EPI Newsletter

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Pertussis Outbreaks in the Americas

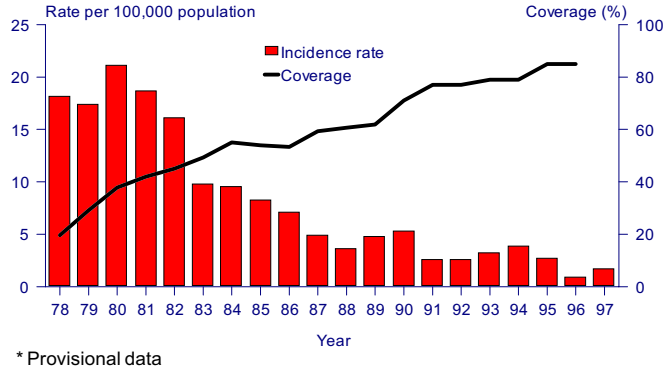
In 1997-1998, several outbreaks of pertussis have been reported in the Region. The following article summarizes preliminary information on the outbreaks occurring in Guatemala and Brazil.

Guatemala

An outbreak of pertussis is affecting the Department of Quiche in Guatemala since November of 1997. The outbreak started in Ilom, a community inhabited primarily by indigenous populations that live in geographical isolation. Vaccination coverage in these communities is estimated to be approximately 13%. The village of Ilom has a health post attended by a health worker.

Two months elapsed between the occurrence of the first cases and deaths and the actual notification to health authorities. By that time, 324 cases had been reported. The outbreak affected over 10% of the population living in the village. Of the total reported cases, 17 persons died (case fatality rate = 5.2%). Highest age-specific incidence rates (48.9%) and case-fatality rates (9.4%) were observed in the population 0-5 years of age. *Bordetella pertussis* was isolated in a nasopharyngeal sample from a four-year-old child and serology was also positive in four blood samples from the outbreak.

Figure 1
Annual incidence of pertussis and vaccine coverage with DPT3 in children less than 1 year of age Region of the Americas, 1978-1997*



* Provisional data
Source: SVI/PAHO

During the second week of January of 1998, more cases occurred affecting several neighboring communities (they share the road to the market). As of the end of January, there were an additional 269 cases reported, predominantly among children 5 to 9 years of age, who accounted for approximately 50% of the cases.

Contributing factors to the outbreak include a large number of susceptibles due to low vaccination coverage and the prolonged absence of *B. pertussis* circulation in an isolated community with relatively low population mobility. This area was also hard-hit by the long armed conflict in Guatemala, which ended in December of 1996. Factors contributing to the high case-fatality rate observed in Ilom include malnutrition, especially among children under 5, poor hygiene and crowded conditions.

Different control measures were put into place during the outbreak. There was a change in the vaccination schedule for DPT. The first of 3 doses was moved forward from 2 months to 1 month, and intervals between vaccination were moved from 2 months to every 4 weeks. Following the initiation of the outbreak, vaccination with DPT was performed house-to-house in all communities. As the outbreak developed and because of the control measures, it was observed that there were reduced number of cases among infants and young children. All cases and contacts have been treated with the appropriate antibiotics.

Source: Ministry of Health, Guatemala.

Brazil

Starting at the end of October 1997, several cases of pertussis were reported among indigenous communities in the state of Acre. These territories are near the Peruvian border and there is frequent contact between the indigenous populations on both sides. During December, a group of vaccinators coordinated by the Ministry of Health visited the

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Upper Enviera River area in the municipality of Feijo, to investigate the outbreak and vaccinate children under 7 years of age with DPT vaccine. This opportunity was also used to vaccinate people with other antigens. The total population living in the area is approximately 2,500.

Since a non-governmental organization left the area at the end of 1995, vaccination coverage with three doses of DPT has fallen from 73% in 1995 to 16% in 1996, and 9% in 1997. A total of 98 pertussis cases were clinically-confirmed by the physician who accompanied the investigation team. The paroxysmal cough, cyanosis, and post-tussive vomiting were some of the pertussis symptoms found in the children. Information was collected for 91 (93%) of the cases: 17 (19%) occurred in children under 1 year, 40 (44%) in children 1-4 years, 22 (24%) in children 10-14 years, and 6 (7%) in persons over 15 years of age. Age was not known in 2 cases. Forty-three (47%) cases had unknown vaccination status, 42 (46%) were unvaccinated, and 2 (2%) occurred in persons who had completed their DPT vaccination schedule. Four (4%) cases occurred in persons who had been partially vaccinated. Of the total cases reported, there were 9 deaths (case-fatality rate = 10%), all occurring in children under 2 years of age, six of whom were less than 1 year of age. The last 3 cases were reported in week 52 of 1997.

As part of the outbreak control activities in the Upper Enviera River, 91 children under 1 year of age were vaccinated with DPT, 52 of whom received their first dose. In addition, 455 children 1-6 years of age were vaccinated. The second and third doses of DPT will need to be applied, as well as vaccination of nearly 14,500 infants from other hard-to-reach indigenous populations in Acre.

In December, cases were notified in the Rio Purus area of the Santa Rosa municipality, also in the state of Acre. Preliminary data was obtained in only 3 of the 19 villages, which reported a total of approximately 100 cases with 5 deaths.

Source: GT Diphtheria and Pertussis, National Health Foundation, Ministry of Health, Brazil.

Editorial note: Pertussis is a highly transmissible bacteria (up to 90% in susceptile individuals), it affects all age groups and can be deadly. Deaths occur primarily in children under 2 years of age, with those less than 12 months at highest risk. Unlike measles, maternal antibodies do not confer immunity to newborns, so infants are susceptible from birth.

Vaccination coverage with three doses of DPT vaccine has improved notably in the Region during the past 20 years—from 12% in 1978 to 86% in 1996. This has produced a steady decline in reported cases over the same period. In 1978, over 100,000 cases were reported, compared with 17,000 cases reported in 1996 (Figure 1).

There are, however, persistent problems with pertussis, including difficult diagnosis, poor surveillance, inadequate laboratory support and high underreporting of cases in adolescents and adults. Given its clinical presentation, pertussis may often be confused with other acute respiratory infections and pneumoniae. One of the major difficulties in establishing pertussis surveillance is the variety of symptoms which can accompany the disease. Symptoms range from slight to fatal paroxysmal coughing and vomiting, and complications include pneumonia, encephalitis and nutritional impairment. The severity of the disease is also related to the age and vaccination status of the patient.

As mentioned above, in 1996, Regional coverage with DPT vaccine was 86%. National average was below 80% in only three countries—Brazil, Guatemala and Venezuela (75%, 73% and 57%, respectively). During the last meeting of the Technical Advisory Group on Vaccine-Preventable Diseases (TAG) held in Guatemala in 1997, countries were encouraged to strengthen surveillance activities, standardize case reporting and laboratory diagnosis, reinforce routine immunization to achieve and maintain DPT3 coverage above 90%, and to implement selective investigation on distribution by age and sex, case vaccination status, case-fatality and inci-dence rates, particularly during outbreaks.

These recent outbreaks in Brazil and Guatemala have occurred primarily among indigenous people living in remote areas. They were preventable and therefore, increased efforts are needed to provide all recommended EPI vaccines to the target populations throughout the Region, especially persons living in areas with poor access to health services.

Importation of Measles to Costa Rica

From July through October of 1997, Costa Rica experienced a measles outbreak with a total of 12 laboratory-confirmed measles cases. Ten clinically-confirmed measles cases were reported for the entire year. The following article summarizes the findings of the team that investigated the outbreak.

The measles elimination initiative was launched in Costa Rica in 1993, but only 75% vaccination coverage was achieved in children under 15 years of age during the attack phase (*catch-up* campaign). Since 1995, selective vaccination campaigns have been held annually, most recently in April 1997. The age for vaccination with measles-mumps-rubella (MMR) vaccine was 12 months of age prior to 1991, 18 months of age from 1991-1994, and 15 months of age from 1994 onward. In 1992, a booster dose was implemented at the age of 7 years (first grade of school). The last measles epidemic occurred from 1990 to 1992, producing more than 8,000 cases and 56 deaths. The last confirmed case of measles corresponds to that time.

From January through June 1997, there had been 49 suspected measles cases reported. Of these, 38 were discarded, 10 were under investigation and one case was clinically confirmed.

Investigation

The first laboratory-confirmed measles case (index case), was a 27 year-old from the county of Liberia in the Northwest province of Guanacaste, who worked as a cook at a restaurant on the El Tamarindo beach, a tourist complex located approximately 60 km from Liberia with at least 60 hotels. The case had rash onset on 22 July 1997, accompanied by conjunctivitis and poor general condition. On 25 July, the patient developed a generalized maculopapular rash, and was admitted to Liberia Hospital for three days. A specimen from the patient tested positive for measles at the national laboratory (INCIENSA). The result was confirmed by the Measles Reference Laboratory of the Gorgas Center in Panama.

Twenty days prior to the illness, the patient had moved from Liberia to El Tamarindo beach to work in a restaurant. The patient was living in Santa Rosa, approximately 10 km from El Tamarindo, with a population of approximately 1,000. As cook, he did not have much contact with the restaurant's clients. Community investigation did not show any suspected measles cases in Santa Rosa. The patient does not remember being vaccinated against measles.

The second documented case, a woman 33 years of age, had rash onset on 11 August, and was hospitalized for five days. On 21 August, a third case was reported in a 12 month old child from Cuajiniquil in La Cruz county, who was hospitalized that same day in Liberia Hospital. The mother revealed that her child had been previously hospitalized on 8-9 August, with asthmatic bronchitis. There were two additional cases in Cuajiniquil, in children 13 and 14 months of age, who had direct contact with this patient.

On 9 September, two more cases were reported in Liberia. One, a girl of 7 months, was hospitalized from 21 to 25 August, with viral meningitis in Liberia Hospital. Fever and rash began ten days after her discharge, on 2 September. The other case was a girl 6 months of age, for whom there was no determined source of infection. All cases in this series were confirmed by INCIENSA and the Gorgas Laboratory.

A detailed investigation took place from 4-8 October, 1997. An analysis of vaccination coverage showed that at least 3 of the 12 counties in the province of Guanacaste did not achieve the required coverage rates for measles (more than 90%) in children under 1 year of age in the last two years.

The epidemiological history of the index case indicates that he likely contracted the virus at El Tamarindo beach, a popular tourist attraction. Most visitors come from Europe, North America, Canada, South America, and some from Central America. The largest hotels register between 35,000 and 40,000 tourists per year.

All contacts of the index case at the restaurant were interviewed without result. Next, selected hotels were visited. The manager of one said that in early July, three Brazilian tourists were lodged, one of which presented fever upon arrival and subsequently rash appeared. A physician diagnosed measles but did not report the case. The three guests left the hotel around 19 August 1997. This hotel is less than 100 meters from the restaurant where the index case worked, and it is probable that the tourists went to eat in that restaurant. Two other suspected measles cases were found during the active search.

PAHO contacted the Ministry of Health in Brazil to investigate the suspected measles case from this Brazilian tourist. The case was confirmed as measles and it was also determined that the case was from the Sao Paulo area.

An analysis was carried out of all patients that entered the Hospital of Liberia from mid-July through the end of September, to determine whether these patients had disseminated the virus to other regions of the country upon leaving the hospital. It was found that patients from all 12 counties of the Guanacaste province had been hospitalized, as well as people from five other counties of the country, including San José, and two patients from Nicaragua.

Control Measures

Selective vaccination was carried out in the county of Liberia targeting the entire population under 15 years of age. A national vaccination campaign against measles was implemented on 20 October 1997.

All countries in the Region of the Americas were alerted, particularly those in Central America, of the high risk of importations, especially in areas with low vaccination coverage.

Conclusions

Measles virus circulated in the province of Guanacaste from July to October 1997. The first case was presented in an adult of 27 years, hospitalized on 25 July in the hospital of Liberia. Eleven more cases were confirmed, the last in October. No other cases have been confirmed either in the Guanacaste province or in the rest of the country. Almost all the cases in the first generation in the counties of Liberia and La Cruz had contact with the Liberia Hospital as source of infection and were linked to the index case. This suggests that transmission took place within Liberia Hospital.

As recommended by the XII Technical Advisory Group on Vaccine-Preventable Diseases (TAG) in Guatemala, it is necessary to monitor vaccination coverage by district and to characterize districts at high-risk for measles (coverage less than 90%). Viral isolation is required from all chains of transmission. An adequate sample of urine should be taken in sterile container at first contact (preferably within one week of rash onset) with suspected measles cases.

Source: Ministry of Health, Costa Rica.

Visit the new **Measles News** section on the World Wide Web page of the Special Program for Vaccines and Immunization at **http://www.paho.org/english/svihome.htm** This section contains up-to-date information on the Regional measles initiative, including the latest news, figures and graphs.

Measles Vaccination Campaigns

Region	Country/Territory	Campaign 1-14 (*Catch-up*)		Average routine coverage 1994-1996 (*Keep-up*)	Campaign 1-4 (*Follow-up*)		Next *Follow-up* Due
		Year	Coverage (%)		Year	Coverage (%)	
Andean	Bolivia	1994	98	90	…	…	**1998**
	Colombia	1993	96	93	1995	90	1999
	Ecuador	1994	100	70	…	…	**1998**
	Peru	1992	75	87	1995	97	1999
	Venezuela	1994	100	75	…	…	**1998**
Brazil	Brazil	1992	96	80	1995	77	1999
Central America	Belize	1993	82	82	1995	85	1999
	Costa Rica	1993	75	90	-	-	***1998****
	El Salvador	1993	96	89	1996	82	2000
	Guatemala	1993	85	73	1996	60	2000
	Honduras	1993	96	91	1996	85	2000
	Nicaragua	1993	94	81	1996	97	2000
	Panama	1993	88	86	1996	94	2000
English-speaking Caribbean and Suriname	Anguilla	1991	99	97	1996	100	2000
	Antigua & Barbuda	1991	96	95	1996	92	2000
	Bahamas	1991	87	91	1997	78	2001
	Barbados	1991	96	98	1996	91	2000
	British Virgin Islands	1991	88	100	1996	90	2000
	Cayman Islands	1991	85	92	-	-	-
	Dominica	1991	95	95	1996	100	2000
	Grenada	1991	98	89	1996	81	2000
	Guyana	1991	94	84	1996	90	2000
	Jamaica	1991	71	87	1995/6	85	1999
	Montserrat	1991	100	100	1996	100	2000
	St. Kitts & Nevis	1991	98	100	1996	100	2000
	St. Lucia	1991	97	94	1996	85	2000
	St. Vincent & Grenadines	1991	97	100	1995	84	1999
	Suriname	1991	89	75	1997	…	…
	Trinidad & Tobago	1991	90	88	1997	96	2001
	Turks & Caicos	1991	81	98	1996	95	2000
Latin Caribbean	Cuba	1987	98	100	1993	99	***1998****
	Dominican Republic	1993	77	84	…	…	***1998****
	Haiti	1994	94	28	…	…	***1998****
Mexico	Mexico	1993	88	91	…	…	***1998****
Southern Cone	Argentina	1993	97	98	…	…	***1998****
	Chile	1992	99	94	1996	100	2000
	Paraguay	1995	70	78	…	…	1999
	Uruguay	1994	95	88	…	…	**1998**

... Data not available - No campaign * Overdue
Data as of 21 January, 1998.

Follow-up vaccination campaigns are an essential component of PAHO's measles eradication strategy. A ***follow-up*** campaign is defined as a periodic measles vaccination campaign which targets all children 1 to 4 years of age, regardless of prior vaccination status or disease history.

However efficient the *catch-up* (vaccination campaign aimed at all children 1-14 years of age) and *keep-up* (vaccination through routine services) vaccination efforts are, there will inevitably be an accumulation of measles susceptible preschool-aged children over time. The primary purpose of ***follow-up*** campaigns is to prevent this accumulation of susceptible children from reaching dangerous levels which can increase the risk of a measles outbreak.

Two factors contribute to the build-up of susceptible children. *First,* measles vaccine is less than 100% effective, thus leaving some children unprotected following vaccination. *Second,* measles vaccination coverage for each birth cohort will almost always fall short of reaching all children.

PAHO's measles eradication strategy recommends that periodic ***follow-up*** vaccination campaigns be conducted whenever the estimated number of measles susceptible preschool-aged children (children 1-4 years of age) approaches the size of an average birth-cohort. The interval between campaigns will depend upon the vaccination coverage obtained among infants through routine services since

the last campaign. The lower the average routine vaccination coverage, the shorter the interval between campaigns. For example, if an average of only 60% routine coverage is obtained, a ***follow-up*** vaccination campaign would be needed approximately every two years; if 80% average coverage is obtained, then campaigns will be needed approximately every four years. The maximum allowable interval between campaigns is 4 years. Most countries of the Americas are able to maintain an average routine coverage of at least 80% and conduct ***follow-up*** campaigns every 4 years.

The table on page 4 summarizes available data concerning measles vaccination activities by country. At this point there are several countries which are overdue for ***follow-up*** campaigns or are due for campaigns in 1998. The following countries **overdue** for a campaign are at relatively increased risk for measles outbreaks and should conduct ***follow-up*** campaigns as soon as possible: **Argentina, Costa Rica, Cuba, Dominican Republic, Haiti, and Mexico**. The following countries are due to conduct ***follow-up*** campaigns in 1998: Bolivia, Ecuador, Venezuela and Uruguay.

Update: Sao Paulo Measles Outbreak

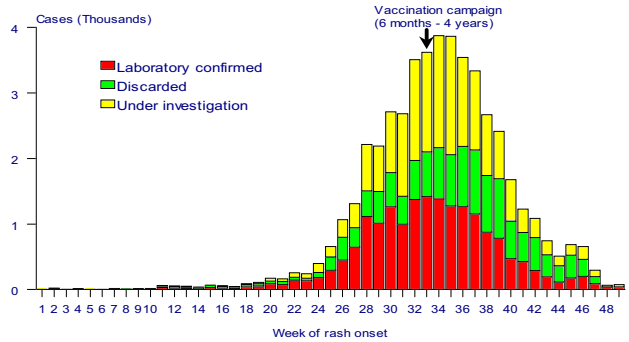
This article updates the information published in the June 1997 edition of the ***EPI Newsletter****.*

During 1997 and through 20 January 1998, a provisional total of 26,722 confirmed measles cases was reported from the countries of the Americas. Of these, 25,599 (96%) were reported from Brazil. Of the Brazil cases, 20,459 (80%) occurred in the state of Sao Paulo. The outbreak began during late 1996 with a total of 27 confirmed cases. During 1997, cases were reported from over 250 of the state's 645 municipalities. Of the total cases, 18,542 (91%) were reported from the Greater Sao Paulo metropolitan area.

The age-groups most affected by the Sao Paulo outbreak were infants under 1 year of age, (440 cases/100,000 population), followed by young adults 20-29 years, (164 cases/100,000), children 1-4 years (47 cases/100,000) and children 5-9 years (32 cases/100,000).

As of 20 January, a total of 20 measles deaths were reported (1 death per 1,022 reported cases, total case-fatality rate of 0.10%); 17 (85%) were residents of the Greater Sao Paulo metropolitan area.

Figure 1
Classification of suspected measles cases by week of rash onset
Sao Paulo, Brazil, 1997*



*As of 15 January 1998
Source: Center for Epidemiological Surveillance, Sao Paulo.

The age distribution of persons dying of measles is as follows: 11 (55%) were infants less than one year of age, 3 (15%) were children 1-4 years of age, 2 (10%) were children 5-9 years of age, and 4 (20%) were young adults 20-29 years of age. The following age-specific case-fatality rates were observed: in infants < 1 year of age (0.38%), children 1-4 years of age (0.25%), children 5-9 years of age (0.20%) and young adults 20-29 years of age (0.04%).

The following strategies were implemented with the goal of reducing measles virus circulation:

- Lowering the age of routine measles vaccination from 9 months to 6 months.
- Selective vaccination of unvaccinated children under 5 years of age in June 1997 (161,987 doses administered).
- Vaccination of health workers (182,562 doses administered).
- Extended contact vaccination of persons under 30 years of age, to reach those possibly exposed to cases of measles, including households, neighborhoods, workplace, schools and other high-risk groups (856,534 doses administered).
- Indiscriminate vaccination of children 6 months through 4 years 11 months of age in August 1997 (3,085,221 doses administered). Coverage is estimated to be 100% using official population data.
- Selective vaccination of school-aged children between 5-15 years of age between September and November 1997 (298,039 doses administered).
- Intensification of routine vaccination against measles for children between the ages of 9 and 15 months of age.

These interventions appeared to have been effective in slowing the epidemic. From week 36 on (two weeks after the indiscriminate vaccination campaign) there was a sharp drop in the number of cases (Figure 1). In addition to this drop, there was a marked reduction in the proportion of suspected measles cases that were confirmed by laboratory testing. Prior to the campaign (weeks 24 to 33), 67% of suspected measles cases were confirmed by laboratory, and following the campaign (weeks 36 to 45) only 43% were confirmed.

The Center for Epidemiological Surveillance of the Sao Paulo State Health Secretariat, in collaboration with the National Health Foundation of the Ministry of Health and the State Promotion for Mass Immunization and Education (FESIMA), along with PAHO are conducting a detailed

study to determine the risk factors for acquiring measles in this outbreak. This study seeks to track the dynamic of measles virus transmission and other factors that may explain the occurrence of this epidemic.

Source: Center for Epidemiological Surveillance, Sao Paulo State Health Secretariat, Brazil.

Editorial Note: Although the outbreak investigation is continuing, the Sao Paulo experience clearly demonstrates both the infectiousness and lethality of measles virus. Following a prolonged period of low measles incidence, the virus returned with a vengeance in Sao Paulo State. Measles has demonstrated its ability to find susceptible persons, even in areas with high vaccination coverage.

Several factors appear to have combined to create conditions which facilitated measles transmission in Sao Paulo. First, the failure to conduct a *follow-up* vaccination campaign in 1995, combined with low routine vaccination coverage (*keep-up* vaccination) among infants allowed for the accumulation of susceptible children in Sao Paulo. Second, the presence of large numbers of susceptible young adults who, for a variety of reasons, escaped both natural measles infection and measles vaccination increased the risk of a measles outbreak. Third, measles virus was imported into Sao Paulo, most probably from Europe. Finally, the high population density of the city facilitated contact between persons infected with measles and susceptible persons.

Available surveillance data suggest that the major outbreak control activities implemented in Sao Paulo helped to reduce the number of susceptibles and slow the epidemic. However, these control measures were very expensive in terms of financial and human resources, not to mention the opportunity cost of the interventions. Over 4.5 million persons were vaccinated in these efforts. Combined with the direct costs associated with medical care and the indirect costs due to decreased productivity, both acutely and chronically, this outbreak was very costly.

The overriding objective of PAHO's measles eradication strategy is the prevention of measles outbreaks. It is far better (and cheaper) to prevent an outbreak than to be forced to attempt to control an outbreak. Measles outbreaks can be prevented by achieving and maintaining high population immunity in susceptible populations, combined with the absence of imported measles virus.

Sao Paulo will now need to redouble its efforts to prevent future measles outbreaks. High coverage levels of measles vaccination must be achieved and maintained for infants at their first birthday. *Follow-up* campaigns must be conducted every four years to assure the highest possible level of measles population immunity. A two-dose schedule is clearly not an appropriate measles eradication strategy unless nearly universal coverage can be assured in a timely manner for **both** doses of measles vaccine. Moreover, efforts need to be made to assure immunity in adolescents and young adults who are at highest risk for exposure to measles virus. These interventions, combined with a the reduction of measles importations from other regions of the world, will greatly decrease the risk of another major measles outbreak in Sao Paulo or elsewhere in the Americas.

Polio Surveillance

In 1998, the Region of the Americas will complete its seventh year since the last case of poliomyelitis was detected, and the fourth year since polio was declared eradicated in the Western Hemisphere by the International Commission for the Certification of Poliomyelitis Eradication. Still in front of us, however, is the projected worldwide eradication of polio by the year 2000. While polio circulates in other regions of the world, the Americas must remain alert in the surveillance for cases of acute flaccid paralysis (AFP).

The table at right compares countries' fulfillment of AFP surveillance criteria in 1994, the year polio was declared eradicated, and in 1997. For the most part, countries have been consistent in maintaining AFP surveillance. However, the indicator measuring AFP rate per 100,000 has declined sharply. This is an indication that fewer AFP cases are being detected and entered into the surveillance system, which subsequently impacts the other surveillance criteria.

AFP Surveillance Indicators, 1994 and 1997*

Country	80% weekly reporting units		80% of cases investigated within 48 hours		80% of cases with 1 adequate stool sample taken		AFP Rate ≥ 1:100,000 in children < 15 years	
	1994	1997	1994	1997	1994	1997	1994	1997
Argentina	■		■				■	
Bolivia	■		■		■		■	
Brazil	■		■				■	
Chile	■		■		■		■	
Colombia	■		■		■		■	
Costa Rica	■						■	
Cuba	■		■		■		■	
Dominican Republic	■		■		■		■	
Ecuador	■		■		■		■	
El Salvador	■		■		■		■	
Guatemala			■		■		■	
Haiti								
Honduras	■		■		■		■	
Mexico	■		■				■	
Nicaragua	■		■		■		■	
Panama	■		■				■	
Paraguay	■		■				■	
Peru	■		■				■	
Uruguay	■							
Venezuela	■		■		■		■	
Total Countries	**18**	**17**	**18**	**17**	**11**	**12**	**18**	**12**

Meet criteria in 1997 ■ Meet criteria in 1994

* Data as of 3 January 1998 (Week 53) *Source:* SVI/PAHO (PESS)

Reported Cases of Selected Diseases

Number of reported cases of measles, poliomyelitis, tetanus, diphtheria, and whooping cough, from 1 January 1997 to date of last report, and the same epidemiological period in 1996, by country.

Country/Territory	Date of last report	Measles				Polio		Tetanus				Diphtheria		Whooping Cough	
		Confirmed 1997			Confirmed* 1996			Non Neonatal		Neonatal					
		Laboratory	Clinically	Total		1997	1996	1997	1996	1997	1996	1997	1996	1997	1996
Anguilla	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Antigua & Barbuda	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Argentina	3 Jan	48	10	58	59	0	0	18	41	3	4	0	0	321	767
Bahamas	3 Jan	1	0	1	0	0	0	0	1	0	0	0	0	0	0
Barbados	3 Jan	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Belize	3 Jan	0	0	0	0	0	0	1	3	0	0	0	0	0	1
Bermuda	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	3	0
Bolivia	3 Jan	1	0	1	7	0	0	4	4	8	14	3	1	125	43
Brazil	3 Jan	25,145	454	25,599	580	0	0	304	815	45	83	160	181	546	1,245
British Virgin Islands	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Canada	3 Jan	580	—	580	327	0	0	3	2	…	…	1	…	2,914	4,809
Cayman Islands	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Chile	3 Jan	54	0	54	0	0	0	4	17	0	0	0	1	825	1,094
Colombia	3 Jan	5	5	10	160	0	0	21	7	24	26	2	40	425	111
Costa Rica	3 Jan	12	3	15	24	0	0	3	3	0	0	0	0	30	20
Cuba	3 Jan	0	0	0	0	0	0	0	3	0	0	0	0	0	0
Dominica	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dominican Republic	3 Jan	1	0	1	0	0	0	14	17	0	0	25	6	1	2
Ecuador	3 Jan	0	0	0	42	0	0	39	88	25	36	19	22	245	163
El Salvador	3 Jan	0	0	0	1	0	0	3	10	2	5	0	0	2	3
French Guiana	…	0	0	0	…	0	0	…	…	…	…	…	…	…	…
Grenada	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Guadeloupe	3 Jan	116	0	116	13	0	0	…	…	…	…	…	…	…	…
Guatemala	3 Jan	2	0	2	1	0	0	5	2	6	12	0	0	92	66
Guyana	3 Jan	0	0	0	0	0	0	0	2	0	0	0	0	0	44
Haiti	26 Jul	0	0	0	1	0	0	0	…	33	…	0	…	0	…
Honduras	3 Jan	1	5	6	4	0	0	10	20	1	4	0	0	160	200
Jamaica	3 Jan	0	0	0	4	0	0	6	13	0	0	0	0	4	22
Martinique	…	0	0	0	…	0	0	…	…	…	…	…	…	…	…
Mexico	3 Jan	0	0	0	180	0	0	163	229	41	64	0	0	206	32
Montserrat	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Netherlands Antilles	…	0	0	0	…	0	0	…	…	…	…	…	…	…	…
Nicaragua	3 Jan	0	0	0	0	0	0	13	9	1	1	0	0	330	14
Panama	3 Jan	0	0	0	0	0	0	1	3	1	0	0	0	103	44
Paraguay	3 Jan	124	0	124	13	0	0	28	16	15	10	0	0	27	40
Peru	3 Jan	0	1	1	105	0	0	63	57	35	46	2	4	989	355
Puerto Rico	3 Jan	0	—	0	8	0	0	…	…	…	…	…	…	…	…
St Vincent/Grenadines	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	0	0
St. Kitts/Nevis	3 Jan	0	0	0	0	0	0	0	1	0	0	0	0	0	0
St. Lucia	3 Jan	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Suriname	3 Jan	0	0	0	0	0	0	0	4	0	0	0	0	0	2
Trinidad & Tobago	3 Jan	1	0	1	0	0	0	4	5	0	0	0	0	1	0
Turks & Caicos	3 Jan	0	0	0	0	0	0	0	0	0	0	0	0	0	0
United States	3 Jan	135	—	135	489	0	0	42	…	…	…	5	0	5,461	7,796
Uruguay	3 Jan	0	0	0	2	0	0	1	1	0	0	0	0	12	17
Venezuela	3 Jan	3	15	18	89	0	0	12	65	7	14	0	0	609	443
TOTAL		**26,229**	**493**	**26,722**	**2,109**	**0**	**0**	**763**	**1,439**	**247**	**319**	**217**	**255**	**13,432**	**17,333**

… Data not available.
— Clinically confirmed cases are not reported.
* Laboratory and clinically confirmed cases.

Vaccines of Quality

This article is the first of a series summarizing quality control tests performed by manufacturers and National Control Authorities (NCA), to determine if a particular vaccine lot is of known quality. This article focuses on the various safety tests that can be performed and their role. Future articles will address the topics of safety tests used for specific vaccines, potency testing, and the importance of planning to maintain adequate vaccine stocks.

The quality of a vaccine or vaccine lot is not only determined by the results of testing. Quality begins during the manufacturing process, as early as at the selection of the seed lot (bacterial or viral strain used to initiate the growth that will lead to the final product), culture media, reagents, and through the quality of the manufacturing process (adherence to Good Manufacturing Practices).

The NCA, through its National Control Laboratory, may decide not to perform all the tests, however, the manufacturer's protocol must be thoroughly evaluated to assure that testing has been performed.

Quality control of a vaccine consists of two main components: safety, and potency or efficacy of the vaccine. Safety evaluations ensure that the vaccine does not contain ingredients harmful to people or animal. These may include:

- the agent itself in the case of a toxin, or the bacterial or viral strain;
- chemicals added during the process intentionally that are not completely removed;
- the substrate used, such as culture medium, culture cells, eggs, serum or liquids;
- chemicals or agents added unintentionally.

Tests have been devised to address these different problems:

a. Specific-toxicity tests have been designed to detect residual toxicity (in the case of toxoids) or virulence (incomplete inactivation of vaccine strain).

b. An identity test can also be included among the safety tests, as it ensures that the antigen in the vaccine is the same as indicated in the label.

c. Chemicals and substances are added to the vaccine during the production processes: anti-foaming agents, inactivating agents, solvents, chemical reagents and finally adjuvants and/or preservatives. The concentration of these agents is usually monitored by chemical reactions to ensure that the concentration is within accepted specifications.

d. Other chemicals added unintentionally through contaminated equipment or reagents can be present and pass undetected. The abnormal toxicity test or innocuity test has been devised for this purpose.

e. Substrates used for the fermentation processes or cell growth are a special risk factor. Animal components of culture media may be contaminated with microorganisms, or products thereof that are a serious threat to human health. Attention is thus being paid to detect microbial contamination through the sterility test.

f. Microorganism contamination during the production process can be also monitored through the pyrogen test and/or the endotoxin test, which detect membrane components (lipopolysaccharides) of Gram negative bacteria.

It is important to note that each of the tests mentioned above is used to evaluate a specific area of vaccine safety, and that these test results can only be interpreted within that context. One cannot demand more from a test than what it was developed to do.

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References to commercial products and the publication of signed articles in this *Newsletter* do not constitute endorsement by PAHO/WHO, nor do they necessarily represent the policy of the Organization.

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