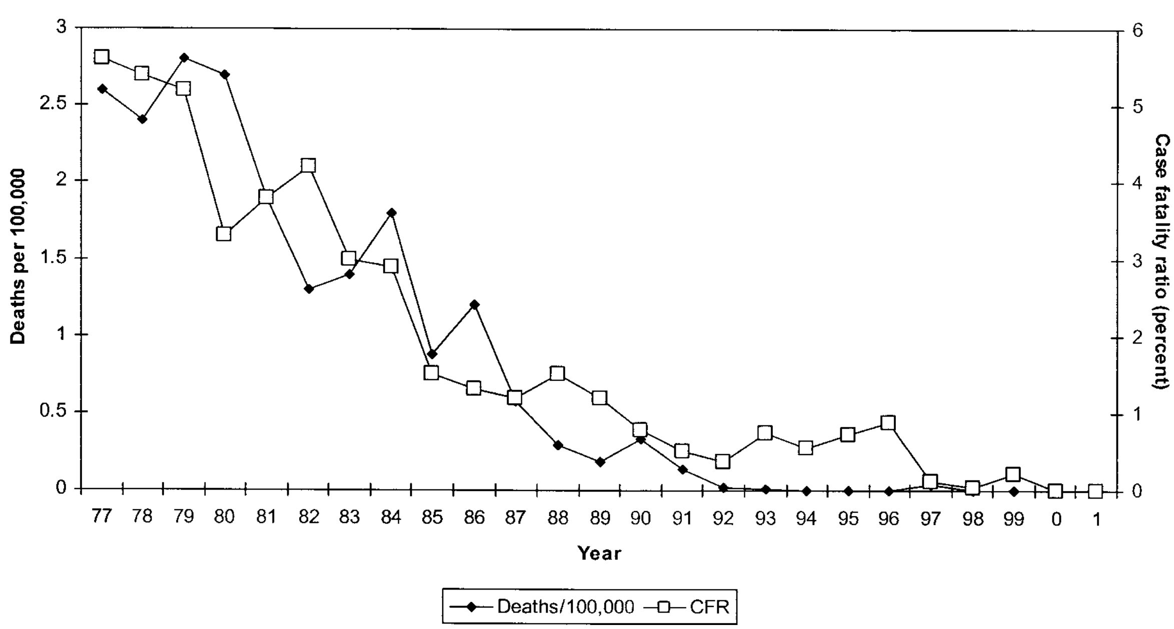

Figure 3. Measles mortality and measles case fatality ratio (CFR), Brazil—1977–2001

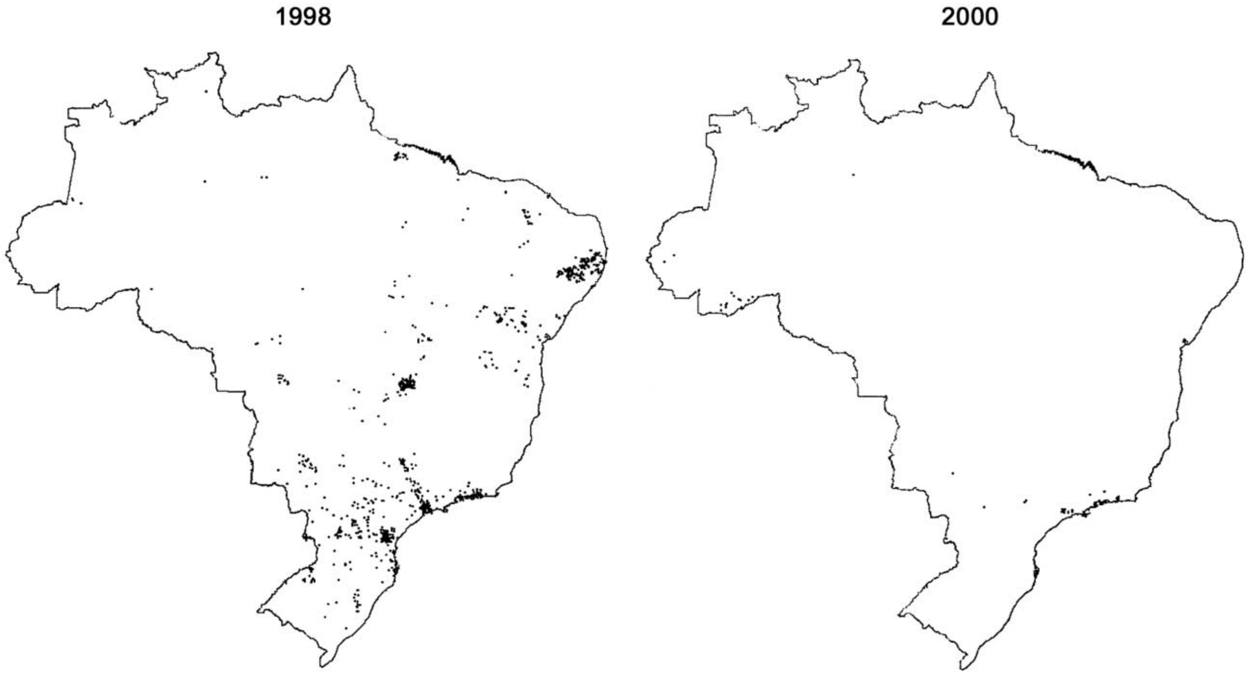

Figure 4. Measles cases by municipality of residence, Brazil—1998 and 2000. Each dot represents 1 case.

among persons aged 20–29 years included lack of measles vaccination, male sex, recent migration to São Paulo from predominantly rural states in northeastern Brazil, contact in the workplace with someone with measles, and use of public transportation for commuting between home and workplace. Among children aged <5 years, being unvaccinated for measles was a consistent risk factor [7]. Mathematical modeling identified the lack of a timely follow-up campaign among children aged 1–4 years in 1995 as a risk factor for epidemic spread [16]. Studies conducted in Rio de Janeiro and Minas Gerais found an increased risk among unvaccinated young adults, particularly in persons originating in the northeast area of the country [17] and in persons born before initiation of routine vaccination or after the last follow-up campaign [18].

Data on the molecular epidemiology of measles viruses in Brazil has allowed more precise definition of transmission pathways. Characterization of measles viruses isolated during the outbreak in 1997 identified the circulation of the D6 genotype [19, 20]. This same genotype was identified in subsequent measles outbreaks in Argentina [21] and Uruguay in 1998 [22] as well as in Chile, Bolivia, and the Dominican Republic [23] during 1999–2001. The C2 genotype was identified from a localized outbreak in the state of Santa Catarina in 1996. The C2 and D6 genotypes circulate primarily in Western Europe and have been linked to importation into a number of countries [23].

The outbreak control strategies included (1) intensification of surveillance, (2) vaccination (after the reporting of suspected cases) of contacts aged 6 months to 39 years who did not have evidence of prior measles vaccination, (3) vaccination in schools, identifying children through 11 years of age not previously vaccinated for measles, and (4) the second national follow-up campaign (see above), which was targeted to children aged 6 months to 4 years and achieved a coverage of 66%. By 1998, the number of measles cases in Brazil had declined to 2930 (figure 4).

Measles surveillance task force. A key component of the intensified measles elimination activities following the outbreak was the adoption in mid-1999 of the Measles Eradication Task Force. One surveillance technician was assigned to each state to assist the State Secretariats of Health in strengthening surveillance through the following strategies: weekly negative notification; timely and complete investigation of cases and outbreaks, with rapid implementation of control measures; active case-finding; assisting and guiding immunization efforts, including identification and vaccination of high-risk groups; analysis and feedback of surveillance data to key partners (e.g., pediatricians); and strengthening partnerships with governmental and nongovernmental institutions (e.g., educational sector) for enhanced surveillance and immunization activities.

Decentralization and the role of training. In the context of a decentralized health care system with high staff turnover, ongoing training at all levels of the health care system has been a key component of the measles elimination plan in Brazil. This training alerts health care providers to the national and regional importance of measles elimination and their role in notification

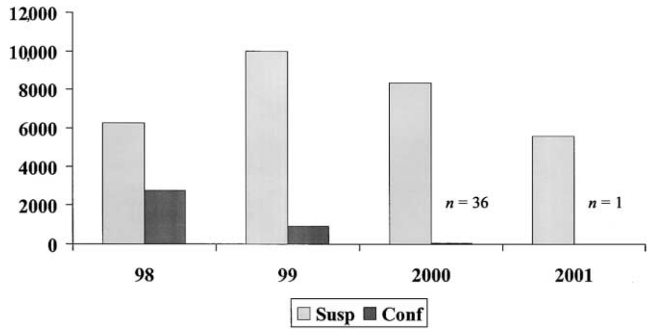

Figure 5. Suspected (Susp) and confirmed (Conf) measles cases, Brazil—1998–2001.

of suspected cases. A second function of training is to build local capacity in disease surveillance, particularly in case investigation. Following the introduction of the measles task force in May 1999, national, state, and local training was intensified. From July 1999 through June 2001, a total of 424 trainings were held at the state or local level, involving a total of 17,914 health care professionals. In addition, oversight of surveillance activities at all levels of the system was intensified: During this same period (1999–2001), there were 94, 334, and 2076 site visits at the national, regional (subnational), and municipality levels, respectively.

Intensification of measles surveillance and vaccination, 1999–2001. The sensitivity and specificity of the surveillance system showed substantial improvement following the implementation of this measles surveillance task force. In 1999, the national reporting network for negative weekly reporting included ~8000 reporting units, of which only 50% were reporting weekly. Of 10,007 suspected cases of measles reported during 1999, 908 (9.1%) were confirmed, and 378 of those (42%) were confirmed by laboratory or epidemiologic link to a laboratory-confirmed case (epi-link). By 2000, the reporting network, had expanded to 9213 reporting units, of which 81% were reporting weekly. Of 8358 suspected cases notified through 30 December 2000, 36 (0.4%) were confirmed (30 [83%] by laboratory or epi-link). Among discarded suspected measles cases, 92% were discarded on the basis of laboratory testing. Of 5599 suspected measles cases in 2001, only 1, an imported case from Japan, was confirmed (figure 5). Laboratory testing was timely during 2000–2001: In 2000, results were available for 67% of samples within 4 days of receipt, and for 2001, this figure was 73% (these data are not available prior to 2000). The last confirmed measles case in Brazil occurred in March 2002, and it was also an imported case from Japan.

During periods of low or absent measles transmission, measles may be mistaken for other more common rash illnesses. Brazil experienced large rubella outbreaks nationwide during 1999–2000, a period when measles transmission was declining. In 1998, 11,987 suspected rubella cases were reported, of which 6729 (56%) were confirmed. In 1999, of 31,911 suspected rubella cases, 14,502 (45%) were confirmed. By 2000, 47,434 cases were reported, of which 15,228 (32%) were confirmed (figure 6). Thus, although the number of confirmed rubella cases was similar during 1999–2000, the number of suspected cases increased, reflecting increased sensitivity of the surveillance during that time period. The decreased numbers of suspected cases of measles and rubella from 2000 to 2001 reflects decreases in rubella transmission in 2001, as evidenced by the confirmation of 5409 (16%) of the 33,943 suspected rubella cases (figure 6).

The last remaining foci of measles transmission in Brazil were eliminated during 1999–2000. In 1999, 908 confirmed cases were distributed in 24 (89%) of the 27 federal units (26 states and the Federal District). Overall, cases were concentrated in the northeastern region of the country, which reported 369 (41%) of the 908 confirmed cases. Of these confirmed cases, 240 (65%) were reported from the state of Pernambuco in northeastern Brazil. Detailed data were available for 196 laboratory-confirmed cases in Pernambuco during 1999. Most cases occurred among unvaccinated children or young adults: 41% of the cases occurred among children aged 5–14 years, and an additional 38% occurred among adults >15 years of age; 75% of case-patients aged 5–29 years were unvaccinated.

Measles elimination was achieved in Pernambuco through intensification of routine vaccination, indiscriminate vaccination of children through age 15 in areas with suspected cases, and vaccination of high-risk groups (personnel in health care and tourism and migrant farm workers). The last case of measles in Pernambuco occurred in December 1999.

The last outbreak of measles in Brazil occurred in Acre, a state bordering Bolivia in northwestern Brazil (figure 4). The outbreak occurred in February and March 2000, with a total of 15 confirmed cases occurring primarily among unvaccinated children: 13 (87%) of the case-patients were unvaccinated, and 9 (60%) were aged 1–14 years. Of the remaining cases, 4 (27%) were aged <1 year and 2 (13%) were 15–29 years old. The outbreak was controlled through house-to-house vaccination, which was targeted to persons 6 months to 39 years of age in

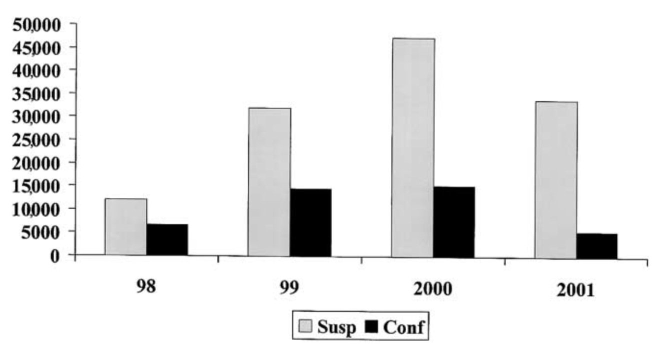

Figure 6. Suspected (Susp) and confirmed (Conf) rubella cases, Brazil—1998–2001.

the affected areas; active case-finding in the community; and mobilization of health case professionals for enhanced surveillance and vaccination activities.

The remaining 21 of the 36 confirmed cases reported during 2000 were sporadic, with no source of infection identified nor evidence of secondary transmission despite extensive investigation and active case-finding in the community, including health facilities, schools, and days care centers. Of these 21 sporadic cases, 14 (67%) were reported from the state of São Paulo (figure 4), and 9 occurred among children aged 9–12 months, all of whom had received a dose of measles-containing vaccine within the previous 30 days. The median interval between vaccination and rash onset was 20 days (range, 17–30).

Periodic active case-finding activities have confirmed the completeness of reporting for measles cases. From July 2000 through March 2001, 917 active-case searches were conducted in 25 states. These active case-findings included 402 hospitals, 515 primary health care units, and 44 other types of health care facilities, with a total of 2,581,542 charts reviewed in 25 states and federal units. In addition, 18,118 interviews were conducted with health care professionals. Of 180 suspected measles cases detected, 142 (79%) had been reported previously. Of 1070 suspected rubella cases, 740 (69%) had been reported previously. No new cases were confirmed as a result of these community-based active case-findings.

Following a period of 14 months with no measles transmission detected, an imported case from Japan was reported from São Paulo in June 2001. A 7-month-old child visiting from Tokyo and unvaccinated for measles arrived by airplane in São Paulo accompanied by 4 family members. The child had rash onset within 1 day after arrival in São Paulo, and the following day, the infant was taken to a private pediatrician who diagnosed and immediately reported the case. Investigation and control measures were initiated the same day. Laboratory results showing measles-specific IgM antibodies were available within 5 days. Two weeks prior to onset of symptoms, the child had had contact with an uncle in Japan who had been hospitalized with measles. Investigation included a national and international alert, with tracing of airline passengers to 10 states in Brazil and 3 other countries (Bolivia, Argentina, and Uruguay). Despite extensive follow-up, no secondary cases were identified. Measles virus isolated from this patient was characterized as belonging to clade D [24]. In March 2002 another case imported from Japan into São Paulo was detected in a 2-year-old unvaccinated child. The child was IgM positive and epidemiologically linked to a confirmed case in Japan. A response similar to the one above was mounted, and no secondary cases were identified. To date, this is the last confirmed measles case in Brazil.

DISCUSSION

Analysis of current surveillance data suggests that the interruption of indigenous measles transmission in Brazil during the year 2000 has been sustained through 2002. Despite an increase in the sensitivity of the surveillance system during 1999–2000, no outbreaks of measles have been detected since February 2000. The interruption of transmission reflects the intensive efforts to achieve high coverage in routine and supplementary vaccination activities (2000 follow-up campaign) during 1999–2000 as well as the intensive efforts to increase the timeliness and sensitivity of measles surveillance, with detection of cases linked to rapid implementation of control measures. The substantial improvement in the quality of surveillance following the designation of the Measles Eradication Task Force to support the state health departments emphasizes the importance of focused resource allocation to achieve the elimination goal.

The detection and predominance of sporadic cases during periods of low or absent measles virus transmission, as was seen in Brazil during 2000, is expected and characteristic of a sensitive surveillance system in countries with low-level or interrupted transmission [25, 26], conditions that result in a decline of the positive predictive value of serologic assays. A high proportion of the sporadic cases detected in Brazil was among children ⩽1 year old who were recently (range, 17–30 days; median, 20) vaccinated for measles. Although measles IgM antibodies may last up to 56 days [27], postvaccination rash generally occurs within 5–14 days [28]. Because these children had rash onset more than 14 days after vaccination, they were likely experiencing symptoms similar to measles but caused by another virus. The IgM detected may have been due to a cross-reaction with non-measles IgM or coincidental rather than causal. Although specificity of the currently used measles tests is high and is increased by retesting all IgM-positive samples, some false-positive results are expected. In Brazil, all measles IgM-positive samples are also tested for dengue and rubella. Other studies have shown that in addition to dengue and rubella, parvovirus B19 and human herpesvirus 6 (HHV-6) are known to cause false-positive results for measles [29]. A study in Brazil involving laboratory testing of all febrile rash illnesses found that a variety of etiologic agents (dengue, rubella, measles, parvovirus B19, and HHV-6) were associated with clinical features similar to measles [30].

Since the inclusion of rubella notification in 1997, the measles surveillance system has been useful for evaluating rubella control strategies. Prior to introduction of rubella vaccination, up to 43% of suspected measles cases were classified as rubella on the basis of IgM testing [31]. The increased recognition of the disease burden of rubella and congenital rubella syndrome has been critical in guiding control strategies. During

1999–2000, identification of the shift in rubella from young children to young adults [32] led to the development of a rubella vaccination campaign targeted to young women of childbearing age conducted in two phases during 2001–2002 [33].

Overall national trends may obscure local weaknesses in surveillance or pockets of low coverage. Thus, reported sporadic or imported cases may overrepresent states or areas with more sensitive surveillance systems. The scope of this article does not permit analysis of local variability in surveillance. Nonetheless, the sensitivity and specificity of the system, as measured by weekly negative reporting, periodic active case-findings, and percent of cases that are confirmed or discarded by laboratory testing, indicates a general consistently high quality of surveillance across states. Further efforts are needed to improve surveillance and coverage in areas identified as suboptimal on the basis of local data.

The past decade of experience with measles elimination in Brazil has led to several key insights relevant to current measles strategies. First, initial catch-up campaigns targeted to a broad age group (9 months to 14 years) can have an immediate and dramatic impact on measles transmission. With reduced numbers of cases, more intensive and timely surveillance is feasible. Second, the measles epidemic in São Paulo in 1997 highlighted the importance of susceptible young adults in disease introduction and transmission. As the vaccination program has matured, a new risk group has become apparent—cohorts of young adults without exposure to natural disease and also lacking vaccine-induced immunity because they were outside of the target age group when the program was initiated. Most of these adults are young males who have immigrated from rural areas to cities in search of work. Third, timely implementation of follow-up campaigns with high coverage is critical to prevent or reduce epidemic spread. Mathematical modeling of the São Paulo outbreak indicates that while a follow-up campaign might not have prevented the outbreak, it would have had a substantial impact on overall incidence. Thus, maintenance of high routine coverage and timely implementation of follow-up campaigns are critical components of the measles elimination strategy. In addition, identification and vaccination of young adults at high risk (e.g., migrant, health care, and tourist industry workers) are now integrated into national and state measles elimination efforts. Last, a key lesson has been the need for maintaining political will in the absence of disease transmission.

Sustaining interruption of measles transmission in Brazil will require continued high-quality surveillance and high routine coverage at the state, municipal, and local levels. Measles virus circulation worldwide continues, with an estimated 31 million measles cases and 770,000 measles deaths in 2000 [34]. Brazil is at high risk for disease importations. In 1999, 4.9 million persons arrived on international airline flights to Brazil, including 1.2 million persons from Europe, 41,294 from Africa, and 104,701 from Asia. Another 4.1 million travelers left from international airports in Brazil to other regions, including 896,500 to Europe, 62,100 to Asia, and 36,000 to Africa [35]. In March 2001 a 5-year global measles strategic plan was finalized [36]. However, until regional and global control advance further, maintenance of sensitive and timely national surveillance along with high routine and follow-up campaign coverage is critical.

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Acknowledgments

We thank all state, regional, municipal, and other local surveillance and immunization coordinators for their dedication to improving measles surveillance; Maria de Lourdes Sousa Maia for her dedication to improving immunization coverage through leadership of the National Immunization Program; Regilma Oliveira for commitment to supporting laboratory aspects of the national measles elimination plan; all members of the measles elimination task force for their commitment and intensive efforts toward improving measles surveillance; Marcia Mesquita for high-quality data management; Claudio Silveira and Vance Dietz for review of the manuscript; and João Batista Risi for providing historical insight on public health and disease eradication programs in Brazil.

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