# MEASLES ERADICATION

## FIELD GUIDE

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# PREFACE

*Measles Eradication* mainly aims at providing health authorities, medical officers, and other health personnel involved in measles eradication at national, state, and local levels with a step-by-step manual for setting up and carrying out measles eradication activities. This guide incorporates experiences acquired by the countries of the Americas over the past seven years, but it can be used by any country working towards the eradication of measles. It emphasizes appropriate vaccination and surveillance strategies that are required to eradicate measles and to continually monitor progress towards that goal. Some of the measures described may need to be adapted to local conditions. Several prototype forms are included in the appendices and may be copied or modified to meet particular needs.

Much of the information contained in this manual was taken directly from technical papers previously prepared by the Pan American Health Organization; several textbooks and other publications also were consulted. Many of these documents are listed in the bibliography at the end of this guide.

The Pan American Health Organization acknowledges the outstanding accomplishment of all the health workers in the Americas involved in measles eradication activities. In confronting the formidable challenge of eradicating one of the most infectious and lethal agents known to man, these persons have persevered and continued to learn from their experiences. It is hoped that the lessons learned from the measles eradication experience in the Americas can be adapted and applied in all countries and Regions of the world, and that the ultimate goal of global measles eradication can be achieved.

PAHO (C. Gaggero)

**In September 1994, the Ministers of Health of the Americas adopted the goal of measles virus eradication from the Western Hemisphere by the year 2000.**

# 1 INTRODUCTION

## 1.1 Background

A major goal of the 1990 World Summit for Children, held in New York (U.S.A.), was to reduce the number of deaths caused by measles by 95% and the number of cases by 90%, compared to pre-immunization levels. Despite increased vaccination coverage against measles and a drop in the number of reported cases, measles continues to cause a considerable amount of illness and death among children in many parts of the world. New strategies to further reduce measles incidence are clearly needed.

Over the past few years the countries of the Caribbean and Latin America have adopted a new vaccination approach that is having a major impact on measles virus circulation and appears to have corrected many of the shortcomings experienced by previous measles prevention programs. In light of the success demonstrated by the Caribbean countries in interrupting measles virus circulation (Figures 1 and 2), as well as the certification of polio eradication from the Americas, in September 1994 the Ministers of Health of the Americas adopted the goal of measles virus eradication from the Western Hemisphere by the year 2000.[1]

To embark upon a measles eradication program is an ambitious task and requires the collaboration of ministries of health, the private sector, nongovernmental organizations (NGOs), and multilateral and bilateral international partners. At the time of publication of this field guide, a variety of international partners have collaborated and/or are still working with PAHO to reach the goal of measles eradication in the Americas, including the governments of Belgium, Brazil, France, Japan, the Netherlands, Spain, Sweden, and the United States of America.

The intensification of measles eradication activities should take place within the wider context of accelerated activities of the Expanded Program on Immunization (EPI), and should build upon the recent accomplishments of the polio eradication program. In order to be successful, activities should start simultaneously in all countries within a major geographic area.

Since measles virus is so infectious, outbreaks may occur on occasion despite the implementation of measles eradication activities. Even small pockets of susceptible children are capable of sustaining measles virus circulation. However, given full implementation of the measles eradication strategy, such outbreaks should become increasingly rare and should only result in a small number of measles cases.

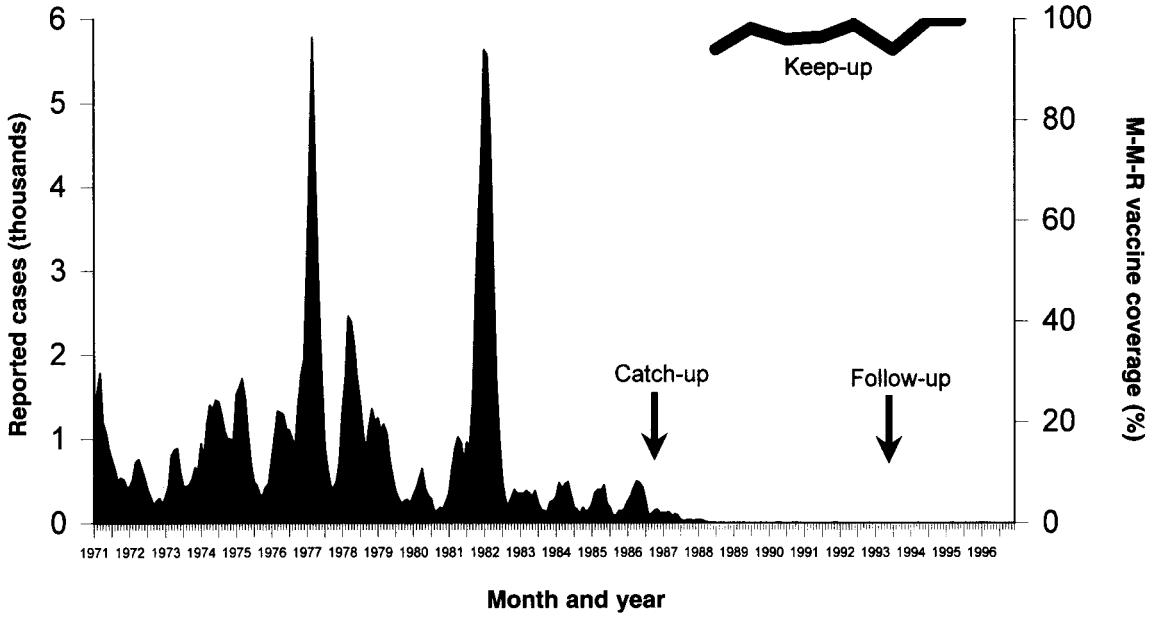
The primary aim of the *Measles Eradication Field Guide* is to provide health personnel involved in measles eradication efforts at national, state, and local levels with a management guide for setting up and carrying out eradication activities.

This guide incorporates knowledge acquired from the measles eradication activities conducted throughout the Caribbean and Latin America between 1987 and 1996 and emphasizes issues related to enhanced surveillance, special immunization campaigns, mop-up efforts, and outbreak response activities. Routine immunization activities are only briefly described, since such activities are well covered in other PAHO documents related to immunization programs. Prototype forms are included in the appendices, and they may be copied or modified to meet particular local needs.

***Note on terminology:*** The terminology for measles has been a source of some confusion. The proper English scientific term is rubeola, although the illness has commonly been referred to as 10-day measles, hard measles, red measles, and morbilli. However, in Spanish, *rubeola* means German measles (rubella). Alternative Spanish terms are *sarampión* or *morbilli* for measles and *sarampión alemán* for rubella. The French terms are *rougeole* for measles and *rubeole* for rubella.

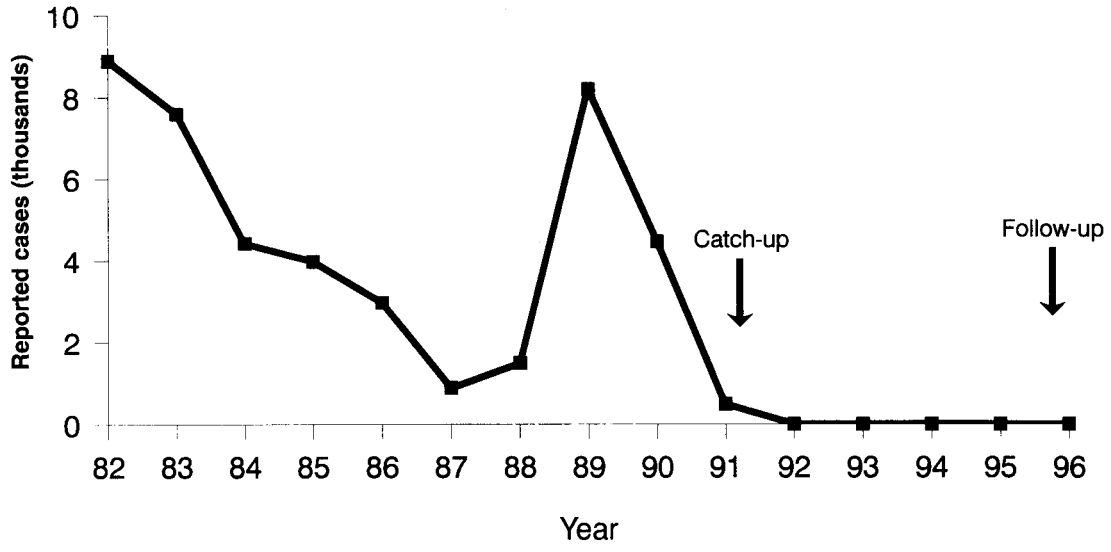
[1]Resolution XVI of the XXIV Pan American Sanitary Conference.

## FIGURE 1
## Mass vaccination campaign impact on morbidity: Cuba, 1971–1996*




***Source:*** Cuba, Ministry of Health.
*Measles cases reported through 31 December 1996.

## FIGURE 2
## Mass vaccination campaign impact on morbidity: English-speaking Caribbean, 1982–1996*




***Source:*** PAHO/EPI.
**Measles cases reported through 31 December 1996.*

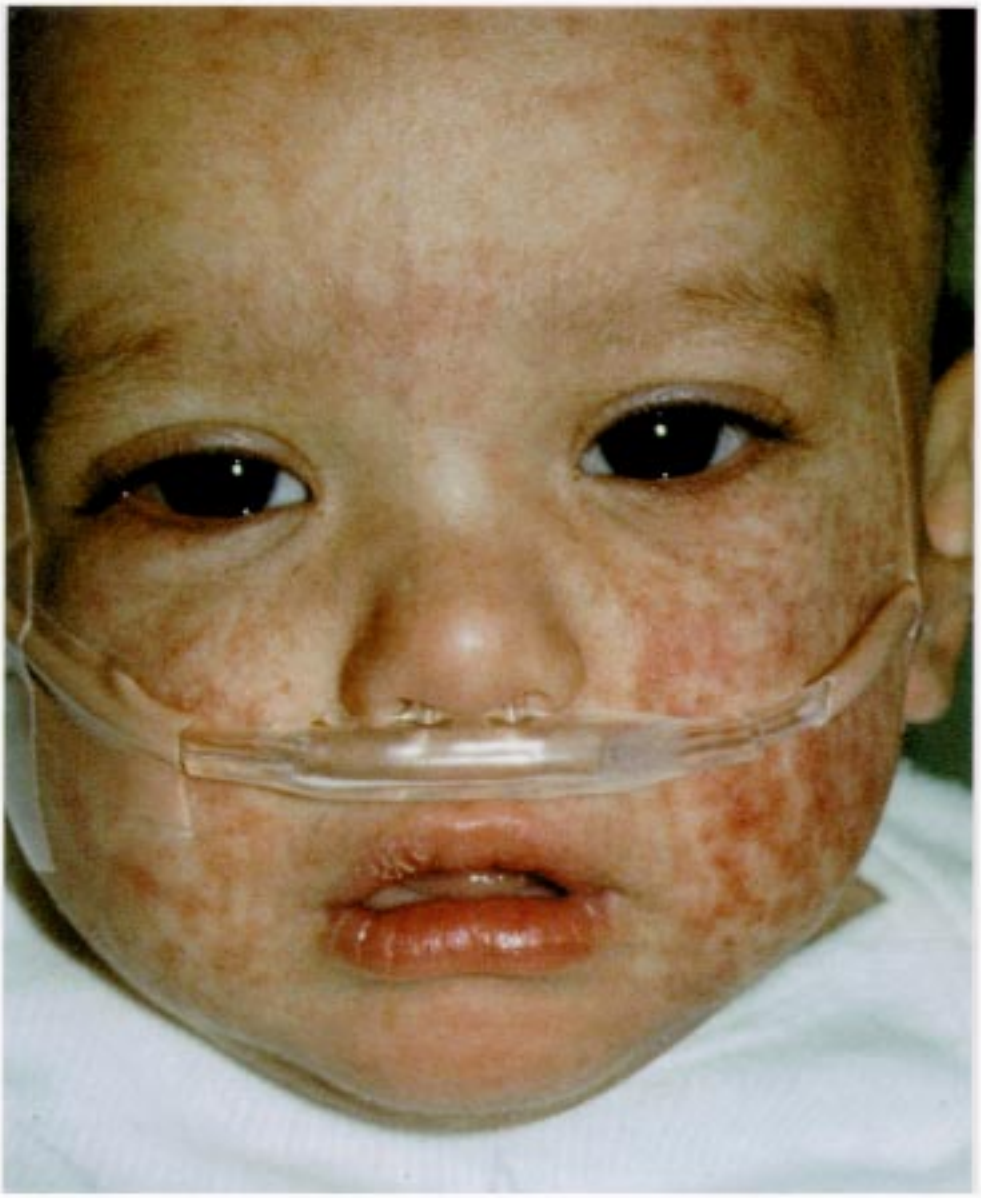


Photo courtesy of Professor Samuel Katz, Duke University Medical Center

**Measles virus is highly contagious and lethal. Over 40 million cases occur worldwide each year, resulting in more than a million deaths.**

# 2 EPIDEMIOLOGY

## 2.1 Infectious Agent

Measles virus is a member of the genus *Morbillivirus* of the *Paramyxoviridae* family. The virus appears to be antigenically stable—there is no evidence that the viral antigens have significantly changed over time. The virus is sensitive to ultraviolet light, heat, and drying.

## 2.2 Occurrence

Measles occurs worldwide. It is seasonal. In temperate climates, outbreaks generally occur in late winter and early spring. In tropical climates, transmission appears to increase after the rainy season. Measles produces a significant amount of illness, death, and disability in developing countries. The World Health Organization estimates that over 40 million cases still occur worldwide each year, contributing to approximately 1 million deaths.

In developing countries with low vaccination coverage, epidemics often occur every 2 to 3 years and usually last between 2 and 3 months, although their duration varies according to population size, crowding, and the population's immune status. Outbreaks last longer where family size, and hence the number of household contacts, is large. In the absence of measles vaccination, virtually all children will have been infected with measles by the time they are 10 years old.

Countries with relatively high vaccination coverage levels usually have five- to seven-year periods when case numbers remain small. However, as the number of susceptible children becomes large enough to sustain widespread transmission, explosive outbreaks may occur.

The introduction of measles vaccine in the Americas in the 1960s resulted in a marked decrease in the number of reported measles cases. The creation of the EPI in 1977, and the ensuing increase in vaccination coverage, contributed to a further drop in the number of reported measles cases and a tendency towards longer intervals between epidemic years (Figure 3).

## 2.3 Transmission

Measles virus is transmitted primarily by respiratory droplets or airborne spray to mucous membranes in the upper respiratory tract or the conjunctiva. Common-source outbreaks associated with airborne transmission of measles virus have been documented.

## 2.4 Reservoir

Man is the only natural host of measles virus. Although monkeys may become infected, transmission among them in the wild does not appear to be an important mechanism by which the virus persists in nature.

## 2.5 Incubation

The incubation period is approximately 10 days (with a range of 8 to 13 days) from the time of exposure to the onset of fever and about 14 days from exposure to the appearance of the rash.

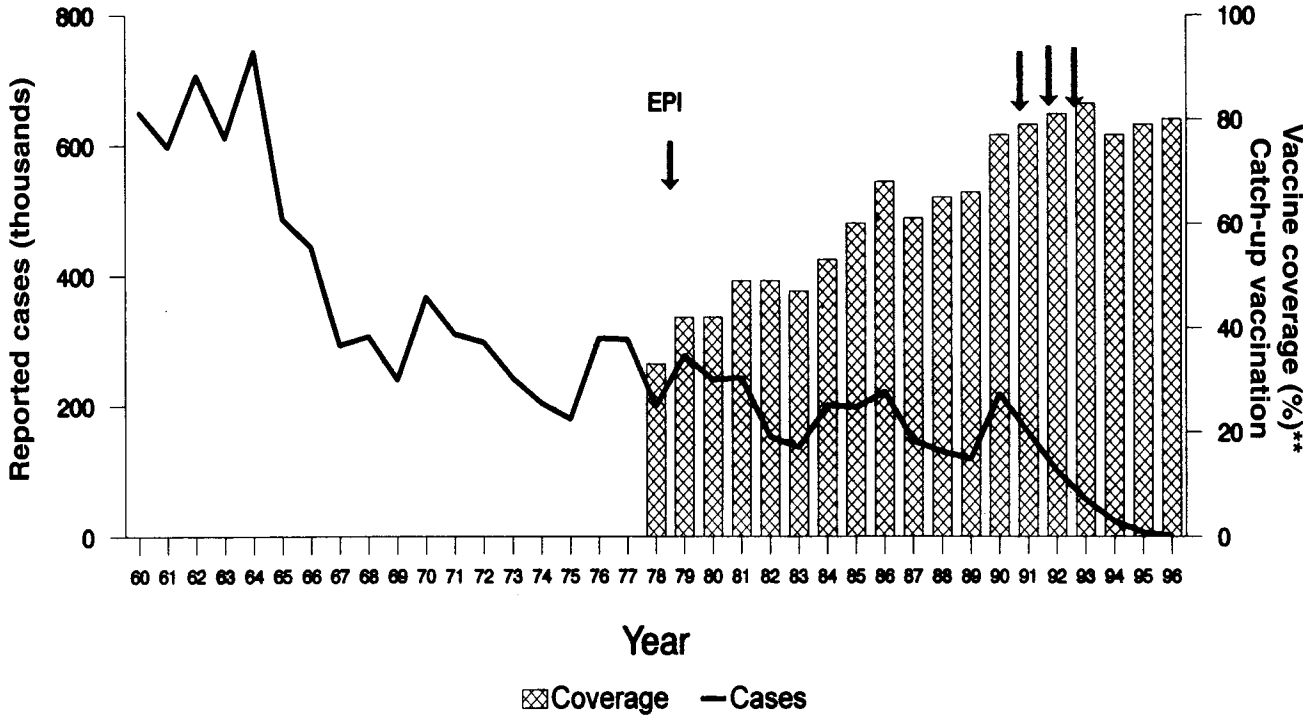
## 2.6 Communicability

Measles is highly contagious and is most communicable 1–3 days before the onset of fever and cough. Communicability decreases rapidly after rash onset. Secondary attack rates among susceptible household contacts have been reported to be over 80%. Due to the high transmission efficiency of measles, outbreaks have been reported in populations where only 3% to 7% of the individuals were susceptible.

## 2.7 Immunity

Prior to the availability of measles vaccine, measles infection was virtually universal. Infants are generally

**FIGURE 3**
**Measles incidence and vaccination coverage, Region of the Americas, 1960–1996***




*Source:* PAHO/WHO
*Data as of 31 December 1996.
**Coverage for children at 1 year of age.

protected until 5–9 months of age by passively acquired maternal measles antibody. Some infants who are immunized before they are 9 months old may not develop detectable immunity because of interference by maternal measles antibody. Immunity following natural infection is believed to be lifelong, and vaccination with measles vaccine has been shown to be protective for at least 20 years.

## 2.8 Changing Epidemiology

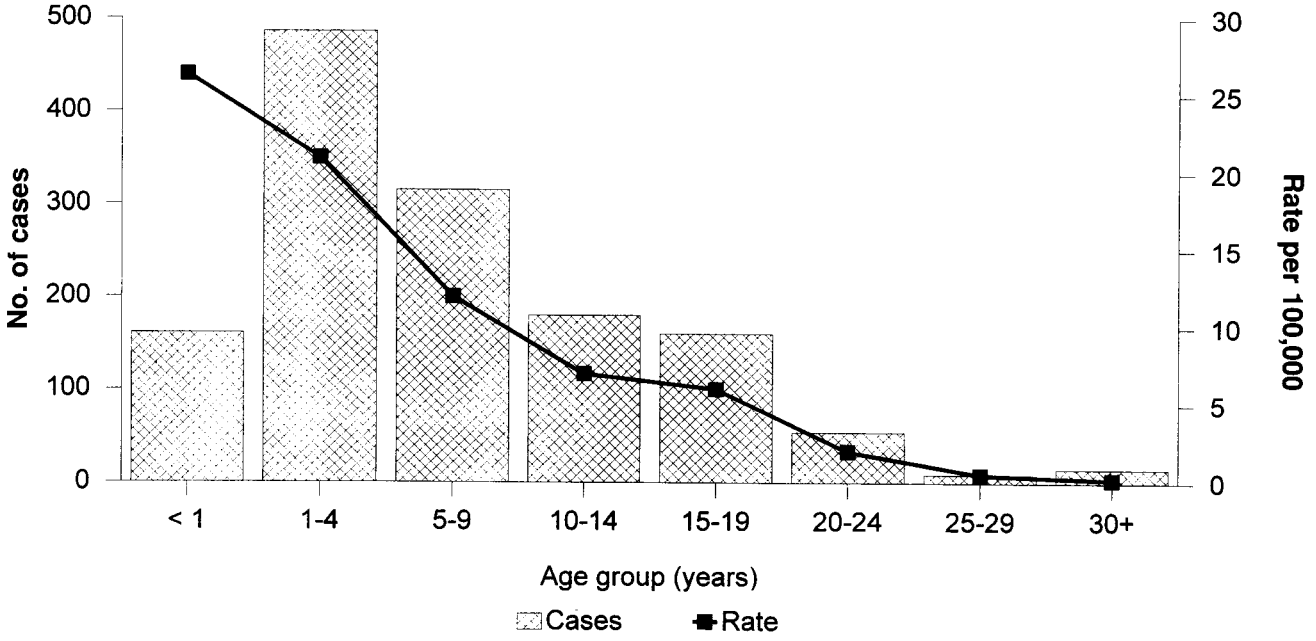
Since the introduction of effective measles vaccines, the epidemiology of measles has changed in both developed and developing countries. As vaccine coverage has increased, there has been a marked reduction in measles incidence; and, with decreased measles virus circulation, the average age at which infection occurs has increased.

Even in areas where coverage rates are high, outbreaks may still occur. Periods of low incidence (the "honeymoon" effect) may be followed by a pattern of periodic measles outbreaks, with an increase in the number of years between epidemics. Outbreaks are generally due to the accumulation of measles-susceptible persons, including both unvaccinated children and those who were vaccinated but failed to seroconvert. Approximately 15% of children vaccinated at 9 months and 5%–10% of those vaccinated at 12 months of age are not protected after vaccination.

**Developed Countries.** After the introduction of measles vaccine during the 1960s, many developed countries experienced a 98% or greater reduction in the number of reported cases. However, periodic measles epidemics continued to occur, especially in large urban areas. These outbreaks have occurred primarily among unvaccinated preschool-aged children, but cases and outbreaks have also been reported among fully vaccinated school-aged children.

**Developing Countries.** Measles virus continues to circulate in many developing countries. Unvaccinated infants and preschool-aged children are at greatest risk for measles infection (Figure 4). Outbreaks among

**FIGURE 4**
**Measles cases and age-specific attack rates, Peru, 1991**

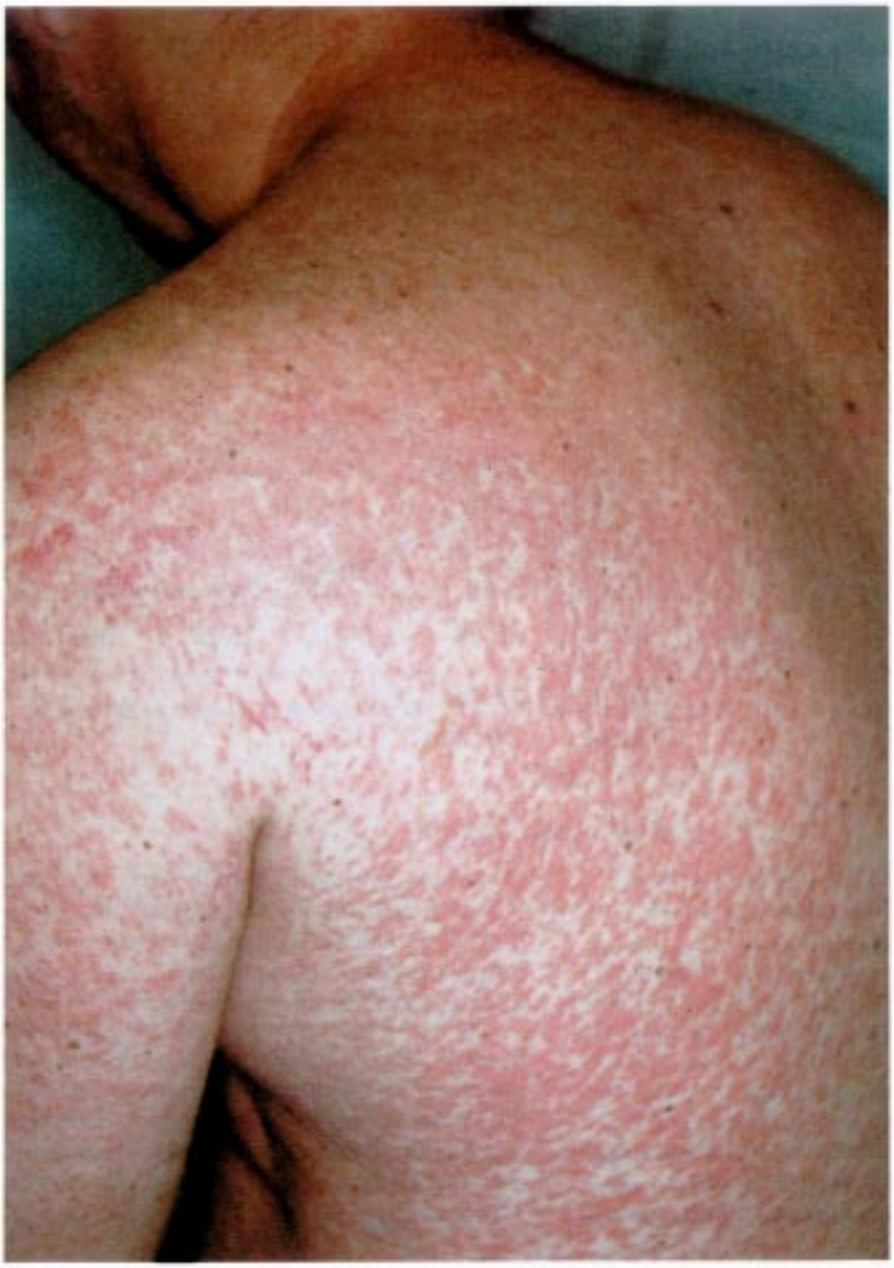



***Source:*** Peru, Ministry of Health.

older children also occur and usually involve those children who have not been vaccinated and have previously escaped natural measles infection because of the relatively low measles incidence. Since measles vaccine is less than 100% effective, vaccinated children may also contract measles, especially during periods of intense transmission.

In large urban areas, even where measles vaccine coverage is high, the number of susceptible infants and children may still be sufficient to sustain transmission. Conditions such as high birth rates, overcrowding, and influx of large numbers of susceptible children from rural areas can facilitate measles transmission. Measles remains endemic in such areas, and a large proportion of cases occur in infants before their first birthday.

In areas where measles remains endemic, only a brief period (or "window of opportunity") exists between the waning of maternal antibody and children's exposure to circulating measles virus. The highest age-specific measles case-fatality rates occur in children under 1 year of age.



PAHO (B. Hersh)

**Within two to four days after prodrome symptoms begin, a characteristic rash made up of large, blotchy, red areas appears behind the ears and on the face. The rash peaks in two or three days, then concentrating on the trunk and upper arms.**

# 3 CLINICAL ASPECTS

During periods of high measles virus circulation, measles infection can be diagnosed clinically with reasonable accuracy. However, the large number of rashlike illnesses that may occur in childhood makes laboratory support the key to definitive diagnosis, especially during periods of low measles incidence. A summarized description of the pathogenesis of measles virus infection and its clinical manifestations is presented in Figure 5.

## 3.1 Clinical Features

**Prodrome and General Symptoms.** Measles infection presents with a 2- to 3-day prodrome of fever, malaise, cough, and a runny nose (coryza). Conjunctivitis and bronchitis are commonly present. Although there is no rash at the onset, the patient is shedding virus and is highly contagious. A harsh, nonproductive cough is present throughout the febrile period, persists for 1 to 2 weeks in uncomplicated cases, and is often the last symptom to disappear. Generalized lymphadenopathy commonly occurs in young children. Older children may complain of photophobia and, occasionally, of arthralgias. A typical clinical course of measles is illustrated in Figure 6.

**Koplik's Spots.** Koplik's spots may be seen on the buccal mucosa in over 80% of cases, if careful daily examinations are performed shortly before rash onset. Koplik's spots are slightly raised white dots 2–3 mm in diameter on an erythematous base. Initially, there are usually one to five of these lesions, but as rash onset approaches there may be as many as several hundred. They have been described as resembling "grains of salt sprinkled on a red background." The lesions persist for only 1 to 3 days, disappearing soon after rash onset.

**Rash.** Within 2 to 4 days after the prodromal symptoms begin, a characteristic rash made up of large, blotchy red areas initially appears behind the ears and on the face. At the same time a high fever develops. The rash peaks in 2 to 3 days and becomes most concentrated on the trunk and upper extremities. The density of the rash can vary. It may be less evident in children with dark skin. The rash typically lasts from 3 to 7 days and may be followed by a fine desquamation. Some children develop severe exfoliation, especially if they are malnourished.

## 3.2 Differential Diagnosis

Many illnesses are accompanied by fever, rash, and a variety of nonspecific symptoms. In examining for measles, it is important to consider rubella, scarlet fever, roseola, dengue fever, and the early stages of chickenpox in the differential diagnosis (Figures 7a–e). Moreover, there are other conditions that may present in a similar form, including enterovirus or adenovirus infections, Kawasaki's disease, toxic shock syndrome, rickettsial diseases, and drug hypersensitivity reactions.

"Modified" forms of measles, with generally mild symptoms, may occur in infants who still have partial protection from maternal antibody, and occasionally in persons who only received partial protection from the vaccine.

## 3.3 Complications

Complications from measles include otitis media, pneumonia, diarrhea, blindness, and encephalitis. It is estimated that otitis media plus pneumonia occurs in 10% to 30% of infants and young children with measles.

**Diarrheal Illness.** A large number of infants and children in developing countries develop diarrhea both during and following acute measles illness.

**Respiratory Infections.** Respiratory infections are the most common cause of significant morbidity and mortality in infants and children with measles. Pneumonia may be due to the measles virus alone or to secondary infection with other viral agents—especially herpes simplex and adenoviruses—or bacterial organisms.

**Malnutrition.** Diarrhea is one of the major factors contributing to the adverse impact of measles on the nutri-

## FIGURE 5
## Pathogenesis of measles virus infection and clinical manifestations

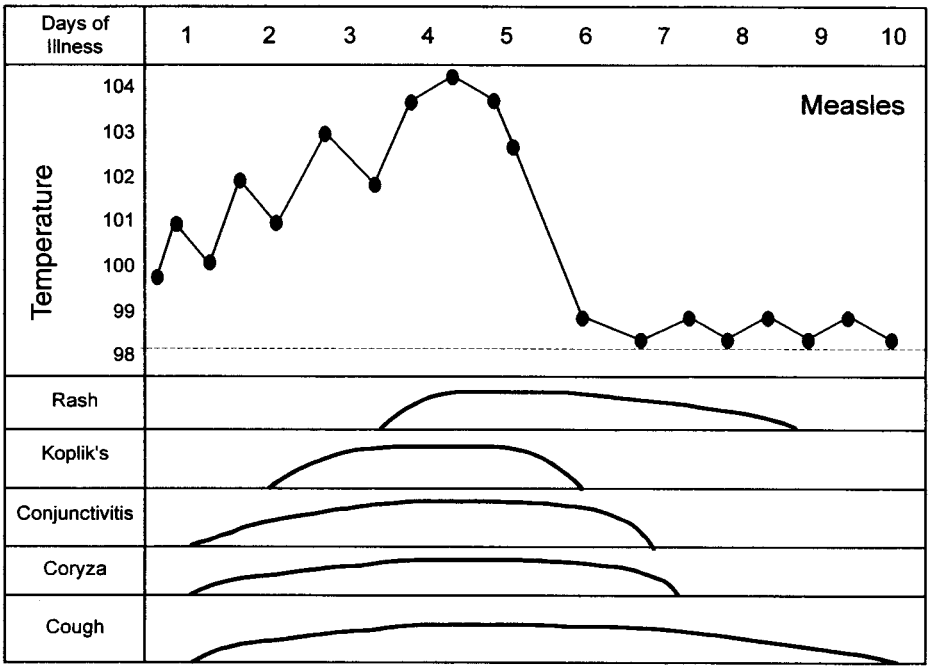
| Infection | Incubation (8–13 days) | Complications |
|---|---|---|
| Aerosol | | |
| Nasal epithelium | | |
| ↓ | | |
| Lymph nodes, blood | | |
| ↓ | | |
| Lympho-reticular system, spleen, liver, bone marrow | | |
| ↓ | ↓ | |
| Blood | **Virema** | |
| ↓ | ↓ | |
| Kidney, skin, upper and lower respiratory tract, brain, giant cells, mononuclear cells, mucosa | Leucopenia | |
| | **Prodrome (2–4 days)** | |
| | Rhinitis, cough, inflamed conjunctivae, tonsillitis, mild fever, red buccal membrane, Koplik's spots | |
| ↓ | ↓ | |
| Immunological response | **Rash (3–7 days)** | ↓ |
| ↓ | Macular (starting on face, spreading to body) | Ear infections |
| Antibody development | High fever | Viral pneumonia |
| ↓ | Rash fading | Bacterial pneumonia |
| (Continued excretion in urine) | Fever decreasing | Encephalitis |
| ↓ | ↓ | |
| Decreasing virus in organs | Temperature normal | |
| ↓ | Desquamation | |
| Virus cleared | | |
| ↓ | ↓ | ↓ |
| **Immunity** | **Recovery** | **Death, Disability** |

tional status in children in developing countries. Measles infection is more severe among children who are already malnourished. Moreover, measles may exacerbate malnutrition because of decreased food intake due to malaise, increased metabolic requirements in the presence of fever, or the mistaken belief of parents and health practitioners that a child's food should be withheld during an acute illness. Undernutrition may lead, in turn, to vitamin A deficiency and keratitis, resulting in a high incidence of childhood blindness during measles outbreaks.

**Neurological Complications.** These occur in 1 to 4 of every 1,000 infected children. The most common manifestation is febrile convulsions, which are not usually associated with persistent residual sequelae. Encephalitis or postinfectious encephalopathy occurs in approximately 1 of every 1,000 infected children. Subacute sclerosing panencephalitis (SSPE) is a rare (incidence of approximately 1 per 100,000 measles cases), chronic, degenerative neurological disorder associated with the persistence of the measles virus in the central nervous system. It may develop several years after a measles infection.

**Mortality.** In developed countries the case-fatality rate for measles tends to be low (between 0.1 and 1.0 per 1,000 cases). In developing countries the overall case-

**FIGURE 6**
**Clinical features of measles**




***Source:*** *Infectious Diseases of Children*, 9th Edition, Figure 13-1, page 224. Krugman S, Katz SL, Gershon AA, Wilfert CM, eds. St. Louis: Mosby, 1992. Used with permission of Mosby Year Book, St. Louis, Missouri.

fatality rate has been estimated at between 3% and 6%; the highest case-fatality rate occurs in infants 6 to 11 months of age, with malnourished infants at greatest risk. These rates may underestimate the true lethality of measles because of incomplete reporting of outcomes of measles illness, such as deaths related to chronic diarrhea that occur after the acute illness has passed. In addition, some deaths may be missed when death certificates are miscoded or hospital records are incomplete. In certain high-risk populations, case-fatality rates as high as 20% or 30% have been reported in infants under 1 year of age.

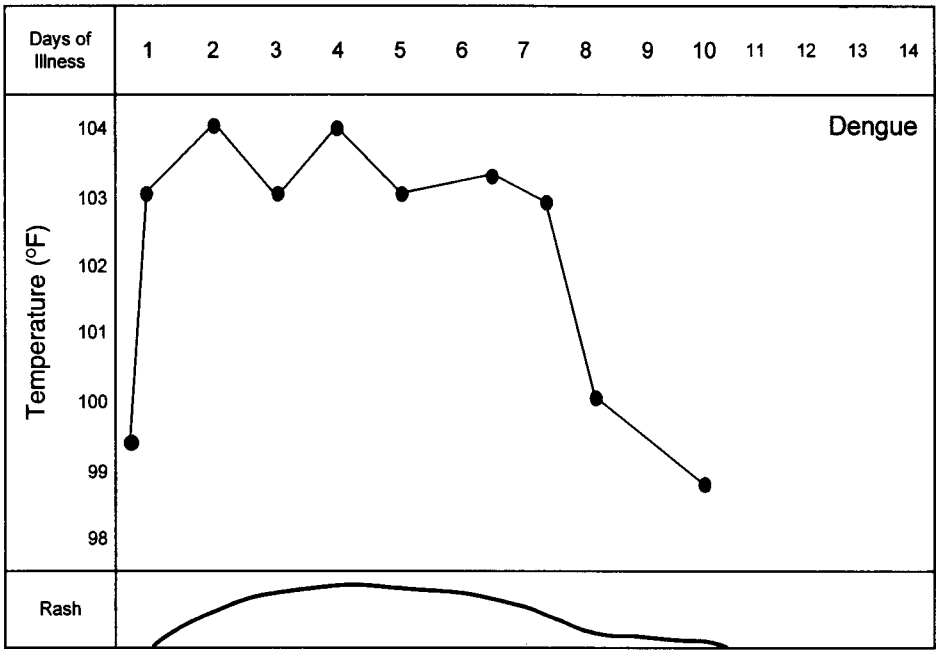
## 3.4 Treatment

There is currently no specific treatment for measles infection. Administration of vitamin A to children at the time of measles diagnosis has been shown to decrease both the severity of disease and the case-fatality rate. Accordingly, the World Health Organization (WHO) has recommended that vitamin A be administered to all children diagnosed with measles infection. One dose (200,000 I.U. for children $\geq$ 12 months, 100,000 I.U. for children 6–12 months, and 50,000 I.U. for infants $<$ 6 months of age) should be administered on the day of measles diagnosis and one dose should be administered the following day.

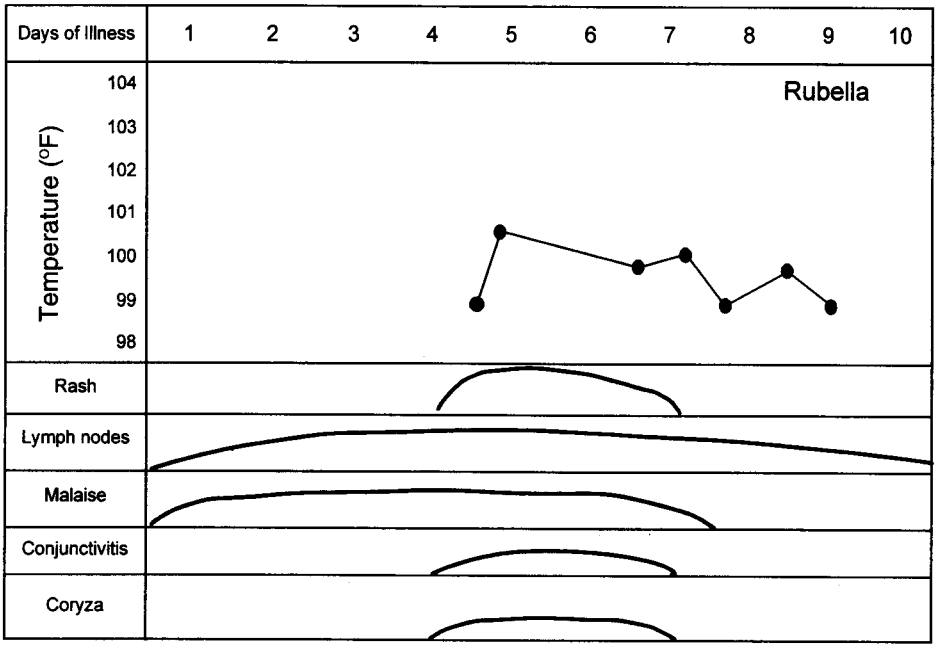
Supportive treatment should be provided for a number of measles complications. For uncomplicated cases, fluids (such as oral rehydration salts solution), antipyretics, and nutritional therapy are commonly indicated. Many children require 4–8 weeks to fully recover their premeasles nutritional status.

Other measles complications, such as diarrhea, pneumonia, otitis media, etc., should be treated following the guidelines in the WHO protocol for Integrated Management of Childhood Illness.

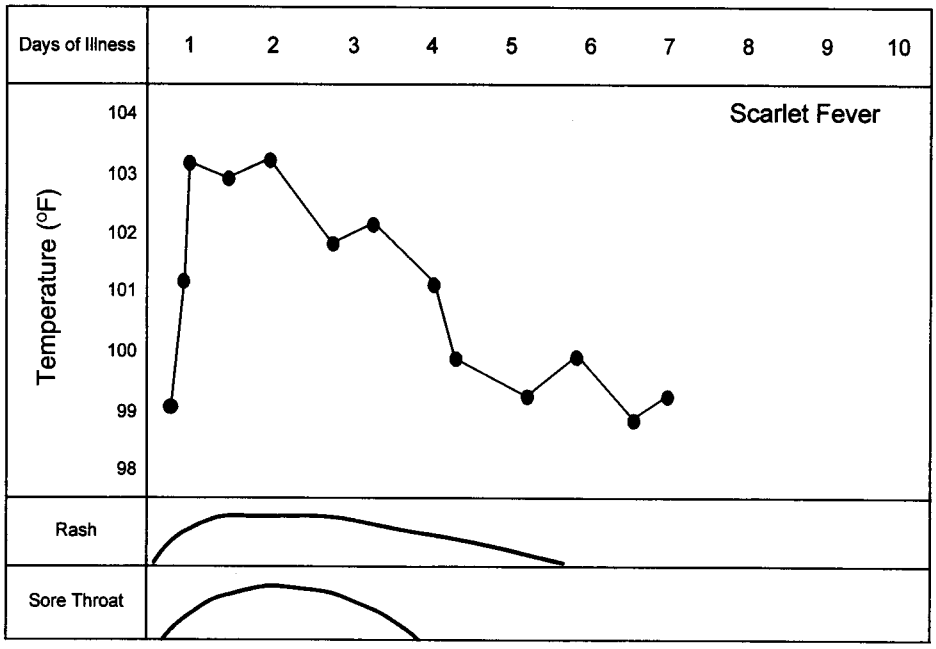
## FIGURE 7a
## Clinical features of certain rash illnesses



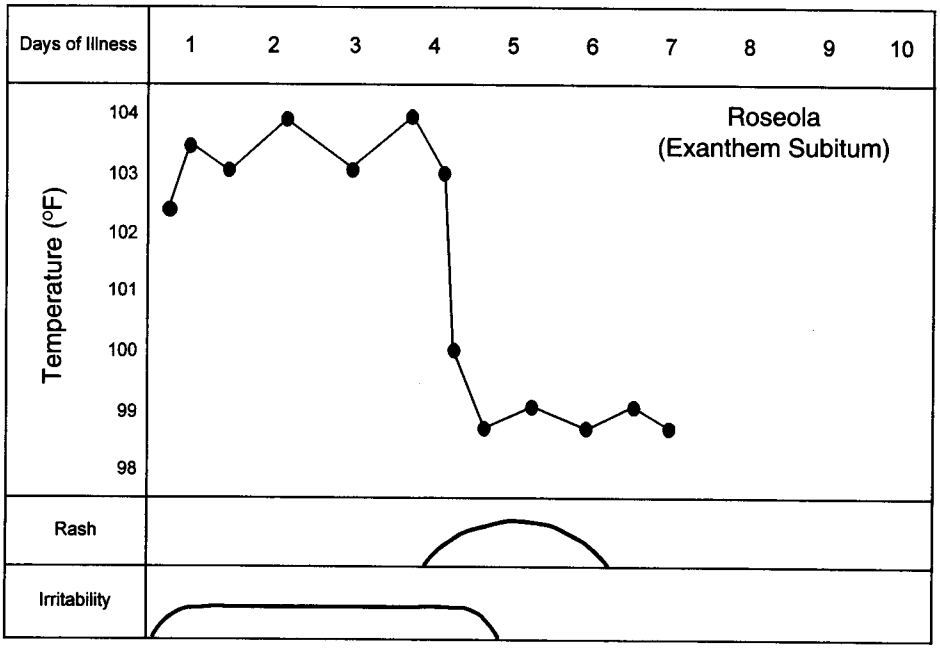

## Figure 7b



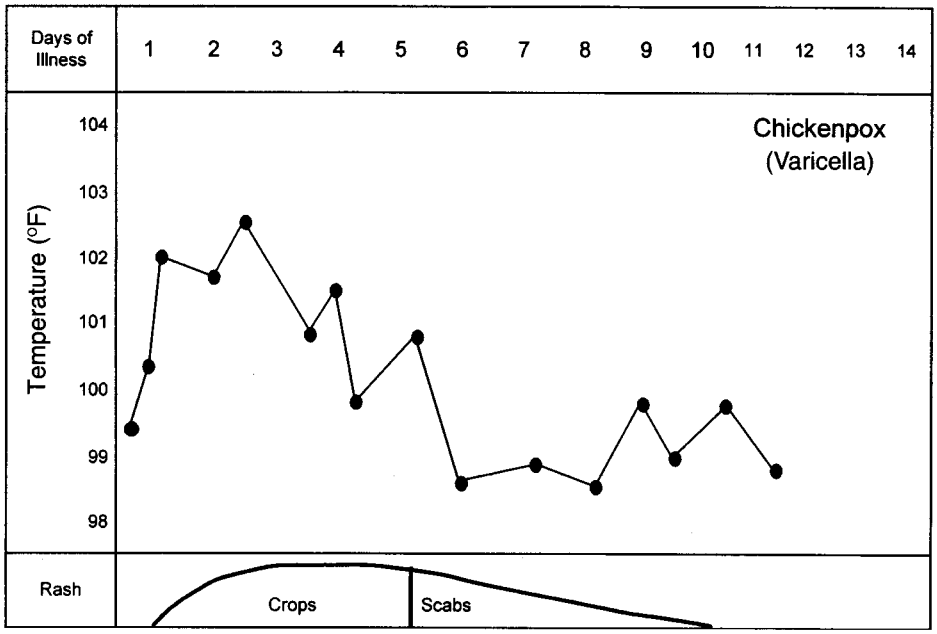
## Figure 7c

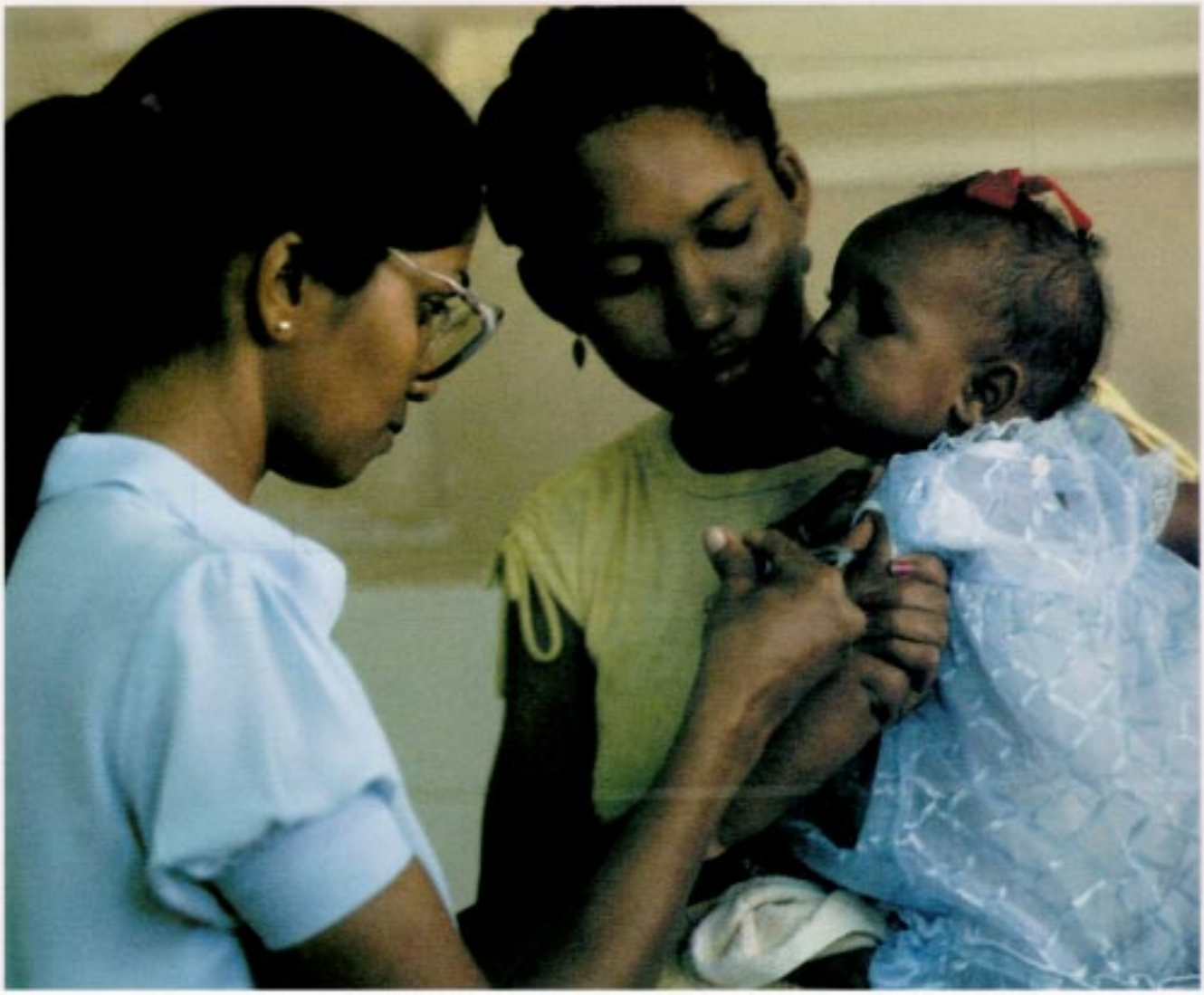



## Figure 7d



## Figure 7e


Days of Illness
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Temperature (°F)
104
103
102
101
100
99
98
Chickenpox
(Varicella)
Rash
Crops
Scabs



PAHO (C. Gaggero)

**There are virtually no contraindications to measles vaccination. Measles vaccine can be safely and effectively administered to children with mild and acute illnesses.**

# 4 MEASLES VACCINES

The original measles vaccines approved for use in children in 1963 were either inactivated or attenuated live virus vaccines. These vaccines are no longer used. The vaccines currently employed in most countries are further-attenuated live measles virus vaccines, which are generally derived from the original Edmonston strain. The Moraten strain vaccine is used principally in the United States, while the Schwartz strain vaccine has been most commonly used in other countries.

All vaccine preparations containing standard titers of live measles virus may be used. The combined measles-mumps-rubella (MMR) vaccine is preferred to ensure that immunity is obtained against all three viruses. The use of MMR vaccine in measles campaigns will result in the reduction of rubella and mumps circulation among children and decrease the incidence of congenital rubella syndrome (CRS). Programs that add rubella vaccine to their schedule should develop a complementary comprehensive rubella control plan to ensure that women of childbearing age are also protected against rubella (see Appendix A).

## 4.1 Immunity

Serologic studies have demonstrated that measles vaccines induce seroconversion in about 95% of recipients who are old enough to have lost all passively acquired maternal measles antibody (this usually occurs by 12 months of age). Both the development and the persistence of serum antibodies following measles vaccination are lower than, but parallel to, the response following natural measles infection. The peak antibody response occurs 6 to 8 weeks after infection or vaccination. Immunity conferred by vaccination against measles has been shown to persist for at least 20 years and is generally thought to be lifelong for most individuals.

For combined vaccines, studies indicate that the antibody response to all antigens is equivalent to the response when each is administered separately.

## 4.2 Schedule

In countries that have conducted successful "catch-up" measles vaccination campaigns, the routine age of infant immunization should be increased from 9 months to 12 months, since the interruption of measles virus circulation following the campaign makes it extremely unlikely that an infant will be exposed to circulating measles virus. Moreover, the three-month delay in administering measles vaccine should result in higher vaccine effectiveness.

If an outbreak does occur and a significant proportion of the cases are among infants under 9 months of age, consideration may be given to lowering the age of routine infant vaccination to 6 months. However, all infants vaccinated before their first birthday ***must*** receive a second dose of measles-containing vaccine at 12 months of age.

Revaccination of previously vaccinated persons with measles vaccine alone or in combination with rubella and mumps vaccines is not contraindicated. The vaccines have an excellent safety record when given to persons who have previously received one or more doses of measles vaccine. Recent studies have shown that when measles virus is reintroduced into a community, it can spread even among populations with high rates of vaccination coverage. During such events, revaccination provides an additional safeguard.

## 4.3 Contraindications

***There are virtually no contraindications to measles vaccination.*** Measles vaccine can be safely and effectively administered to children with mild acute illnesses, such as low fever, diarrhea, and upper respiratory tract infections. However, vaccine should not be administered to severely ill children with high fevers because of the likelihood of a concurrent severe infection that may interfere with seroconversion.

Malnutrition is ***not*** a contraindication, but rather a strong indication for measles vaccination. If a malnour-

ished child is infected, the disease may aggravate his/her nutritional status and increase the chances of complications or death.

In countries where human immunodeficiency virus (HIV) infection is prevalent, infants and children should be immunized with the EPI antigens according to standard schedules. This also applies to individuals with asymptomatic HIV infection. Screening for HIV infection prior to vaccination should not be conducted. For persons with advanced HIV infection, the potential risks of measles vaccination must be weighed against the potential risk of being exposed to circulating measles virus.

Since measles and MMR vaccines contain live viruses, they should not be administered to pregnant women. However, there is currently no evidence to suggest that children born to pregnant women who received these vaccines during pregnancy are adversely affected. Moreover, prospective studies of the offspring of women vaccinated with rubella vaccine during pregnancy have not found vaccination to be a risk factor for development of congenital rubella syndrome.

## 4.4 Adverse Events Associated with Vaccination

**Measles.** Approximately 10% of infants vaccinated with measles vaccines may develop a low-grade fever, and approximately 5% develop a generalized rash that lasts for 1 to 3 days, beginning 7 to 10 days after vaccination. These reactions are generally mild and well tolerated. Neurological complications following vaccination are reported to occur in less than 1 in 1,000,000 vaccinees (see Table 1 below). The benefit of using the vaccine clearly outweighs the costs associated with having the disease, both in human and monetary terms.

**Mumps.** Adverse events following mumps vaccination are rare. Most common are parotitis and mild fever. However, the Urabe strain mumps vaccine has been repeatedly associated with an increased incidence of postvaccination meningitis, compared to other vaccine strains, including the Jeryl Lynn strain. For this reason, several countries have discontinued use of the Urabe strain mumps vaccine and are now using vaccines containing the Jeryl Lynn strain.

**Rubella.** Adverse events associated with rubella vaccine include rash, fever, and lymphadenopathy 5 to 12 days after vaccination in a small percentage of children. In addition, joint pain, usually in small peripheral joints, may occur; it tends to be more frequent in postpubertal females. Joint involvement usually begins 7 to 21 days after vaccination and is transient. Central nervous system complications with fever and thrombocytopenia have been reported, but no cause-and-effect relationship with the vaccine has been established.

## 4.5 Dosage and Administration

Measles vaccine is lyophilized and reconstituted with sterile water immediately prior to administration by injection. Given as a single antigen or combined with mumps and rubella vaccines, the volume of injection is 0.5 ml and should be administered subcutaneously in the anterior thigh, although it may also be administered in the upper arm. Each 0.5 ml dose of reconstituted vaccine should contain a minimum infective dose of at least 1,000 viral $TCID_{50}$ (median tissue culture infective doses). Other live and inactivated bacterial and viral vaccines can be administered simultaneously without problem. Health care providers should collect used disposable needles and syringes following vaccination and burn them in order to prevent their reuse.

## 4.6 Storage and Supply

Measles vaccine is relatively heat stable before reconstitution. However, breaks in the cold chain that result in temperatures higher than 37 °C may render the vaccine completely ineffective. Measles vaccine, MR, and MMR can be safely frozen without loss of potency. When stored at 0 to 8 °C, a minimum infective dose can be maintained in unreconstituted vaccine for two or more years. Storage at temperatures over 8 °C will reduce potency. Reconstituted vaccine should be disposed of after 8 hours, regardless of the temperature at which it was maintained. Vaccine should never be left at room temperature, especially in tropical climates. When used in the field, it should be transported on dry or wet ice in isothermic containers.

Measles single antigen, MR, and MMR vaccine stored at the national level should be kept frozen. At the local level, vaccine should always be placed in the center of a storage refrigerator used only for vaccines. To assist in temperature maintenance in the event of a power failure, bottles or other containers full of water should also be stored on the lower shelves of the refrigerator. Care should be taken to minimize the frequency with which the refrigerator door is opened.

| TABLE 1. Adverse reactions associated with measles vaccine compared with the natural disease | | | |
|---|---|---|---|
| ADVERSE EFFECT | ESTIMATED RISK ASSOCIATED WITH VACCINATION | RATE ASSOCIATED WITH NATURAL DISEASE | RANGE OF RELATIVE RISK DISEASE/VACCINE |
| Fever ≥39.4 °C | 1/16–1/6 | 1 | 6–16 |
| Rash | 1/100–1/5 | 1 | 5–100 |
| Febrile convulsions | 1/2,500–1/100 | 1/200–1/100 | 1–25 |
| Encephalitis/ encephalopathy (other neurologic disorders) | 1/1,000,000–1/17,600 | 1/1,000 | 17.6–1,000 |
| Subacute sclerosing panencephalitis (SSPE) | 1/1,000,000[a] | 1/200,000–1/50,000 | 5–20 |
| Thrombocytopenic purpura | Very Rare | + to + + + | Positive[b] |

[a]No cases of SSPE have been proven to be caused by measles vaccine.
[b]The rate following natural disease is higher than that following vaccination, but the ratio is unknown.

Effective distribution of potent vaccine in sufficient quantities is critical to the success of a measles eradication program. All locations that provide immunization should have a sufficient vaccine supply on hand to last until the next shipment is likely to be received: at the local level, a supply of 1–3 months; at the regional and state level, 3–6 months; and at the national level, 6–12 months. Order and supply dates should be checked to determine whether previous vaccine shipments were received before the vaccine supply was exhausted. No expired vaccine should be kept. Recent monthly usage rates should be compared with the amount of vaccine remaining to determine if the vaccine on hand can be used up prior to its expiration date.

## 4.7 Cold Chain

If cases of measles occur in individuals who have been vaccinated or in areas where there have been mass campaigns and coverage rates of 1-year-old children are high, the adequacy of the cold chain should be checked. A special study may be warranted for this purpose.

During mass campaigns special attention must be paid to establishing and maintaining a cold chain that is equipped to handle the increased quantity of vaccine. In particular, it is necessary to ensure the availability of sufficient amounts of ice, appropriate storage capacity (for example, through the use of local ice houses), and adequate private refrigeration. In addition, power backup systems need to be established.

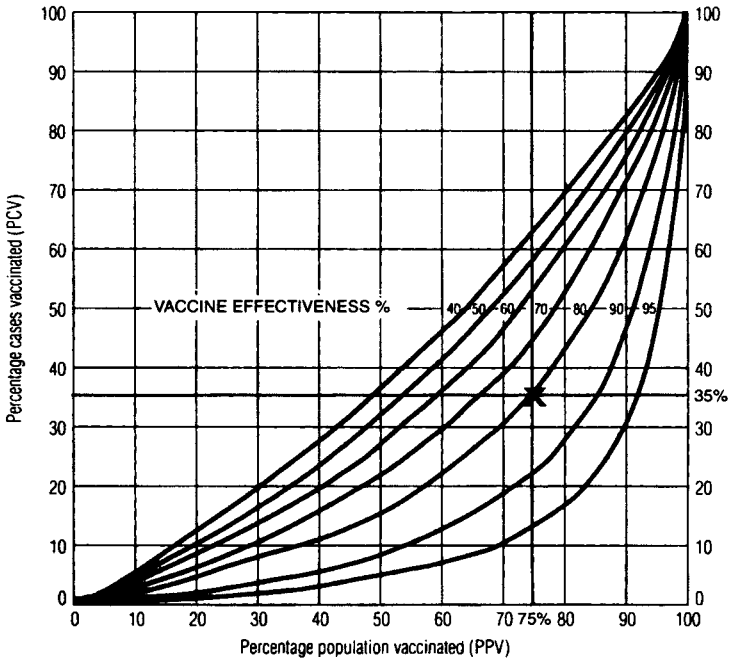
***Box 1. WHAT TO CHECK WHEN VISITING ANY FACILITY WHERE VACCINE IS STORED:***

- *Check that the refrigerator/freezer and thermometer function properly. Check temperature on arrival (normal 0–8 °C).*
- *Determine that the temperature of the refrigerator is recorded twice daily and the records maintained. If the temperature is not in the appropriate range, was a problem found and has it been reported to a technician? If the refrigerator is not electric, is there enough gas or kerosene to last until the next order is expected?*
- *Are there enough cold boxes for routine as well as outreach activities? Are the boxes in good condition? Do they close properly and seal tightly?*
- *Are there enough frozen ice packs for the number of cold boxes being used?*
- *Was the last vaccine shipment received with ice packs surrounding all sides? Was the temperature of the vaccine recorded when the last shipment was received?*
- *Is there enough diluent for the vaccine, and is it appropriately stored? Is any expired vaccine being stored?*

On visits to any facility where vaccine is stored, the following should be reviewed:

- vaccine availability;
- vaccine expiration dates; and
- cold chain mechanics (see Box 1).

**FIGURE 8**
**Sample of graph used to estimate vaccine effectiveness**




***Source:*** Orenstein WA et al. Field evaluation of vaccine efficacy. *Bull* WHO 1985; 63(6): 1055-1068.

## 4.8 Vaccine Efficacy and Effectiveness

Vaccine efficacy may be defined as how well a vaccine performs under the idealized conditions of a premarketing evaluation or a controlled clinical trial. Vaccine effectiveness, on the other hand, is considered to be the ability of a vaccine to provide protection under the normal conditions of a public health vaccination program.

Since no vaccine is 100% effective, not all persons given measles vaccine are necessarily protected against measles. Therefore, during a measles outbreak the occurrence of measles cases among persons with documentation of measles vaccination is to be expected. If vaccination coverage is high, a significant number of cases may occur among vaccinated persons. The occurrence of measles cases in these persons often leads to doubts about the effectiveness of measles vaccine.

Several approaches can be used to estimate vaccine effectiveness. They include prospective cohort trials and case-control studies as part of an outbreak investigation. These methods are time-consuming and their discussion is beyond the scope of this field guide. However, an alternative method (described below) which allows a rapid estimation of vaccine effectiveness has been developed. If effectiveness is found to be low (for example, below 80%), it may indicate that there were problems either with the production of the vaccine or with the cold chain.

Vaccine effectiveness can be estimated if the following two variables are known: the proportion of cases occurring in vaccinated individuals (PCV), and the proportion of the population that is vaccinated (PPV). The curves in Figure 8 indicate the vaccine effectiveness levels based upon the distributions of PCV and PPV.

In the example shown in Figure 8, the percentage of cases with a known measles vaccination status who received one or more doses of measles vaccine (PCV) is 35.9%, and from prior coverage assessments it is known that the percentage of the population at risk (<10 years of age) who were vaccinated (PPV) is 75%. The intersection of these two lines is plotted on the graph with an X. Since the X is to the left of the 90% curve and to the right of the 80% curve, the vaccine efficacy can be estimated in this case as approximately 82%. Such a screening does not provide an exact estimate of vaccine effectiveness, but does serve as a rough guide as to whether further evaluation is necessary.


PAHO (C. Gaggero)

**The build-up of susceptible children over time is the most serious obstacle to measles eradication. Measles can be eradicated by routine infant vaccination, supplemented by "catch-up" and "follow-up" vaccination campaigns.**

# 5 VACCINATION STRATEGY FOR MEASLES ERADICATION

The strategy currently used to control measles in many countries has been to immunize each successive birth cohort with a single dose of measles vaccine through the routine health services delivery system. While measles vaccination coverage has increased markedly, significant and troublesome measles outbreaks continue to occur.

Since measles vaccine is less than 100% effective and vaccination coverage is rarely universal via routine health services, an accumulation of nonimmune children will result. With each successive birth cohort, the number of children susceptible to measles inevitably increases, including both children who escaped vaccination and those who were vaccinated but failed to respond to the vaccine. ***The build-up of susceptible children over time in a population is the most serious obstacle to measles eradication.*** High vaccination coverage through routine health services is essential, yet that alone is clearly not sufficient for measles eradication.

To improve measles control, a number of countries have adopted a two-dose measles vaccination schedule. The second dose is often given when children start school. For those countries with sufficient resources, a well-developed health services delivery system, and school attendance by the majority of children, this schedule will help to reduce the number of susceptible children and may ultimately interrupt measles transmission.

However, the routine addition of a second dose is not an appropriate strategy for measles eradication in those countries where large segments of the population do not have access to routine health services and/or where many children do not attend school. A two-dose strategy is intended, in fact, to protect the 5% to 10% of children who were vaccinated but failed to respond to the vaccine. Thus, the majority of second doses are given to children who are already protected. Moreover, the addition of a second dose to the vaccination schedule will not increase immunity among children who still do not receive even a single dose of measles vaccine.

To rectify shortcomings of the above strategies, the Pan American Health Organization has developed a novel measles eradication vaccination strategy with three principal components. First, measles virus circulation in a community is rapidly interrupted by conducting a one-time-only ***"catch-up"*** measles vaccination campaign over a wide age-cohort of infants, children, and adolescents. Second, to maintain the interruption of measles virus circulation, routine immunization programs (or ***"keep-up"*** vaccination) ***must*** provide measles vaccine to at least 90% of each new birth cohort of infants before the age of 2 years in every district of the country. Finally, periodic ***"follow-up"*** vaccination campaigns among preschool-aged children will be necessary every four years, because of the inevitable build-up of children susceptible to measles. In addition to the above components, special intensive efforts, known as ***"mop-up"*** vaccination, may be required to provide measles vaccine to children living in high-risk areas who missed routine vaccination and also escaped vaccination during the "catch-up" and "follow-up" campaigns.

When the PAHO strategy is fully implemented, virtually all children will have received one dose of measles vaccine, and most will have received more than one dose. Indeed, the PAHO strategy offers a second opportunity for preschool-aged children to receive measles vaccine. The paramount objective of the PAHO measles eradication strategy is, therefore, to ensure that as many infants and children as possible receive at least one dose of measles vaccine. This strategy is described in detail below.

## 5.1 "Catch-up" Measles Vaccination Campaigns

The "catch-up" measles vaccination campaign is a one-time-only vaccination activity conducted over a short period of time across a wide age-cohort of chil-

dren. The goal is to rapidly interrupt chains of measles transmission in a geographic area by the achievement of high levels of population immunity. These campaigns should be conducted during periods of low measles transmission.

All children 1 through 14 years of age, regardless of vaccination history or history of measles disease, are targeted for measles vaccination. Even if immunization levels are high among infants, older children may be less likely to have been vaccinated and also may have escaped measles infection. Indeed, several outbreak investigations conducted in areas with strong immunization programs and high measles vaccine coverage among infants have found that older children and adolescents are likely to be at relatively high risk for measles and are often responsible for infecting their younger siblings.

"Catch-up" campaigns should be carried out within a brief time frame, usually one week to one month. The campaign is planned and coordinated at the national level by the Ministry of Health and implemented by personnel of state and local health services (see Box 2). Before the campaign begins, financial resources should be secured so that funds will be available to health officials at the district level, where the vaccination effort is undertaken.

Intensive use is made of mass media communication in order to attract the target population to the vaccination sites. Health officials can take advantage of the campaign to deliver other vaccines, such as OPV and DTP. Key to success is strong coordination between the government, NGOs, and the private sector. Moreover, a detailed logistics plan and proper social communication will increase the probability of success. Such campaigns result in a rapid increase in population immunity, and, if high enough coverage is achieved, measles virus circulation is interrupted.

Children 5 to 14 years of age attending school can generally be vaccinated through the school system. Preschool-aged children and those who do not attend school are more difficult to reach. Vaccinations should be offered at many sites in addition to the traditional clinics. Locales such as churches, community centers, markets and shopping areas, plazas, schools, transportation centers, and other easily accessible areas where people congregate should be considered.

Special attention should be paid to high-risk areas, districts, or municipalities where routine coverage levels are below the national average. It may be necessary to assign additional personnel and logistical resources to these areas to address problems such as inadequate access or poorly staffed and equipped health services.

Once a "catch-up" campaign has been completed, the coverage achieved by every district should be analyzed. Those districts with low coverage rates should carry out supplementary vaccination activities, including house-to-house vaccination (see Section 5.4 on "mop-up" efforts).

**Mobilizing the Community.** Measles eradication requires active community participation. The community needs to be made aware of the benefits of eradicating measles and convinced that they can contribute to this goal (see Box 3). Community resources—human, material, and financial—should be sought for staffing clinics, providing publicity, storing vaccine, furnishing freezers, and supporting volunteers.

Community leaders should be contacted as soon as possible during the planning stages of a mass campaign. They should understand that by quickly implementing vaccination activities for an entire district or larger geopolitical unit, many measles cases and deaths can be prevented. They should be informed of the activities and offered a role in them. The briefing provided should be simple and direct, emphasizing the following specific points:

- The existence of a measles case or low vaccine coverage places the community at risk of measles epidemics.
- A campaign is necessary to protect all children in the community quickly.
- Community mobilization should complement resources from the health sector and should provide volunteers.
- Community leaders' help is needed to determine how best to gain access to hard-to-reach populations.
- Leaders' opinions will be taken into account when decisions on the proposed times and places to hold clinics and to train volunteers are made.
- Local assistance is required to access community equipment for storing ice packs and/or vaccine.
- Participation is needed for the distribution of posters and flyers.
- The leaders' assistance will be sought in setting up committees within the community to deal with mass media, business contributions, churches, etc.
- School representatives should be included in planning and implementing the vaccination campaign.

**Box 2. STEPS FOR PLANNING AND CONDUCTING A "CATCH-UP" CAMPAIGN**

1. Develop a preliminary plan for campaign with a general time line for activities.
2. Determine resources required.
3. Discuss resource availability within Ministry and with other cooperating agencies.
4. Obtain further political commitment.
5. Obtain professional community commitment.
6. Hold social communication workshop to prepare guidelines for campaign.
7. Determine if a sufficient supply of vaccine is available, and if there is sufficient refrigeration space for vaccine and other essential supplies on their arrival.
8. Determine if cold chain is sufficient to reach remote areas.
9. Ministry of Health to designate a planning/coordination committee including a chief medical officer of health, epidemiologist, EPI manager, health educator, central vaccine storekeeper, and procurement officer.
10. The planning/coordination committee to plan and develop national guidelines and refine time line of activities, including overall strategy and policy, types of promotion, and locations and methods of vaccine delivery.
11. Order measles vaccine and other EPI vaccines if included. Include disposable syringes with needles, containers for disposing of used syringes and needles, vaccine carriers, cold boxes, forms, and stationery for keeping records.
12. Seek assistance, especially in promotion, through schools, social workers, health educators, community groups, government, nongovernmental agencies, and influential members of communities.
13. Prepare special strategies to gain access to hard-to-reach groups, including grass-roots and neighborhood-level involvement.
14. Health officials to explain details of program over radio and television, including panel discussions and newspaper coverage.
15. Distribute vaccines, syringes with needles, needle destructors, vaccine carriers, cold boxes, forms, and stationery.
16. Conduct final briefings and discussions to ensure that all staff—including drivers, teachers, health educators, social workers, community groups, and government and nongovernmental agencies, as well as influential members of communities—know their responsibilities.
17. Check to ensure that health centers, schools, and all other places at which the vaccine will be administered are prepared with staff and the necessary supplies. Emphasize keeping accurate records in order to be able to derive "before" and "after" coverage statistics.
18. Officials of the government to officially launch the program over radio and television the day before the campaign begins.
19. Ensure adequate and proper supervision for guidance and corrective actions.
20. Calculate coverage achieved among children <1, 1–4, 5–9, and 10–14 if applicable.
21. Hold meeting of planning/coordination committee to report outcome; include coverage achieved, problems encountered, solutions applied, problems outstanding.
22. Distribute final report to all who participated in program.

**Box 3. KEY GROUPS TO CONTACT**

- All schools and preschools
- Religious organizations
- Local organizations, mothers' groups, parent/teacher associations
- Volunteer groups
- Rotary and Lions clubs
- Municipal and provincial government offices
- Private sector health providers, doctors, clinics, pharmacies

**Grass-Roots/Neighborhood Involvement.** One of the principal aims of any campaign should be to identify and reach populations of high-risk children. Such pockets of need may be in urban or rural areas. Volunteers need to be recruited to go door-to-door to inform parents of the upcoming campaign and to encourage them to bring their children to the vaccinating center during the campaign.

Volunteers should inquire whether any problem would keep the parents from bringing children to a center, such as lack of transportation or lack of a babysitter for older children. The volunteer should help arrange for transport or other needed assistance. It is best to have a volunteer coordinator trained for each geographic area. This type of program works most smoothly when each volunteer knows exactly the num-

ber of houses he or she is responsible for and keeps records of the visits, using a standardized data collection form. It is critical that the volunteer revisit the homes on the day or days of the clinic. Volunteer work should be carried out just prior to and during the clinic events. A variety of motivational techniques can be used to reward volunteers, and local clubs may be a good source of such rewards.

Youth groups and other volunteer groups are helpful in distributing flyers and other materials. Simple messages should be developed, and television and radio stations should be requested to provide public service announcements.

## 5.2 Routine Vaccination Services ("Keep-up" Vaccination)

After the initial "catch-up" campaign, routine immunization services should assure that all infants receive one dose of measles-containing vaccine as soon as possible after their first birthday. Without high coverage through routine services, the population of susceptible infants and children will rapidly expand and increase the probability of a large measles outbreak, should the virus be reintroduced. ***High measles vaccine coverage in every new birth cohort through routine services is absolutely necessary if the interruption of measles virus circulation is to be maintained over time.***

Various approaches are used to ensure that at least 90% of each new birth cohort receives measles-containing vaccine. These include:

- improving access to vaccination services;
- integrating vaccination services within routine health services;
- reducing missed vaccination opportunities;
- utilizing infant immunization tracking systems;
- conducting special outreach activities, including house-to-house vaccination, when necessary;
- developing school programs and school immunization laws.

The efficiency of routine vaccination activities can be monitored by conducting monthly reviews of the immunization records of the 1-year-old population (12–23 months of age). The reasons for failure to have been vaccinated should be determined and vaccination strategies should be altered accordingly.

**Vaccination Coverage Assessment.** Vaccination coverage should be analyzed regularly at the municipality, county, or district level. Where possible, birth cohorts should be monitored closely on a regular basis. Community vaccination coverage surveys are not generally advisable, as they are time-consuming and labor-intensive and divert critical resources which can be better used to improve vaccination coverage.

Assessment of measles vaccination coverage should be done every 6 months at the health facility and district level. Coverage data from each district should be aggregated at the provincial and national level on a quarterly or semi-annual basis. Districts should then be categorized by coverage level reached: $<90\%$ or $\geq 90\%$. Districts that present coverage below 90% should conduct "mop-up" activities.

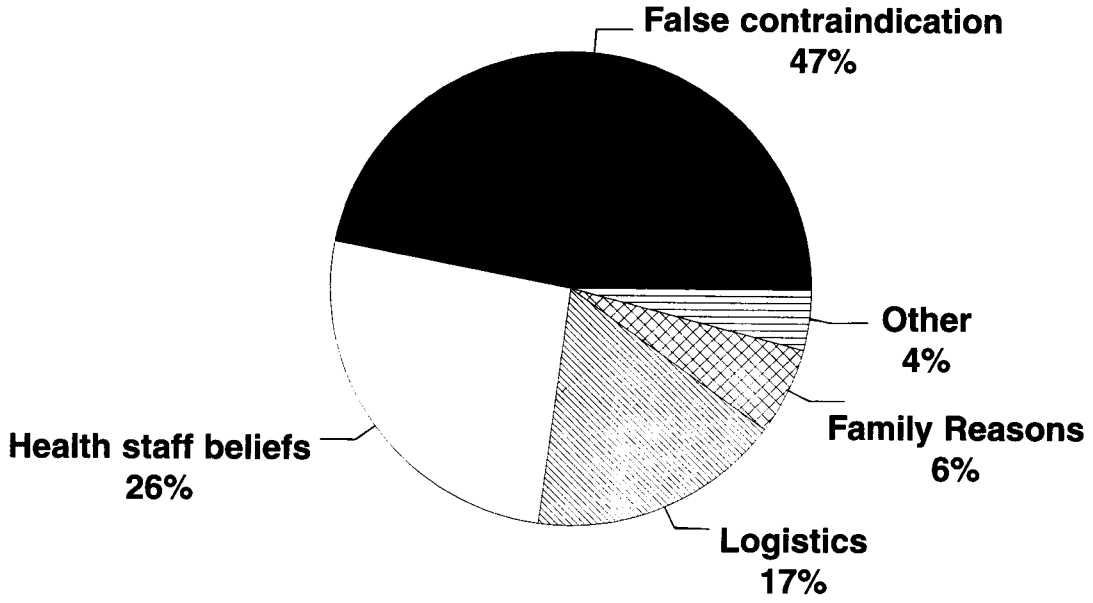
**Missed Opportunities for Vaccination.** Studies of missed opportunities for vaccination indicate that it is necessary to inform health personnel that there are virtually no contraindications to receiving measles vaccination. Otherwise, these personnel will continue to impose unwarranted barriers to achieving the goal of measles eradication. Steps should be taken to ensure that whenever infants and children have contact with the health care system, all vaccines they may need are offered.

Missed opportunities are generally due to one or more of the following four causes (see Figure 9):

- False contraindications to vaccination, including mild fever, diarrhea, vomiting, colds, and coughing, often prevent health workers from vaccinating children, despite the existence of clear national standards in this regard. The health workers erroneously fear that these symptoms will be exacerbated by the vaccine.
- Health workers often do not remember to ask whether a child who visits a clinic for some other reason is fully vaccinated. Other times, they may be reluctant to open a multi-dose vial of vaccine for a single child because they believe it would be a waste of resources.
- The supply and distribution of vaccines to health centers is sometimes inadequate.
- The limited hours or days during which some health centers are open is commonly cited as a factor that has prevented children's access to vaccination services.

Family beliefs, religion, or past negative experiences with vaccination are also sometimes cited as reasons for missed opportunities.

**FIGURE 9**
**Reasons for missed vaccination opportunities in Latin America**




***Source:*** Review of 13 studies performed in the Americas, 1988-1990, PAHO.

## 5.3 "Follow-up" Vaccination Campaigns

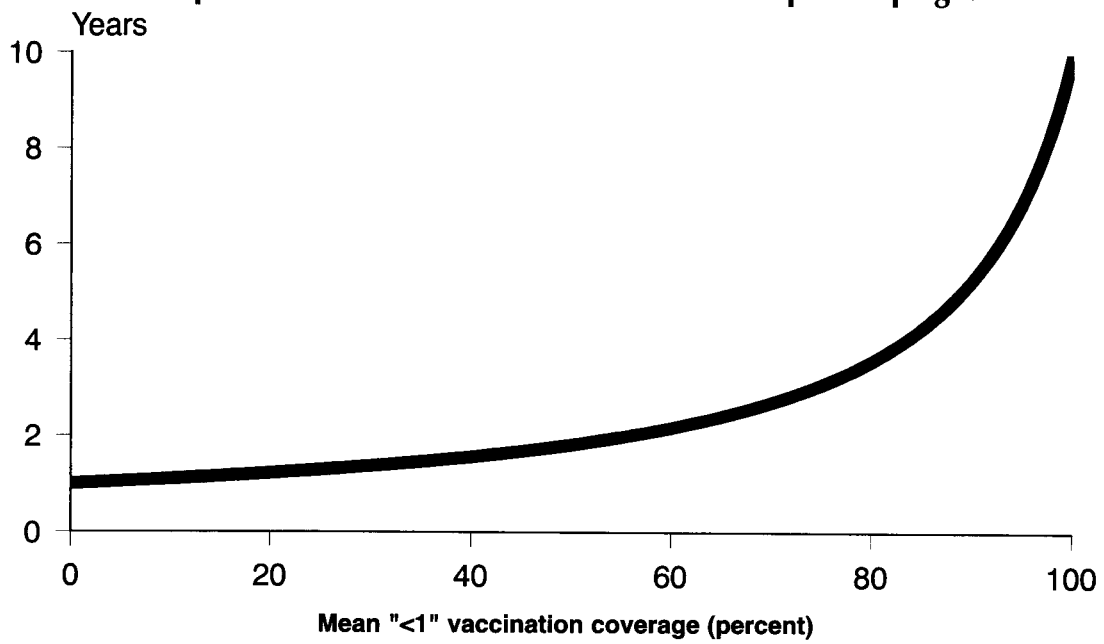
However efficient the "catch-up" and routine immunization efforts are, there will inevitably be an accumulation of measles-susceptible preschool-aged children over time. Two major factors contribute to the build-up of susceptible children. First, measles vaccine is less than 100% effective, thus leaving some children unprotected following vaccination. Second, measles vaccination coverage for each birth cohort will almost always fall short of reaching all children.

The accumulation of susceptible preschool-aged children can be illustrated by the following hypothetical situation in a country with a population of 20 million and 500,000 births per year. If 90% of newborns receive measles vaccination through routine health services at 12 months of age, and if measles vaccine effectiveness is 90%, then each year only 405,000 children (81%) of the newborn cohort will be protected against measles (500,000 × 0.9 × 0.9) and 95,000 children (19%) will remain susceptible to measles. Thus, each year, 95,000 children will be added to the pool of measles-susceptible children. In approximately five years, the number of measles-susceptible children in the population will approximate the number of children in an average birth cohort. This large number of measles-susceptible children will increase the risk of a large measles outbreak should the virus be reintroduced through an importation.

Thus, the PAHO measles eradication strategy recommends that periodic "follow-up" vaccination campaigns be conducted among preschool-aged children. These campaigns should be conducted whenever the estimated number of measles susceptible preschool-aged children (aged 1–4 years) 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. Thus, if only 60% coverage is obtained, a "follow-up" vaccination campaign would be needed approximately every two years; if 80% coverage, approximately every four years; and if 90% coverage, approximately every five years (Figure 10). In practice, these campaigns are conducted every four years and target all children 1–4 years of age.

"Follow-up" campaigns are conducted in a manner similar to that of the "catch-up" campaigns described above, with the exception that the target age group is narrower. For example, if four years have passed since the "catch-up," the target for the "follow-up" will be children 1–4 years of age. As with a "catch-up" cam-

**FIGURE 10**
**Graph to estimate interval between "follow-up" campaigns***




***Assuming vaccine effectiveness of 90%**

***Source:*** de Quadros, CA, et al. (*JAMA* 1996; 275:224-229.) Measles elimination in the Americas: evolving strategies.

paign, after a "follow-up" campaign there may be remaining pockets of susceptible children. Therefore, it may be necessary to carry out "mop-up" vaccination efforts, as discussed below.

## 5.4 "Mop-up" Vaccination Efforts

After the "catch-up" and "follow-up" campaigns have been conducted, pockets of unvaccinated children may still remain, especially in disadvantaged urban areas and in hard-to-reach rural areas. Protecting these children requires intensive vaccination efforts, which may include house-to-house vaccination. These special efforts are referred to as "mop-up" vaccination.

"Mop-ups" usually include the same age group that was targeted in the mass campaign. High-risk areas are usually selected on the basis of coverage results from the campaign; however, other criteria may also be used, such as areas with:

- cases of measles within the last three months;
- poor measles surveillance;
- poor access to health services; and
- large concentrations of urban poor, especially with frequent migration.

Although varying approaches are used in urban, periurban, and rural areas, the overall principles remain the same. Some basic information should be obtained as quickly as possible:

- population data (by age group);
- estimated number of households;
- maps (as recent as possible) showing the urban, rural, or other geographic divisions in detail, including the number of households per block or other unit; and
- measles immunization coverage by health district.

When the number of houses, the number of children living in the houses, the distance between them, and the topography of the area (hills, mountains, or rivers) are known, it is then possible to calculate the number of vaccinators and supervisors required, as well as how long the "mop-up" effort will last. Estimates must also be made regarding needs for vaccine carriers, ice, transportation, supplies, etc.

A supervisor (one for each 10–15 vaccinators) should be assigned to ensure that no areas or blocks of houses are left unvisited and that all children in the target age group are vaccinated. The supervisor also must ensure that the logistics of moving vaccinators and sup-

**Box 4. MOP-UPS IN THE AMERICAS HAVE SHOWN THAT:**

1. ***To properly plan the distribution of personnel, supervisors must be familiar with the areas to be covered****, that is, which areas are more commercial buildings and less family housing, and which neighborhoods have a higher concentration of children.*
2. *In urban areas one vaccinator can generally* ***vaccinate between 50 and 80 children per day going house-to-house*** *(vaccinators generally do not fill out vaccination card histories during mop-up efforts).*
3. *Because of possible fatigue and logistical* ***considerations in hilly areas****, many vaccinators should be assigned to cover these areas quickly and in the early morning hours. This will permit them to descend as the morning progresses and complete the less hilly areas in the afternoon. In very warm climates, provision of water must be taken into account.*
4. *Perhaps the most underestimated task, and one which is sometimes difficult to organize, is the* ***freezing of large quantities of ice overnight*** *to have ready for the vaccine carriers on the day of the campaign. This task requires careful advance planning.*
5. *Training of both health workers and community volunteers* ***needs to be carried out quickly****. Training of community volunteers should be done in the one or two days before the start of vaccination activities to reduce volunteer drop-out.*
6. *On the first morning of the house-to-house vaccination, it is advisable that* ***operations be decentralized*** *and that vaccinators and supervisor start work immediately at the designated locations, so that critical time is not wasted transporting personnel to their respective vaccination sites.*

plies are well planned. Experience has shown that a supervisor is most effective when accompanying vaccinators rather than covering large areas in a vehicle on his or her own. At the end of the day all supervisors should meet with the campaign coordinator(s) to review and discuss accomplishments and problems and to make any adjustments that may be necessary for the next day's work. In rural areas, supervision methods should be adjusted to the topography and size of the area covered (see Box 4).

At the end of the "mop-up" effort, the total number of children who have been vaccinated should be tallied for each health center, post, or other unit. This total should be compared to the goal. If there are pockets of unvaccinated children, teams of vaccinators accompanied by supervisors should return to the households at a time, such as evening, when the children are likely to be there.

The results of the "mop-up" vaccination should be made known to the community as soon as available. The health team should provide community leaders with any other information they may find useful. The local radio station should be requested to air the results of the "mop-up" and to congratulate the community for its participation.

## 5.5 Vaccination of "High-Risk" Groups

The measles eradication vaccination strategy primarily targets infants and children, but small percentages of adolescents and young adults may have escaped both natural measles infection and measles vaccination and, thus, remain susceptible to measles. For practical purposes, persons born before 1960 in most countries of the Americas can be assumed to have been exposed to naturally circulating measles virus and thus be immune to the disease. Therefore, the overwhelming majority of adults are already immune and most susceptible adults are at low risk for being exposed to measles virus. ***Countrywide mass campaigns among adults are, therefore, not recommended.***

In recent years economic factors in many countries have led young adults to migrate from rural to urban areas. Because measles circulates more readily in cities with high population densities, persons who have recently migrated from rural areas with low population densities (and therefore lower risk for being previously exposed to circulating measles virus) may be at relatively increased risk for measles susceptibility. When these persons congregate in settings that can facilitate measles virus transmission due to high contact rates between persons, they are at increased risk for acquiring measles, should the virus be introduced.

Certain institutional settings such as colleges and universities, military barracks, health care facilities, large factories, and prisons can facilitate measles transmission, if measles virus is introduced. Indeed, many measles outbreaks among adolescents and young adults have been documented in these settings, even in institutions with very high measles vaccination coverage.

In addition to persons living or working in institutional settings, adolescents and young adults who travel to countries with endemic measles transmission are at increased risk for being exposed to the virus. To prevent the occurrence of measles outbreaks among adolescents and adults, efforts need to be made to assure measles immunity in persons potentially at "high-risk" for being exposed to the measles virus.

PAHO (C. Gaggero)

**The primary purpose of measles surveillance is to detect in a timely manner *all* areas in which measles virus is circulating**

# 6 MEASLES SURVEILLANCE

A sensitive surveillance system is essential for monitoring progress toward measles eradication. The primary purpose of measles surveillance is to detect, in a timely manner, ***all areas*** in which measles virus is circulating, not necessarily to detect every possible measles case. This requires the notification and timely case investigation of all suspected measles infections. Laboratory investigation for anti-measles IgM antibodies of suspected measles cases is important to permit health authorities to confirm or exclude measles virus infection. To be discarded, a suspected measles case must have a thorough epidemiologic investigation, including a negative laboratory result for measles antibodies.

Even after indigenous transmission has been interrupted, the maintenance of a surveillance system is important so that any imported measles cases can be detected early. Weekly measles surveillance bulletins—summarizing reporting, current outbreaks, cases under investigation, and confirmed measles cases by geographic area—should be distributed.

## 6.1 Case Definitions

Health care providers are asked to report all patients in whom they suspect the possibility of measles virus infection. Suspected measles cases are carefully investigated, including the collection of an adequate blood specimen for serologic analysis, and then are classified as being either *discarded* or *confirmed*. The purpose of the classification system is to provide a guide for program action (Figure 11). The following case definitions are used to classify cases for measles surveillance:

**Suspected Measles.** The category of suspected measles case has a wide catchment and is intended to provide an early alert for health workers at the lowest level that measles virus may be circulating in the community. A patient in whom a health care provider suspects the possibility of measles virus infection is, for surveillance purposes, considered to be a ***suspected measles case***.

All suspected measles cases should have a single blood specimen collected for laboratory analysis of measles virus infection and should be immediately reported to local surveillance authorities. The notification of a suspected measles case should result in the immediate careful investigation of the case and should stimulate an active search for additional suspected measles cases in the area.

**Confirmed Measles Case.** There are two categories of confirmed measles cases: ***laboratory-confirmed*** and ***clinically-confirmed***. The total number of confirmed measles cases is the sum of the cases in these categories. The definitions of these categories are as follows:

***Laboratory-confirmed measles:*** A laboratory-confirmed measles case is a suspected measles case that after complete investigation satisfies at least one of the following criteria:

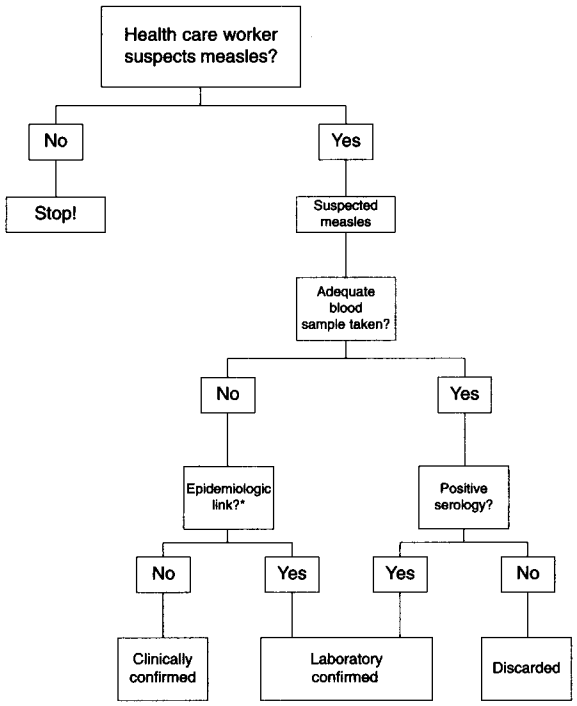
- laboratory confirmation of measles virus infection,
  AND/OR
- epidemiologic linkage to another laboratory-confirmed measles case.

A suspected measles case is considered to be laboratory-confirmed if measles-specific IgM antibodies are detected using the enzyme immunoassay (EIA) IgM technique in a blood specimen collected from the patient (see Chapter 7).

Once measles virus circulation has been confirmed by the laboratory, it is not necessary to collect a blood sample from every suspected measles case. To avoid overwhelming the laboratory with specimens, blood may be collected from every third or fourth suspected measles case. This is useful for documenting the end of the outbreak.

Other suspected measles cases can be empirically considered to be laboratory-confirmed if they are epidemiologically linked to another laboratory-confirmed measles case. Epidemiologic linkage is defined as direct contact with another laboratory-confirmed measles case whose rash onset was 7–18 days before the present case.

## FIGURE 11
## Decision tree for measles surveillance case classification




**To another case that has been laboratory confirmed.*

***Clinically-confirmed measles case:*** A suspected measles case that, for any reason, is not completely investigated is considered to be clinically confirmed. Since measles virus infection was suspected by a health care provider and the possibility of measles virus infection could not be excluded, these cases cannot be discarded. Cases may be classified under this category because the patient died before the investigation was complete, the patient could not be located or was lost to follow-up, or the patient received only a clinical diagnosis from a health care provider without laboratory investigation.

Since an epidemiologic investigation was not conducted and measles virus infection could neither be confirmed nor excluded, these cases are considered to be failures of the surveillance system. In an eradication program, the goal of the measles surveillance system is to conduct a complete epidemiologic investigation of ***every*** reported suspected measles case and to have as few clinically confirmed measles cases as possible. Of the total confirmed measles cases, at least 80% should have laboratory confirmation of measles infection (see surveillance indicators, Section 6.5).

**Discarded Case (Not Measles).** A suspected measles case that has been completely investigated, including the collection of an adequate blood specimen, and lacks serologic evidence of measles virus infection can be classified as discarded. Moreover, if there was laboratory evidence of another infection that is usually associated with a fever and rash illness, such as rubella or dengue, this provides ample support for discarding the case.

The national epidemiology office should receive a copy of all case investigation forms so that it can periodically review the distribution of diagnoses and evaluate the clinical basis for discarded cases (see Appendix B).

**Imported Measles Case.** An imported measles case is defined as a confirmed measles case in a person who traveled in another country with documented measles virus circulation during the possible exposure period (7–18 days prior to rash onset) and was in an area where measles cases were occurring. For a case to be confirmed as imported, the possibility of local exposure to measles must be excluded after a careful community investigation. Data obtained from molecular

**FIGURE 12**
**Sample of the weekly special surveillance report**

**WEEKLY SPECIAL SURVEILLANCE REPORT**

REPORTING UNIT _____

DATES: from _____ to _____

1. NUMBER OF SUSPECTED MEASLES CASES: _____
   (Attach forms on any case; if no cases to report, indicate 0.)

2. NUMBER OF ACUTE FLACCID PARALYSIS: _____
   (Attach forms on any case; if no cases to report, indicate 0.)

3. OTHER _____: _____
   (Other designated disease or condition)

PERSON FILLING OUT REPORT: _____ DATE _____

PLEASE SEND BY MESSENGER, TELEPHONE, OR FAX BY TUESDAY.

epidemiology of the measles virus isolated from the patient may provide additional information concerning the probable source of the measles importation.

## 6.2 Identification and Notification of Suspected Measles Cases

Routine reporting is the backbone of a surveillance system. Monitoring of suspected cases should be carried out by an established network, including health facilities, private practitioners, hospitals, and laboratories. Investigation of notified suspected measles cases should take place rapidly (within 24 to 48 hours). The monitoring system should include at least one reporting source identified in each municipality.

It may be necessary to convince public and private health personnel of the importance of measles reporting, since many consider the disease an unavoidable fact of childhood. Additionally, many private practitioners may not have seen a measles case or remember what one looks like, and therefore may be reluctant to report. To increase physician and nurse participation, visits should be made to association meetings and, if necessary, directly to clinics. It is advisable to provide a specific form indicating key information to report; such a form may include other specially reportable diseases or conditions (Figure 12). It is crucial that when zero cases are reported, such reports actually reflect the absence of suspected cases in the community.

**Health Facilities.** Every health facility should designate one individual and one or two alternates to be responsible for keeping track of suspected measles cases and immediately reporting all new suspected measles cases. Reports should be submitted to local and/or state surveillance coordinators. A special "hot line" should be established to convey this information by the fastest means possible (aerogram, telegram, telephone, fax, e-mail, etc.). State, regional, and provincial officials should, in turn, transmit weekly to the national level the reports they receive from the health facilities in their jurisdiction, and national authorities should report weekly to coordinating agencies (see Box 5).

All health professionals who are likely to be in contact with suspected measles cases should be provided written material that describes their responsibilities and duties. Training and close ongoing supervision are important, as staff turnover may be frequent in many areas. National and provincial/state surveillance personnel should visit all clinic staff to train them. Presentations on surveillance should be made to doctors, nurses, allied health personnel, and record clerks. The design and use of posters and other visual materials illustrating responsibilities should be encouraged. Key points to consider are the following:

**Box 5. SAMPLE HEALTH CENTER MEASLES SURVEILLANCE PROCEDURE**

1. Ensure that all patients sick with fever and rash illnesses have the **Case Investigation Form attached to the medical chart** when seeing the doctor/nurse.
2. Nurses and/or doctors should ask parents whether there are any fever and rash illnesses occurring in their villages/towns.
3. When a health care provider suspects measles virus infection, the **District Health Officer should be notified immediately**. The surveillance case definition for a "suspected measles case" is any patient of any age in whom a health care provider suspects measles infection.
4. For all suspected measles cases a blood specimen should be collected immediately. **A copy of the measles case investigation form should be sent with the acute blood.**
5. Plans should be made to visit the home of the patient and the surrounding area to find additional cases.
6. Whenever suspected measles cases are identified, the doctor or nursing director should call the epidemiologist in charge of measles surveillance.
7. Each Tuesday, the **Weekly Surveillance Report** summarizing the number of suspected cases seen or reporting ZERO cases seen in the previous week should be telephoned, faxed, or sent by messenger to the epidemiologist. A copy of the Case Investigation Form should be included.

- Repeated visits by the program surveillance officers will be required in order to establish and monitor all levels of the reporting system.
- All suspected cases should be investigated by epidemiologists or other specially trained staff, and an appropriate laboratory specimen should be obtained from each case and tested promptly.
- Each suspected case should be given a unique identification number, which should be used whenever the case is cited. The case numbers should begin with one or more three-letter combinations to designate the geographic location, followed by the year and the case number (for example, MEX-JAL-97-001 = case number 1 of 1997 for the state of Jalisco in Mexico).
- Regular reports should be made each week, even when no suspected cases of measles have been identified. Consideration should be given to developing a special report form for measles which would include other vaccine-preventable diseases.

**Private Practitioners.** It is important that private medical practitioners be included in the surveillance system (Figure 13), as they may be the first to see suspected measles cases. In some areas, sentinel reporting systems can be set up among a community's key pediatricians. A successful system requires good coordination, training, frequent contact, and feedback.

**Hospitals.** Case-finding through the emergency department and pediatrics ward is critical to the success of a measles surveillance system. A doctor or nurse should be assigned at each hospital to check pediatric and infectious disease wards visually and to review admission records for suspected measles cases. Reports may be submitted by telephone, e-mail, facsimile, courier service, etc.

**Community Sources.** In addition to all health facilities, a network of community reporters needs to be organized to report suspected measles cases. These reporters may include pharmacists, private practitioners, health workers at private clinics, village leaders, school personnel, and anyone else likely to learn of or have contact with sick children.

**Laboratory Reporting.** Every effort must be made to ensure that laboratory, epidemiologic, and operational personnel work closely together. It is important to establish routine communications with all local laboratories that may receive serum specimens for diagnosis of suspected measles cases. Laboratory personnel should be instructed to notify the surveillance coordinator immediately when specimens are labeled "measles," or any other rash illness with fever. In any local laboratory, the log book should be checked once each week to ensure that all suspected cases are being reported promptly (see Appendix C).

## 6.3 Case Investigation

Suspected measles cases should receive a case identification number, as described in Section 6.2, to aid in case tracking. All communications and forms related to the case should cite the identification number. A visit should be made to the home of the initial suspected cases of an outbreak to obtain basic demographic and clinical information. The following steps should be taken as part of the investigation (see also Box 6):

## FIGURE 13
## Sample letter to private physicians

26 September 1996

Dear Doctor,

The Ministry of Health has joined with other World Health Organization member countries in a Measles Eradication Campaign. You probably remember the successful immunization campaign which was conducted in May of 1991.

A national Measles Surveillance System has been developed to keep track of all suspected cases of measles. As the incidence of measles falls, the need to monitor other infectious diseases with exanthems becomes more important; these include dengue, scarlet fever, rubella, coxsackie, chickenpox, roseola, etc.

Measles is a highly transmissible acute infectious viral disease. You should suspect measles in patients presenting with the following signs and symptoms:

- high fever
- generalized blotchy rash
- cough, or coryza, or conjunctivitis.

We are requesting your participation in our Measles Surveillance System. Please report any patient of any age in whom you suspect measles infection. Enclosed is the surveillance form we are asking that you complete on each patient with suspected measles. May we suggest that your receptionist/nurse be provided with these forms and instructed to include this form whenever a patient has suspected measles.

In addition, if you see a patient with suspected measles infection, please contact your local Health Officer, Dr. Eric Smith, at (555) 674-2432 as soon as possible. In order to confirm measles infection in the laboratory, we will need to collect a blood specimen. If needed, we can assist either with the collection or pick-up of the specimen.

I am personally looking forward to working with you on this program.

Thank you for your cooperation.

Yours faithfully,

Dr. Samuel Jones
Senior Medical Officer of Health

- Complete the Case Investigation Form (Figure 14).
- Update the Suspected Case Line Listing (Appendix D).
- Obtain blood specimens from suspected measles cases. Once the outbreak has been laboratory confirmed, it is not necessary to take blood from every suspected measles case.
- Establish the time for a follow-up visit at the patient's home to evaluate the family/friends for evidence of illness and to provide immunizations as needed.
- Inform surveillance sites and surveillance coordinators in nearby areas that a suspected case has been identified. If the case is located close to a national border, the neighboring country should be informed.
- Conduct contact tracing to identify the source of infection and determine whether other areas have been exposed or are also experiencing outbreaks.
- Evaluate vaccination coverage levels and provide measles vaccination to unvaccinated persons (see Section 6.6, Outbreak Response, below).

Transmission is likely to have occurred from a person who had a rashlike illness or prodromal symptoms and

**Box 6. INVESTIGATION PROCEDURES**

***NOTE: During the first contact, the health care provider must make every effort to obtain the basic information, clinical data, and a blood sample, as it may be the only contact with the patient.***

1. *As soon as a health care provider suspects measles infection, the patient or parent of the patient should be informed that a public health nurse will be visiting their home. Explain about the measles eradication program, and why a visit is necessary.*
2. *Arrange for a time to visit the family when all family members are expected to be at home; this may mean an evening visit.*
3. *On the field visit, take measles case investigation forms and measles vaccine. Only suspected measles cases should have blood drawn.*
4. *Ask about additional cases in the home, adjacent homes, or in the neighborhood. Remember that some cases may be in either the incubation period or at the early stages of the illness, with only a fever and cold symptoms. It is important that the families know who to contact if a rash should occur. In addition, a visit/call should be made every 2 days for a period of 2 weeks to ask if any new cases have occurred in the household.*
5. *All families should be advised to keep the patient at home and to keep the number of visitors to a minimum until the rash disappears.*
6. *Ask the family if they know where the patient got the illness. It will be necessary to explain the incubation period to them, and that after exposure occurs it takes about 10 days for symptoms to start. Remember that the case may have been exposed to someone who did not have a rash. This is important, as measles is highly contagious even before the rash appears.*
7. *Visit adjacent homes (for example, within a radius of 100 to 1,000 yards around the case or in the same block or neighborhood) and ask in person whether any cases of fever and rash have occurred during the previous month. Also check the immunization status of all children under 15 years of age living in the households.*
8. *Investigate any reports of either rash illnesses or general fever/colds. It may be necessary to request that other clinics go to the homes of possible sources to see if there has been a rash illness and to fully investigate the case.*
9. *In addition, preschools, nurseries, schools, church groups, etc., in the area should be visited to find out if any fever and rash illnesses have been occurring.*
10. *Vaccinate or revaccinate immediate household members and any neighbors, playmates, or schoolmates who have been exposed directly to the case during the illness. This usually includes children 9 months to 14 years of age. Remember to take vaccination consent forms so that, if necessary, teachers can pass them on to the parents for permission to vaccinate.*
11. *Send out pamphlets or notify the neighborhood and other preschools and schools by word of mouth that there is a suspected measles case in the area, and that anyone between 9 months and 14 years of age who has not been vaccinated needs to be vaccinated as soon as possible.*
12. *Call local private medical doctors to inform them about the suspected measles outbreak and to ask if they have seen any cases of fever and rash illness.*

later developed a rash illness. Inquiries should be made to determine whether cases are occurring in places that the case under investigation visited between 7 and 18 days prior to the onset of the rash, such as a preschool center, school, or another town or village. If there are more than 10 suspected cases in a single outbreak area, the household visits should be reduced or eliminated, depending upon the availability of investigators. However, the Suspected Case Line Listing should be filled out for each suspected case and particular attention paid to obtaining basic demographic data, including the age and vaccine history of the patient.

**Case Finding.** In order to find additional suspected measles cases in the community, the public should be kept well informed and community leaders should be asked to assist in case finding. Health staff in the affected and nearby areas should use every contact with patients as an opportunity to inquire about rash and fever illnesses in the neighborhood. Efforts to identify additional cases should also extend well beyond the neighborhood community in which the suspected case lives. Case finding activities may include:

## FIGURE 14
## Suspected measles case investigation form

### Suspected measles case definition:

Complete this form for: **All cases for which a health worker suspects measles**

### Identification

State or province: _____
County: _____
City: _____

Name: _____
Name of mother or father: _____
Address: _____

Case # _____
Date of notification ____/____/____
Source of notification:

Sex: ☐ A = Masculine B = Feminine Z = Unknown

Age: ☐☐ Years ☐☐ Months

# of documented doses: ☐ of measles vaccine ZZ = Unknown

Date of last dose ____/____/____

☐ A = Urban B = Rural Z = Unknown

☐ A = Public B = Private C = Laboratory D = Community E = Active search Y = Other Z = Unknown

### Clinical data

Date of investigation: ____/____/____

Fever: ☐ A = Yes B = No Z = Unknown
Date of onset of fever ____/____/____

Date of rash onset ____/____/____
Type of rash ☐ A = Maculopapular B = Vesicular Y = Other Z = Unknown

Conjunctivitis: ☐
Coryza: ☐
Cough: ☐
Lymph Nodes: ☐
Hospitalized: ☐
Death: ☐

A = Yes B = No Z = Unknown

Name of hospital: _____
Date of death: ____/____/____

### Laboratory data

| Date sample taken | Laboratory | Received in laboratory | Type of test | Antibody | Result | Date of result |
|---|---|---|---|---|---|---|
| ____/____/____ | _____ | ____/____/____ | ☐ A = HI B = IgM Capture C = NT D = CF E = Indirect IgM F = IgG - EIA Y = Other Z = Unknown | ☐ A = Measles B = Rubella C = Dengue Y = Other Z = Unknown | ☐ A = Positive B = Negative Z = Unknown | ____/____/____ |
| | _____ | ____/____/____ | | | | ____/____/____ |
| | _____ | ____/____/____ | | | | ____/____/____ |
| | _____ | ____/____/____ | | | | ____/____/____ |

### Classification

A - Suspected ☐ B - Discarded ☐ F = Rubella I = Dengue Y = Other Z = Unknown C - Confirmed ☐ A = Laboratory B = Epidemiologic link C = Clinical Diagnosis

Date of diagnosis or final classification: ____/____/____

### Possible source of infection

Travel during 7-18 days prior to rash onset? ☐ A = Yes B = No Z = Unknown

Was there contact with another confirmed measles case 7-18 days prior to rash onset? ☐ A = Yes B = No Z = Unknown

Was there a confirmed case of measles in this area prior to this case? ☐ A = Yes B = No Z = Unknown

### Investigator

Name: _____ Position: _____

Signature: _____ Date of investigation: ____/____/____

Comments: _____

- visiting blocks adjacent to the affected household;
- sending notices to health care providers asking if they have seen or heard of persons with fever and rash illnesses;
- conducting visits and reviewing records at the local health centers, hospitals, and clinics.

## 6.4 Monitoring and Feedback

The number of units reporting and the timeliness of the reports should be monitored weekly. To evaluate the weekly reporting system (particularly in areas with all negative reports), interviews should be conducted with personnel involved in surveillance at the regional level and in selected districts, and with individuals from reporting units within a state or area.

Feedback includes providing surveillance participants with the following: (1) the number and location of reported cases, (2) an assessment of the level of promptness and accuracy of their surveillance reports, (3) information on the effectiveness of vaccination and control activities, (4) specific recommendations on how to solve common problems, and (5) commendations of personnel doing excellent work. Feedback can be provided effectively by sending weekly measles surveillance bulletins to the reporting sites and to interested parties (Figure 15).

## 6.5 Surveillance Indicators

The following indicators are used to monitor, on an ongoing basis, the quality of measles surveillance (see Appendix E):

***Proportion of reporting sites that report each week:*** At least 80% of surveillance sites should report each week on the presence or absence of suspected measles cases.

***Proportion of sites reporting at least one suspected measles case per year:*** At least 80% of surveillance sites should report one or more suspected measles cases per year.

***Interval between notification and investigation:*** At least 80% of the reported suspected cases should be investigated within 48 hours of report. This indicator shows how quickly the health staff is responding to reports.

***Proportion of suspected measles cases with blood specimen collected or epidemiologic linkage to a laboratory-confirmed measles case:*** At least 80% of reported suspected measles cases must have a complete epidemiologic investigation, which will include collection of a blood specimen if there is not epidemiologic linkage to a laboratory-confirmed case. Blood specimens must be accompanied by the following basic information: case identification number, county/municipality, name, age, number of vaccine doses received, date of last measles vaccination, date of rash onset, date of notification, date of investigation, date of blood sample collection, and case classification.

***Proportion of total laboratory-confirmed cases with known source of infection:*** Following a complete epidemiologic investigation, at least 80% of the total laboratory-confirmed measles cases should have a known source of infection.

***Ratio of discarded to confirmed cases:*** An effective surveillance program should be identifying at least twice as many "discarded" as "confirmed" cases. This would mean that at least 2 out of 3 reported suspected cases are ultimately classified as discarded.

***Proportion of blood specimens for which results were received within 7 days of receipt in laboratory:*** At least 80% of specimens must be tested and the results reported back to the surveillance unit within 7 days of receipt of the specimen in the laboratory. Lab turnaround time must be as short as possible.

## 6.6 Outbreak Response

Because measles virus continues to circulate in many parts of the world and international travel is readily available, importations of measles virus into measles-free areas can be expected to occur. Therefore, it is necessary to maintain high levels of population immunity among persons living in these areas. Maintaining high levels of measles immunity will reduce the possibility that measles will spread following an importation.

Experience has shown that, because of the very high communicability of measles, many susceptible persons will already have been infected with measles virus before an outbreak is recognized and control activities can be implemented. Although effective control of an outbreak may be very difficult, and resources are best expended on outbreak prevention, an appropriate public health response must be made (see Box 7).

## FIGURE 15
## PAHO weekly measles bulletin (sample)

# PAN AMERICAN HEALTH ORGANIZATION

PAN AMERICAN SANITARY BUREAU REGIONAL OFFICE OF THE
WORLD HEALTH ORGANIZATION

*Special Program for Vaccines and Immunization*

*Expanded Program on Immunization*

*Measles Surveillance in the Americas*

*Vol. 2 No. 52*

*Weekly Bulletin for the week ending 28 December 1996*

| Region | Country | Week of Report | Suspected Cases Notified for Current Week | Year to Date - 1996 | | | | | | Total Confirmed Cases 1995 |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Total Suspected Cases Notified | Suspected Cases Under Investi-gation | Discarded Cases | Confirmed Cases | | | |
| | | | | | | | Clinic-ally* | Labora-tory♣ | Total | |
| AND | BOL | 52 | 7 | 91 | 19 | 68 | 4 | 0 | 4 | 76 |
| | COL | 51 | ... | 1,068 | 614 | 412 | 38 | 4 | 42 | 410 |
| | ECU | 52 | 0 | 286 | 72 | 184 | 30 | 0 | 30 | 919 |
| | PER | 52 | 0 | 843 | 370 | 408 | 64 | 1 | 65 | 353 |
| | VEN | 52 | 58 | 604 | 143 | 425 | 32 | 4 | 36 | 172 |
| BRA | BRA | 45 | ... | 2,226 | 852 | 1,165 | 190 | 19 | 209 | 793 |
| CAP | BLZ | 52 | 2 | 38 | 15 | 23 | 0 | 0 | 0 | 4 |
| | COR | 49 | ... | 139 | 45 | 87 | 3 | 4 | 7 | 35 |
| | ELS | 52 | 6 | 326 | 7 | 318 | 0 | 1 | 1 | 0 |
| | GUT | 52 | 0 | 119 | 14 | 105 | 0 | 0 | 0 | 23 |
| | HON | 52 | 0 | 40 | 18 | 19 | 3 | 0 | 3 | 0 |
| | NIC | 52 | 0 | 277 | 1 | 276 | 0 | 0 | 0 | 5 |
| | PAN | 52 | 0 | 201 | 13 | 188 | 0 | 0 | 0 | 19 |
| CAR | ANG | 52 | 0 | 6 | 1 | 5 | 0 | 0 | 0 | 0 |
| | ANT | 52 | 0 | 3 | 1 | 2 | 0 | 0 | 0 | 0 |
| | BAH | 52 | 0 | 5 | 0 | 5 | 0 | 0 | 0 | 0 |
| | BAR | 52 | 0 | 72 | 6 | 66 | 0 | 0 | 0 | 0 |
| | CAY | 51 | ... | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | DOM | 51 | ... | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| | GRE | 52 | 1 | 17 | 5 | 12 | 0 | 0 | 0 | 3 |
| | GUY | 52 | 0 | 62 | 36 | 26 | 0 | 0 | 0 | 0 |
| | JAM | 52 | 0 | 37 | 9 | 28 | 0 | 0 | 0 | 15 |
| | MON | 51 | ... | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | NAN | ... | ... | ... | ... | ... | ... | ... | ... | ... |
| | SCN | 52 | 0 | 9 | 0 | 9 | 0 | 0 | 0 | 1 |
| | STL | 52 | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 2 |
| | STV | 52 | 0 | 6 | 1 | 5 | 0 | 0 | 0 | 0 |
| | SUR | 52 | 0 | 15 | 1 | 14 | 0 | 0 | 0 | 0 |
| | TRT | 52 | 0 | 101 | 26 | 75 | 0 | 0 | 0 | 0 |
| | TUR | 51 | ... | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| | VIB | 52 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 |
| | VIU | 51 | ... | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LAC | CUB | 52 | 9 | 108 | 56 | 52 | 0 | 0 | 0 | 1 |
| | DOR | 52 | 0 | 37 | 4 | 33 | 0 | 0 | 0 | 0 |
| | FGU | ... | ... | ... | ... | ... | ... | ... | ... | ... |
| | GUA | 51 | ... | 17 | 4 | 7 | 1 | 5 | 6 | 0 |
| | HAI | ... | ... | ... | ... | ... | ... | ... | ... | ... |
| | MAR | ... | ... | ... | ... | ... | ... | ... | ... | ... |
| | PUR | 52 | 0 | 8 | 0 | 0 | 0 | 8 | 8 | 11 |
| MEX | MEX | 52 | 4 | 1,687 | 153 | 1,430 | 102 | 2 | 104 | 244 |
| NOA | BER | 51 | ... | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | CAN | 52 | 0 | 325 | 0 | 0 | 0 | 325 | 325 | 2,357 |
| | USA | 52 | 0 | 488 | 0 | 0 | 0 | 488 | 488 | 309 |
| SOC | ARG | 39 | ... | 260 | 105 | 117 | 38 | 0 | 38 | 655 |
| | CHI | 52 | 1 | 96 | 21 | 75 | 0 | 0 | 0 | 0 |
| | PAR | 40 | ... | 39 | 11 | 23 | 5 | 0 | 5 | 73 |
| | URU | 32 | ... | 0 | 0 | 0 | 0 | 0 | 0 | 5 |
| Total | | | 88 | 9,660 | 2,624 | 5,665 | 510 | 861 | 1,371 | 6,489 |

... No information provided
* Clinical suspicion of measles without laboratory investigation.
♣ Includes epidemiologically linked cases.

**Box 7. STEPS IN OUTBREAK RESPONSE**

- *Isolate in household and investigate suspected measles case(s).*
- *Obtain appropriate blood specimens for laboratory confirmation.*
- *Inform other health authorities.*
- *Assess coverage in affected and surrounding areas.*
- *Provide measles vaccine to unvaccinated persons.*
- *Enhance surveillance.*
- *Analyze/summarize outbreak.*

**Isolation Instructions.** At home, a suspected measles case should only be permitted contact with immediate family members until 5 days after the rash appears. Communicability greatly decreases after the second day of rash. In hospitals, patients with suspected measles should be isolated from the onset of symptoms through the fifth day of rash. However, suspected measles cases should not be hospitalized unless absolutely necessary because of the high risk of intrahospital transmission.

***Close contacts:***

- Contacts are defined as all persons living in a household or other close quarters with the case during the infectious period (5 days before to 5 days after the onset of the rash).
- Contacts without evidence of measles immunity should immediately be vaccinated. They should also be instructed about the symptoms of measles prodrome and told to avoid contact with other persons for two full weeks after exposure.
- If less than 14 days have elapsed since the case's rash began, all contacts should receive the isolation instructions whether or not they have been immunized.
- During the second week after exposure, at the first sign of possible measles (fever, runny nose, cough, or eyes bothered by light), the contact should be instructed to stay at home. The contact should not attend school, preschool, work, church, clubs, meetings, parties, baby-sitting groups, etc. If the illness is measles, it will become apparent in one or two days by the severity of the illness and the presence of a rash. Parents should be advised to notify the health care provider immediately upon rash onset.

**Outbreak Investigation.** A suspected measles outbreak may be defined as two or more suspected cases in a defined geographic area within a one-month period. A single laboratory-confirmed measles case is considered to be a confirmed measles outbreak. General guidelines for outbreak investigation are given in Box 8.

When a measles outbreak occurs in a defined geographic area and includes more than 20 cases, data gathering efforts should be limited to obtaining basic information from each case, such as name, address, age, immunization history, date of rash onset, and outcome (see Appendix D). At this point, visits to affected households should be greatly reduced, as they are time-consuming and may divert attention from the more important control measures, such as vaccinating previously unvaccinated children.

Once the presence of measles virus circulation has been confirmed in the laboratory and appropriate specimens have been collected for viral isolation, blood does not need to be collected from every suspected measles case. During an outbreak, patients in whom a health care provider strongly suspects measles infection may, for surveillance purposes, be considered to be confirmed via epidemiologic linkage. When the number of reported suspected cases has decreased to low levels, the collection of blood specimens may be useful in order to document the end of the outbreak. Limiting the number of blood specimens collected will save valuable staff time and prevent overloading of the laboratories.

**Evaluation of Vaccination Coverage.** Vaccination coverage data should be reviewed as soon as a measles outbreak is suspected (see Box 9). Persons and areas potentially at risk for measles transmission should be identified. The priority of the vaccination activity is to provide measles vaccination to previously unvaccinated infants and children (see "Measles Vaccination," below).

**Cross-Notification.** Health authorities at all levels should be informed of and involved in all aspects of surveillance and outbreak response. Health officials in nearby jurisdictions also should be notified and updated as frequently as possible, so that they may begin appropriate preventive actions as needed. If an importation may have occurred, the local health officials in the country from which it was imported should be provided with full details of the case (Figure 16). If a suspected case has traveled or had close contact with individuals from other areas of the country 7–18 days before the onset of the illness, the surveillance coordinator in those areas should be notified immediately. Neighboring countries should be

**Box 8. GENERAL GUIDELINES FOR INVESTIGATION OF MEASLES OUTBREAKS**

1. ***Confirm the diagnosis.***
   - *Serologic testing of suspected measles cases:*
     *— collect one blood specimen at first contact*
   - *Appropriate specimens for viral isolation:*
     *— collect midstream urine specimen in sterile container*

2. ***Identify and investigate suspected measles cases.***
   - *Basic surveillance variables:*
     *— age, sex, residence*
     *— date of rash onset*
     *— date of last measles vaccination/number of doses received*
     *— date of collection of blood specimen*
     *— date of collection of urine specimen*
     *— possible source of exposure 12–17 days prior to rash onset*
     *— exposure to another laboratory-confirmed measles case?*
     *— travel to foreign country with known measles virus circulation?*
     *— possible transmission to others 3 days prior to rash onset to 3 days after rash onset?*
   - *Questions to be asked:*
     *— where was patient born?*
     *— when did patient move to current residence?*
     *— have there been other cases within the household?*
     *— have there been other cases in the neighborhood?*
     *— where does patient work/study?*
     *— how does the patient travel to work/school?*
     *— are there other cases in the workplace/school?*
     *— where does the patient socialize? (market, church, club, school, etc.)*
     *— are there other cases in these social groups?*

3. ***Describe the outbreak (descriptive epidemiology).***
   - *Total number of confirmed cases*
   - *Age distribution and vaccination status of confirmed measles cases*
   - *Which municipios have measles circulation occurring? (maps)*
   - *In each affected municipio, what was the age and vaccination status of the first case?*
   - *In each affected household, what was the age and vaccination status of the first case?*
   - *How long did the epidemic last? (epi-curve)*

4. ***Determine source of outbreak.***
   - *Classical epidemiology (who acquired infection from whom)*
   - *Molecular epidemiology via genotypic analysis of measles virus isolates*

5. ***Determine risk factor for measles infection (analytical epidemiology).***
   - *Age and vaccination status of cases*
   - *Place of exposure (school, office, church, etc.)*
   - *Attack rates*
   - *Possible risk factors:*
     *— age group and vaccination status*
     *— travel to areas where measles is endemic*
     *— occupation (e.g., health care, tourism industry, etc.)*
     *— school, church attendance*
     *— visit to health facility*

| *Box 9. POINTS TO CONSIDER AT THE START OF AN OUTBREAK* | |
|---|---|
| *POPULATION DATA* | *Obtain most recent population size and age distribution.* |
| *WHAT'S BEEN DONE* | *List any actions already taken.* |
| *CASE REVIEW* | *List reports of cases in area during previous six months.* |
| *COVERAGE RATES* | *Obtain existing coverage data and include unofficial estimates.* |
| *SPOT MAP* | *Use pins or a pen to mark the location(s) of case(s) and areas targeted for immunization on a map.* |
| *RESOURCES* | *Determine what resources are available at all levels for outbreak control (transportation, vaccine, cold chain materials, promotional materials, etc.). Human resources should include field staff to assist in the outbreak, including staff from other programs, district staff, medical and nursing students, interpreters, and drivers. Arrange for transport and for travel advances.* |
| *ARRIVALS* | *Inform appropriate health/community authorities when and where any special teams will be arriving, and ensure that specific health staff/community representatives will be present.* |
| *SUPPLIES* | *Organize necessary supplies:*<br>*1. Adequate vaccine based on estimated target population.*<br>*2. Cold chain materials: ice packs, cold boxes, vaccine carriers, thermometers, refrigeration capacity (locally available or must be brought in), possibility of purchasing ice locally.*<br>*3. Adequate supply of forms*<br>• *Line Listings of Suspected Cases*<br>• *Case Investigation Forms*<br>• *Outbreak Control Summary*<br>• *Mop-up Work Sheets*<br>*4. Promotional materials: pamphlets, posters, etc.* |

notified as well. The public should be informed through the media about the outbreak and any control efforts (see Appendix F).

**Measles Vaccination.** There are virtually no contraindications to receiving measles vaccine. The following recommendations serve as a general guide. Specific measures must be based on the prevailing epidemiologic situation in the outbreak area.

***Whom to vaccinate:*** When a measles outbreak is suspected, all children 1 to 15 years of age without history of measles vaccination should be vaccinated. If the outbreak is large and many cases are occurring in infants under 12 months of age, the age of routine vaccination should be decreased to 6 months. These infants should be revaccinated when they reach 1 year of age. In addition, consideration should be given to providing measles vaccination to adolescents and young adults residing or working in certain institutions where they may be at risk for measles virus transmission, including military bases, university dormitories, hospitals, and factories. Finally, children hospitalized or attending outpatient clinics for any reason who cannot provide written proof of measles vaccination should be vaccinated with measles vaccine, if not contraindicated.

***When to vaccinate:*** Vaccination of previously unvaccinated persons should start immediately when a measles outbreak is suspected, without waiting for laboratory confirmation of the suspected measles cases. If the suspected cases are eventually confirmed in a laboratory, the vaccination intervention should help to decrease the number of susceptible children, and perhaps result in the interruption of measles virus circulation. If the initial suspected cases do not turn out to be measles, then the vaccination activity has helped to raise the level of measles immunity in the community and prevent measles outbreaks in the future.

## FIGURE 16
## Sample letter on possible importation

May 28, 1993

Dr. Edmond Jones
Health Officer
New York City

Dear Dr. Jones:

On May 26th, we were informed by Dr. Mukerjee, the Medical Officer of Health at one of our clinics, that he had seen what appeared to be a case of measles (rubeola). The affected child, Marissa Smith, had just returned from a trip visiting family in Brooklyn, New York. Marissa, female 20 months of age, started her illness with two days of "high" fever (no temperature was taken), followed by a maculopapular rash which appeared blotchy on the face by the second day. Dr. Mukerjee saw the patient on the second day of rash and observed Koplik's spots at that time. The rash had started on the face. The patient also had a cough and a runny nose and the mother relates that the child's eyes had bothered her. The child was visited by health staff on May 28; at that time she had virtually completely recovered from her illness, and only a fine, faint rash could be seen. The child had stayed with family in Brooklyn and also was cared for at a day-care center there.

Below are some details of the case:
Date of Birth: Sept. 30, 1991 (born in Barbados)
Date Onset of Rash: May 24, 1993
Date Onset of Fever: May 21, 1993
Duration of Rash: 3–4 days
Vaccination History: MMR December 9, 1992 (from vaccine record)
Serum Specimen: Collected May 26, 1993 (to be tested for measles IgM)
Possible Source of Infection: Aunt's home in Brooklyn, New York. Visited from May 7 to May 18.
Father's Name: Vincent Smith, resides in Barbados
Relative's House in Brooklyn: Ms. Glynis Smith. Tel: 718 555-1234 (Ms. Smith is reportedly a nurse. We have been unable to get the address as of this time.)
Name of Day-Care Center: Has not been provided at this time.

The children in the household have the last name of Williams. Children under 15 years of age at the Brooklyn home (vaccination status unknown) are: Damion, 10 years; Michael, 4 years; Martin, 20 months.

As soon as we receive the results from the laboratory we will be forwarding this information to you. We are also interested in hearing about the results of your investigation in Brooklyn when such information is available.

Sincerely,

Senior Medical Officer of Health
Ministry of Health Barbados
Surveillance Program
Jemmotts Lane
*ST. MICHAEL*
TEL: 809 427-5130
FAX: 809 427-9434

cc: CDC

***Where to vaccinate:*** In both urban and rural areas, the focus of vaccination efforts should be any potential pockets of susceptible (i.e., unvaccinated) infants and children. The largest possible area should be covered. Gathering points such as schools, churches, health posts, etc., may also be chosen as mass vaccination sites.

**Measles Cases at a Port of Entry.** A number of issues have been raised regarding how to handle international passengers who are suspected of being infected with measles. The following guidelines may be useful in approaching such situations.

Any traveler who is suspected of having measles should immediately be referred to local health authorities. The passenger should be informed of his/her illness and its potential for complications and transmission to others. If hospitalization is not necessary, the patient with suspected measles infection should remain at a residence (hotel or other living quarters) until at least 5 days after rash onset.

A health information card should be given routinely to all travelers arriving or visiting from other countries. It should inform them of the measles eradication program and request that they assist by seeking immediate medical attention if they experience any fever and rash illness.

**Enhancement of Surveillance.** Measles surveillance should be intensified to search for additional suspected cases. All reporting units should be notified of the suspected measles outbreak and be alerted to be "on the look-out" for additional cases. Daily calls or visits to schools, hospital emergency rooms, and selected pediatricians may prove useful, especially in urban areas.

**Outbreak Monitoring.** The most recent information on suspected and confirmed measles cases, vaccination activities, and areas visited should be monitored and updated continuously during an outbreak. This information should be recorded in such a way that it can be summarized quickly on the Measles Outbreak Response Summary form (Appendix G). When no new cases are reported during a three-week period, despite the presence of enhanced surveillance, the outbreak may be considered to be over.

**Outbreak Summary.** Careful investigation of measles outbreaks can provide useful information regarding factors that may have facilitated measles virus circulation. The investigation may help to identify risk factors for measles infection and provide information that can be used to refine and improve the measles eradication strategy.

In order to benefit from the investigation and outbreak control activities, it is necessary to organize and report on data related to the outbreak. The report should include at least the following sections:

1. Introduction;
2. Surveillance methods;
3. Description of the outbreak;
4. Analysis of the outbreak;
5. Control measures;
6. Problems;
7. Conclusions and recommendations.

## 6.7 Information Systems and Analysis

An important aspect of a successful measles eradication program is a well-developed and decentralized information system that provides program managers and health workers with the information they need for taking appropriate actions. Information from the surveillance system is used to produce regular summary reports, which are distributed to the personnel responsible for taking actions on identified problems. All surveillance information should be standardized.

**Data Collection.** Whether or not the information system is computer-based, it should cover two basic areas:

***Case tracking:*** At the state and district levels there should be a system that is capable of tracking all reported suspected measles cases until they are either confirmed or discarded. Such a system is characterized by several important elements:

- uniform case identification numbering;
- a standardized case investigation form;
- basic demographic data on each case;
- basic clinical data on each case;
- the recording and monitoring of laboratory specimens from collection to final laboratory results.

At the central level, essential information, as presented in the Suspected Case Line Listing, should be available for monitoring the basic surveillance indicators of the program.

***Site reporting:*** At the country level and the subregional level, a system capable of keeping track of

reporting units is needed (Appendices H and I). Such units may be a geopolitical jurisdiction such as a county, district, or municipality, or a service unit such as a hospital, private clinic, or private practitioner. The critical data to maintain on such sites are:

- submission of weekly reports, including negative reporting; and
- timeliness of reporting (on time or late).

**Data Analysis.** Each geopolitical subdivision within a country should be part of the weekly reporting system and should summarize its experience with measles and other rashlike illnesses on a regular basis. Data from a region should be presented in as standardized a format as possible and should include, at a minimum:

- monthly numbers of reported cases and case rates;
- laboratory results;
- final diagnoses of discarded cases;
- age distribution of confirmed cases;
- vaccination status of confirmed cases;
- geographic distribution (urban versus rural); and
- number of cases with case investigation form.

Data from case investigation forms and line listings should be analyzed to provide a descriptive picture of the cases and determine whether standards for case reporting and investigation are being met.

***Age distribution:*** It is useful to know the age distribution of cases in order to detect any changes in the epidemiology of the disease and to establish which age groups to target for vaccination.

***Geographic location:*** Cases should be plotted on a map according to their place of residence, and the map compared with vaccination coverage data and surveillance reporting sites. These maps can be useful for coordinating activities (such as setting up vaccination points, etc.).

***Source of infection:*** This information will help to identify areas where the measles virus is still actively circulating.

***Source of notification:*** This knowledge will help to determine whether improvements are needed regarding notification sources. For example, if cases are being reported only from public health facilities, then additional contacts with private medical doctors and private clinics are required.

***Vaccination history of cases:*** Accurate information on the vaccination history of persons with measles is essential for evaluating vaccine effectiveness and detecting potential problems with the cold chain.

**Information Dissemination.** At the country level, a bulletin, preferably updated on a weekly basis, should be issued with results on reported and confirmed cases. In addition, this newsletter should indicate the number of units reporting each week (including negative reporting). Information about the current epidemiology of acute flaccid paralysis, neonatal tetanus, and other EPI target diseases should also be included. Bulletins should be distributed to all health care providers and other interested health care personnel on a weekly or monthly basis.

PAHO (A. Waak)

**Measles infection can be confirmed by documenting a measles-specific immune response in the patient and/or by culture and isolation of the measles virus from a clinical specimen.**

# 7 LABORATORY CONFIRMATION OF MEASLES INFECTION

Since clinical diagnosis is not sufficient to confirm measles infection, the laboratory has a very important role to play in a measles eradication program. Measles infection can be confirmed by documenting a measles-specific immune response in the patient and/or by culture and isolation of the measles virus from a clinical specimen.

The most common technique used to confirm the diagnosis of measles is a test for the presence of measles-specific IgM antibodies in sera collected from suspected measles cases. For measles surveillance, a single blood specimen obtained shortly after rash onset is sufficient to confirm or discard suspected measles cases.

Although technically more difficult than serologic assays, the culture, isolation, and genetic analysis of the measles virus obtained from measles outbreaks can provide important information about the circulation of measles virus. Therefore, appropriate clinical specimens for viral culture must be collected from every chain of measles transmission (see Section 7.2).

In order to promote high-quality measles laboratory testing throughout the Region of the Americas, PAHO has established a regional network of measles reference laboratories. There are currently 12 international measles reference laboratories located in 11 different countries of the Americas. Each international reference laboratory provides technical support and confirmatory measles testing for one or more national measles laboratories.

## 7.1 Measles Serology

Following primary infection with measles virus, measles-specific antibodies appear in the blood shortly after rash onset (Figure 17). IgM, IgG, and IgA antibodies are produced initially, but the detection of IgA antibodies is not used to confirm measles infection.

IgM antibodies appear first and can be detected shortly after rash onset. They attain peak levels approximately one week later, then gradually decline and are rarely detectable at six weeks after rash onset. The detection of measles IgM antibodies in the blood of a suspected measles case can be considered confirmation of measles virus infection. Using currently available serologic assays, IgM is generally not detected in an immune individual following re-exposure to measles virus.

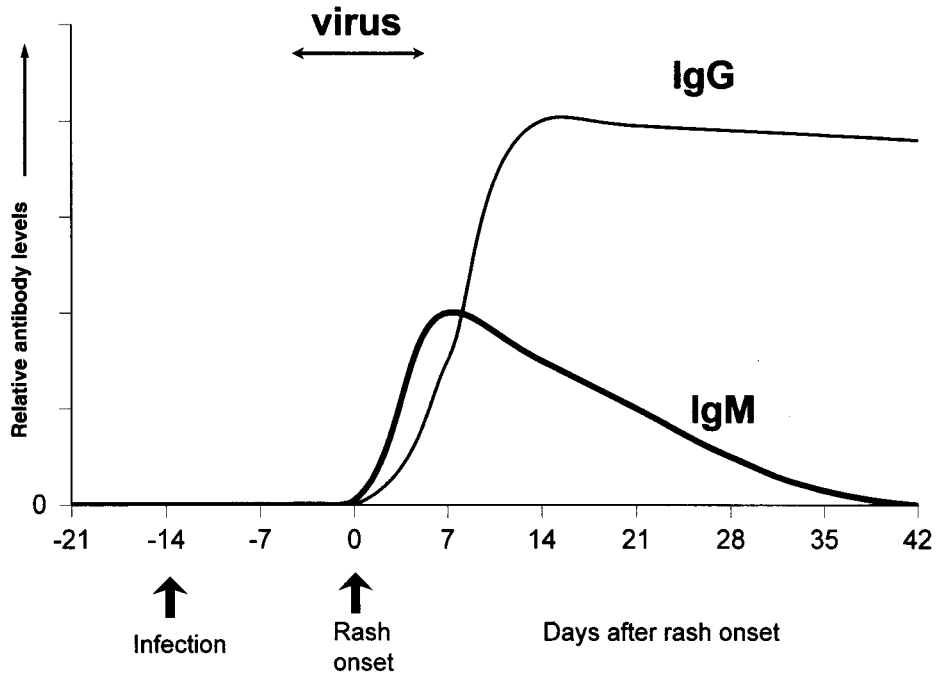
IgG antibodies peak about two weeks following rash onset and are detectable for years after infection. Re-exposure to measles virus in a person with pre-existing measles immunity induces a characteristic anamnestic immunologic response, with a rapid boosting of IgG antibody levels.

At present, there is no single optimal serologic test for confirmation of measles virus infection—that is, a test that is both 100% sensitive and 100% specific, is quick, and can be easily performed in most basic laboratories.

In the past, the documentation of measles IgG seroconversion (a fourfold increase in antibody titers between acute and convalescent sera) using paired specimens was *sine qua non* for measles serologic confirmation. However, with the recent development of sensitive and specific IgM enzyme immunoassays (EIA), it is now possible to confirm measles infection using only a single serum specimen obtained shortly after rash onset.

Measles-specific IgM antibodies can be detected using both indirect and capture EIAs. There are several indirect measles assays available as commercial kits (Behring, Clark, Organon, etc.). These tests are relatively easy to perform, require only 2–3 hours, and have a fairly high sensitivity and specificity for measles. The major shortcoming of the indirect assays, however, is that in periods of low measles incidence false-positive results may be expected because of the less-than-100% specificity of the tests.

**FIGURE 17**
**Graph of antibody responses to acute measles infection**




The measles laboratory of the U.S. Centers for Disease Control and Prevention (CDC) has developed a capture IgM EIA. Overall, sensitivity and specificity have been found to be over 97%. This test will detect IgM antibodies in about 75% of measles cases on the first day of rash; by day three of rash, the test will detect close to 100% of measles cases. Moreover, false-positive results are extremely rare with this assay. While the CDC capture assay has produced excellent results in regional measles reference laboratories, the test's relative complexity and length (6–7 hours) have made it difficult to implement in all state and national virology laboratories.

To counter the disadvantages of both types of assays and to allow a large number of laboratories throughout the Region to test for measles, the PAHO measles laboratory network has developed a two-step testing algorithm. First, sera from suspected measles cases are tested in state or national laboratories using an indirect IgM EIA. Second, all indeterminate samples and samples which are considered to be "problematic" by the indirect assay are sent to a regional measles reference laboratory for measles confirmation via IgM capture EIA. A "problematic" serum specimen is one for which epidemiologic information suggests that the indirect assay result may be either false-negative or false-positive.

**Collection and Shipment of Sera.** In order to obtain sera from a high proportion of suspected measles cases, blood specimens should be collected at the suspected case's first contact with the health care system. While EIA tests are most sensitive in sera taken on day 3 of rash or later, ***a single serum sample obtained at the first contact with the health care system, regardless of day following rash onset, is considered adequate for measles surveillance.***

The serum sample should be sent to the state or national laboratory as soon as possible after collection. ***Each blood specimen must be accompanied by a copy of the case investigation form.***

EPI staff should train health workers in the proper techniques of venous blood collection and ensure the availability of specimen collection kits that will be shipped to the laboratory.

Meetings with public health laboratory personnel are essential to establish clear procedures, at all levels of the health system, for the receipt and transport of any

specimens that are submitted for measles serology. These procedures include ensuring that the proper forms accompany the specimen and that the person receiving the specimen signs a receipt.

***Preparation of specimens:***

- Specimens may be serum or whole blood. To separate serum, use a centrifuge if available. If it is not, keep whole blood (3 ml) at room temperature until there is complete retraction of the clot from the serum. Blood can be stored at 4 °C for up to 24 hours before the serum is separated.
- Transfer serum aseptically to a sterile vial.
- Store serum at 0–8 °C until shipment. Sera may be frozen. ***Do not freeze whole blood.***
- Fill in case investigation forms completely. Three dates are very important:
  (1) date of last measles vaccination;
  (2) date of rash onset;
  (3) date of collection of sample.

***Shipment of specimens:***

- Specimens should be shipped to the laboratory as soon as possible; do not wait to collect additional specimens before shipping.
- Place specimens in zip-lock or plastic bags.
- Use Styrofoam boxes or a thermos bottle.
- Place specimen form and investigation form in plastic bag and tape to inner top of Styrofoam box.
- Vials containing serum samples should be sealed and may be frozen, but whole blood samples should be stored at 0 to 8 °C.
- If using ice packs (which should be frozen), place them at the bottom of the box and along the sides, place samples in the center, then place more ice packs on top.
- Arrange shipping date.
- When arrangements are finalized, inform receiver of time and manner of transport.

**Results.** ***Only patients who have a positive result with an IgM EIA or have epidemiologic linkage to another laboratory-confirmed case are considered to be laboratory-confirmed measles cases.*** On rare occasions, a second blood specimen may be required. For example, if a blood specimen collected from a suspected measles case has a negative result and the clinician or epidemiologist strongly suspects measles infection, then it may be reasonable to collect a second blood specimen 7 to 14 days after rash onset. Similarly, if a clinician needs to make a definitive diagnosis on an individual patient with an initial negative result, a second sample may be useful.

Since measles vaccine and natural measles infection can both stimulate an IgM response in the host, a surveillance dilemma occurs when a suspected measles case has a history of measles vaccination within 6 weeks of rash onset. Measles vaccine can cause fever and rash in about 10% of vaccinees, and most first-time vaccinees are expected to have detectable measles IgM after vaccination. Moreover, other medical conditions, such as rubella, dengue, etc., may produce fever and rash in persons who have recently received measles vaccine. Therefore, a suspected measles case with a positive IgM result is not necessarily due to wild measles virus infection. An operational definition is needed to investigate and classify these cases.

A practical approach to this problem is as follows: If a suspected measles case with positive IgM serology has a history of measles vaccination within 6 weeks of rash onset AND (1) an active search of the community does not find any further evidence of measles transmission and (2) the patient has not recently traveled to areas where measles virus is known to be circulating, the case may be discarded as not being measles. If, on the other hand, an active search finds other laboratory-confirmed cases of measles, the suspected measles case with history of recent vaccination must be classified as being laboratory-confirmed.

## 7.2 Viral Isolation

The isolation of measles virus from clinical specimens can also be used to confirm measles diagnosis, but it is relatively time-consuming and requires more sophisticated laboratory support than serology. However, recent advances in the molecular epidemiology of measles virus have made it possible to analyze viral nucleotide sequences and classify measles isolates according to probable geographic origin.

During periods of low measles incidence, the isolation and molecular analysis of measles isolates can provide very important information concerning the likely geographic origin of measles importations. Information obtained through molecular epidemiology can complement information obtained from the standard epidemiologic investigation. ***Therefore, appropriate clinical specimens must be obtained for viral culture from every chain of measles transmission.***

The measles virus genome contains approximately 16,000 ribonucleotides. Measles has been considered to be an antigenically stable virus, but recent analyses of nucleotide sequences from measles isolates obtained from various regions of the world have found important genetic differences between isolates, especially in the areas of the genome which code for the hemaglutinin protein.

Humans are the only natural host of measles, but measles virus can be grown *in vitro* in a variety of cell cultures and lines. The most sensitive cell line for isolation of measles virus is the B95-8 line, which is composed of Epstein-Barr virus (EBV)-transformed marmoset lymphocyte cells. However, great care must be exercised in using this cell line because of the presence of EBV in the culture medium.

**Specimen Collection.** Suitable samples for isolation of measles virus are leukocytes, serum, throat and nasopharyngeal secretions, and urine. ***In practice, urine is the preferred sample for measles virus isolation.*** Specimens for virus isolation should be collected early in the acute phase of infection (the prodrome phase through the first few days of rash), when the virus is present in high concentration. They should be refrigerated and transported to a laboratory within 48 hours.

Throat and nasopharyngeal secretions are taken either by aspiration, by lavage, or by swabbing the mucous membranes. Nasal aspirates or bronchial lavage samples yield virus more frequently than throat swabs.

For isolation of the virus from urine, midstream urine should be collected into a sterile container. The urine should then be centrifuged for 30 minutes, the supernatant discarded, and the sediment resuspended in 1–2 ml of viral transport media (e.g., Hanks' balanced salts solution). The resuspended sediment may be frozen and transported to the appropriate regional measles reference laboratory.

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Slides, folders, posters, and other materials are available from PAHO country offices upon request.

# APPENDIX A

## RUBELLA CONTROL

As use of MMR or MR vaccines increases and measles eradication programs adopt these vaccines, consideration should be given to certain issues related to the control of rubella and of congenital rubella syndrome (CRS):

1. The development of a specific rubella control strategy.
2. Assessment of the likelihood of achieving and maintaining a high level of immunization coverage in the target groups.
3. Review of CRS surveillance methodologies.

### Epidemiology

Rubella is transmitted chiefly through respiratory droplets. Subclinical infection is common, occurring in 40% to 60% of all cases. Peak incidence is in the late winter and early spring. The incubation period ranges from 14 to 21 days, and the disease is most communicable several days before onset of rash until 5 to 7 days after onset of rash. Infants with congenitally acquired rubella may shed the virus in nasopharyngeal secretions and urine for up to one year.

Prior to the widespread use of rubella vaccine, the disease was epidemic in 6–9 year cycles. However, when the vaccine is in wide use and populations achieve higher rubella coverage, the period between outbreaks increases. In addition, as a result of the reduction of rubella circulation among infants and children due to vaccination, unvaccinated children are less likely to come into contact with the wild virus and therefore remain susceptible as young adults.

Of principal concern in rubella control is the prevention of CRS. The most commonly observed anomalies of CRS are ophthalmologic (cataracts, microphthalmia, glaucoma, chorioretinitis), cardiac (patent ductus arteriosus, peripheral pulmonary artery stenosis, atrial or ventricular septal defects), auditory (sensorineural deafness), and neurologic (microcephaly, meningoencephalitis, mental retardation). Also, infants with congenital rubella frequently are growth-retarded and have radiolucent bone disease, hepatosplenomegaly, thrombocytopenia, jaundice, and purpuric skin lesions ("blueberry muffin" appearance).

### Laboratory

As with measles, laboratory confirmation is required for rubella and CRS. Virus may be isolated from the blood and nasopharynx during the prodrome until several days after onset of the rash. Rubella virus can be excreted by CRS cases for up to a year after birth. Serologic testing of a single blood specimen for rubella IgM antibodies is commonly used to confirm the presence of acute rubella infection. In CRS, IgM antibodies may be detected for up to a year after birth.

### Vaccine Effectiveness

For rubella, vaccine effectiveness has been found to be about 90%. Results from serologic studies on the duration of rubella vaccine-induced antibodies have not been uniform; however, newer, more sensitive tests indicate that loss of antibody does not appear to be a significant problem. Rubella vaccine should not be given to pregnant women or to those likely to become pregnant within 3 months after receiving the vaccine, because of a small theoretical risk to the fetus.

## Control Strategies

The primary rationale for rubella immunization is the prevention of CRS. Cost-benefit analysis reveals that the benefits gained from prevention of CRS far outweigh the costs of immunization.

Studies throughout the world have found different levels of susceptibility among populations of women of childbearing age. Even in countries where susceptibility is extremely low, CRS cases still occur. CRS is preventable through immunization, and three different approaches are commonly followed:

1. Universal immunization of young children, often at the same time as measles immunization. This approach aims at interrupting transmission of rubella. Susceptible pregnant women are therefore protected through decreased risk of exposure to circulating rubella virus.
2. Selective immunization of high-risk groups. Under this approach, girls are immunized around the age of puberty, and vaccine is offered to any susceptible adult women or given post partum to those found to be susceptible on screening during pregnancy. This strategy is based on providing individual protection.
3. Combination of the above two strategies, where both universal immunization of children and immunization of targeted females are provided. Although the most expensive, this approach provides the most rapid and effective control of rubella and prevention of CRS, through interruption of transmission and protection of high-risk groups, as well as reduced circulation of the wild virus by universal immunization.

## APPENDIX B

### DISTRIBUTION OF DIAGNOSES FOR DISCARDED CASES OF SUSPECTED MEASLES

*JURISDICTION* _____

| YEAR | | | | | | |
|---|---|---|---|---|---|---|
| DIAGNOSIS | # | % | # | % | # | % |
| RUBELLA | | | | | | |
| SCARLET FEVER | | | | | | |
| DENGUE | | | | | | |
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| WITHOUT DIAGNOSIS | | | | | | |
| TOTALS | | | | | | |

## APPENDIX C

### LABORATORY LINE LISTING (MEASLES SEROLOGY)

*LABORATORY* _____

| COUNTRY | CASE ID | DATE OF MEASLES VACCINATION | DATE ONSET OF RASH | DATE BLOOD TAKEN | DATE SPECIMEN RECEIVED | CONDITION OF SPECIMEN | TYPE OF TEST | DATE OF RESULTS | RESULTS | OBSERVATIONS |
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# APPENDIX D

## LINE LISTING OF SUSPECTED MEASLES CASES

*COUNTRY:* _____ *REPORT YEAR:* _____

| CASE ID | NAME | COUNTY/ MUNICIPALITY | AGE | DOSES RECEIVED | DATE OF LAST VACCINE | NOTIFI-CATION DATE | CONTACT WITH OTHER CONFIRMED CASE (Y/N) | FEVER (Y/N) | DATE OF RASH ONSET | OTHER SYMPTOMS (Y/N) | | | DATE LAB. SAMPLE TAKEN | FINAL CLASSIFICATION** | | | OBSERVATIONS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | COUGH | CORYZA | CONJUNC-TIVITIS | | CONFIRMED LAB/EPI | CONFIRMED CLINICAL | DISCARDED | |
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## APPENDIX E

### SUMMARY OF MEASLES SURVEILLANCE DATA AND SURVEILLANCE INDICATORS

*COUNTRY* _____

| | 19____ | 20____ | 20____ |
|---|---|---|---|
| MEASLES SURVEILLANCE DATA | | | |
| # OF SUSPECTED MEASLES CASES REPORTED | | | |
| # OF LAB CONFIRMED MEASLES CASES | | | |
| # OF CLINICALLY CONFIRMED MEASLES CASES | | | |
| # OF DISCARDED MEASLES CASES | | | |
| SURVEILLANCE INDICATORS | | | |
| % OF SURVEILLANCE UNITS THAT NOTIFY WEEKLY | | | |
| % OF REPORTING SITES THAT REPORTED AT LEAST ONE SUSPECTED MEASLES CASE | | | |
| % SUSPECTED MEASLES CASES INVESTIGATED WITHIN 48 HOURS OF NOTIFICATION | | | |
| % SUSPECTED MEASLES CASES FULLY INVESTIGATED, INCLUDING COLLECTION OF A BLOOD SPECIMEN | | | |
| % OUTBREAKS WITH KNOWN SOURCE OF INFECTION | | | |
| % LABORATORY RESULTS RECEIVED WITHIN 7 DAYS OF SAMPLES' RECEIPT BY THE LABORATORY | | | |

## APPENDIX F

# SAMPLE
# MEASLES ALERT NOTICE

Children with measles have been found in your neighborhood, and YOUR CHILD MAY BE AT RISK of getting this disease!

This type of measles is also called the 10-day red measles and can cause SEVERE ILLNESS with pneumonia, ear infections, brain disease, and EVEN DEATH.

If your child has a FEVER AND RASH ILLNESS, inform a doctor or health worker of this illness now.

Measles can be PREVENTED BY MEASLES VACCINE. ALL CHILDREN 6 MONTHS OF AGE AND OLDER should NOW receive the vaccine. Even if your child has already had a measles vaccination, an additional dose should be given to be sure that this disease will be prevented.

The measles vaccine is very safe and effective and will help to keep YOUR CHILD HEALTHY. Please contact your doctor or clinic to get your vaccine.

## APPENDIX G

# MEASLES OUTBREAK RESPONSE SUMMARY FORM

Name of index case _____ CASE ID _____

PROVINCE/STATE _____ COUNTRY _____

MUNICIPALITY/COUNTY _____ VILLAGE/CITY _____

List neighboring areas which also have measles outbreaks: _____

Date of measles rash onset of earliest case: ___/___/___ Date of measles rash onset of last case: ___/___/___

NUMBER OF CASES BY AGE (YEARS)

| | <1 | 1 | 2 | 3 | 4 | 5–9 | 10–14 | >15 | TOTALS |
|---|---|---|---|---|---|---|---|---|---|
| Suspected | | | | | | | | | |
| Confirmed | | | | | | | | | |

IMMUNIZATION STATUS OF CASES

| AGE | CONFIRMED MEASLES CASES | | | | |
|---|---|---|---|---|---|
| | Not Immunized | Documented Vac. History: 1 Dose | Documented Vac. History: 2+ Doses | Unknown | Total No. |
| <1 | | | | | |
| 1–2 | | | | | |
| 3–4 | | | | | |
| 5–9 | | | | | |
| 10–14 | | | | | |
| 15+ | | | | | |
| TOTALS | | | | | |

COMMUNITY COVERAGE

| AGE | 1+ DOSES % |
|---|---|
| <1 | |
| 1–2 | |
| 3–4 | |
| 5–9 | |
| 10–14 | |
| 15+ | |
| TOTALS | |

IMMUNIZATIONS FOR OUTBREAK CONTROL

| <1 | 1–4 | >5 | TOTAL |
|---|---|---|---|
| | | | |

Date first started ___/___/___ Number vaccinations given:

Date ended ___/___/___ Number of households visited _____

LIST VILLAGES/CITIES WHICH WERE VISITED IN THE COURSE OF THE INVESTIGATION

| Name | Date | # Immunized | Comments (cases found?) |
|---|---|---|---|
| _____ | ___/___/___ | _____ | _____ |
| _____ | ___/___/___ | _____ | _____ |
| _____ | ___/___/___ | _____ | _____ |
| _____ | ___/___/___ | _____ | _____ |

Describe control activities: _____

_____

Describe follow-up activities: _____

_____

Name of investigator _____ Place _____ Date ___/___/___

# APPENDIX H

## WEEKLY REPORTING MONITOR FORM (Part I)

*INSTRUCTIONS* *1) Mark with a check each week a report is received on time, mark with an X when a report is received late.*
*2) Calculate percentage of sites reporting on time by dividing the number reporting on time by the total number of sites.*

| *REPORTING UNITS* | *WEEK #* 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 |
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| *TOTAL # REPORTING* | | | | | | | | | | | | | | | | | | | | | | | | | | |
| *% REPORTING ON TIME* | | | | | | | | | | | | | | | | | | | | | | | | | | |

# APPENDIX H

## WEEKLY REPORTING MONITOR FORM (Part I)

*INSTRUCTIONS* *1) Mark with a check each week a report is received on time, mark with an X when a report is received late.*
*2) Calculate percentage of sites reporting on time by dividing the number reporting on time by the total number of sites.*

| *REPORTING UNITS* | *WEEK #* 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 |
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| *TOTAL # REPORTING* | | | | | | | | | | | | | | | | | | | | | | | | | | |
| *% REPORTING ON TIME* | | | | | | | | | | | | | | | | | | | | | | | | | | |

## Appendix I

### WEEKLY REPORTS SUMMARY

*COUNTRY* _____ *YEAR* _____

| *WK #* | *# SITES IN SYSTEM* | *# SITES NOTIFYING* | *% REPORTING* | *WK #* | *# SITES IN SYSTEM* | *# SITES NOTIFYING* | *% REPORTING* |
|---|---|---|---|---|---|---|---|
| 1 | | | | 27 | | | |
| 2 | | | | 28 | | | |
| 3 | | | | 29 | | | |
| 4 | | | | 30 | | | |
| 5 | | | | 31 | | | |
| 6 | | | | 32 | | | |
| 7 | | | | 33 | | | |
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| 9 | | | | 35 | | | |
| 10 | | | | 36 | | | |
| 11 | | | | 37 | | | |
| 12 | | | | 38 | | | |
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| 14 | | | | 40 | | | |
| 15 | | | | 41 | | | |
| 16 | | | | 42 | | | |
| 17 | | | | 43 | | | |
| 18 | | | | 44 | | | |
| 19 | | | | 45 | | | |
| 20 | | | | 46 | | | |
| 21 | | | | 47 | | | |
| 22 | | | | 48 | | | |
| 23 | | | | 49 | | | |
| 24 | | | | 50 | | | |
| 25 | | | | 51 | | | |
| 26 | | | | 52 | | | |
| | | | | 53 | | | |