

Measles elimination in South Africa - policy and implementation

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SUMMARY

With the advent of an effective and safe vaccine against measles, the control of measles has been astounding. In several countries the success of immunisation have led to the attempt to eliminate measles transmission entirely, through the use of vaccination strategies originally developed in the polio eradication programme. These strategies are to increase and maintain high routine coverage, to conduct periodic supplemental mass immunisation campaigns and case based, laboratory confirmed surveillance.

In South Africa, measles mass vaccination was added to the existing polio mass vaccination campaigns in 1996 and 1997, and the combined strategies were formulated for the South African context in this document.

This document is targeted at decision makers in the national and provincial Departments of Health, to enable a coordinated and effective South African measles elimination programme.

OPSOMMING

Sedert 'n effektiewe en veilige entstof gevind is teen masels, het die gebruik daarvan 'n dramatiese dalingseffek gehad op die voorkoms van die siekte. In verskeie lande het die sukses van immuniseringsprogramme daartoe aanleiding gegee dat die volledige uitwissing van masels nou verwesenlik kan word deur gebruik te maak van inentings strategieë wat oorspronklik gebruik is vir die polio uitwissingsprogram. Hierdie strategieë sluit in die handhawing en verbetering van 'n hoë roetine inentingsvlak, die gebruik van herhalende addisionele immuniseringsveldtogte en verder ook laboratorium bevestiging van elke masels geval.

Die masels veldtogte in Suid Afrika is gekoppel aan reeds beplande polio veldtogte in beide 1996 en 1997. Die gesamentlike strategieë word saamgevat in hierdie dokument.

Hierdie dokument is gemik op besluitnemers in beide die nasionale en provinsiale Departemente van Gesondheid om sodoende 'n gekoördineerde en ook effektiewe maselsuitwissingsprogram te kan loods.

KEYWORDS

measles elimination, South Africa, policy, implementation, strategies, mass immunisation campaigns, surveillance, routine immunization

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CHAPTER 1 - BACKGROUND

1.1 Disease

1.1.1 Virus and transmission

Measles virus is an RNA virus and is a member of the genus *Morbillivirus* in the family Paramyxoviridae¹. 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 haemagglutinin protein. This has resulted in 8 distinct genotypes being identified, including a genotype predominant on the African continent.

Measles is an ubiquitous, highly infectious disease affecting nearly every person in a given population by adolescence in the absence of immunisation programmes². Measles is transmitted primarily from person-to-person by large respiratory droplets, but can also be spread by the airborne route as aerosolized droplet nuclei³.

1.1.2 Clinical aspects

Measles is most infectious during the prodrome. First there is localized infection of the respiratory epithelium of the nasopharynx and possibly the conjunctivae, with spread to regional lymphatics. Primary viraemia occurs 2 to 3 days following exposure, and an intense secondary viraemia occurs 3 to 4 days later. The secondary viraemia leads to infection of and further replication in the skin, conjunctivae, respiratory tract and other distant organs. The amount of virus in blood and infected tissues peaks 11 to 14 days after exposure and then falls off rapidly over the next 2 to 3 days.

Prodrome and General symptoms: Measles infection presents with a 2-3 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 highly contagious. A harsh, non-productive cough is present throughout the febrile period, persisting for 1 to 2 weeks in uncomplicated cases, and it is often the last symptom to disappear. Generalized lymphadenopathy commonly occurs in young children. Older children usually complain of photophobia and, occasionally, of arthralgia.

Koplik's spots: Koplik's spots may be seen on the buccal mucosa in over 80 percent of cases, if careful daily examinations are performed shortly before rash onset. The spots, however, may be confused with other vascular lesions and are present in other conditions. Koplik spots are slightly raised white dots 2 to 3 mm in diameter on an erythematous base. Initially, there are usually 1 to 5 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, and disappear soon after rash onset.

Rash: Within two to four days after the prodrome symptoms begin, a characteristic rash made up of large blotchy red areas usually appears behind the ears and on the face. At the same time a high fever occurs. In dark skinned children the rash may not be as evident. The rash peaks in 2 to 3 days, and becomes most concentrated on the trunk and upper extremities. The density of the rash varies; young infants may have rashes that cover the face and trunk. The rash lasts from 3 to 7 days and may be followed by a brawny or fine desquamation. Some children develop severe exfoliation, especially if they are malnourished or have vitamin deficiencies.

Differential Diagnosis: Many febrile illnesses are accompanied by a rash and a variety of non-specific symptoms (see adjacent box).

Mild or "modified" forms of measles with generally mild symptoms occur in persons with partial protection from maternal antibody, and rarely from vaccine failures.

1.1.3 Complications and permanent sequelae

Though usually a mild or moderately severe illness of childhood, measles can result in residual neurological impairment from encephalitis in approximately 5–10 cases per 10,000 and in death in approximately 1–3 cases per 1,000.⁴

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

Diarrhoeal Diseases: A large number of infants and children in developing countries develop diarrhoeal illness both during and following acute measles illness. Dehydration and the concomitant loss of Vitamin A may have disastrous consequences, raising the probability of dying from measles in these infants considerably.

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

Differential diagnosis:

Common:

- rubella
- roseola
- enterovirus infection
- rickettsial diseases
- drug hypersensitivity reactions

Rare:

- adenovirus infections
- Meningococcal septicaemia
- dengue fever
- scarlet fever
- Kawasaki's disease
- Toxic Shock Syndrome

other viral agents, especially herpes simplex and adenoviruses, or bacterial organisms.

Malnourished Children: Measles infection is more severe among malnourished children. Diarrhoea is one of the major factors contributing to the adverse impact of measles on the nutritional status in children in developing countries. Measles may exacerbate malnutrition because of decreased food intake due to malaise, increased metabolic requirements in the presence of fever, or because parents and health practitioners inappropriately withhold a child's food during an acute illness. Undernutrition may in turn lead 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 1/100,000 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 and is usually fatal within 7 years.

Mortality: Case fatality rates vary depending on the age of infection, intensity of exposure, nutritional status and availability of treatment. 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-fatality rate has been estimated at between 3 and 6%. The highest case-fatality rate occurs in infants 6 to 11 months of age. These rates may underestimate the true lethality of measles because of incomplete reporting of outcomes of measles illness, such as delayed deaths related to chronic diarrhea. 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 percent have been reported in infants under 1 year of age.

1.1.4 Immunological response to natural infection and immunisation

In primary acute infection, T-cell⁵ and B-cell⁶ responses can be detected to most of the six measles virus proteins. Both IgG and IgM antibodies are initially produced, however IgM antibodies peak at 7 to 10 days after rash onset and fall rapidly, rarely being detectable more than 4 weeks after rash onset (Figure 1). Serum and secretory IgA are also produced but are usually transient⁷.

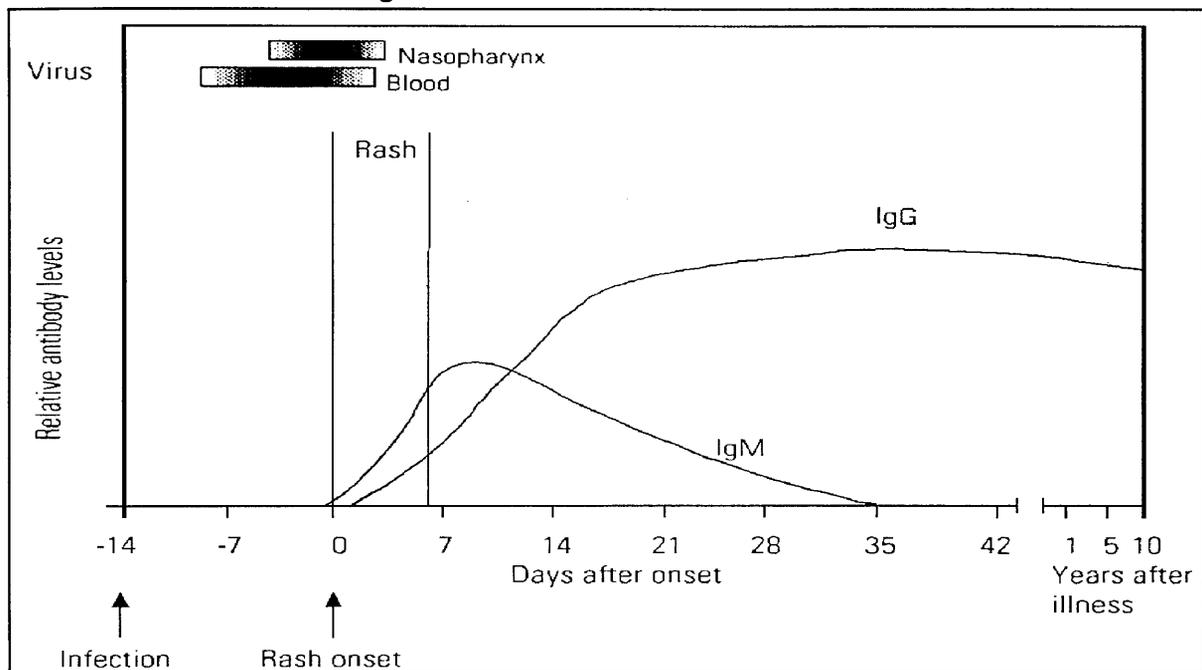
The presence of IgM is generally accepted as evidence of primary measles infection (by disease or vaccine). However, absence of IgM does not exclude infection, as the sensitivity of some IgM assays is low⁸, and the timing of specimen collection is important, because of the short-lived IgM response⁹. Furthermore, IgM has been detected in secondary responses to some other viral infections such as rubella¹⁰, and it is theoretically possible that this may occur in measles.

IgG becomes detectable in the serum soon after rash onset, peaks within about 4 weeks and subsequently declines, but persists for life¹¹ and therefore immunity after natural infection is usually lifelong¹².

Cell-mediated immunity plays an important role in recovery from, and possibly, prevention of measles, and it has been postulated that sufficient stimulation of cell-mediated immunity may be a prerequisite for the development of lifelong protection¹³. However, tests for cell-mediated immunity are less readily available than those for humoral immunity.

Acute measles infection is associated with a wide range of immunological abnormalities, including depressed general cellular reactivity (manifest, for example,

Figure 1: The antibody response in acute measles infection (Adapted from: WHO/EPI: The Immunological Basis for Immunization: Measles)



in a depressed delayed hypersensitivity reaction to the tuberculin test¹⁴) and cytokine production abnormalities. Studies are in progress to elucidate further the mechanisms of immune disruption after measles and possible variation by age at infection.

Prior to the availability of measles vaccine, measles infection was virtually universal. Infants born to mothers with measles antibodies due to natural infection or vaccination are protected until 5-9 months of age. Some infants who are immunized before they are 9 months old may not develop detectable immunity due to interference by passively-acquired maternal antibody.

At present, no serological tests can distinguish between antibody, whether IgG or IgM, produced by measles infection and that produced by immunization. The levels of antibody induced by immunisation with attenuated measles virus vary with an approximately log-normal distribution, and reach lower peak levels than those induced by wild virus¹⁵. Antibody loss is quicker after further attenuated vaccines than after the early vaccines. Some data suggest that the rate of antibody decline is faster among persons who attain the highest antibody levels post-immunization, so that the range of

levels narrows with time¹⁶.

Antibody persists longer when there is boosting from exposure to circulating wild virus^{17,18}. However, even in isolated communities, antibodies have been shown to persist for at least 16 years after immunization^{17,18,19}. The mechanism for maintenance of detectable antibody levels in the absence of re-exposure is not known²⁰.

When measles antibody falls to low levels, re-exposure to measles virus (wild or vaccine virus) stimulates memory cells, which remain dormant after the initial infection and are primed to produce a measles-specific response. An anamnestic (secondary) immune response occurs, in which IgG levels rise rapidly and peak approximately 12 days after reinfection. If antibody levels are high prior to exposure, reinfection is prevented and a boost is rarely seen.

1.1.5 Treatment of measles and referral criteria

There is currently no specific treatment for measles infection. However, 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 rate²¹. The South African Standard Treatment Guideline indicates the following treatment at primary health care level:



If the patient is older than six months, well nourished and uncomplicated, treat at home with:

- * *paracetamol* for fever or discomfort children: 10mg/kg every 4-6 hours
- * if diarrhoea, rehydrate for 24 hours
- * if bronchitis or otitis media, treat with appropriate antibiotic
- * if purulent conjunctivitis, treat with *tetracycline ophthalmic ointment*
- * all children with an acute attack of measles should be given *retinol* (vitamin A)

- < 12 months : 100 000 IU Vitamin A orally as a single dose
- > 12 months : 200 000 IU Vitamin A orally as a single dose

In the following situations, refer the patient to hospital:

- younger than 6 months old;
- signs of severe or unresponsive bronchitis or pneumonia present;
- malnutrition (below 3rd percentile);
- dehydration;
- neurological signs or symptoms, for example confusion;
- associated illness such as AIDS, TB, asthma;
- immuno-compromised and severely ill adults.

Some paediatricians advise the use of chloramphenicol eye ointment instead of the tetracycline ointment mentioned above. In addition, the *Manual on the Integrated Management of Childhood Illnesses (IMCI)* which is currently being prepared includes a section on measles management. Following the general assessment of the child and the assessment for diarrhoeal disease, the manual proceeds to febrile illnesses. The following instructions are given in the case where the child has measles now or within the last 3 months:

- Does the child have fever? (By history or feels hot or temperature 37.5 C or above.)
- Look and feel:
 - Look for mouth ulcers. Are they deep and extensive?
 - Look for pus draining from the eyes.
 - Look for clouding of the cornea.
- Classify:

<ul style="list-style-type: none"> ■ Any general danger signs or ■ clouding of cornea or ■ deep or extensive mouth ulcers 	SEVERE COMPLICATED MEASLES	<ul style="list-style-type: none"> ■ Give Vitamin A ■ Give first dose of an appropriate antibiotic ■ If clouding of the cornea or pus draining from the eye, apply tetracycline ointment ■ Refer URGENTLY to hospital
<ul style="list-style-type: none"> ■ Pus draining from the eye or ■ Mouth ulcers 	MEASLES WITH EYE OR MOUTH COMPLICATIONS	<ul style="list-style-type: none"> ■ Give Vitamin A ■ If pus draining from eye, treat eye infection with tetracycline eye ointment ■ If mouth ulcers, treat with Gentian violet ■ Follow-up in 2 days
<ul style="list-style-type: none"> ■ Measles now or within the last 3 months 	MEASLES	<ul style="list-style-type: none"> ■ Give Vitamin A

1.2 Vaccine

1.2.1 Vaccine types

In South Africa, eleven measles containing vaccines are available (six measles only vaccine, one measles-mumps combination vaccine and four measles-mumps-rubella combination vaccines). Measles-mumps-rubella (MMR) vaccines are available in the private sector and are generally purchased by some parents for their children. Ignorance by parents and private health care providers of the importance of the cold chain have however occasionally led to the administration of MMR of dubious potency,

leading to “vaccine failures” in these children and subsequent outbreaks in “vaccinated” children. However, MMR vaccine that has been kept in appropriate conditions has been shown to be as efficacious as monovalent measles vaccine.

1.2.2 Vaccine stability, storage and supply

Prior to 1980, measles vaccines were extremely heat-labile, causing difficulty in their use in tropical²² and subtropical climates. The development of effective stabilizers and the formulation of the WHO requirements for heat stability for freeze-dried measles vaccine²³ have considerably improved the quality of measles vaccines available since 1980, although there are still variations in the stability of vaccines produced by different manufacturers.

In the freeze-dried state, present measles vaccines which meet WHO requirements retain a minimum potency of at least 3.0 log₁₀ live virus particles per human dose after exposure to a temperature of 37°C for at least one week, and the virus titre does not decrease by more than 1.0 log₁₀ during incubation²⁴. However, reconstituted measles vaccines quickly lose their potency at exposure to room temperatures. At 22°C to 25°C, reconstituted measles vaccine suffer approximately 50% loss in potency in one hour. At temperatures over 37°C, it is inactivated within one hour. It is therefore extremely important to keep reconstituted measles vaccine cool (below 8° C) and protected from sunlight.

Measles vaccine is fragile. Breaks in the cold chain (temperatures greater than 10° C) may quickly render the reconstituted vaccine completely ineffective. Measles vaccine, MR, and MMR can however be frozen without loss of potency. When stored at 0 to 8° C, a minimum infective dose can be maintained in unreconstituted vaccine for 2 or more years. Reconstituted vaccine should be disposed of after 8 hours, regardless of the temperature maintained. Vaccine should never be left at room temperature. When used in the field, it should be transported on wet ice in isothermic containers.

Measles single antigen, MR, and MMR vaccine should be kept frozen at the national level. At the district and health facility level, vaccine should always be placed on the upper shelves of a storage refrigerator which is used only for vaccines.

Effective distribution of viable vaccine in sufficient quantities is critical to the success of the measles eradication program. All locations that provide immunization should have a sufficient vaccine supply on hand to last until the next consignment is likely to be received. Order frequency, stock control and other cold chain and vaccine operations issues are discussed in detail in the *South African Cold Chain & Immunisation Operations Manual*.

1.2.3 Vaccine efficacy

Not all persons given measles vaccine are necessarily protected against measles, since no vaccine is 100% effective. The appropriate way to evaluate whether the proportion of cases with a history of vaccination is high in an outbreak, is to estimate vaccine effectiveness. There are several approaches to calculating vaccine effectiveness. They include:

- use of coverage data, and
- outbreak investigation with case-control studies.

These methods are too detailed for presentation in this guide. If effectiveness is low (for example below 80%), this may indicate that there are problems either with the cold chain, age at vaccination, or with the vaccine's ability to produce protection as manufactured.

Table 1: Seroconversion rates in selected developing countries by age at measles immunisation (adapted from Halsey 1983²⁵; Source: WHO/EPI: Immunological basis for Immunization: Measles)

Country	Seroconversion(%) by age in months								Reference
	5	6	7	8	9	10	11	12	
Haiti	-	45	71	77	84	94	95	100	²⁶
Kenya	<50	40	93	90	93	94	100	100	²⁷
Latin America	-	58	69	82	85	92	89	92	²⁸

Serologic studies summarised in table 1 have demonstrated that measles vaccines induce seroconversion in 84 to 93 percent of recipients who are old enough to have lost all passively acquired maternal measles antibody (this usually occurs by 9 months of age). The development and persistence of serum antibodies following measles vaccination have been lower than, but parallel to the response following natural measles infection. Peak antibody responses occur 6 to 8 weeks after infection or vaccination.

For combined vaccines (such as MMR), studies indicate that the antibody response to all antigens is equivalent to the response when each is administered separately, provided the vaccine has been handled correctly and has not lost its potency.

1.2.4 Adverse reactions and side effects²⁹

The following comparative rates of serious adverse events in the case of measles disease and measles immunisation were found³⁰ (Table 2).

Table 2 : Estimated rates of adverse events following measles immunisation to complication rates of natural measles infection.

Condition	Measles disease (per 100,000 cases)	Measles immunisation (per 100,000 doses)
Encephalopathy/encephalitis	50 - 400	0.1
Convulsions	500 - 1,000	0.02 - 190
Death	10 - 10,000	0.02 - 0.03

More than 240 million doses of measles containing vaccine were distributed in the United States from 1963 through 1993. The vaccine has an excellent record of safety. Mild side effects include fever and between 5% and 15% of vaccinees may develop a temperature of greater than 39.4° C beginning 5 - 12 days after vaccination and usually lasting several days³¹. Most persons with fever are otherwise asymptomatic. Transient rashes have been reported for approximately 5% of vaccinees. Central nervous system (CNS) conditions, including encephalitis and encephalopathy, have been reported with a frequency of less than one per million doses administered. The incidence of encephalitis or encephalopathy after measles vaccination of healthy children is lower than the observed incidence of encephalitis of unknown etiology. This finding suggests that the reported severe neurologic disorders temporally associated with measles vaccination were not caused by the vaccine. These adverse events should be anticipated only in susceptible vaccinees and do not appear to be age-related. After revaccination, most reactions should be expected to occur only among the small proportion of persons who failed to respond to the first dose.

Convulsions and febrile seizures

As with the administration of any agent that can produce fever, some children may have a febrile seizure. Although children with a personal or family history of seizures are at increased risk for developing idiopathic epilepsy, febrile seizures following vaccinations do not in themselves increase the probability of subsequent epilepsy or other neurologic disorders. Most convulsions following measles vaccination are simple febrile seizures, and they affect children without known risk factors. It should be stressed that

the likelihood of seizures during an attack of measles is far greater than seizures following measles vaccination.

An increased risk of these convulsions may occur among children with a prior history of convulsions or those with a history of convulsions in first-degree family members (i.e. siblings or parents)³². Although the precise risk cannot be determined, it appears to be low.

Because the period for developing vaccine-induced fever occurs approximately 5-12 days after vaccination, prevention of febrile seizures is difficult. Prophylaxis with antipyretics has been suggested as one alternative, but these agents may not be effective if given after the onset of fever. To be effective, such agents would have to be initiated before the expected onset of fever and continued for 5-7 days. However, parents should be alert to the occurrence of fever after vaccination and should treat their children appropriately.

Children who are being treated with anticonvulsants should continue to take them after measles vaccination. Because protective levels of most currently available anti-convulsant drugs (e.g., phenobarbital) are not achieved for some time after therapy is initiated, prophylactic use of these drugs does not seem feasible.

The parents of children who have either a personal or family history of seizures should be advised of the small increased risk of seizures following measles vaccination. In particular, they should be told in advance what to do in the unlikely event that a seizure occurs. The permanent medical record should document that the small risk of postimmunization seizures and the benefits of vaccination have been discussed.

Subacute Sclerosing Panencephalitis (SSPE)

Measles vaccine significantly reduces the likelihood of developing SSPE, as evidenced by the near elimination of SSPE cases after widespread measles vaccination began in

the USA. SSPE has been reported rarely in children who do not have a history of natural measles infection but who have received measles vaccine. The available evidence suggests that at least some of these children may have had an unidentified measles infection before vaccination and that the SSPE probably resulted from the natural measles infection. The administration of live measles vaccine does not increase the risk for SSPE, regardless of whether the vaccinees has had measles infection or has previously received live measles vaccine^{33,34}.

Thrombocytopenia

Surveillance of adverse reactions in the United States and other countries indicates that Measles/Mumps/Rubella (MMR) vaccine can, in rare circumstances, cause clinically apparent thrombocytopenia within the 2 months after vaccination. In prospective studies, the reported incidence of clinically apparent thrombocytopenia after MMR vaccination ranged from one case per 30,000 vaccinated children in Finland³⁵ and Great Britain³⁶ to one case per 40,000 in Sweden, with a temporal clustering of cases occurring 2-3 weeks after vaccination³⁷. With passive surveillance, the reported incidence was approximately one case per 100,000 vaccine doses distributed in Canada and France³⁸, and approximately one case per 1 million doses distributed in the United States³⁹. The clinical course of these cases was usually transient and benign, although haemorrhage occurred rarely³³. Furthermore, the risk for thrombocytopenia during rubella or measles infection is much greater than the risk after vaccination. Of 30,000 schoolchildren in one Pennsylvania county who had been infected with rubella during the 1963-64 measles epidemic, 10 children developed thrombocytopenic purpura (incidence: one case per 3,000 children)⁴⁰. Based on case reports, the risk for thrombocytopenia may be higher for persons who previously have had idiopathic thrombocytopenic purpura, particularly for those who had thrombocytopenic purpura after an earlier dose of MMR vaccine.

Revaccination Risks

There is no evidence of an increased risk for adverse reactions after administration of live measles vaccine to persons who are already immune to measles as a result of either previous vaccination or natural disease.

1.2.5 Contraindications and Precautions²⁴

Measles vaccine can be safely and effectively administered to children with mild acute illnesses. Malnutrition is a strong indication to vaccinate, not a contraindication. If a malnourished child is infected, the disease may aggravate his/her nutritional status and increase the chances of complications or death.

Pregnancy

Since measles and MMR vaccines are live viruses, they should theoretically not be administered to pregnant women. There is currently no evidence, however, to suggest that children born to pregnant women vaccinated with these vaccines during pregnancy will be adversely affected. This precaution is based on the theoretical risk of fetal infection, although no evidence substantiates this theoretical risk. Considering the importance of protecting adolescents and young adults against measles, asking women if they are pregnant, excluding those who are, and explaining the theoretical risks to the others before vaccination are sufficient precautions.

Allergic Reactions

Hypersensitivity reactions rarely occur after the administration of measles containing vaccines. Most of these reactions are minor and consist of a wheel and flare or urticaria at the injection site. Immediate, anaphylactic reactions to measles containing vaccine are extremely rare. Although >70 million of MMR vaccine have been distributed in the United States since the Vaccine Adverse Events Reporting System (VAERS) was implemented in 1990, only 33 cases of anaphylactic reactions that occurred after MMR vaccination have been reported. Furthermore, only 11 of these cases a) occurred

immediately after vaccination and b) occurred in persons who had symptoms consistent with anaphylaxis (CDC, unpublished data).

In the past, persons who had a history of anaphylactic reactions (i.e., hives, swelling of the mouth or throat, difficulty breathing, hypotension, and shock) following egg ingestion were considered to be at increased risk for serious reactions after receipt of measles-containing vaccines, which are produced in chick embryo fibroblasts. Protocols requiring caution were developed for skin testing and vaccinating persons who had had anaphylactic reactions after egg ingestion^{41,42,43,44,45}. However, the predictive value of such skin testing and the need for special protocols when vaccinating egg-allergic persons with measles-containing vaccines is uncertain. The results of recent studies suggest that anaphylactic reactions to measles-containing vaccines are not associated with hypersensitivity to egg antigens but with some other component of the vaccines. The risk for serious allergic reaction to these vaccines in egg-allergic patients is extremely low, and skin testing is not necessarily predictive of vaccine hypersensitivity^{46,47}. In South Africa, a measles vaccine grown on human diploid cells can be used if parents are greatly concerned about egg-allergy in their child.

Measles vaccine may contain trace amounts of neomycin as a precaution to bacterial growth. Although the amount present is less than that usually used for a skin test to determine hypersensitivity, persons who have experienced anaphylactic reactions to neomycin should not be given these vaccines. Most often, neomycin allergy is manifested by contact dermatitis rather than anaphylaxis. A history of contact dermatitis to neomycin is not a contraindication to receiving measles vaccine. Live measles virus vaccine does not contain penicillin.

Thrombocytopenia

Children who have a history of thrombocytopenic purpura or thrombocytopenia may be at increased risk for developing clinically significant thrombocytopenia after measles containing vaccination. The decision to vaccinate should depend on the benefits of

immunity to measles, mumps, and rubella and the risks for recurrence or exacerbation of thrombocytopenia after vaccination or during natural infections with measles or rubella. The benefits of immunization are usually greater than the potential risks, and administration of measles containing vaccine is justified - particularly with regard to the even greater risk for thrombocytopenia after measles or rubella disease. However, avoiding a subsequent dose might be prudent if the previous episode of thrombocytopenia occurred in close temporal proximity to (i.e., within 6 weeks after the previous vaccination). Serologic evidence of measles immunity in such persons may be sought in lieu of vaccination.

HIV-infected Persons

Because of the increased risk for severe complications associated with measles infection and the absence of serious adverse events after measles vaccination among HIV-infected persons^{48,49}, the Advisory Committee on Immunization Practices (ACIP) in the USA has recommended that measles containing vaccine be administered to all asymptomatic HIV-infected persons and that measles containing vaccine be considered for administration to all symptomatic HIV-infected persons who would otherwise be eligible for measles vaccine- even though the immune response may be attenuated in such persons. There is a theoretical risk for an increase (probably transient) in HIV viral load following measles vaccination because such effects have been observed with other vaccines^{50,51}.

ACIP continues to recommend measles containing vaccine for HIV-infected persons without evidence of measles immunity⁴⁷ who are not severely immunocompromised^{52,53}. Severely immunocompromised and other symptomatic HIV-infected patients who are exposed to measles should receive immune globulin (IG), regardless of prior vaccination status⁵⁴. In addition, health-care providers should weigh the risks and benefits of measles vaccination or IG prophylaxis for severely immunocompromised HIV-infected patients who are at risk for measles exposure because of outbreaks or international travel.

Because the immunologic response to both live and killed antigen vaccines may decrease as HIV disease progresses, vaccination early in the course of HIV infection may be more likely to induce an immune response. Therefore, HIV-infected infants without severe immunosuppression should routinely receive measles vaccine as soon as possible within the routine immunisation schedule.

Even though HIV infection prevalence is high in South Africa, all 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 compared with the potential risk of being exposed to circulating measles virus.

CHAPTER 2 - GLOBAL CONTEXT AND EXPERIENCES OF MEASLES ELIMINATION

2.1 Terminology

Eradication is defined as the interruption of measles transmission globally such that vaccination would not need to be continued. **Elimination** refers to interruption of transmission in a sizeable geographical area but, because of the continued threat of re-introduction of the virus, vaccination would need to be continued. Global eradication basically represents the sum of successful elimination efforts in all countries. Elimination has been achieved already in some areas for limited periods of time.

Catch-up campaign in measles elimination refers to a nationwide mass campaign targeting a broad age-group and designed to immunise measles susceptibles in the population and achieve a level of herd immunity sufficient to interrupt virus transmission.

Follow-up campaign refers to specific campaigns often targeted at a narrower age-group and designed to immunise susceptibles which have accumulated in the population since the catch-up campaign.

2.2 Global context and progress to elimination

In July 1996, a meeting was held in Atlanta, USA, to document the advances in global measles elimination. A summary of this meeting was published in the *Weekly Epidemiological Record*⁶⁵ and is quoted in part here.

This consultative meeting represented a significant landmark in the history of measles control. The data presented demonstrated both the theoretical and technical feasibility of eliminating measles transmission for prolonged periods over wide geographical areas. The recent development of molecular tools to accurately identify individual strains of measles has supported these claims through the differentiation of indigenous

and imported viruses. In addition, global experience has now demonstrated that an important distinction must be made between the limited measles immunization campaigns that have targeted urban or poorly served areas in many countries, and the mass immunizing strategy which has been employed to interrupt transmission in the Americas and the United Kingdom. Geographically limited campaigns which target only young children may raise immunization coverage, but they will not be sufficient by themselves to interrupt transmission of the virus.

Of particular importance in the meeting were the country and regional presentations documenting the considerable political and public interest in the eradication of measles, particularly in developing countries. It has become increasingly evident, however, that an international consensus and commitment to measles eradication is essential as supplementary immunisation activities will be required in industrialized as well as developing countries. A global plan of action for the elimination/eradication of measles is needed to facilitate coordination between countries, donors, technical agencies and international organizations so as to ensure that activities are conducted in an efficient manner. At the same time there is an urgent need to strengthen poliomyelitis eradication efforts in countries and regions with endemic polio virus transmission to ensure that the introduction of measles elimination activities sustains rather than compromises the poliomyelitis eradication initiative.

The meeting found that, based on the success in controlling measles in the Americas and in the United Kingdom, global measles eradication is technically feasible with currently available vaccines. National, subregional, and regional elimination of measles can and should be accomplished. Although non-human primates can be infected with measles virus, it is very unlikely that non-human reservoirs could sustain measles transmission. Asymptomatic and non-classical cases of measles may occur in vaccinated persons but would not impede elimination or eradication of the virus. Waning immunity does not appear to play a major role in vaccine failure.

It was recommended that a goal of global measles eradication should be established,

with a target date within the next 10-15 years (i.e. between 2005 and 2010). Measles eradication is a logical addition and follow-on to the current poliomyelitis eradication initiative but needs to build on the success of poliomyelitis eradication. Because of the rapid accumulation of susceptibles to measles, the implementation phase of an eradication effort should be compressed into as brief a time as possible. Further research to understand molecular pathogenesis and the immune response to measles virus infection should be continued.

The major obstacles to measles eradication are perceptual, political, and financial. The full significance of measles is often not understood and it is frequently perceived as a illness of little consequence. Measles eradication will quickly pay for itself due to savings in vaccinations, hospitalisations and deaths prevented.

There is a need to educate parents, medical practitioners, and public health professionals about the global burden of disease due to measles.

2.3 Experiences in measles elimination

2.3.1 United States of America (USA)⁵⁶

Beginning in 1966, a federally supported effort to eradicate measles was undertaken and federally-supplied vaccine became available in the public sector as well. Federal funds supported purchase of vaccine, public information and education, surveillance and investigation, and coordination, but could not be used for actual delivery of immunisations. The eradication strategy had four main elements:

- 1) routine vaccination of infants at one year of age;
- 2) vaccination of all remaining susceptible children at the time of school entry (age 4-6);
- 3) improved surveillance of measles; and
- 4) prompt epidemic control when outbreaks are first recognised.

Over the next 3 years, considerable effort and resources were devoted to measles eradication, with the result that reported measles dropped to 22,231 cases by 1968, a more than 95% decline from the prevaccine era. Unfortunately, the effort was not sustained, and in 1969 major public sector emphasis shifted to rubella vaccine, which had just been licensed. As a result, the number of reported cases rose, reaching a peak of 75,290 cases in 1971. Cases remained in the 20-60,000 range throughout the mid-1970s.

Because of evidence of low immunisation levels in children and a resurgence of measles, in 1977 a national Childhood Immunization Initiative was announced with the aim of raising immunisation levels in the nation's children to 90% and putting in place a system to maintain those levels thereafter. Major emphasis was placed on reviewing immunisation records of children in primary and secondary schools and on enacting and enforcing school entry immunisation laws. More than 28 million records were reviewed and children needing immunisations were given them. The result was that, since 1981, more than 96% of children entering school have had evidence of immunity to measles, defined as a record of having received measles vaccine on or after the first birthday, documentation of physician-diagnosed measles, or laboratory evidence of immunity. The early success of this effort led to the announcement, in October 1978, of an initiative aimed at eliminating indigenous measles from the USA by October 1, 1982. The main elements of this effort were threefold:

- 1) Achieve and maintain high levels of immunity;
- 2) Conduct effective surveillance for measles; and
- 3) Aggressive response to cases.

Elimination was defined as the absence of indigenous transmission, with the expectation that any reported case could be traced to a foreign source within two generations before its onset. It was anticipated there would probably be about 500 cases reported per year -100 importations and 4 spread cases for each, on average. Considerable effort was placed on this program, with every case being investigated,

and reported incidence declined to a record low of 1497 cases in 1983. This represented an incidence rate of $<1/100,000$ and a $>99\%$ decrease compared to the pre-vaccine era.

Although the USA had come close to the target of elimination, they had not achieved it. Analysis of the measles continuing to occur in the 1980s revealed 3 main patterns depending on the primary age involved - preschool, school-aged, and adult. Outbreaks in preschool-aged children tended to be small (median number of cases 13 in 1985/1986) and to occur primarily in children who had not been vaccinated; approximately $\frac{1}{3}$ because they were too young for vaccination, and the remainder for a variety of reasons, usually not related to contraindications. Outbreaks in school-aged children were more numerous and larger (median 25 cases) with most cases occurring in children who had been vaccinated (i.e., were vaccine failures). As an indication of the infectiousness of measles, transmission was documented in a secondary school in Texas where documented vaccination levels were 99% and serological evidence of immunity was present in 96% of students! The third pattern, cases in adults, involved those who had never been vaccinated (many because they were "too old" to have received measles vaccine) as well as vaccine failures.

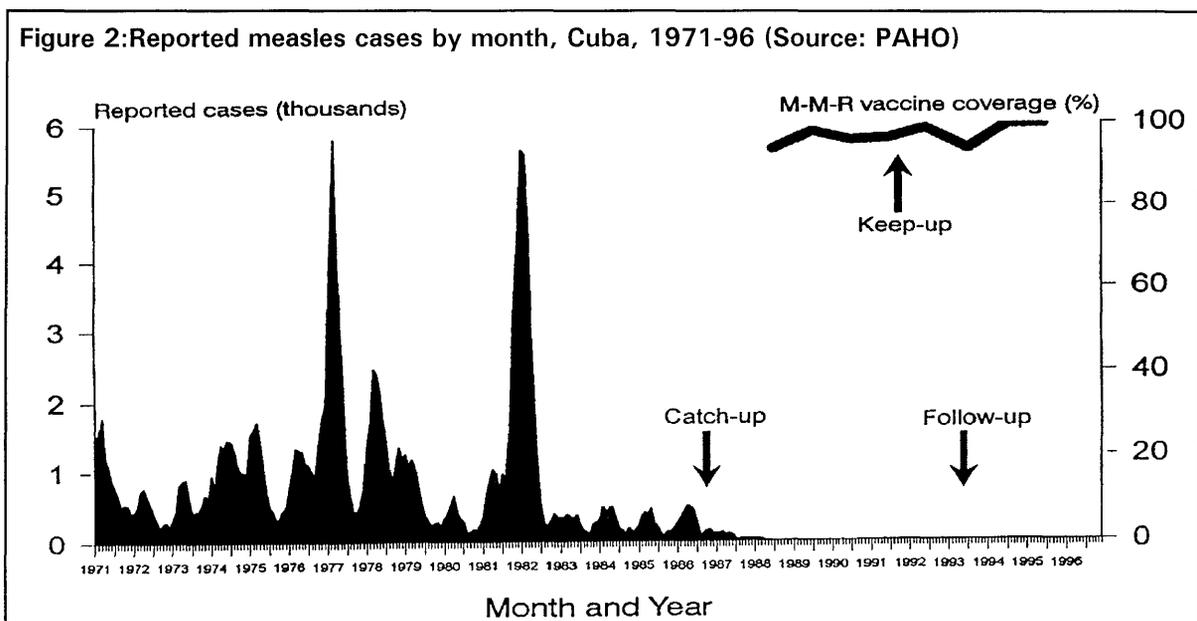
In 1989-1991 there was a major resurgence of measles, focused primarily in unimmunized pre-schoolaged children living in crowded inner city populations. The poor and members of racial and ethnic minorities were disproportionately represented. When President Clinton took office in early 1993, he markedly increased the level of support through a new Childhood Immunization Initiative, focused on getting infants and young children immunised on time. He also announced a new measles elimination target date for 1996. This initiative has had striking results, with nearly 90% of children now receiving individual antigens before their 2nd birthdays and 77% nationwide having received a basic 4 DTP, 3 OPV, and 1 MMR. Uptake with the more recently recommended hepatitis B and varicella vaccines is not as great.

Measles incidence has fallen even further and only 309 cases were reported in 1995,

a record low. Both epidemiological and laboratory evidence indicates that indigenous transmission of measles was interrupted in 1993. During a 16 week period only 4 cases of measles were reported which were not clearly related to importation and these cases occurred in widely separated parts of the country. In addition, no isolates having the characteristics of strains circulating in the USA before 1993 have been isolated since then. All recent isolates have shared characteristics with viruses circulating in other countries, even in the instances in which no direct epidemiological link has been established. It is believed in the USA that their goal of interruption of indigenous transmission of measles was achieved. The challenge now is to ensure that imported cases do not re-establish transmission and maintain this status until global eradication can be achieved.

2.3.2 Cuba

In Cuba, measles vaccine was introduced at the beginning of the 1970s. Despite improved coverage, 2 large epidemics occurred with an interval of 4 years, in 1976-1977 and 1981-1982 (Figure 2). In 1986, since another epidemic was predicted, a catch-up campaign targeting all children from 1-14 years of age was organized. This vaccination campaign was completed over a 6-month period. A total of nearly 2.5



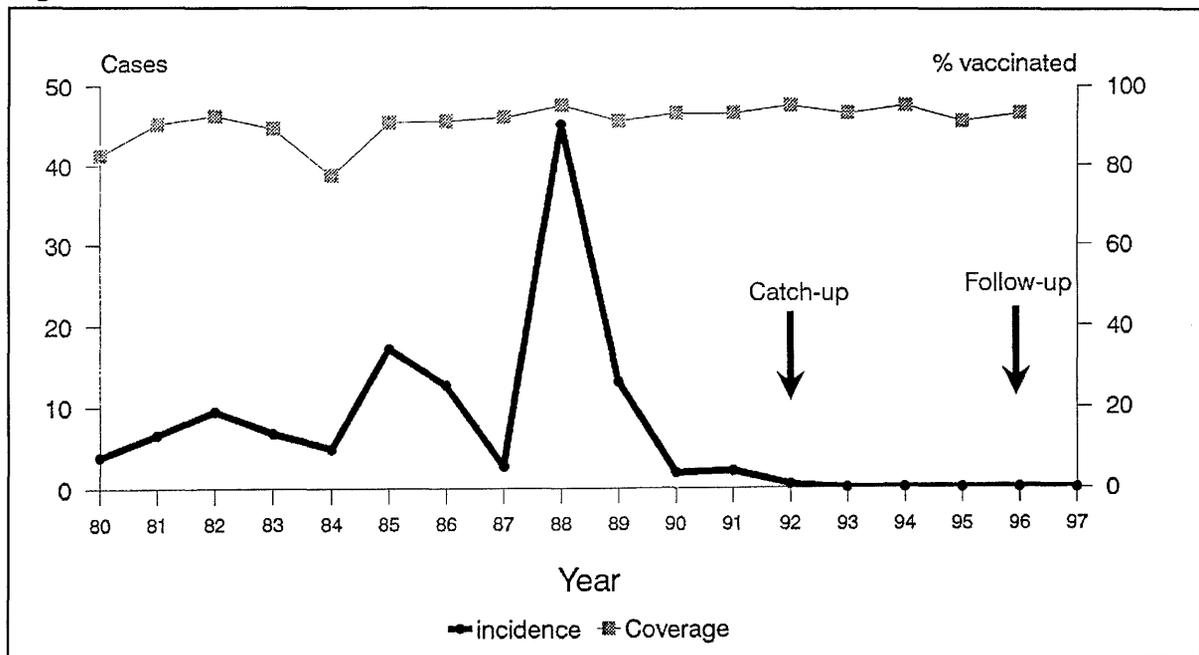
million children were immunized, achieving a 97.6% coverage.

After the campaign surveillance was enhanced and reported measles rapidly decreased to a 20-year low, with 858 cases reported in 1987 (a morbidity rate of 8.34 per 100,000 population). Since that time, cases have continued to decrease, with <20 reported cases occurring per year between 1989-1992, and the last confirmed case occurring in June 1993. Apparently transmission has been interrupted in Cuba. Because of accumulation of susceptible preschool-age children since the catch-up campaign, a follow-up campaign was conducted in 1993 targeting all children 2-6 years of age, regardless of prior measles immunization history. Over 880,000 children were vaccinated during this campaign, resulting in a 98% coverage. No confirmed measles cases were reported in 1994 and 1995 in spite of improved measles surveillance.

2.3.3 Chile

In Chile, measles vaccine was introduced in the mid-1960s and coverage rates gradually increased to reach a plateau around 90% from 1978. Measles incidence was

Figure 3: Measles in Chile (Source: PAHO)



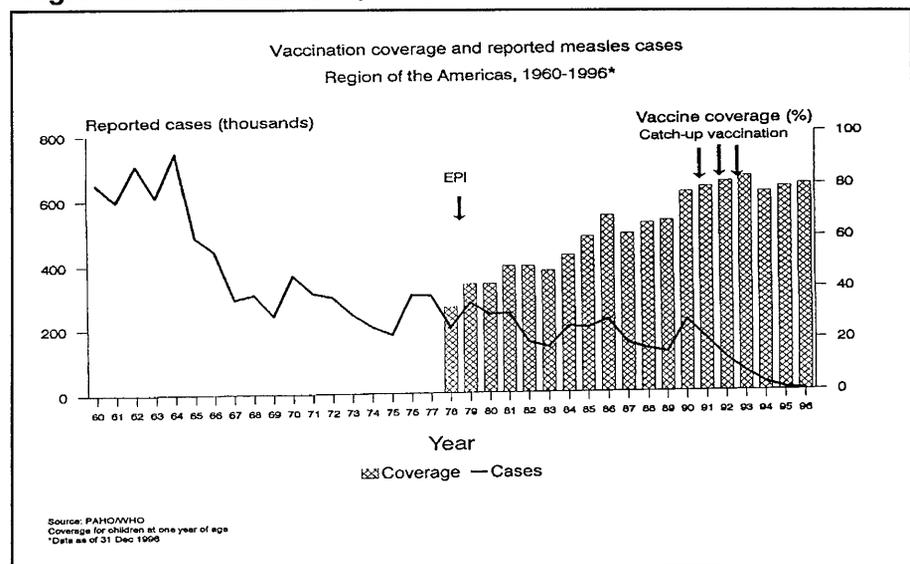
reduced with the introduction of the vaccine but epidemics regularly occurred at 3-4 years intervals, in spite of high vaccination coverage. In 1982, with the intention of improving further measles control, a 2-dose measles schedule was implemented but discontinued after 3 years when an expected epidemic in 1985 was not avoided. Three years later, in 1988, a major measles outbreak occurred which represented the highest number of cases ever recorded in the post-vaccine era. To avoid the predicted measles outbreak in 1992, a catch-up mass campaign was carried out that year in May, the low measles endemicity period, targeting all children from 9 months to 14 years of age. The target comprised a total of 3.9 million children or 29% of the total population. Reported coverage rates for the campaign exceeded 99%.

Following the campaign, in 1992, a country-wide reporting system was established with the weekly reporting of suspected cases. During 1992-93, only 2 cases of measles were confirmed, both imported, and no secondary cases could be found in either case despite intensive epidemiological investigation. From then until to the end of 1995, no confirmed measles cases have been notified in spite of the implementation of intensified measles surveillance with laboratory testing of all suspected cases. Using vaccine coverage rates to estimate the build-up of susceptibles, a follow-up campaign was planned for May 1996.

2.3.4 Elsewhere in the Americas

Similar strategies have been implemented in all countries in Latin America. The circulation of measles has been interrupted in the

Figure 4: Vaccination coverage and reported measles cases, Region of the Americas, 1960 - 1996



English-speaking Caribbean islands since September 1991. In 1995, less than 5,000 cases were notified throughout the Americas, the lowest figure ever reported (Figure 4). Since Canada accounted for >50% of the cases reported in 1995, a similar strategy with the organization of a catch-up campaign was planned and implemented in Spring 1996. Based on this success, and following the declaration in 1994 that polio had been eradicated from the Americas, a goal of measles elimination from the Americas by the year 2000 was set.

2.3.5 United Kingdom (UK)

The UK embarked upon measles control in the 1980s, and estimated coverage reached 92% in 2 year-olds in 1988. This, coupled with a "catch-up" programme targeted at pre-school children, resulted in a marked reduction in the number of notified cases in all age groups. However, the reduced opportunity for unvaccinated older children to acquire immunity through natural infection was reflected in an increase in the proportion of school-children who were susceptible to measles and outbreaks occurred in secondary schools.

Predictions from mathematical models developed in the UK indicated that the accumulation of susceptible school children in recent years would be sufficient to cause a substantial resurgence of measles in older age-groups in the future. An estimated 100,000-200,000 measles cases, approximately half of whom would be secondary school-children, was predicted for 1994/95. An estimated 30-80 deaths would occur during the outbreak. Therefore, a catch-up campaign was conducted in 1994, which targeted children 5-16 years of age, and 92% coverage was achieved. Between January and September 1995, <100 measles cases were confirmed in the UK, with a high proportion traced as importations.

CHAPTER 3 - ELIMINATION STRATEGIES

In the arena of measles elimination in developing countries, the experiences of the Americas stand out. Measles elimination strategies have been developed by the Pan American Health Organisation (PAHO) and have been found to be successful, both in the developing and the developed country health care settings. Detailed descriptions of these strategies were published in the *Journal of the American Medical Association*⁵⁷ and are quoted here.

These strategies aim to rapidly interrupt measles transmission by initially conducting mass campaigns and to maintain interruption of transmission by sustaining high population immunity through vaccination of infants at routine health service facilities supplemented by periodic mass campaigns. Disease surveillance, measles virus surveillance and outbreak response are other key elements of the strategy.

3.1 Mass immunisation campaigns

3.1.1 “Catch-up” campaigns

The “catch-up” campaign is a one-time initial vaccination conducted to rapidly interrupt chains of measles transmission. This campaign is generally conducted during periods of low measles transmission ie. the winter months. All children 9 months through 14 years of age, irrespective of vaccination history or reported history of measles infection, are vaccinated with measles vaccine within a short period, usually 1 week to 1 month in duration. The campaign is coordinated by the Ministry of Health and conducted by the local health services. Mass media communication is used to attract the target population to the vaccination sites. National government finances the campaign, and in some countries external resources have complemented government funding, in which case national resources accounted for more than 80% of the total costs of the campaign. In some instances these campaigns are used for the delivery of other vaccines and interventions, such as oral polio vaccine and Vitamin A supplementation.

These campaigns result in a rapid increase in population immunity, and if high enough coverage is achieved, measles transmission is interrupted.

3.1.2 “Mopping-up” campaigns

After a catch-up campaign has been conducted, groups of susceptible children may remain. An evaluation is conducted to identify these children, and special vaccination (“mop-up”) is carried out in such areas to increase their level of coverage. These mop-up campaigns, which aim at increasing vaccination in areas of low coverage, differ from the ones used during the polio eradication program that aimed to interrupt polio virus transmission in areas with persistent transmission despite high vaccination coverage.

3.1.3 “Follow-up” campaigns

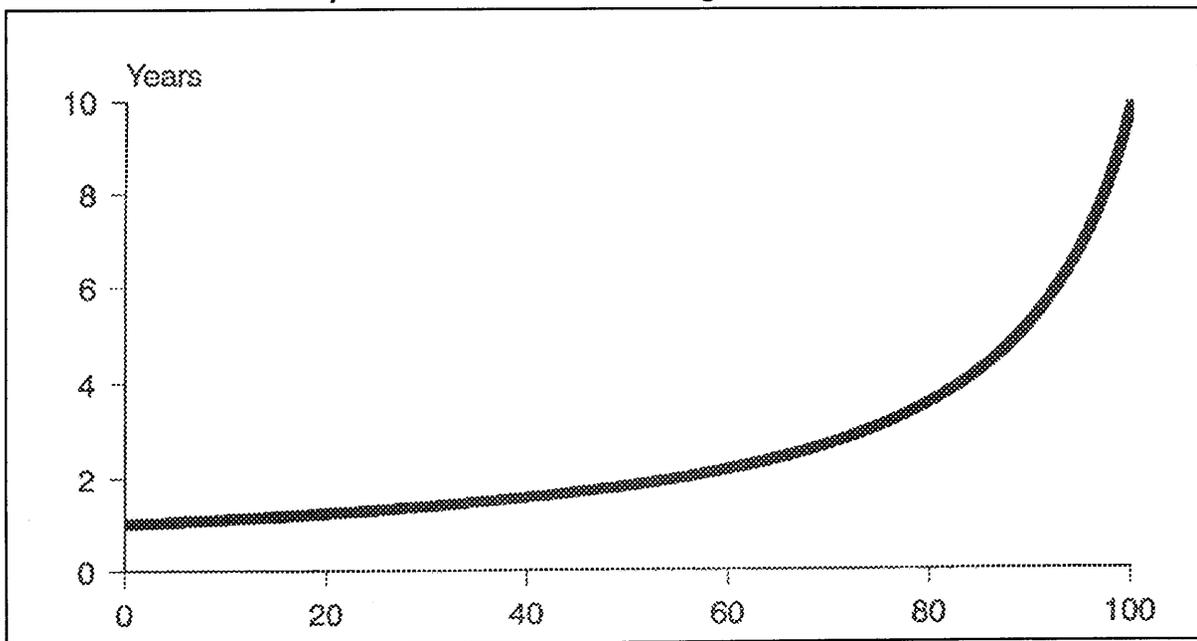
However diligent the immunization efforts, susceptible preschool-aged children will accumulate over time. Two major factors contribute to the accumulation of susceptible children. Firstly, measles vaccine is not 100% effective, thus leaving some children unprotected despite vaccination. Secondly, measles vaccination coverage for each birth cohort will fall short of 100%, however effective the programme.

The accumulation of susceptible pre-school-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 measles vaccine effectiveness is 90%, then each year 405 000 children (81%) of the newborn cohort will be protected ($500\,000 \times 0.9 \times 0.9$) against measles and 95 000 children will be added to the pool of susceptible persons. In approximately 5 years, the cumulative number of susceptible children persons will approximate the number of children in one birth cohort. Almost certainly this number represents enough susceptible children to permit an outbreak to occur should the virus be reintroduced.

Thus, the present strategy calls for periodic vaccination campaigns to be conducted among preschool-aged children. This strategy is recommended whenever the number of susceptible preschool-aged children (children younger than 5 years) approaches the size of an average birth cohort. The interval between campaigns will depend on the vaccination coverage obtained among infants through routine services since the last campaign. Thus, if only 60 % coverage is obtained during routine vaccination services offered to all children younger than 2 years, a follow-up mass campaign would be needed approximately every 2 years; if 80% coverage, approximately every 4 years; and if 90% coverage, approximately every 5 years (Figure 4). It is recognized that setting the epidemic danger point is an arbitrary approximation. Further experience may eventually suggest either a higher or lower threshold.

“Follow-up” campaigns are conducted similar to that of the “catch-up” campaigns described above, with the exception that the target age group is narrower. For example, if 4 years have passed since the “catch-up”, the target for the follow-up may

Figure 5: Required frequency of “follow-up” measles campaigns according to annual mean under 1 year vaccination coverage (Source: JAMA, 17 Jan 1996)



be children 1 to 4 years of age. Similar to “catch-up”, after a “follow-up” campaign there

may be remaining pockets of susceptible children. When such pockets still exist it is necessary to carry out a “mop-up” vaccination efforts as discussed in section 3.1.2 above on page 31.

3.2 Routine vaccination programme

After the initial catch-up and mop-up campaigns, routine immunization services should ensure that all new birth cohorts of children receive the routine doses of measles vaccine as specified in the childhood immunisation schedule. Various approaches are used to ensure that at least 90% of each new birth cohort receives measles vaccine. These approaches include improving access to vaccination, reducing missed opportunities for vaccination, and where necessary, mobile house-to-house vaccination services.

Missed opportunities are generally caused by the following four main reasons, although many other reasons for missed opportunities exist:

- a) The limited hours or days which some health centres are open are a commonly cited example that has prevented access.
- b) Health workers often do not find out whether a child who visits a clinic for some other reason is fully vaccinated. Others 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.
- c) False contraindications to vaccination include mild fever, diarrhoea, vomiting, colds, and coughing. Despite clear national standards, health workers often do not vaccinate children with these symptoms because they erroneously fear that they will be exacerbated.
- d) Sometimes the supply and distribution of vaccines to health centres is inadequate.

The level of coverage reached with the routine vaccination services is critical in the

elimination of measles transmission, as it determines the rate at which the susceptibles increase. As soon as sufficient children are left unimmunised, outbreaks are likely.

3.3 Surveillance

Routine reporting is the backbone of a surveillance system. Monitoring suspected cases should be carried out by an established network including health facilities, private practitioners, hospitals, and laboratories. Follow-up of reported cases should take place rapidly (within 24 to 48 hours) and is the responsibility of the district level staff. The monitoring system should include at least one reporting source identified in each "village/township" (or comparable small geo-political unit).

It may be necessary to convince public and private health personnel of the importance of measles reporting since many consider the disease an unavoidable fate of childhood and subsequently leaving suspected measles cases go unreported. 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 by district coordinators to association meetings, and if necessary directly to clinics. It is advisable to provide a specific form displaying key information to report. It is crucial that when ZERO cases are detected in a reporting unit, a ZERO REPORT is nevertheless sent in to reflect the absence of suspected cases.

3.5 Laboratory support

3.5.1 Serological testing

Measles-specific IgM antibodies can be detected using both indirect and capture EIA's. 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 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 are to be expected because of the less than 100% specificity of the tests.

The measles laboratory of the Centers for Disease Control and Prevention has developed a capture IgM EIA assay. Overall, sensitivity and specificity have been found to be over 97%. This test has been found to 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.

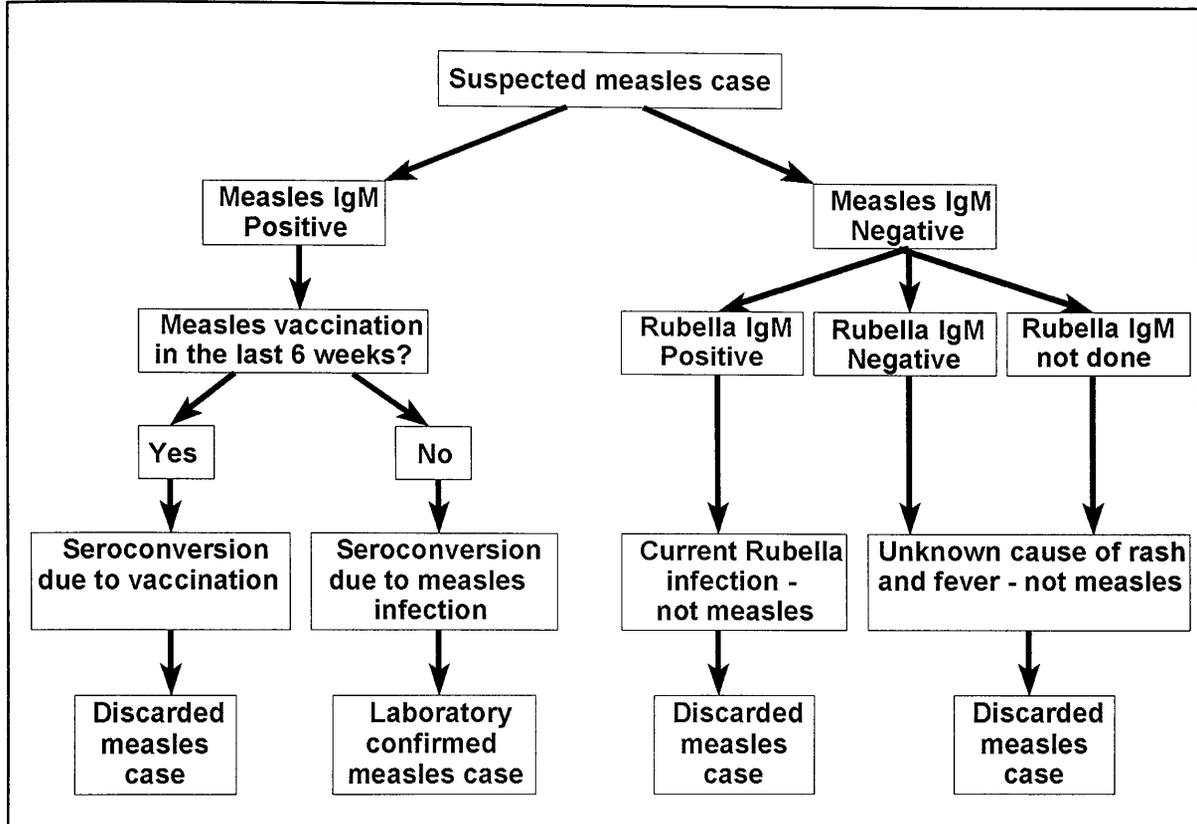
While the CDC capture assay has produced excellent results in regional reference measles laboratories in the Americas, the relative complexity and length of the test (6-7 hours) have made it difficult to implement this assay further afield.

IgG testing for measles requires the demonstration of a rise in the titre of antibody against measles. Two serum specimens per case are always required. The first specimen should be drawn as soon after rash onset as possible, at the latest within 7 days after rash onset. The second specimen should be drawn 10–30 days later. The tests for IgG antibody should be conducted on both acute and convalescent specimens at the same time. The same type of test should be used on both specimens. The specific criteria for documenting an increase in titre depends on the test. ELISA values are not titres and increases in ELISA values do not directly correspond to four-fold or greater titre rises.

Because tests for IgG require two serum specimens and a confirmed diagnosis cannot be made until the second specimen is obtained, IgM tests are generally preferred.

The interpretation of the serology should be based on the following diagram (Figure 6):

Figure 6: Interpretation of laboratory results



3.5.2 Measles virus isolation

Although isolation of measles virus is not recommended as a method to diagnosis measles, virus isolates are extremely important for molecular epidemiologic surveillance to help determine

- the origin of the virus,
- which viral strands are circulating in the country, and
- whether these viral strains have become endemic in the country.

Isolation of measles virus is technically difficult and is generally performed only in research laboratories, in the case of South Africa, at the National Institute for Virology (NIV).

The isolation of measles virus from clinical specimens can also be used to confirm measles diagnosis, but is relatively time consuming and requires more sophisticated laboratory support than serology. However, recent advances in the molecular epidemiology of measles virus has made it possible to analyse 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 source of measles importation. Information obtained through molecular epidemiology can complement information obtained from the standard epidemiologic investigation.

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 concerning the circulation of measles virus. Indeed, information obtained from molecular epidemiology can well complement information obtained from the classic epidemiologic investigation. Therefore, efforts must be made to collect appropriate clinical specimens for viral culture from every chain of measles transmission.

3.6 Outbreak investigations and response

Because measles virus continues to circulate in many parts of the world and international travel is readily available, it is virtually impossible to completely protect a population against measles. However, maintaining high levels of population immunity will decrease the possibility of extended measles transmission following an importation, should one occur into a measles free area.

Experience has shown that due to the very high communicability of measles, many susceptible persons will already have been infected with measles virus before the outbreak is recognized and control activities can be implemented. Although effective

control of an outbreak may not be possible, and resources are best expended on Outbreak Prevention, some appropriate response needs to be made.

STEPS IN OUTBREAK RESPONSE

- + **Confirm the Diagnosis**
- + **Investigate Suspected Measles Case(s)**
- + **Isolate Case(s)**
- + **Inform other Health Authorities**
- + **Assess Coverage in Affected and Surrounding Areas**
- + **Define Target Groups and Immunize Unvaccinated Persons**
- + **Enhance Surveillance**
- + **Analyse/Summarize Outbreak**
- + **Develop New Outbreak Prevention Strategy if Necessary**

CHAPTER 4 - IMPLEMENTATION IN SOUTH AFRICA

4.1 South African Measles Elimination Goal

4.1.1 Justification for measles elimination in South Africa

Although the current EPI(SA) strategy of achieving and maintaining high routine vaccination coverage has had a very positive impact on measles epidemiology by reducing cases, its limitations have become apparent with the occurrence of a major epidemic in 1992. South Africa has enjoyed in the past 2 years the lowest level of measles activity ever recorded. This "honeymoon period" is the result of sustaining relatively high routine vaccination coverage plus the occurrence of the 1992 measles epidemic which immunised many of the susceptibles in the older age groups. Since then, as national coverage rate lies around 85% for children 1 year (12-23 months) of age, the major proportion of susceptibles is accumulating among children <5 years of age.

However, due to the suboptimal vaccine efficacy and inadequate coverage, as shown in both developed and developing countries, measles outbreaks will continue to occur, and this even where virtually 100% of children have documented vaccination. The periodicity of those outbreaks will depend primarily on the level of coverage reached in each newborn cohort and on the uniformity of coverage distribution over the country.

Hence, for South Africa a combination of mass vaccination campaigns and high routine vaccination coverage and measles surveillance with laboratory support is recommended as the most effective strategy for controlling and eventually eliminating measles.

The success of these strategies depends upon achieving very high coverage during the mass campaigns, to reduce the number of susceptibles below the threshold level, and sustaining high routine vaccination coverage between campaigns to keep the rate of accumulation of susceptibles as low as possible. Although substantial resources are

required to implement a combination measles vaccination strategy, analysis in Canada and the United Kingdom suggested that the mass campaign was a cost effective public health intervention in these countries. Additionally to maximize the impact of such a strategy, particularly if the goal is measles elimination, surveillance must be strengthened to allow an immediate clinical and laboratory investigation of all suspected cases.

In South Africa, measles will be the next disease targeted for eradication after poliomyelitis. Wild polio virus circulation has, for all practical purposes, been interrupted in South Africa, but the conditions for the international certification of polio eradication require that active surveillance for acute flaccid paralysis (AFP) cases be continued for the next few years. The measles elimination initiative, with its own comprehensive epidemiological surveillance requirements, can be utilised to sustain EPI's high profile in general and on-going polio surveillance efforts in particular.

4.1.2 Setting the goal

A measles elimination consensus meeting was held in Pretoria on 28 November 1996. Participants in this meeting were health officials from the provincial and national health departments, international and national experts and paediatric and public health academics. The following goal was proposed and with its approval this goal would become a national health goal. A similar goal has been stated by several neighbouring countries, notably Namibia and Botswana.

South African Measles Elimination Goal

To interrupt the indigenous transmission of measles virus in South Africa by the end of the year 2002.

4.2 Historical perspective & current status of measles control in South Africa

4.2.1 Changes in measles vaccination schedules from 1980 to now

Prior to 1980, measles vaccination was given to only to individuals who bought the vaccine on the private market. No public sector measles vaccination took place until it was introduced in 1983. Since then various schedules and vaccine types have been utilized as presented below. The reason to change from the high to medium titre Edmonston-Zagreb vaccine in 1992 was that higher titre measles vaccine was for a time thought to be associated with increased delayed childhood mortality.

Table 3: History of routine measles schedule in South Africa (Source: Personal communication: Dr HGV Küstner, Director: Epidemiology, DoH)

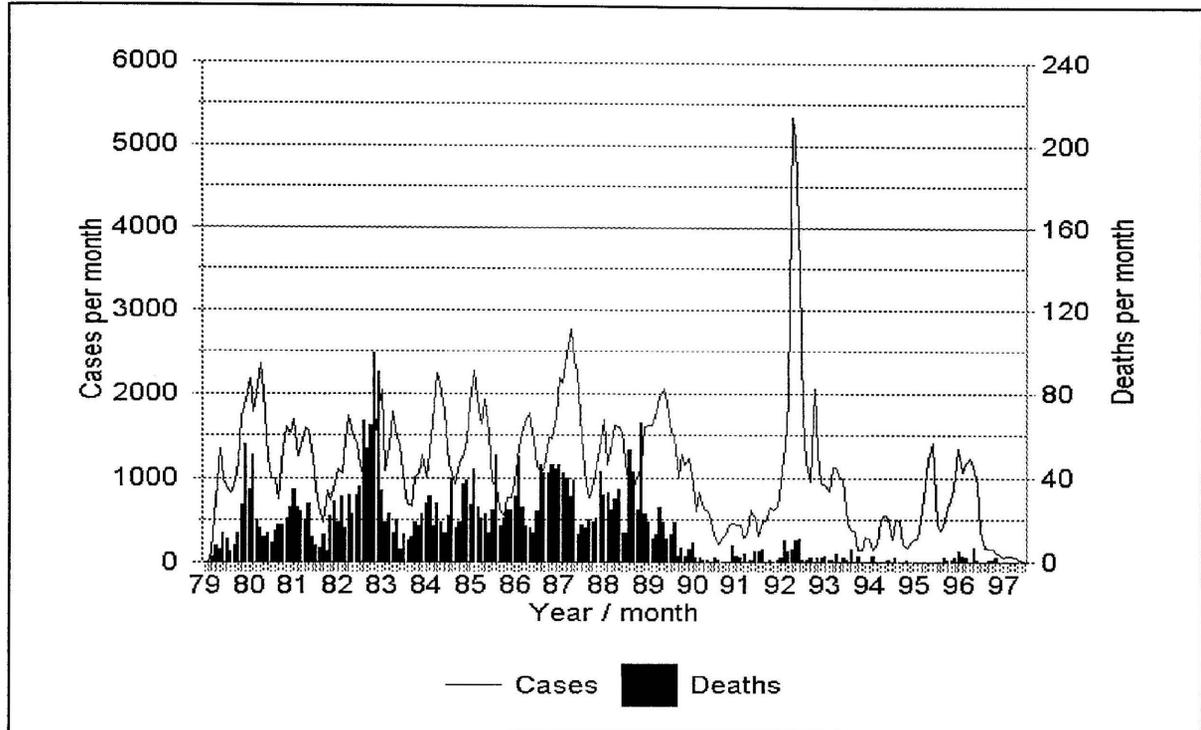
Year	Recommended Age	Vaccine strain	Minimum titre
1983-85	6m, 1st. dose 15m, 2nd dose	Schwartz	10^3 TCDI ₅₀
1986	9-10m	Schwartz	10^3 TCDI ₅₀
1/1991	6m	Edmonston-Zagreb	10^5 TCDI ₅₀
3/1991	6m	Edmonston-Zagreb	$10^{4.5}$ TCDI ₅₀
1992	6m- high risk area	Edmonston-Zagreb	$10^{4.7}$ TCDI ₅₀
	9m - low risk area	Schwartz	10^3 TCDI ₅₀
1993	9m, 1st dose	Schwartz	10^3 TCDI ₅₀
	18m, 2nd dose		
	Additional dose at 6m in high-risk areas		
1995	9m, 1st dose	Schwartz	10^3 TCDI ₅₀
	18m, 2nd dose		

4.2.2 Disease epidemiology in South Africa

Measles was made a notifiable condition in 1980. Prior to this data on disease incidence is found only in occasional reports and in some local authority annual reports.

The seasonal pattern of measles led to a primary peak in cases being experienced in September to November each year, with a secondary peak in March and April each year. In the period from 1980 to 1990, epidemics occurred every year, and case fatality

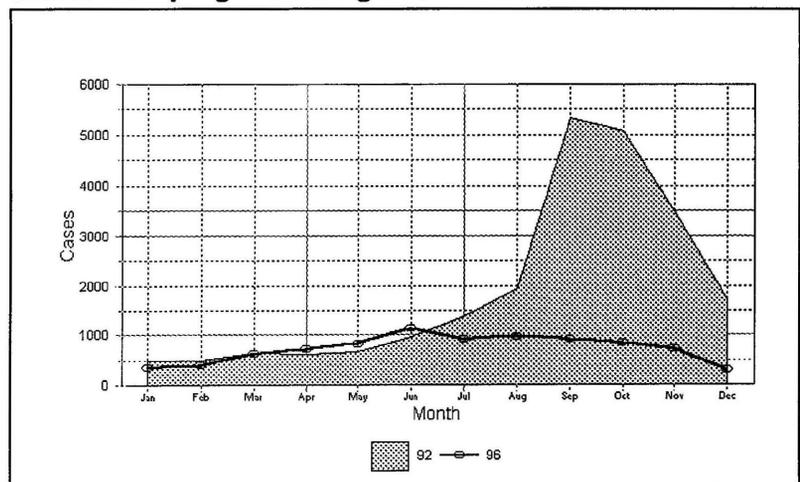
Figure 7: Notified measles cases and deaths, South Africa, 1979 - 1997



ratios of between 3% (1983) and 0.1% (1993) were experienced.

In 1990, the “Measles Strategy” (see below) was put into effect, resulting in the lowest ever annual number of cases being reported in 1991. This was followed in 1992/93 with a “post-honeymoon”

Figure 8: Aborting an epidemic: comparing notified measles cases in 1992 (epidemic year) and 1996 (mass campaigns in August)



epidemic with more cases per month in September and October 1992 than ever before. Fortuitously however, the number of deaths did not rise to the expected levels and most cases occurred in the 5 - 9 year and 10 - 15 year age groups.

Following the 1994 National Immunisation Programme Review, a national measles control goal was set, namely, that less than 4,000 reported measles cases for a period of 5 consecutive years beginning in 1996 should be observed. In fact, this goal was achieved in 1994, but the number of cases exceeded the goal in 1995 and 1996. Comparing the number of measles cases per month in the first few months of 1996 to the pre-epidemic period of 1992, an alarming trend towards another epidemic became visible, only to be curtailed by the mass immunisation campaigns in 1996/97 (Figure 8).

4.2.3 Vaccination coverage

As part of the National EPI Review in 1994, a vaccination coverage survey of children 12-23 months of age was performed⁵⁸ (Table 4) which confirmed the quality of coverage figures reported through the routine notification system: 76% and 85% of the children were vaccinated with measles vaccine before one year and at the

Table 4: Measles vaccination coverage of 12 - 23 month olds by first birthday and by time of the survey

Province	By first birthday	By time of survey (95% CI)
E Cape	66,5	71,6 (62,7 - 80,5)
Free State	74,1	82,9 (76,4 - 89,4)
Gauteng	81,9	89,3 (85,1 - 93,6)
KwaZulu Natal	76,7	86,0 (80,7 - 91,3)
Mpumalanga	71,9	78,6 (71,3 - 86,0)
N Cape	71,6	88,6 (82,5 - 94,6)
N Province	80,3	91,5 (87,4 - 95,7)
North West	71,3	82,0 (75,7 - 88,2)
W Cape	89,1	95,2 (91,0 - 99,5)
SOUTH AFRICA	76,4	84,5 (82,1 - 86,9)

time of the survey, respectively. Another interesting finding of this survey is that a high

proportion of children (28%) were vaccinated before 9 months of age, that is, when vaccine efficacy is estimated around 50-60%.

Due to the restructuring of the health information units at national and provincial levels the routine collection of coverage data has been limited to individual provinces. No complete coverage picture for the country is currently available.

4.2.4 The "Measles Strategy"

In 1990, a "Measles Strategy" was launched, aiming at the improvement of immunization coverage against all 6 target diseases. From the available coverage information, this strategy resulted in a slight increase in vaccination coverage from 63% in 1989 to 71% in 1990 in the former South African and self-governing areas.

This strategy had a dramatic effect on children under 5 years, reducing their proportion in the total number of measles cases considerably. In the subsequent epidemic in 1992, most cases occurred in the older children above 5 years, and consequently only very few deaths were recorded during the epidemic. Also, the average number of reported measles cases per month before the measles strategy was 933, while after the measles strategy (including the epidemic in 1992) average reported measles cases per month dropped to 324.

4.2.5 Mass immunisation campaigns in 1996/97

Following the successful mass immunisation campaigns in 1995 against polio, another set of polio campaigns were planned for August / September 1996. However, national and provincial health managers decided to include measles mass vaccination at the same time.

Due to the structure of decision-making in the South African health system and different financial resources, different provinces decided to target different age groups of

children. It was decided that all provinces would cover the full 9 month to 14 year old age group in mass immunisation campaigns against measles either in 1996 or in 1997. The following age groups were chosen by the provinces:

Table 5: Measles mass immunisation target age groups per province , 96-97

Province	1996	1997
Eastern Cape	6 months - 9 years	9 months - 14 years
Free State	9 months - 15 years	Not done
Gauteng	9 months - 5 years	6 years - 14 years
KwaZulu-Natal	9 months - 4 years	5 years - 14 years
Mpumalanga	9 months - 14 years	Not done
Northern Cape	9 months - 14 years	Repeat selected areas only
Northern Province	9 months - 4 years (selected areas only)	9 months - 14 years (whole province)
North-West Province	9 months - 14 years	Not done
Western Cape	9 months - 4 years	5 years - 14 years

Although the classical “catch-up” campaigns described in the Americas was never conducted in two campaigns one year apart, this split was necessitated by the limited resources available in some provinces. The following levels of coverage were reached in the 96/97 measles mass immunisation campaigns:

Table 6: Coverage obtained during measles mass immunisation, 96/97

Province	96			97		
	Children targeted	Doses given	Coverage (%)	Children targeted	Doses given	Coverage (%)
E Cape	1,644,994	1,624,954	98.8	2,117,000	1,835,795	86.7
Free State	1,049,941	937,414	89.3	-	-	-
Gauteng	854,754	652,175	76.3	1,526,420	1,297,457	85.0
KwaZulu-Natal	984,727	802,778	81.5	2,117,302	1,815,960	85.8
Mpumalanga	1,044,298	1,089,324	104.3	-	-	-
N Cape	246,293	231,042	93.8	15,269	12,609	82.6

N Province	320,000	286,325	89.5	2,049,851	1,508,534	73.6
North-West	1,218,720	1,059,620	86.9	-	-	-
W Cape	334,272	331,095	99.0	778,981	704,000	90.4
South Africa	7,697,999	7,014,727	91.1	8,604,823	7,174,355	83.4

4.3 Strengthening routine immunisation

Seven diseases are targeted through vaccines given routinely in the EPI in South Africa and an eighth (Hib vaccine) is being planned. As the strengthening of the routine immunisations will encompass all these vaccines, this section deals with issues wider than just measles vaccination.

4.3.1 Physical and functional accessibility

Accessibility to routine immunisation services are generally good throughout the country. However, services are occasionally inaccessible for two reasons.

Firstly, not all communities have full access yet to health care within reasonable distance from their dwellings. This would constitute a physical barrier to accessibility. In the short term this problem should be addressed with mobile or outreach activities, delivering services to currently deprived areas.

Urgent attention should be paid by district managers to communities which remain without accessible health services, not only for the sake of immunisations but for all health care programmes. Various methods at district level could be used to identify the unreached areas. Possibly the easiest method and a good starting point would be to request all health facilities to demarcate their approximate area of service delivery on a district map based on their knowledge. These boundaries can, with time, be refined in each health facility by marking off where their patients come from. Finally, areas where no coherent health services, as well as areas of excessive overlap, will become evident through this exercise and district managers can redirect the services appropriately.

The second barrier to accessibility is probably less easy to overcome. Health care services including immunisations, are occasionally denied to clients, because the client did not come on the “right” day for the service, arrived too late at the health facility or was in other ways prevented by circumstance or staff to received full primary health care services when they arrive. This constitutes a functional barrier to accessibility and is much more covert than physical barriers.

The means to overcome these functional barriers include the redirection of primary health care staff to become client orientated much in the way a good hotel would take care of its clients. Also, thought

may be given to opening the health facilities after normal working hours to allow working parents access to health facilities in their spare time. In the case of immunisations, all eligible children should be provided with

Open vial policy:
Opened vials of OPV, DTP, DT, TT and Hepatitis B can be kept for subsequent vaccination sessions provided the vaccine has been kept in the cold chain, is not contaminated and has not left the health facility on an outreach activity.

the appropriate immunisation, even if it means opening a multidose vial for a single child who has come later. Adherence to the open vial policy (see inset) will also decrease the wastage for those vaccines, as they can be kept for subsequent immunisation sessions. **In the case of measles vaccine however, reconstituted measles vaccine should *a/ways* be discarded at the end of each 6 hour session.**

4.3.2 Missed opportunities in the clinic setting

The *Integrated Management of Childhood Illnesses (IMCI)* clearly spells out the need for curative visits to the clinic to be accompanied by the checking of the Road-to-Health card and the provision of missing immunisations. This is the mainsay to ensuring that all contacts with health services are simultaneously used to provide missing immunisations.

Each clinic should be able to define the area in which the population lives that they serve. Ideally, this definition of the catchment area should be done in conjunction with other clinics in the area, as is described in section 4.3.1, page 46.

A register of children born in the area and of those that have presented themselves for previous immunisations needs to be kept. This would allow clinic staff to identify those children who have not received the subsequent immunisation doses. These children can then be traced and immunised.

Often clinics have devised their own ingenious way of finding these children, and clinic staff in some cases know their clients personally over the years, making this task easier.

4.3.3 Missed opportunities in hospitals

Due to previous health care provision legislation in some areas of South Africa, immunisations in local authority areas, even within hospitals, have often been considered a function of local authority health services. Often this would be evident through the fact that local authority staff would regularly visit the maternity and paediatric wards in hospitals in their areas and provide the necessary immunisations. However, this has led to an extraordinary number of missed opportunities^{59,60}. Infants discharged during week-ends often leave unimmunised, as local authority routine would exclude the week-ends. Also, the great number of children seen daily in general and specialist paediatric outpatients are routinely either not checked for completeness of immunisation, or are told to have their missing immunisations completed at a clinic. Both practices let a golden opportunity to reach the children presenting themselves to health facilities pass unused.

All maternity and paediatric wards as well as the paediatric out-patient departments should devise mechanisms that *Road-to-Health* cards of each child are checked and that the necessary immunisations are given *there and then*, without any referral. This

can possibly even be done during the outpatient screening or admission procedures. Similarly, children's homes and "places of safety" should institute a ruling that all entrants require full vaccination including measles at entry.

In addition to this, *all paediatric admissions (even short term) of patients aged six months to four years should receive a dose of measles vaccine on admission, unless written proof of measles vaccination is provided.* This will not only protect the individual child, but prevent catastrophic nosocomial outbreaks of measles disease.

4.3.4 Missed opportunities in the private sector

As in paediatric out-patient departments, children who are present to a private practitioner or paediatrician should bring along their Road-to-Health card, and any missing immunisations should be given immediately and recorded on the Road-to-Health card. Although private health care providers have for a long time not been involved to a great extent in the immunisation programme, more and more private health care providers have now indicated their interest in providing immunisation services.

A national directive on private immunisation has been drawn up and is currently the basis of the interaction between the private sector and the public sector on immunisation. In respect of individual private health care providers, we would encourage their participation in the immunisation programme. Vaccines can be obtained free of charge from the district health authority, provided that the client is not charged for the vaccine, the number of doses given are supplied back to the district and that EPI(SA) policies are adhered to, both regarding the administration of the vaccine and the cold chain.

4.3.5 House-to-house vaccination

In certain circumstances, routine immunisations should be given by a team of

vaccinators moving from house-to-house (“raking”). Especially when it is suspected that groups of people are avoiding the authorities (eg illegal immigrants), have not been informed of health services (eg new informal settlements with high numbers of persons from other areas) or are, for any other reason, not presenting themselves to the clinics, this approach should be attempted.

Vaccinators move from door to door, requesting the residents to produce their Road-to-Health card and providing the missing doses at once. These visits should also be used to provide health promotional material, information on the local health services and other public health interventions (eg preparation of oral rehydration solutions in the case of diarrhoea).

4.4 Mass immunisation campaigns

4.4.1 “Catch-up” campaigns

By the time this policy and implementation plan was created, the “catch-up” campaigns in South Africa had been completed, placing the country squarely on the road to measles elimination. A description of the South African “catch-up” campaigns is given in section 4.2.5 on page 44.

4.4.2 “Mopping-up” activities

In South Africa, the term “mopping-up” is being used for two different activities. To place South Africa in line with international terminology regarding campaigns, we suggest the following use of terms.

Mopping-up campaign

A mass immunisation campaign following a previous campaign where areas in which low campaign coverage was achieved are reselected and redone. Similar to all campaigns, Road-to-Health cards are not checked or marked, and all

children within the target age group in the identified geographical area are reimmunised.

Raking

An activity linked to the provision of routine immunisations. In areas where low routine coverage are found, children who have no documented proof of immunisation are immunised. These immunisations form part of the routine immunisation activity and should be regularly undertaken at clinic level to boost routine coverage.

Although the second activity has often also been called mopping-up the use of the alternate term - raking - will avoid confusion.

In areas or groups where low coverage (<80%) was reached during the 96/97 mass immunisation campaigns mopping up campaigns are planned. In some cases the mopping-up was done immediately following the '97 campaign. However, where large areas or groups were missed, more extensive planning will be done to ensure good reach during the mopping-up campaigns.

Using the data on district level from the '97 campaign any district that reached less than 80% coverage will be required to do mopping-up work. In collaboration with the provincial and regional coordinators the most appropriate strategy to reach those that have been left out should be devised. This will include house-to-house vaccination, targeting creches or schools that have not reached the target. Experience in the "catch-up" campaign have shown that those schools and creches where health workers explained the need for campaigns personally to teachers and parents, a much higher coverage was obtained and refusals were minimal.

A guideline for mopping-up activities has been drawn up separately to assist the provinces in their planning.

4.4.3 “Follow-up” campaigns

The timing of “follow-up” campaigns is dependent on the coverage obtained in the routine measles vaccination programme. A “follow-up” campaign needs to be done when sufficient numbers of susceptibles have accumulated through imperfect coverage and imperfect efficacy to sustain transmission in an epidemic. This accumulation can either be estimated using the routine coverage and vaccine efficacy figures, or by doing cross-sectional serosurveillance studies. In South Africa, this decision is complicated by the current weak surveillance on the number of doses given in the routine immunisation programme and the different strategies and age groups used by the provinces in the 96/97 catch-up campaign.

Any follow-up campaign should be run uniformly across the country to enable effective social mobilisation and probably more effective disease prevention. It is proposed that the timing of the “follow-up” campaign should be calculated by doing seroprevalence studies in the age group 0 to 15 years. The seroprevalence study should be done three years after the end of the first “catch-up” activity, ie. July 1999. As indicated previously it is estimated that the current routine coverage for the first dose of measles is 76% by the first birthday and 83% in the 12 - 23 month old age group. The proposed three year limit will enable a scientific decision by the time the “follow-up” campaign is due. It is expected that “follow-up” campaigns will not be done in South Africa before July 2000.

4.5 Surveillance

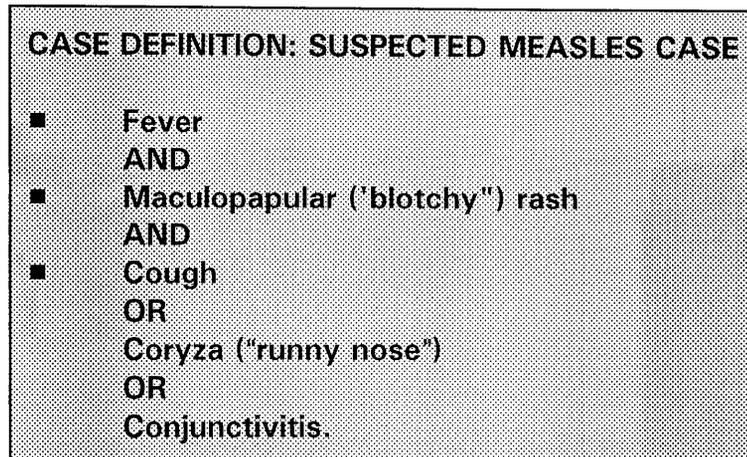
4.5.1 Case definitions

Suspected Measles Case (SMC)

The category of Suspected Measles Case (SMC) is a wide catchment that is intended to provide an early alert for health workers at the health facility level that measles virus may be circulating in the area. A patient in whom a health care worker suspects the

possibility of measles virus infection is, for surveillance purposes, considered to be a SMC.

Although there is not a rigid clinical case definition used for SMCs, a health care worker should suspect measles virus infection when a patient presents with the following clinical picture:



All such cases should have both a single blood specimen for laboratory analysis of measles virus infection and a urine sample for virus isolation collected and should be immediately reported to district surveillance authorities. The notification of a SMC should result in the immediate careful investigation of the case, as well as stimulate an active search for additional SMCs in the area.

Confirmed Measles Case (CMC)

There are two categories of CMCs:

- "Laboratory confirmed" and
- "Clinically confirmed".

The total number of CMCs is the sum of these categories. The definitions of these categories are outlined below:

Laboratory confirmed measles case

A Laboratory CMC is a SMC that after complete investigation satisfies at least one of the following criteria:

- Laboratory confirmation of measles virus infection
- Epidemiologic linkage to another laboratory confirmed measles case

A SMC is considered to be Laboratory Confirmed if measles specific IgM antibodies are detected in a blood specimen collected from the patient.

In an outbreak of more than 3 cases, it is not necessary to collect a blood sample from every SMC. Only the first 3 to 5 cases should have blood drawn for laboratory confirmation. All of the other SMCs can be 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 CMC whose rash onset was 7-18 days before the present case.

Clinically Confirmed Measles Case

A patient who satisfied the definition of a SMC and, for some reason, is not completely investigated is, for surveillance purposes, considered to be a Clinically CMC. Since the possibility of measles virus infection could not be excluded, it is not possible to discard these cases.

A Clinically CMC is a SMC without a complete epidemiologic investigation. Possible reasons include:

- death of the patient before an investigation is complete;
- patient can't be located or is lost to follow up;

- patient receives only a clinical diagnosis from a health care worker without laboratory investigation.

Since an epidemiologic investigation was not conducted and measles virus infection could not 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 on every reported suspected measles case and to have as few Clinically CMCs as possible. Of the total CMCs, at least 80% should be Laboratory CMCs.

Discarded Measles Case

A SMC that has been completely investigated, including the collection of an adequate blood specimen, and lacks serologic evidence of measles virus infection can receive the final case classification of “discarded”. Moreover, if laboratory evidence of another infection that is usually associated with a rash illness was present, such as rubella, this provides ample support to discard the case.

The national EPI office should receive a copy of the case investigation form so that it can periodically review the distribution of diagnoses and evaluate the clinical basis for discarded cases.

Imported Measles Case

An imported measles case is considered a CMC in a person who travelled in another country with documented measles virus circulation during the possible exposure period (7-18 days prior to rash onset), and was in contact with a measles case in that country. For a case to be confirmed as an imported measles case, the possibility of local exposure to measles must be excluded after careful community investigation.

4.5.2 Case finding and routine reporting

Each health facility should identify one individual and one or two alternates who are responsible for keeping track of suspected measles cases and immediately reporting all new suspected measles cases. Reports should be submitted to local and/or district surveillance coordinators by the fastest means possible (telephone, e-mail, fax, etc.). All health professionals who are likely to be in contact with cases should be provided written material that describes their responsibilities and duties. Training and close ongoing supervision are important, as staff turnover may be a problem in many areas. National and provincial/state staff 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 should be encouraged illustrating responsibilities.

Key points to consider are:

- Repeated visits by the program surveillance officers will be required to establish and monitor all levels of the reporting system.
- All suspected cases should be investigated by trained staff, and an appropriate laboratory specimen should be obtained and tested promptly for the first three cases in an outbreak.
- Each suspected case should be given a unique identification number, that should be used whenever referring to the case.
- Regular reports should be made each week, even when no suspected cases of measles have been identified.

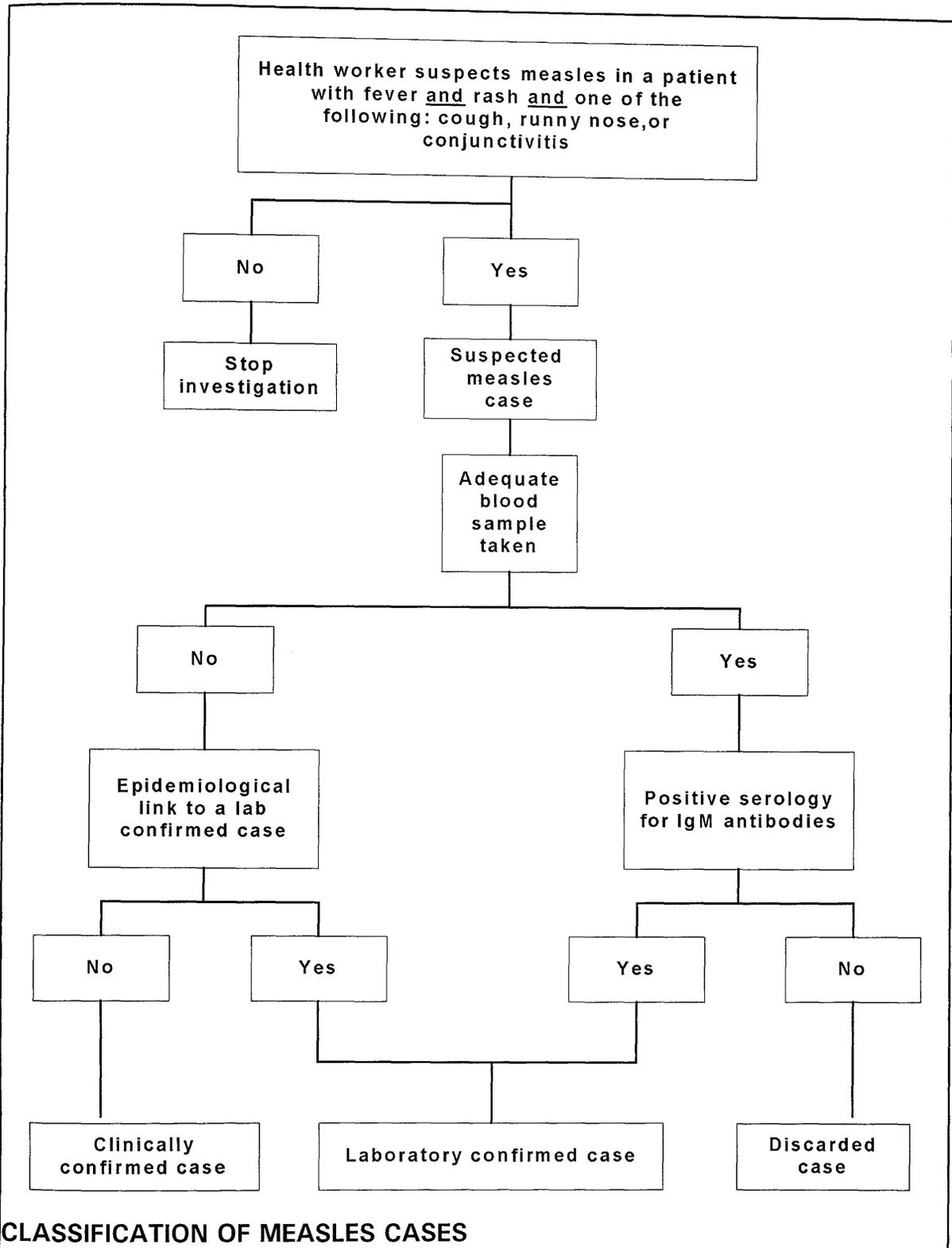
Private Practitioners: It is important that private medical practitioners be included in the surveillance system. In many areas it is likely that they will be the first to see

suspected cases. In some areas, sentinel reporting systems can be set up among a community's key pediatricians. Success of the 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 surveillance system. The infection control nurse or a deputy should be assigned at each hospital to check pediatric and infectious disease wards visually and 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 need to be organized to report suspected cases. These may include pharmacists, private practitioners, private clinics, village leaders, schools, and anyone else likely to come in contact with such illnesses.

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. Health care workers 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.

As measles incidence declines, additional effort may be required to ensure that appropriate and timely diagnosis of rash illnesses and reporting of suspected cases continues. In addition, the rapid investigation and reporting of all suspected cases, and recording vaccination history and import status for all cases, will become increasingly important.

The activities listed below can further improve the detection and reporting of measles cases and improve the comprehensiveness and quality of reporting.

Searching hospital and other records. Hospital records may be searched yearly to evaluate the comprehensiveness of the reporting of hospitalized patients.

Mortality data are available through the vital records systems. Mortality data should be reviewed each year to identify deaths that may be due to measles. Any previously unreported cases identified through this review should be reported. At a minimum, mortality data should be reviewed annually.

Investigating contacts. Determining the source or chain of disease transmission, identifying all contacts (household, daycare, and other close contacts), and following-up of susceptible persons may reveal previously undiagnosed and unreported cases.

Active surveillance. Active surveillance may have a role in measles disease control; district health departments should consider making regular contact with health providers in high-risk areas (i.e., large hospital outpatient services in inner city areas) to obtain case-reports. These activities are especially important in large cities and in cities that have large numbers of international visitors. Active surveillance also may be conducted during outbreaks, when a cluster of suspected cases is reported, and when poor routine surveillance is suspected.

Special projects. Special projects such as reviewing emergency department logs to

identify rash illnesses that may have been unreported cases of measles may be used to evaluate surveillance sensitivity and reporting efficiency.

Monitoring surveillance indicators. Regular monitoring of surveillance indicators including time intervals between diagnosis and reporting, and completeness of reporting may identify specific areas of the surveillance and reporting system that need improvement.

Surveillance indicators for measles:

1. The proportion of confirmed cases reported to the national EPI with complete information.
2. The median interval between rash onset and notification of a public health authority, for confirmed cases.
3. The proportion of confirmed cases that are laboratory confirmed.
4. The number of cases that meet the clinical case definition, but are not confirmed.
5. The number of cases that meet the clinical case definition in which measles is ruled-out by appropriate laboratory testing.
6. The number of chains of transmission that have an imported source.
7. The number of chains of transmission for which at least one clinical specimen for virus isolation was collected and submitted to the national EPI office.

4.6 Case investigation and reporting

4.6.1 Steps in the investigation of a suspected case

All suspected cases of measles should be investigated so that the case can be classified as either discarded or confirmed. Once a case has been identified by a health worker using the case definition for a suspected measles case (SMC) the district EPI or CDC coordinator should be immediately informed by the quickest means possible (phone, fax or email). While the responsibility to investigate and follow-up the case ultimately lies with the district or regional coordinator, the health worker should be involved in the initial investigation. At the first contact with the suspected measles case, it should be confirmed that the case meets the case definition. The provincial EPI coordinator should also be informed that a case is under investigation.

An EPID number should then be assigned to each case. The EPID number consists of five elements, namely the disease code (MSL), a provincial code (eg FS for the Free State), a district code (eg BLM for Bloemfontein), the year (eg 97) and a sequential number (eg 002). The full EPID number in this example would thus read:
MSL-FS-BLM-97-002.

A case investigation form (Appendix A) for measles should be used to collect all data in a systematic way. With the first contact all information in the first section needs to be collected and noted on the form. The following fields contain critical information:

- all demographic data;
- date of onset of rash;
- date of last vaccination; and
- date of serum sample taken.

A sample of venous blood should be obtained. This may be collected either by venepuncture in regular glass tubes (without any additives - red top), or using a heelprick and a capillary collection system such as Microtainer®. The sample should be sent to the nearest university virological department. If regular blood collection tubes were used, the sample should be sent on ice, while in the capillary collection tube it does not require the sample to be sent on ice. Both the sample and the laboratory request forms should be marked with the EPID number. The laboratories will conduct a measles IgM ELISA test on the sample.

In addition to the blood sample, a urine sample should be sent along with the blood sample to the virological laboratory as well. The urine sample will enable the isolation of the measles virus itself. The urine sample should accompany the original serum sample to the nearest university virological laboratory. Should the measles IgM be positive, the laboratory will send on the urine sample to the National Institute for Virology (NIV).

The investigator should enquire about other cases in the area, and if further cases are found follow the instructions in the outbreak investigation described in section 4.7 on page 69. Also, the investigator should inform other health workers in the vicinity as well as the district coordinators in adjacent districts of the occurrence of a suspected measles case so that they can be on the look-out for further cases.

The district Suspected Measles Case Line List (Annexure B) should be updated with the information of the case or cases.

Transmission is likely to have occurred from a person who had a rash-like illness or prodromal symptoms, and developed a rash illness later. Inquiries should be made to determine whether cases are occurring in places that the case visited within four weeks prior to the onset of the rash, such as a pre-school centre, school, or another town or village. If there are more than 10 suspected cases in a single outbreak area, the household visits should be cut back or eliminated depending upon available manpower. However, the district Suspected Case Line Listing should be filled out with particular attention to obtaining basic demographic data, including the age and vaccine history of the patient.

Isolation of the case and contacts

At home, a case should be limited to contact with immediate family members until 5 days after the rash appears. Communicability greatly decreases after the second day of rash. In hospitals, cases should be isolated from the onset of symptoms through the 5th day of rash. All children hospitalized or attending outpatient clinics, who cannot provide written proof of measles vaccination, should be vaccinated .

Management of close contacts

Definition of a contact:

All persons living in a household or other close quarters with the case during the infectious period (five days before to five days after the onset of the rash).

- 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 stay at home. The child 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 contact the health or medical case provider immediately.
- Contacts who were susceptible at the time of a visit should be vaccinated and stay home and avoid contact with other children until two full weeks after exposure.

Searching for additional cases

In order to find additional suspected measles cases, the public should be kept well informed and community leaders should be asked to assist in case finding. Activities may include:

- 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 record reviews at the local centres, hospitals and clinics;
- Health staff in the affected areas should use every contact with patients as an opportunity to inquire about rash and fever illnesses in the neighbourhood;
- Efforts to identify additional cases should extend well beyond the neighbourhood community in which the suspected case lives.

4.6.2 Laboratory investigations

Collection and delivery of sera

While collecting sera on the first day of rash may result in some false-negative lab results, the majority of cases will be properly classified. Collecting a measles specimen soon after rash onset is clearly preferable to losing a patient to follow-up and not being able to collect any specimens.

Many patients, however, present to a health facility on or after day 2 of rash; the majority of these cases will have correct lab results and be properly classified. Moreover, if measles virus is circulating at high levels in a population, there will be more suspected measles cases and the laboratory will have other opportunities to confirm the presence of measles virus. Thus, a single serum specimen obtained at first contact with the health care system is considered to be adequate for measles surveillance.

The serum sample should be sent to the nearest academic virological department as soon as possible after collection.



SERUM COLLECTION AND SHIPMENT PROCEDURES

- Whole blood (3 ml) should be collected in a Microtainer® or normal blood collection tube. It may be kept 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. Do not freeze whole blood.
- If blood is collected in a Microtainer® tube, it can be sent without refrigeration or separation of the serum.
- If normal blood collection tubes were used:
 - transfer serum aseptically to a sterile vial.
 - If available, use a centrifuge to separate the serum.
 - Store serum at 0-8° C until it is ready for shipment. Sera may be frozen;
 - 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 flask;
 - 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 frozen, with the exception of whole blood, which should be stored at 0 - 8° C.
 - If using ice packs (these should be frozen) place ice packs at the bottom of the box, and along the sides, place samples in the centre, then place more ice packs on top.
- Arrange shipping date
- When arrangements are finalized inform receiver of time and manner of transport.

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. This includes ensuring that the proper forms accompany the specimen.

Serum sent from the peripheral laboratory will be analysed for measles IgM and IgG antibodies using an indirect enzyme-linked immunoassay (ELISA) test. This test will be

standardized throughout the country and the kits will be supplied to the seven virological laboratories.

Serum found to be negative for measles IgM (ie. no current active measles disease or vaccination) will be tested for rubella, as the public health implication of a proven case of rubella is important.

Results

Patients that have a positive result with the IgM assay are considered to be laboratory confirmed measles cases. Any suspected measles case who was in contact with a laboratory confirmed case will also be considered to be laboratory confirmed.

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 suspect 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 both 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 vaccinees are expected to have detectable IgM after vaccination. Moreover, other medical conditions such as rubella, dengue, etc. may cause fever and rash illnesses 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 an active search of the community does not find any further evidence of measles transmission, the case may be **discarded** as not being measles.

If, on the other hand, an active search finds other laboratory confirmed cases of measles in the community, the suspected measles case with history of recent vaccination should be classified as **laboratory confirmed**.

From this it is amply clear that the date of the last measles vaccination is a crucial data item and it needs to be collected on all suspected measles cases.

Viral isolation

The best clinical specimens for isolating measles virus are respiratory secretions, white blood cells and urine. Specimens are best collected during the prodromal phase through the first few days of rash. Specimens (urine, nasopharyngeal aspirates, heparinized blood, or throat swabs) for virus culture should be obtained from every clinically suspected case of measles and should be shipped with the serum to the nearest university virological department. If the measles IgM is positive, the virus isolation sample will be forwarded to the National Institute for Virology. Clinical specimens for viral isolation should be collected at the same time as, and in addition to, samples taken for serologic testing. Because virus is more likely to be isolated when the specimens are collected within 3 days of rash onset, collection of specimens for virus isolation should not be delayed until laboratory confirmation is obtained. Clinical specimens should ideally be obtained within 7 days of rash onset, and should not be collected if the opportunity to collect a specimen is more than 10 days after rash onset.

Specimen collection for viral isolation

Specimens for virus isolation should be collected early in the acute phase of infection, when the virus is present in high concentration. They should be refrigerated and transported to a laboratory within 48 hours. Suitable samples for isolation of measles virus are leukocytes, serum, throat and nasopharyngeal secretions and urine.

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 (1000 - 1500 rpm); the supernatant should be discarded and the sediment should be resuspended in 1-2 ml of viral transport media (e.g. Hanks' BSS). The resuspended sediment may be frozen and transported to the NIV.

4.6.3 Completing the case investigation

Once the results from the laboratory investigation have been received back, the case investigation form should be completed and all missing information added. The completed case investigation form should be faxed to the provincial EPI coordinator who is responsible to ensure that all the details of the case investigation forms are correct and complete.

The final case classification is made by the provincial EPI coordinator using the information on the case investigation form. The completed form with the classification should then be sent to the national EPI office where the information will be collated and reported. The national EPI office will also verify the final classification and if necessary request further information.

Feedback to the district coordinator and the health worker who detected the case is the responsibility of the provincial EPI coordinator.

4.7 Outbreak investigation and response

4.7.1 Confirm the Diagnosis

Suspected cases of measles should be investigated immediately as indicated above, and blood specimens for serologic confirmation should be collected. Also, urine samples or throat swabs for virus isolation should be taken and sent to the National Institute for Virology.

A suspected measles outbreak may be defined as 3 or more suspected measles cases in a defined geographical area within a one month period. In this context, once a single laboratory-confirmed measles occurs it is considered to be a confirmed measles outbreak.

When a measles outbreak occurs in a defined geographic area and has 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 (Appendix - Suspected Case Line Listings). 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, efforts are not needed to collect blood from every suspected measles case. During an outbreak, patients in whom a health care worker has a strong suspicion of measles infection, may for surveillance purpose, 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. This limitation on the number of blood specimens collected will save valuable staff time, and prevent overloading the laboratories.

4.7.2 Evaluate Vaccination Coverage

Vaccination coverage data should be reviewed as soon as a measles outbreak is suspected. If immunization coverage is not high or there is not good coverage data, this presents a good opportunity to undertake a rapid vaccination program and to complete it within 1-2 weeks. The priority of the vaccination activity is to provide measles vaccination to previously unvaccinated preschool-aged and school-aged children.

4.7.3 Control actions and outbreak response

Control activities should not be delayed pending the return of laboratory results on suspected or probable cases.

The primary strategy for control of measles outbreaks is achieving a high level of immunity in the population in which the outbreak is occurring. In practice, the population affected is usually rather narrowly defined (such as one or more schools); high level immunity is obtained by achieving high coverage with 2 doses of measles vaccine in the affected population. Persons who cannot readily provide documentation of measles immunity should be vaccinated or excluded from the setting (school, hospital, etc.). Only doses of vaccine with written documentation of the date of receipt should be accepted as valid. Verbal reports of vaccination without written documentation should not be accepted. Persons who have been exempted from measles vaccination for medical, religious, or other reasons should be excluded from affected institutions in the outbreak area until 21 days after the onset of rash in the last case of measles. The recent experience in measles outbreaks in South America has been that almost all persons who are excluded from an outbreak area because they lack documentation of immunity quickly comply with vaccination requirements.

If cases are occurring among infants <12 months of age, measles vaccination of infants as young as 6 months of age may be undertaken as an outbreak control measure.

Monovalent measles vaccine is preferred. In practice, this recommendation may take several months to implement, and several months to halt once the outbreak has ended.

Health authorities at all levels should be informed and involved in all aspects of outbreak control. Health officials in nearby jurisdictions also should be notified and kept up to date as frequently as possible, so that they may begin appropriate preventive actions, as needed. If a suspected case has travelled or had close contact with individuals from other areas of the country within 15 days before the onset of the illness, the surveillance coordinator in those areas should be notified immediately. When appropriate, other countries should be notified. The public should also be informed through the media about any outbreak and control efforts that have been implemented.

The most recent information on cases, immunization activities, and villages visited should be monitored continuously during an outbreak. This information should be kept in a form that can be summarized quickly in an Outbreak Summary (see below). No new cases should be occurring four weeks after vaccination efforts are completed. Special reviews and checks should be made at this time to ensure that no new cases have occurred.

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:

The age group of the cases in an outbreak is critical to determine the target group of supplemental outbreak vaccination. In general, the measles cases indicate the group where susceptibles exist and should be targeted first.

When fewer than 3 suspected cases are identified in an area, vaccinate all close

contacts, and the children between the ages of 9 months and 5 years in the immediate neighbourhood who documented proof of measles vaccination. When 3 or more suspected cases are identified in an area, depending on the estimated vaccination coverage in the area, a broader vaccination effort may be needed.

If many of the cases are occurring in infants under 9 months of age, vaccinate infants between 6 and 9 months of age (these infants should be revaccinated when they reach one year of age). Vaccination of older age groups should be considered, if high attack rates are observed in children 5 years of age or older, or if the coverage achieved during the "catch-up" vaccination did not reach 90% among the 9 month-14 year olds. All children without a history of vaccination after their first birthday should be targeted for vaccination.

- When to vaccinate

Start vaccination activities immediately when a measles outbreak is first suspected. Do not wait for laboratory confirmation of the suspected measles cases. If the suspected cases are eventually found to be laboratory confirmed, 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 due to measles infection, then the vaccination activity has helped to raise the level of community measles immunity and prevent measles outbreaks in the future.

- Where to vaccinate:

In both urban and rural areas the focus of vaccination efforts should be any potential pockets of susceptible children. The largest area possible should be covered. Door-to-door vaccination requires greater resources, but is likely to yield the better results. Gathering points such as schools, churches, health posts, etc., may also be chosen as mass vaccination sites.

4.7.4 Outbreaks in special circumstances:

Control of outbreaks in schools and other institutions.

During outbreaks in elementary, primary, and high school, and colleges and other institutions of higher education, as well as other institutions where young adults may have close contact (such as prisons or army camps), a program of revaccination with measles vaccine is recommended in the affected schools or institutions.

The scope of vaccination effort needed will depend on

- age-appropriate measles coverage in the community,
- population density, and
- patterns of social contacts within the community.

During an outbreak, strong consideration should be given to expanding vaccination efforts to all schools in the community, unless measles coverage is high in those other schools.

All students and their siblings, and all school personnel who cannot provide documentation that they have received two doses of measles containing vaccine or cannot provide other evidence of measles immunity (such as serologic testing), should be re-vaccinated. Persons who cannot readily provide documentation of measles immunity should be vaccinated or excluded from the school or other institution. Persons revaccinated, as well as previously unvaccinated persons receiving their first dose as part of the outbreak control program, may be immediately readmitted to school. Persons who continue to be exempted from or who refuse measles vaccination should be excluded from the school, day care, or other institution until 21 days after the onset of rash in the last case of measles.

Control of outbreaks in medical settings.

If an outbreak occurs within, or in the areas served by a hospital, clinic, or other medical or nursing facility, all personnel (including volunteers, trainees, nurses, physicians, technicians, receptionists, and other clerical and support staff) with patient contact should receive a dose of measles vaccine, regardless of their age, unless they have documentation of measles immunity or vaccination. If indicated, health-care workers who have not been immunised against measles should receive a dose of measles vaccine. Serologic screening of health care workers during an outbreak to determine measles immunity is not generally recommended, because arresting measles transmission requires the rapid vaccination of susceptible health-care workers which can be impeded by the need to screen, wait for results, and then contact and vaccinate the susceptible persons.

Susceptible (unimmunised) personnel who have been exposed to measles should be relieved from all patient contact if possible and should be excluded from the facility from the 5th to the 21st day after exposure. Personnel who become ill should be relieved from all patient contact and excluded from the facility for 7 days after they develop rash.

Further discussion on the prevention of nosocomial transmission can be found in section 4.8 on page 77

Role of community wide vaccination efforts in outbreak control.

Mass revaccination of entire communities is not of demonstrated benefit in control of measles outbreaks. Such activities may sometimes have to be undertaken because of political or other community demands for “action” and concerns about the acceptability of targeted interventions directed toward selected, high risk populations, but there is no epidemiological evidence that they are feasible or useful in controlling measles outbreaks.

Quarantine.

Quarantine is of limited usefulness in control of measles outbreaks. Imposing quarantine measures for outbreak control is usually both difficult and disruptive to schools and other institutions. Under special circumstances, such as during outbreaks in schools attended by large numbers of persons who refuse vaccination, restriction of an event or other quarantine measures might be warranted. However, such actions are not recommended as a routine measure for control of most outbreaks.

Post-exposure vaccination and use of immunoglobulin to prevent measles in exposed persons.

If given within 72 hours of exposure to measles, measles vaccine may provide some protection. In most settings, post-exposure vaccination is preferable to use of immunoglobulin. Immunoglobulin may be preferred for infants <1 year of age who are household contacts of measles patients because it is likely that they will have been exposed more than 72 hours prior to measles diagnosis in the household member, and they are at highest risk of complications from the disease.

Measles cases at port of entry.

A number of issues have been raised regarding how to handle international passengers who are suspected of being infected with measles. Below are some guidelines which may be useful in approaching such situations.

Any traveller 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 spread 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 travellers arriving or visiting from other countries informing them of the measles eradication program, and requesting that they assist by seeking immediate medical attention if they experience any rash illness with fever.

4.7.5 Additional surveillance strategies

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

4.7.6 Outbreak monitoring

Information on suspected and confirmed measles cases, vaccination activities, and areas visited should be monitored and updated continuously during an outbreak. The Outbreak Summary form should be completed. When no new cases are reported during a 3 week period despite the presence of enhanced surveillance, the outbreak may be considered to be over.

4.7.7 Outbreak Summary

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

Sections in an outbreak summary report:

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

In order to benefit from the investigation and

outbreak control activities it is necessary to organize and report data related to the outbreak (see adjacent box).

4.8 Minimising nosocomial measles transmission⁶¹

It is vital to maximize awareness among health staff that a child with measles could enter any health facility at any time. Staff must assume that there exists a continual risk of nosocomial spread of measles to non-immune persons. There needs to be a constant state of preparedness to minimize the risk of nosocomial measles transmission.

The following recommendations are made to prevent measles transmission specifically in health facilities. General recommendations such as maintaining high measles coverage in the community and avoiding missed opportunities is discussed elsewhere in this document.

4.8.1 Ensure adequate measles immunization status among hospitalized patients

The immunization status of all hospitalized patients should be rigorously checked. A dose of measles vaccine be given to all *unimmunized* infants aged six months to nine years upon admission to hospital. In cases of outbreaks or where there is a lot of measles circulating in the community, this may be extended to *all* children, even if there is documented evidence of previous measles immunization, but the precise age range may be adjusted in light of local conditions.

In addition, to guarantee that no opportunities are missed, the immunization status of patients should be checked again before discharge. Immunization of those without documentation of previous measles immunization will reduce the chances of a child returning home while incubating a nosocomially-acquired measles infection. Failure to do this could result in the infection of children in the community with measles originating in the hospital.

Exposed non-immune contacts of hospitalized measles cases, such as patients sharing the same ward and visitors, aged six months to nine years, should receive one dose of measles vaccine, where possible, within 72 hours of exposure. Hyper-immune measles gamma globulin is less effective and much more costly than measles vaccine for use with non-immunocompromised patients.

4.8.2 Isolate fever and rash cases upon arrival

Cases of fever and rash should be considered as suspected measles until proven otherwise. To reduce the chance of exposure, cases of fever and rash presenting at a health facility should ideally not enter the common waiting areas. Where available, such cases should be fitted with a mask and taken directly to a different room reserved for diseases subject to respiratory isolation. Where possible, an area should be designated in the clinic to see all cases of rash illness.

If possible, waiting and treatment areas should be well-ventilated, and care should be taken to ensure that sick and well children do not subsequently share the same room or same staff for weighing, clinical examination, immunization or other consultation, since this would clearly defeat the purpose of their initial separation by allowing the possibility of measles transmission.

If it is not normally possible to provide a special waiting area because of lack of space, at least during a measles outbreak such an area should be created, and information disseminated that children with a rash illness should not wait in the common waiting area. Where female literacy is more common, a sign may be mounted outside the health facility instructing parents/guardians bringing a child with rash to wait outside and ask another person to inform the staff that the child has arrived.

4.8.3 Inform the hospital infection control authorities

Measles is a notifiable disease in South Africa. In addition, where appropriate,

nosocomially-acquired measles cases should be reported immediately to hospital infection control authorities for immediate investigation and response.

4.8.4 Ensure adequate measles immunization status among health facility staff

To prevent nosocomial spread of measles in the hospital setting, all staff should be immune. Any staff member who cannot provide documentary proof of measles immunization or adequate measles antibody titres at the time of employment should be considered for a dose of measles vaccine. Candidates should first be screened for contra-indications such as pregnancy and immune suppression.

4.8.5 Administer gamma globulin to immuno-compromised contacts of measles cases

Due to the risk of overwhelming viraemia, live virus vaccines such as measles vaccine are contra-indicated in individuals with congenital disorders of immune function or those receiving immuno-suppressive therapy. Hence, immuno-compromised contacts of measles cases should receive hyper-immune measles gamma globulin, as soon as possible after exposure. However, persons infected with the human immuno-deficiency virus (HIV) or with suspected or confirmed acquired immuno-deficiency syndrome (AIDS) may receive live measles vaccine.

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ANNEXURE A: MEASLES CASE INVESTIGATION FORM

ANNEXURE B: DISTRICT SUSPECTED MEASLES CASE LINE LISTING



INSTRUCTIONS: This form should be completed in full for each suspected measles cases. The minimal clinical criteria for suspected measles cases are: **FEVER AND BLOTCHY RED (MACULOPAPULAR) RASH AND ONE OF THE FOLLOWING: COUGH OR RUNNY NOSE (CORYZA) OR CONJUNCTIVITIS**

Official use only: **EPIDNUMBER:** _____ Received on ___/___/19___

IDENTIFICATION OF PATIENT

Surname of patient: _____

First names of patient: _____

Names of father/mother: _____

Sex Male Fem. Date of birth ___/___/19___ Age ___ months ___ yrs

Res. address / Contact information: _____ Clinic/Hospital name: _____

_____ Town: _____

_____ District: _____

_____ Province: _____

NOTIFICATION / INVESTIGATION / RESPONSE

Date district notified: ___/___/19___ Date case investigation ___/___/19___ Date of response

CLINICAL INFORMATION / ADMISSION TO HOSPITAL / COMPLICATIONS

Date of onset of rash ___/___/19___

Admitted to hospital? Yes No Unk If yes, date of admission: ___/___/19___

Name of hospital: _____ Hospital number: _____

Did patient die? Yes No Unk If yes, date of death: ___/___/19___

IMMUNISATION HISTORY

Number of documented doses of measles vaccine Date of last dose: ___/___/19___

LABORATORY DATA

	Date collected	Date sent to lab	Date received at lab	Date received at NIV
Serum sample for IgM				
Urine sample for virus isolation				

SEROLOGY RESULTS

	Results			Date of result
Measles IgM (indirect)	Positive	Negative	Indetermin.	
Rubella IgM (indirect)	Positive	Negative	Indetermin.	
Other				

Result of virus isolation: _____

POSSIBLE SOURCE OF INFECTION

Travel 7 -18 days prior to onset of	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk	Contact with lab confirmed cases	Yes	No	Unk
		Other measles cases in the area	Yes	No	Unk

FINAL DIAGNOSIS (MADE BY PROVINCIAL EPI COORDINATOR)

Date of final diagnosis ___/___/19___ Imported? Yes No Unk

CLASSIFICATION

DISCARDED		CONFIRMED	
Rubella positive		Laboratory confirmed	
Other _____		Epidemiolog. linked	
		Clinical confirmation	

INVESTIGATOR: Name _____ Tel: _____

Position and facility/district _____ Fax: _____



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