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**WHO Guidelines for Epidemic Preparedness and Response
to Measles Outbreaks**

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**World Health Organization
Communicable Disease Surveillance and Response**

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WHO Guidelines for Epidemic Preparedness and Response to Measles Outbreaks

These technical guidelines are part of a series developed by the Communicable Diseases Cluster (CDS) at the World Health Organization. The purpose of this series is to update current knowledge on diseases with epidemic potential, to help health officials detect and control outbreaks, and to strengthen the capacity for emergency response to an epidemic situation.

These guidelines have been prepared jointly with the Health Technology and Pharmaceuticals Cluster (HTP). The contribution of the Government of Ireland to the production of this document is gratefully acknowledged.

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EPIDEMIC PREPAREDNESS AND RESPONSE TO MEASLES

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PART ONE: THE ORGANISM AND THE DISEASE

1.1 The nature and magnitude of the problem

Measles ranks as one of the leading causes of childhood mortality in the world. Before measles vaccine became available, virtually all individuals contracted measles with an estimated 130 million cases each year. Humans are the only natural host. Measles is a highly communicable infection. Despite the remarkable progress made in measles control with the introduction of measles vaccination, it is estimated that in 1997 nearly one million deaths from measles still occurred, half of them in Africa. Outbreaks of measles continue to occur even in highly vaccinated populations.

1.2 The organism

Measles virus is a paramyxovirus of a single serological type, closely related to the viruses causing canine distemper and rinderpest in cattle. Virions consist of an inner nucleocapsid that is a coiled helix of three proteins (N, P, L) and RNA and an envelope containing three proteins (M, H, F). A haemagglutinin (H) protein mediates absorption of the virus to receptors on the host cell and a fusion (F) protein is responsible for the membrane fusion of virus and host cell and penetration of virus into the host cell.

1.3 The disease (pathogenesis and clinical problems)

The incubation period usually lasts 10 days (with a range from 7 to 18 days) from exposure to the onset of fever. The disease is characterised by prodromal fever, conjunctivitis, coryza, cough and the presence of Koplik spots (reddish spots with a white centre) on the buccal mucosa. A characteristic red rash appears on the third to seventh day beginning on the face, becoming generalised and lasting 4-7 days.

Clinical case definition:

Any person in whom a clinician suspects measles infection

OR

Any person with fever, and maculopapular rash (i.e. non-vesicular), and cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes)

Laboratory criteria for diagnosis*

At least a four-fold increase in antibody titre, or isolation of measles virus, or presence of measles-specific IgM antibodies.

** only recommended for countries in the measles elimination phase (see page 4)*

Measles case definitions also given in Annex 1

The rash is caused by an allergic response due to the union of sensitised lymphoid cells and measles antibody with the virus in the skin. A similar reaction occurs in the epithelium, leading to conjunctivitis, stomatitis, pneumonitis and acute inflammation of the gastro-intestinal tract. This allergic reaction clears the virus and is followed by a period of anergy during which many immune responses are greatly diminished. This immuno-suppression, which may last for many weeks, results in increased susceptibility to other infections such as those caused by pneumococcus.

The frequency of complications varies in different parts of the world. In industrialised countries, complications occur in around 10-15% of cases and include diarrhoea, otitis media, pneumonia, croup and, typically, encephalitis.

The frequency of complications in developing countries is less well known. At least three-quarters of cases in developing countries can be expected to have at least one complication and some have multiple systems involvement.

The three major causes contributing to the high case-fatality rate are pneumonia, diarrhoea and croup. Measles can also lead to life-long disabilities, including blindness, brain damage and deafness. Low vitamin A status has been associated with a higher rate of complications and a higher death rate, as it has similar pathological effects on epithelia and the immune system. Most measles deaths (98%) occur in developing countries, where vitamin A deficiency is common. The case fatality rates in developing countries are normally estimated to be 3-5%, but may reach 10-30% in some situations. This compares with 0.1% in many industrialised countries. Through synergy with measles infection, vitamin A deficiency contributes to the estimated 1 million childhood deaths from measles every year. Half of the childhood corneal blindness in developing countries is attributable to vitamin A deficiency, and half to measles infection.

1.4 Transmission and immunity

Transmission is airborne, by droplet spread or by direct contact with the nasal and throat secretions of infected persons. Measles is one of the most highly communicable diseases in man, with a basic reproductive rate of 17-20 (i.e., the introduction of one case of measles in a completely susceptible community generates 17-20 new cases).

The disease is communicable from slightly before the prodromal period to four days after the appearance of the rash. Natural infection produces a lifelong immunity. Measles vaccine induces long-term and probably lifelong immunity in most individuals; the vaccine virus has not been shown communicable.

1.5 Treatment

Under normal circumstances, uncomplicated measles only requires supportive therapy, with access to further care if complications develop. Case-fatality rates can be reduced by effective case management, including the use of vitamin A supplements.

See Annex 2 for Case management, complications and vitamin A

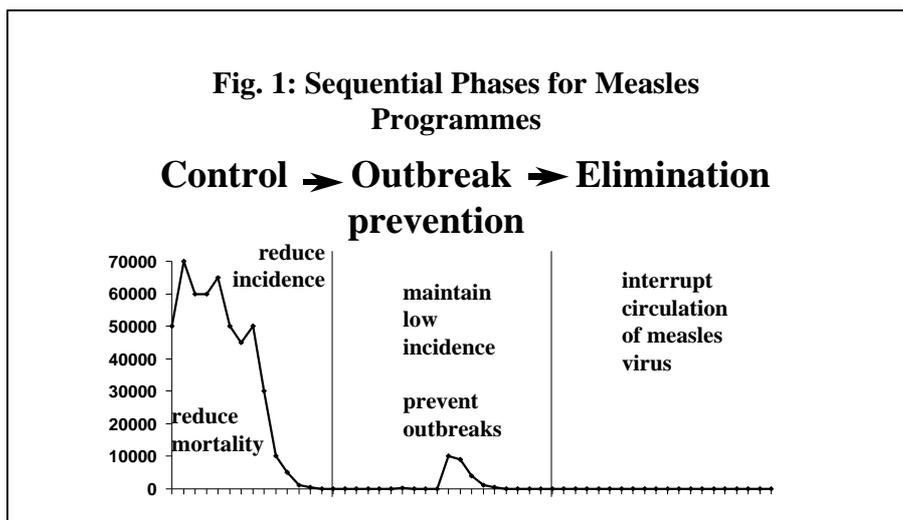
PART TWO: PREVENTION AND CONTROL

2.1 Phases of measles control

The introduction of measles vaccine into routine immunization programmes results in a marked reduction in incidence of the disease and its associated morbidity and mortality.

There are three sequential phases for measles immunization programmes (Fig. 1).

- measles control phase
- measles outbreak prevention phase
- measles elimination phase



2.2 Measles control phase

Measles control is defined as a significant reduction in measles incidence and mortality. When high levels of vaccine coverage are attained (i.e. vaccine coverage >80%), measles incidence decreases and the intervals between outbreaks are lengthened (e.g., 4-8 years) when compared to those observed during the pre-vaccine era (e.g., 2-4 years). As high levels of vaccine coverage are maintained, an increasing proportion of cases will occur among individuals in older age-groups. As vaccine coverage improves, the proportion of cases with a vaccination history increases.

See Annex 3 for List of vaccine suppliers to United Nations agencies

2.3 Outbreak prevention phase

Once measles have been drastically and persistently reduced through a sustained increase in immunization coverage, countries may wish to implement strategies aiming at the prevention of periodic measles outbreaks. These strategies include improved surveillance in order to understand the changing epidemiology of the disease (e.g., changes in the age distribution of cases, etc.) and in order to identify populations at higher risk.

It is possible to predict outbreaks and to prevent them by timely immunization of susceptible individuals in populations at higher risk and by improving overall levels of vaccine coverage in the population. If an outbreak is anticipated, supplementary immunization activities may be considered.

See Annex 4 for measles outbreak prevention strategies

2.4 Measles elimination phase

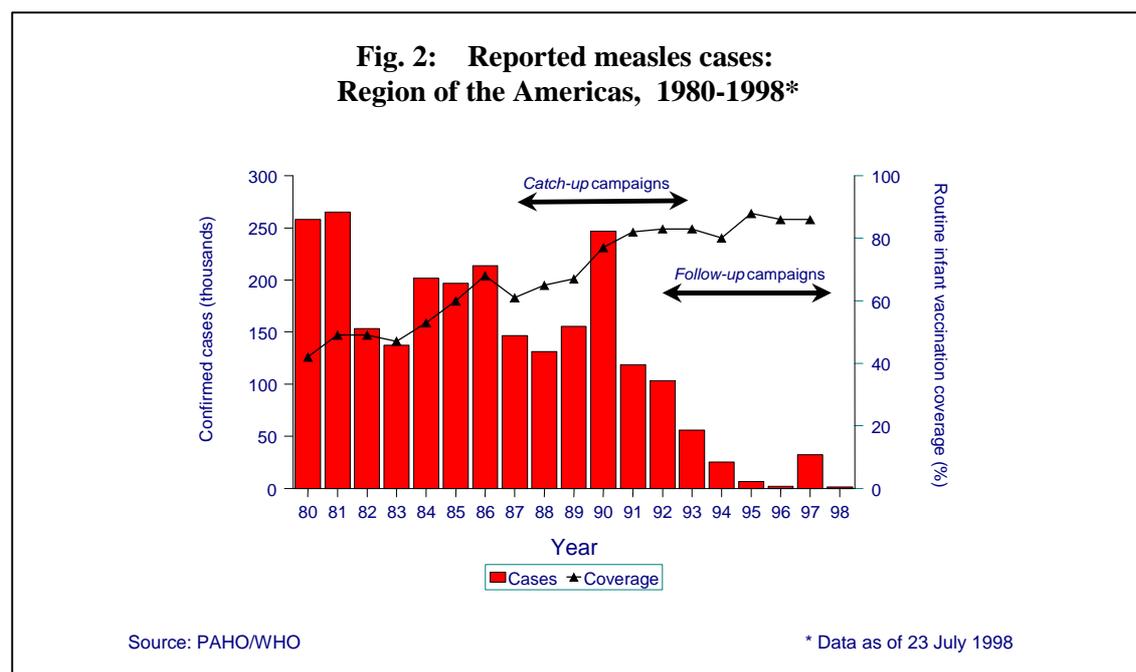
Both developing and industrialised nations have begun to implement innovative measles immunization and surveillance strategies in an effort to eliminate indigenous transmission of measles virus. The development of these strategies has been prompted by the persistence in these countries of low-level transmission and intermittent outbreaks, despite high coverage with either one-dose or two-dose immunization schedules.

A common principle to all measles strategies currently implemented is the need to maintain the number of susceptible individuals in the population below the critical number that is required to sustain transmission of the measles virus.

Measles strategies

- Drastically and speedily reduce the number of susceptible individuals in those age-groups where most susceptible individuals have accumulated and where the nature of contact among them facilitates virus transmission (*Catch-up*).
- Maintain the build-up of susceptible individuals at very low levels by immunising a large proportion (>95%) of each new birth cohort (*Keep-up* – as shown by the immunization coverage curve in Fig. 2).
- Implement additional vaccination activities to periodically protect susceptible individuals who have accumulated (*Follow-up*).

See Annex 5 for Measles elimination strategies



Because of the continued threat of virus re-introduction, vaccination will need to continue until measles eradication is achieved. Measles eradication is defined as the world-wide interruption of transmission of the virus, and represents the sum of successful elimination efforts in all countries and regions.

PART THREE: EPIDEMIC CONTROL

3.1 Management

The term “outbreak” is generally used when the number of cases observed is greater than the number normally expected in the same geographic area for the same period of time. The definition of an “outbreak” will vary according to the phase of measles control. For instance, a single case may mark an outbreak in a country aiming at elimination. The occurrence of a measles outbreak in a highly immunised population does not necessarily represent a failure of the routine immunization programme. Investigation of outbreaks provides an opportunity to identify high-risk groups, changes in measles epidemiology, weaknesses in the routine immunization programme or in the management of measles cases. When an outbreak occurs that has not been predicted, or could not be prevented, the response needs to be rapid, since measles is highly infectious and spreads rapidly.

See Annex 6 for surveillance and outbreak thresholds

3.2 Detection

Detection of an outbreak relies on the ability of the responsible authority to recognise an increase in measles cases significantly above the number normally expected. This recognition is simpler if a routine surveillance system collects either summary or case-based information on clinical and confirmed cases of measles. The availability of such data allows for the establishment of background activity levels and the establishment of a local outbreak (or epidemic) threshold. This threshold value is usually a number of cases in a defined period in excess of (a predetermined) expected number. The attainment of a threshold value should be considered as signalling an outbreak and should trigger specific responses.

In the absence of an effective surveillance system it may be difficult to detect small or limited outbreaks. However, large outbreaks may be detected by the existence of large numbers of cases, health clinic attendances, admissions to hospital, deaths or media reports. In all these situations it will be important to confirm the outbreak.

3.3 Confirmation

When an outbreak is suspected:

- A preliminary case investigation must be carried out to confirm the diagnosis, assess the extent of the outbreak and identify the population at risk. This is best done by health workers using a standard form, seeking details on cases (e.g. clinical syndrome and immunization status) and contacts.
- It is important that blood samples be collected from the initial 10 reported cases of an outbreak, to confirm or not whether measles virus is the cause of the outbreak.
- For countries in the measles elimination phase, laboratory investigation of all suspected measles cases is mandatory.
- Blood samples should be taken and sent to reference laboratories to allow measles virus isolation for genomic sequencing and mapping purposes. This information will be valuable in tracking measles virus circulation and establishing virus importation.

See Annex 7a for suspected measles case investigation form

See Annex 7b for Measles line listing form

See Annex 8 for Laboratory diagnostic methods

The collected data should be analysed locally and rapidly to determine the extent of the outbreak and consequently the population at risk. This can be done by creating a line listing of cases with key variables or, more efficiently by entering the data into a computer programme such as EPI-INFO.

Analysis should include the construction of an epidemic curve, graphing the age distribution of cases and spot-mapping the cases. Vaccine efficacy and the proportion of cases that could have been prevented through immunization should be calculated (age and immunization status of cases are essential elements). If population data are available, age-specific attack rates should be calculated. In addition, the investigation must document measures taken so far and any identifiable reasons for the outbreak.

See Annex 9 for information of data analysis and epidemiological calculations

3.4 Response

3.4.1 Planning a response

In case of a confirmed epidemic in a population, it is important to plan a systematic response based on the available data. **The immunization response in most outbreaks occurs too late to affect the impact of the outbreak¹.**

Outbreaks provide an opportunity to collect data, identify problems and adjust strategies accordingly. This is best done in consultation with other key players. The convening of a response team (e.g. epidemic committee, rapid epidemic response team) is essential to ensure quality decisions and co-ordination. The main areas to be dealt with by are:

- definition of and agreement on response
- management of response
- resources for response
- public information
- post-outbreak activities
- prediction of, and preparedness for, further outbreaks.

See Annex 10 for Epidemic response team - roles and responsibilities

3.4.2 Definition and agreement on response

The main activities during the response to an outbreak will depend on the phase of the immunization programme. The activities to be implemented as a priority during all measles outbreaks will be:

- to prevent measles complications and deaths through early and effective case management
- to review epidemiological data and immunization programme in order to identify the cause(s) of the outbreak
- to increase public awareness of measles infection, treatment and prevention through immunization
- to strengthen existing routine immunization programmes, with particular attention to the identification of high-risk areas.

See Annex 11 for Prediction of severe disease outbreaks
See Annex 2 for Case management, complications and vitamin A
See Annex 12 for Causes of measles outbreaks

In countries in the measles outbreak prevention phase and elimination phase, a further range of activities may be undertaken, such as:

- intensive measles surveillance (weekly reporting, including reporting that no cases have occurred – zero reporting) and investigation of all suspected cases
- accelerated immunization activities (i.e. improving coverage amongst high risk populations and supplementary immunization in areas not yet affected by the outbreak).

See Annex 6 for Surveillance and outbreak thresholds
See Annex 13 for Supplementary immunization strategies

**PRIORITY DURING OUTBREAKS IS TO PROVIDE APPROPRIATE TREATMENT AND
REDUCE MORTALITY**

In addition, collection of data on the epidemiology of the disease will help identify high risk populations, evaluate and modify current immunization strategies, and predict future outbreaks.

Supplementary immunization activities in the setting of an outbreak undertaken with the aim of interrupting transmission of the virus may not have a substantial impact on the course of the measles outbreak. Supplementary vaccination activities in the course of an outbreak are **not** recommended unless there is substantial political and or community pressure to undertake control measures. If implemented, supplementary vaccination activities should focus on unaffected areas where the epidemic is more likely to spread.

There is one exception to this recommendation. Outbreaks in closed communities or institutions such as refugee camps, hospitals and military barracks may necessitate immediate supplementary immunization activities under any circumstances. In refugee camps, vaccination of all children below five years of age is indicated as soon as they arrive to the camp. Delay in implementing this recommendation may result in high morbidity and mortality.

See Annex 14 for Measles in emergency situations

3.4.3 Management of response

Once a clear strategy has been defined, it is necessary to mobilise and manage the resources required for the response. It is best if an inventory of resources already exists as part of a preparedness plan. If not, such an inventory should be drawn up rapidly. These resources will need to be mobilised in a co-ordinated fashion.

See Annex 10 for resources for outbreak response

It is important to know the roles and responsibilities of national, regional and district levels during an epidemic. Relevant international and non-governmental organizations should be involved as early as possible.

Assigning responsibilities prior to an epidemic reduces the need to divert time and energy during the outbreak. An epidemic response team should co-ordinate epidemic preparedness and response activities at local health centres. It must function on a continuous basis, and meet periodically even when no epidemics are present.

When an epidemic is declared, the epidemic response team must convene more frequently on a regular basis to plan and review activities. These meetings should include a review of the most recent data, an agreement on control measures and the assignment of a person responsible for the implementation of each measure.

The response will need to be monitored regularly and must ultimately be subjected to formal evaluation after the outbreak.

3.4.4 Public information

When an outbreak is declared, there is likely to be widespread public concern and media attention. It is important to keep the public informed about the outbreak and the outbreak response.

Public information can be transmitted by a number of simple means, either directly to the community via schools or community meetings, or via the mass media such as radio, newspapers and television. Simple, clear public information material can help to:

- allay fears
- convey public health messages regarding appropriate treatment of cases and immunization.

It is important that such material:

- give information on the natural history of measles infection, the care of a child with measles and the signs and symptoms that should prompt a parent to seek expert advice
- encourage parents whose children have had a recent onset of rash and fever to notify health workers
- give clear information on the age for immunization and on the locations and time-schedule of any vaccination activities.

The media are useful partners in keeping the population informed. Regular press releases and conferences are essential in that they help the media play their role and help avoid “media hounding” of team members. A single spokesperson must be appointed and made known to the media. This person must receive clear instructions from the team and up-to-date information. The spokesperson can arrange for other team members to be interviewed as necessary.

If the media are to be enlisted in the delivering of health messages to the population, it is essential that these messages are reproduced as exactly as possible. It is not a good idea to rely on media for the interpretation of detailed health education material and for expert decisions on what to publish.

• Predicting further outbreaks

It is important to try and predict the onset of further outbreaks:

1. Imminent outbreaks among other populations

An early determination should be made as to whether an outbreak is localised or if disease is likely to spread to other areas. If disease is likely to spread, efforts to improve immunization coverage by routine or supplementary immunization may be advised in these areas.

2. Future outbreaks in the population currently experiencing an outbreak

Data collected on age-specific attack rates and vaccine coverage during the epidemic will assist in this type of prediction.

3.4.6 Post-outbreak activities

After an outbreak, the Epidemic Response Team must carry out a thorough evaluation of the following:

- cause of the epidemic
- surveillance of measles and detection of the outbreak
- preparedness for the epidemic
- management of the epidemic
- immunization programme goals and operations.

The findings of this evaluation should be documented in a written report containing clear recommendations regarding:

- epidemiological characteristics of the epidemic
- surveillance (assess the surveillance system, recommend actions to enhance measles surveillance in the affected areas)
- preparedness /recommend action to improve outbreak response)
- immunization activities and strategies to increase coverage and cover high-risk areas.

ANNEX 1: CASE DEFINITIONS FOR MEASLES

The recommended case definition depends on the phase of measles control a given country is undergoing.

Clinical case definition:

Any person in whom a clinician suspects measles infection

OR

Any person with fever, and maculopapular rash (i.e. non-vesicular), and cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes)

Laboratory criteria for diagnosis

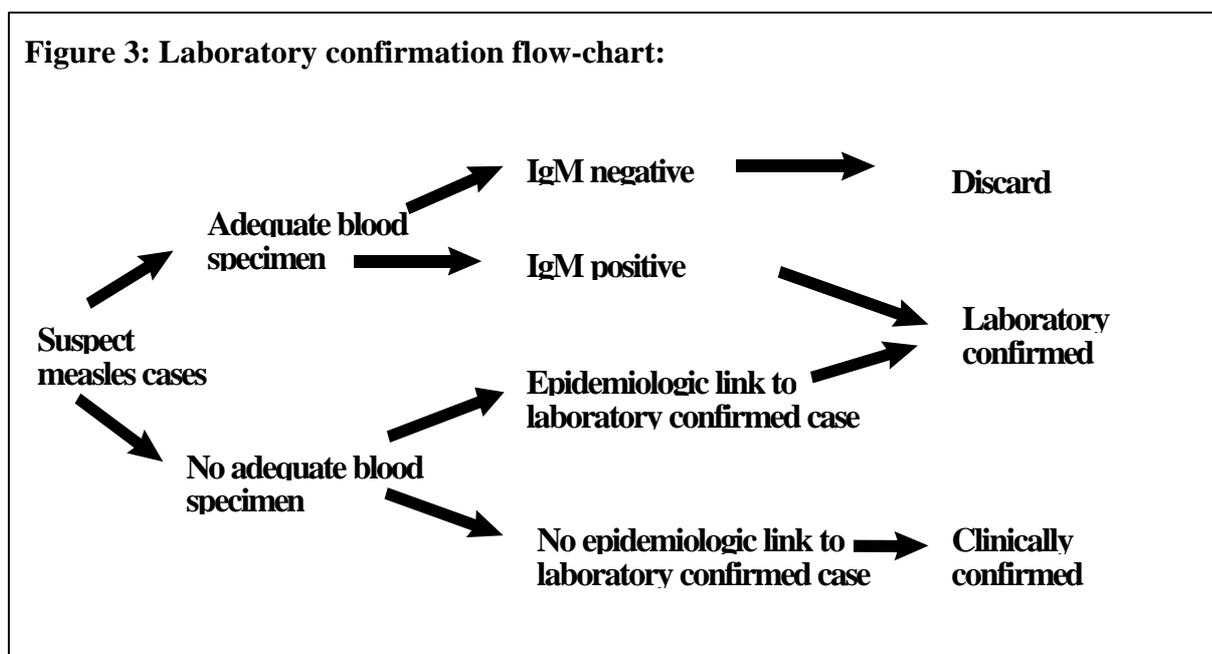
At least a four-fold increase in antibody titre, or isolation of measles virus, or presence of measles-specific IgM antibodies.

Case classification

Clinically confirmed: A case that meets the clinical case definition

Laboratory-confirmed (Only for outbreak confirmation and during the elimination phase): A case that meets the clinical case definition and that is laboratory-confirmed or linked epidemiologically to a laboratory-confirmed case. Epidemiological linkage is defined here as direct contact with another laboratory-confirmed measles case in which rash onset occurred 7-18 days before the present case.

See Annex 8 for Laboratory diagnostic methods



Clinically confirmed:

A suspected measles case that, for any reason, is not completely investigated is considered to be **clinically confirmed**. Since a health care worker suspected a measles virus infection and the possibility of measles virus infection could not be excluded, these cases cannot be discarded and are considered a failure of the surveillance system.

Possible reasons include:

- patient received only a clinical diagnosis from a health care worker without laboratory investigation, or
- patient cannot be located, or
- patient is lost to follow-up, or
- patient died before an investigation was completed.

In an elimination program, the goal of the measles surveillance system is to conduct a complete epidemiological investigation on **every** reported suspected measles case and to have as few **clinically confirmed** measles cases as possible. Of the total confirmed measles cases, at least 80% should show laboratory confirmation of measles infection.

Discarded case (not measles):

A **suspected** measles case that has been completely investigated, including the collection of an adequate blood specimen, and lacks serological evidence of measles virus infection can be classified as **discarded**.

ANNEX 2: CASE MANAGEMENT, COMPLICATIONS AND VITAMIN A

Case management guidelines

Significant morbidity and mortality are associated with measles, particularly during an outbreak. Proper case management must be encouraged and facilitated through the distribution of appropriate materials. Case management should address four points: diagnosis, clinical assessment, severity status, and treatment.

1. **Diagnosis:** use the standard measles case definition (see Annex 1).
2. **Clinical assessment:** initial assessment will normally be carried out in a health centre. Any child with a rash and fever, or suspected for other reasons of being a case of measles, should be kept away from other children, particularly the young. Children must be examined for the following signs and symptoms to ensure that those with severe complications are properly treated:

Ask if the child has had:

- an inappropriate change in the level of consciousness, feeding or drinking
- cough, convulsions, diarrhoea, ear pain
- discharge from eyes or loss of vision

Examine the child for:

- rapid pulse, wasting, sore red mouth
- dehydration (thirst, sunken eyes, skin pinch goes back slowly)
- pneumonia (rapid breathing, chest indrawing)
- ear infection (draining pus, red/immobile eardrum)
- eye disease (pus; corneal ulcer, perforation, clouding)

3. **Classification for management:** Since case management depends on the severity of disease, the degree of severity of the case must be stated:

- uncomplicated measles: a child with measles and none of the signs or symptoms of complicated disease
- complicated measles: a child with measles and at least one of the signs or symptoms of complicated disease as per following table.

Table 1: Complications of measles

Acute complications	Later complications
Diarrhoea	Increased susceptibility to other infections
Pneumonia	Blindness
Laryngo-tracheobronchitis	Subacute sclerosing panencephalitis (SSPE)
Otitis media	
Malnutrition	
Corneal ulceration and blindness (due to vitamin A deficiency)	
Stomatitis	
Acute encephalitis	

4. Case management

Case management of uncomplicated measles

Many children will experience uncomplicated measles and will require only supportive measures:

- give Vitamin A if in an area of known deficiency or high measles case fatality rates (see table 2 for dosage)
- advise mothers to treat the child at home as long as no complications develop
- provide nutritional support: continue breast feeding or give weaning foods and fluids at frequent intervals and treat mouth ulcers
- control fever by keeping the child cool
- instruct to return for further treatment if the child's general condition worsens or any of the danger signs develop
- explain to mothers that there is an increased risk of diarrhoea, acute respiratory infections and other infections in the weeks following measles and encourage them to seek medical advice early
- immunize close contacts, if they are identified within 72 hours of exposure.

Case management of complicated measles

Even in industrialized countries, around 10% of cases can be expected to develop complications of measles; in severe outbreaks in developed countries, this proportion will be higher and some children may have several complications.

In developing countries, at least three-quarters of cases in developing countries can be expected to have at least one complication and some may have multiple systems involvement.

Actions to be taken in cases of complication include:

- refer to health facility for further management
- follow the above recommendations for case management of uncomplicated measles

AND

- ensure that two doses of vitamin A are given
- clean eye lesions and treat with 1% tetracycline eye ointment three times a day for 7 days (for corneal lesions, cover the eye with a patch) - vitamin A administration is particularly important to minimize the risk of potentially blinding eye lesions: in this situation, use a third dose of vitamin A four weeks later using the same dosage and age as in table 2
- clean ear discharge and treat with antibiotics
- refer suspected encephalitis to hospital
- treat malnutrition and diarrhoea with sufficient fluids and a high quality diet
- treat pneumonia with antibiotics.

Table 2. Recommended Vitamin A Schedule for measles treatment

AGE	IMMEDIATELY ON DIAGNOSIS	NEXT DAY
Infants <6 months	50 000 IU	50 000 IU
Infants 6-11 months	100 000 IU	100 000 IU
Children 12 months plus	200 000 IU	200 000 IU

Vitamin A supplementation

In vitamin A deficiency areas, a measles outbreak may provide an important opportunity to administer vitamin A supplementation to all children whose age puts them at risk of measles, whether they have been immunized or not. Supplementary dosage is: infants 6-11 months 100 000 IU; children 12 months and over 200 000 IU.

ANNEX 3: MEASLES VACCINE SUPPLIERS TO UNITED NATIONS AGENCIES**(as of July 1998)**

Name	Address	Phone/fax number
<i>Pasteur-Mérieux Connaught</i>	1755 Steeles Avenue West North York, Ontario M2R 3T4 Canada	Tel: 1 416 667 2701 Fax: 1 416 667 2912
<i>Swiss Serum Institute</i>	P.O. Box 2707 3001 Bern, Switzerland	Tel: 41 31 980 6345 41 31 980 6111 fax: 41 31 980 6785
<i>P.T. BIOFARMA (PERSERO)</i>	28 J.L. Pasteur P.O. Box 1136 Bandung 40161, Indonesia	Tel: 62 22 233755 Fax: 62 22 2041306
<i>Chiron Vaccines</i>	Via Fiorentina, 1 53100, Siena, Italy	Tel: 39 577 243 209 Fax: 39 577 243 443
<i>Serum Institute of India, Limited</i>	212/2 Hadapsar Pune 411028, India	Tel: 91 212 672016 Fax: 91 212 672040
<i>MEDEVA Group Research</i>	Evans House Regents Park, Kingston Road Leatherhead, KT22 /PQ United Kingdom	Tel: 44 1372 364153 Fax: 44 1372 364163
<i>SmithKline Beecham Biologicals</i>	Rue de l'Institut 89 1330 Rixensart Belgium	Tel: 32 2 656 8606 Fax: 32 2 656 8149
<i>EISAI CO, Limited</i>	Department of Export and Asian Operations 610 Loishikawa 4 chome Bunkyo ku Tokyo 11280, Japan	Tel: 81 3 3817 3919 Fax: 81 3 3811 3574
<i>Pasteur-Mérieux Connaught</i>	Bactériologie, Recherche 69280 Marcy l'Etoile, France	Tel: 33 4 78873232 Fax: 33 4 78873081

ANNEX 4: STRATEGIES FOR THE PREVENTION OF OUTBREAKS

Outbreaks of measles can occur during any of the phases of a measles immunization programme, when there are enough susceptible individuals to sustain transmission. In populations with low vaccination coverage, epidemics occur regularly every two or three years. High vaccination coverage will result in lengthened inter-epidemic periods and the outbreaks may not be as prolonged or affect as many individuals. In areas with high vaccination coverage, a higher proportion of the cases may occur in older children and in previously vaccinated children.

Vaccination reduces the incidence of disease by providing immunity to susceptible children. Most, but not all, vaccinated children develop immunity to the disease; even with high vaccine coverage some children (vaccinated children who do not develop immunity and unvaccinated children) will remain *susceptible*. These susceptible individuals provide the potential for periodic outbreaks.

Outbreaks can occur when the accumulated number of susceptible individuals is greater than the critical number of susceptible individuals, or epidemic threshold, for a given population. Because the level of communicability of measles is high, the epidemic threshold is low.

Susceptible individuals tend to accumulate in pockets or clusters, particularly in communities that are hard-to-reach or do not wish to be vaccinated for religious or cultural reasons. Outbreaks may occur in these poorly immunised groups at any time if the disease is introduced and the number of susceptible individuals is greater than the epidemic threshold. Morbidity and mortality from such outbreaks can be particularly high if these groups also present underlying risk factors for severe disease, such as immune suppression, malnutrition and vitamin A deficiency.

Outbreaks can be predicted by monitoring the number of susceptible individuals accumulated and the changing epidemiology of the disease. Estimates of the current number of susceptible individuals can be based on:

- Vaccination
 - elapsed since the introduction of measles vaccine
 - measles vaccine coverage since the introduction of the vaccine
 - supplementary measures such as campaign
- Infection
 - age-specific incidence.

Prediction of outbreaks thus requires data on measles vaccination coverage, on past and current vaccination schedules, on the disease incidence and on the age distribution of the cases over a number of years, as well as demographic information (e.g. birth and mortality rates). When available, data from representative serological surveys constitute an additional tool to assist in the process of outbreak forecasting. However, serological surveys are not routinely recommended.

If an outbreak can be anticipated, preventive measures such as supplementary mass immunization may be undertaken to blunt or avert it. The future susceptibility profile can be estimated on the basis of current susceptibility patterns by age and cohorts and on coverage and vaccine efficiency data, provided there is no endemic transmission, no migration and that the vaccine and coverage data are reliable.

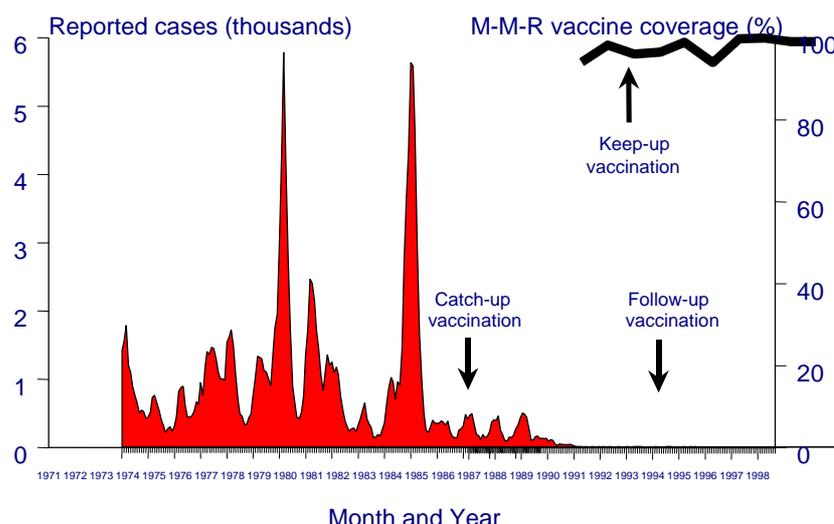
ANNEX 5: MEASLES ELIMINATION STRATEGIES

As more countries implement strategies for the prevention and elimination of outbreaks, experience will accumulate for the organization of mass campaigns, the selection of target populations and the establishment of adequate surveillance. A field guide is in preparation to assist countries in their efforts to control or eliminate the disease.

The following four supplemental strategies should be considered:

1. Conduct a one-time (“catch-up”) mass immunization campaign for the age-group where most susceptible individuals have accumulated. This should effectively reduce the number of susceptible individuals – especially in those age-groups that have an important role in measles transmission because of the number of susceptible individuals accumulated and the nature of contacts among them – and will help reduce circulation of the virus.
2. Sustain high routine measles (“keep-up”) coverage (>90% in each infant cohort) to reduce the speed at which new individuals enter the susceptible population, and the number of cases
3. Subsequently, conduct periodic (“follow-up”) mass campaigns for a limited age-group (e.g., those born after the initial campaign) in order to maintain the number of susceptible individuals at very low levels*. These campaigns may be required every few (possibly five) years to eliminate susceptible individuals from subsequent birth cohorts. An alternative strategy is the introduction of a second dose of measles vaccine. However, this strategy is **ONLY** recommended when coverage with the second dose is likely to be greater than that achieved with the first dose.
4. Monitor the epidemiology of the disease by implementing a sensitive surveillance system including laboratory investigation of all suspected cases to detect high risk areas and continued virus circulation or importation, so that rapid action (e.g., supplemental immunization) can be implemented.

**Fig 1 Reported measles cases by month
Cuba 1971-1998**



Source: Cuban Ministry of Health
Data as of 1 Oct 1998



*In countries with highly developed immunization programmes capable of reaching extremely high coverage (>95%) in all geopolitical units (i.e districts, blocks etc.) on a routine basis and with active follow-up of defaulters, the introduction of a “two-dose plus” strategy can eventually achieve national elimination. It is essential to reach all children with measles vaccine and the “second dose” should provide an opportunity to reach those who missed the first dose; such children should be vaccinated and subsequently receive a second dose.

ANNEX 6 SURVEILLANCE AND OUTBREAK THRESHOLDS

Surveillance is essential for any disease control initiative. Reporting of measles cases should be a component of all routine infectious disease surveillance systems. The document *Using surveillance data and outbreak investigations to strengthen measles immunization programmes*² contains detailed guidelines on the objectives, data analysis and actions of measles surveillance for each phase.

ROUTINE SURVEILLANCE

An adequate measles control programme includes surveillance activities aimed at monitoring susceptible individuals as well as the disease.

Briefly, routine surveillance requires:

- a network of motivated individuals
- a simple, well publicised case definition
- a simple reporting system
- a clear path for upwards transmission of data (either case-based or summary)
- data on population
- regular analysis of the data with downwards feed-back
- performance indicators to monitor the quality of surveillance

The minimum requirement of measles surveillance depend on the phase and goal of the measles immunization programme:

Control phase

- coverage data from each district, on quarterly or semi-annual basis
- age groups and immunization status of reported cases, by district (at least once a month)
- notified measles cases, by month and by district
- interval between measles outbreaks
- number and location of reporting units, with monthly analysis on completeness and timeliness of reports.

Adequate routine reporting allows the analysis of trends in measles incidence and the early detection of any outbreak.

Outbreak prevention phase

- immunization coverage data from each district, on a quarterly or semi-annual basis
- identification of high risk populations (low coverage, poor health care, overcrowding)
- age-groups and immunization status of reported cases, by district (at least monthly)
- notified measles cases, by month and by district
- the intervals between measles outbreaks and the accumulation of susceptible individuals should be monitored to assist in the prediction of outbreaks
- number and location of reporting units, with a monthly analysis on completeness and timeliness of reports
- laboratory investigation of the initial 10 measles cases during a measles outbreak.

During outbreaks, the routine surveillance system can provide key data that will aid in decision-making regarding the causes of the outbreak and the possible response.

Elimination phase

In addition to the elements described in the previous phases, countries with a goal of measles elimination need to carry out more intensive surveillance including:

- adoption of a laboratory confirmed case definition and introduction of laboratory confirmation of probable measles cases
- immediate investigation and laboratory confirmation of any suspected measles case, including data required to establish if the case fulfils the case, data on source of infection, and final outcome of the case
- a line-listing of all measles cases including basic information required to monitor the performance of the surveillance system
- zero weekly reporting (i.e., a report even if no cases have been observed) from all reporting units.

Active case-finding is important, particularly in high-risk areas which have failed consistently to report cases or to provide weekly zero-reports.

STRATEGIES FOR THE INVESTIGATION OF MEASLES OUTBREAKS

The investigation strategies vary according to the different measles phases. In all phases, data collection and analysis should lead to a deeper understanding of why the outbreak occurred, the characteristics of the population affected, and the remedial action required to improve the routine immunization services.

- **Control phase**

- Age of cases
- Immunization status
- Location
- Number of deaths (case-fatality rates)

Data may be obtained through record reviews at hospitals and other health facilities.

- **Outbreak prevention goal**

- Name, address, age, sex
- Date of onset of rash
- Possible source of infection
- Basic clinical information (presence or absence of fever, rash, coryza, cough or conjunctivitis)
- Immunization status age at immunization,
- Outcome (dead or alive)
- Diagnosis (suspected, confirmed or discarded case)

A blood sample should be collected from the initial 10 cases to confirm that the outbreak is due to measles.

- **Elimination phase**

During the elimination phase, a single confirmed case constitutes an outbreak. Case investigation and data collection should be conducted following the guidelines for surveillance during the elimination phase. Laboratory investigation of all suspected measles cases is recommended.

See Annex 10 for data analysis and epidemiological calculations

OUTBREAK THRESHOLDS

Until measles has been eliminated from an area, measles virus transmission will occur to a greater or lesser extent. Factors which determine whether or not cases occur include season, population density and immunization coverage.

Generally, the term "outbreak" is used when the number of cases observed is greater than the number normally expected in the same geographic area for the same period of time. The definition of an "outbreak" will vary according to the phase of measles control. For instance, a single confirmed case signifies an outbreak in a country aiming at elimination.

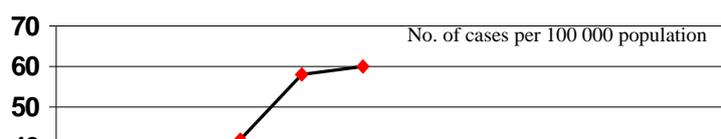
The following are required to predict and detect outbreaks:

- a surveillance system that is sensitive enough to detect an increase in cases,
- measles vaccine coverage data (ideally, since measles vaccine introduction)
- a standard method for determining whether the number of reported cases is higher than expected (a *threshold* for either the number of cases or the *reported incidence rate – the number of reported cases relative to the population* – must be established)
- a determination of whether the increase in reported cases is real or an artefact (an increase in cases may be due to improved surveillance, rather than a real increase in disease occurrence).

The outbreak threshold is a pre-determined number of reported measles cases or a reported incidence rate above which the situation is defined as an outbreak. The specific threshold must be developed on the basis of local epidemiology and of immunization programme objectives. The outbreak threshold may and should change as the incidence of measles and the programme objectives change. Two methods can be used for setting the threshold

- **using local epidemiology to set up thresholds:** a review of case reports from previous years (preferably at least 5 years excluding epidemic years) should be used to set up the threshold. The average number of cases or the average incidence rate, for a defined geographical area during a determined period of time in non-epidemic years can be taken as the threshold above which one should be alerted to the possibility of an outbreak (see Fig. 5).
- **using immunization programme objectives to set thresholds:** in areas where a vigorous measles control programme is in place and high immunization coverage has been achieved, a threshold that is lower than one based solely on previous experience is appropriate. This will quickly focus attention on identifying and correcting problems within the routine programme. For instance, the Region of the Americas has chosen to define an outbreak as three or more cases present in a defined geographical area within a one month period.

Fig. 1 Monthly measles incidence in Federal District of Brasilia, January-June 1983. Maximum expected monthly incidence and average monthly incidence, 1976-1982



If the surveillance system is upgraded, reports may suggest an increased incidence, whereas in reality they simply reflect improved reporting. In such cases, it may be necessary to set a new threshold.

It is important that outbreak thresholds be realistic, particularly where there are large populations in health districts or areas where the disease is endemic. If an outbreak threshold is set too low, valuable resources may be diverted from routine services by triggering a response too often.

ANNEX 7a: SUSPECTED MEASLES CASE INVESTIGATION FORM

1. IDENTIFICATION						
Case No. _____ PROVINCE/REGION _____ DISTRICT/TOWNSHIP _____	URBAN ? RURAL ?					
ADDRESS _____						
NAME _____ SEX M ? F ? MOTHER'S NAME _____						
DATE OF BIRTH: ___/___/___/___/___/___ NO. CERTIF.DOSES ___/___ DATE LAST DOSE ___/___/___ DAY MONTH YEAR						
AGE IN YEARS _____ MONTHS _____ (if date of birth not known)						
2. POSSIBLE SOURCES OF INFECTION						
	YES NO ? COMMENTS					
TRIP WITHIN 21 DAYS PRECEDING ERUPTION CONTACT WITH ANOTHER CONFIRMED CASE IN THE 7 TO 18 PRECEDING DAYS	? ? ? WHERE ? _____					
WAS THERE ANOTHER CASE OF MEASLES IN THE AREA BEFORE THIS ONE	? ? ? WHO AND WHERE ? _____ ? ? ? WHO ? _____					
3. CLINICAL DATA						
RASH Yes ?	DATE OF ONSET OF RASH ___/___/___					
FEVER Yes ?	DATE OF ONSET OF FEVER ___/___/___					
COUGH Yes ? No ?	CORYZA (runny nose) Yes ? No ? CONJUNCTIVITIS (red eyes) Yes ? No ?					
4. LABORATORY DATA						
SAMPLE	DATE TAKEN	RECEIVED LABORATORY	TYPE OF TEST*	DATE OF RESULTS	RESULTS POSITIVE	NEGATIVE
SERUM	___/___/___	___/___/___	_____	___/___/___	?	?
SERUM	___/___/___	___/___/___	_____	___/___/___	?	?
COMMENTS _____						
*IgM Measles, HI Measles, IgM Rubella						
5. FINAL CLASSIFICATION		DATE OF FINAL DIAGNOSIS ___/___/___				
CONFIRMED ? LABORATORY		DISCARDED ? RUBELLA				
? EPIDEMIOLOGICAL LINK		(FINAL DIAG.) ? CHICKENPOX				
? CLINICAL CASE		? DENGUE				
_____		? OTHER (SPECIFY)				
FIELD INVESTIGATOR NAME _____ POSITION _____ SIGNATURE _____						

INSTRUCTIONS FOR COMPLETING THE MEASLES SUSPECTED CASE INVESTIGATION FORM

OUTBREAK PREVENTION PHASE

All suspected cases should be recorded, investigated, and documented. Each line or box of the form should be completed even if the information is not known.

DEFINITION OF SUSPECTED CASE OF MEASLES (CLINICAL CASE):

A person in whom a health professional suspects measles

OR

A person with:

- Fever **and** maculo-papular rash (non-vesicular) **and**
- at least one of the following:
 - cough
 - coryza (runny nose)
 - conjunctivitis (red eyes)

No. 1. IDENTIFICATION

CASE NUMBER: Each health service should list the cases by chronological order of notification and report them to the next level immediately.

ADDRESS: write down the address in detail to facilitate location of the case.

NAME, SEX, MOTHER'S NAME, DATE OF BIRTH or AGE: self-explanatory.

NUMBER OF DOSES: check the vaccination card for the number of doses received and the date on which the last dose of measles vaccine was administered; note the date.

No. 2. POSSIBLE SOURCES OF INFECTION

Investigate with relatives whether the case left the locality and where he or she went, if he or she had contact with a confirmed case in the 7 to 18 preceding days, and if there was another similar case in the community in the 18 days prior to the appearance of the rash.

No. 3. CLINICAL DATA

DATE THAT THE FEVER AND RASH BEGAN: investigate the day the fever began and the day the rash began. Mark in the corresponding box whether the case does or does not meet the criteria for defining a suspected case.

No. 4. LABORATORY DATA

The investigator shall be responsible for collecting one sample of serum (5 cc), immediately upon learning of the case (from initial 10 cases during outbreaks and from all suspected cases in the measles elimination phase).

No. 5. FINAL CLASSIFICATION

The case should be monitored until a final diagnosis that classifies it as confirmed, or discarded, based on the information in the data sheet; the appropriate box should be marked.

No. 6. FIELD INVESTIGATOR

The person responsible for the investigation shall write his or her name and position, sign the form, keep a copy and send the original to the next level.

ANNEX 8 LABORATORY DIAGNOSTIC METHODS³⁻⁶

Laboratory confirmation of measles cases is recommended in the following situations:

- during **outbreaks**, in countries in outbreak prevention or elimination phase: a blood sample, from the initial 3-4 cases, to confirm that measles virus is indeed the cause of the epidemic.
- in countries with measles elimination goals: to **investigate every reported measles case**.
- in all countries: samples from all outbreaks should be collected and sent to reference laboratories in order to **initiate genomic sequencing and genetic epidemiological analysis of measles virus** strains. Decision to collect samples for virus isolation should be made in coordination with the epidemiologist and the laboratory. Co-ordination of number of specimens and timing of collection is especially important for virus isolation to ensure at least 2 virus isolates.

Collection, storage and shipment of specimens for measles diagnosis

1 Specimen collection: (Table 1).

Table 1: Samples for measles serology and measles virus isolation, according to different phases of measles control and elimination⁸.				
<i>Phase</i>	<i>Situation</i>	BLOOD (SEROLOGY)	VIRUS ISOLATION	<i>Remarks</i>
Control	Isolated case	NO	NO	Clinical confirmation of cases is recommended
	Outbreak	YES* Initial 10 cases to confirm outbreak and suspected spread	YES* Approximately 10 specimens	Isolates for genetic characterization and strain banking.
Outbreak Prevention	Isolated case	NO	NO	Clinical confirmation of cases advisable
	Outbreak	YES* Initial 10 cases to confirm outbreak and suspected spread	YES* Approximately 10 specimens	Isolates for genetic characterization and strain banking
Elimination	Isolated case	YES all suspected measles cases	YES* From suspected measles cases	Monitor lack of indigenous transmission of measles virus
	Outbreak	YES, from all suspected cases; during elimination phase one case constitutes an outbreak	YES* Initially 10 specimens; More may be collected from new districts or atypical cases	To investigate measles virus transmission pathways and evaluate the programme

* in coordination between the epidemiologist and the laboratory

1.1 Single blood specimens for IgM serology

Timing

The correct timing of specimens with respect to the clinical signs is important for interpreting results and arriving at an accurate conclusion. While IgM ELISA tests are more sensitive between day 3 and 28 after rash onset, *a single serum obtained at the first contact with the health care system, regardless of which day following the rash onset it is, is considered adequate for measles surveillance.*

Collection procedures:

- Collect 5 ml blood by venepuncture into a sterile tube labelled with patient identification and collection date
- Whole blood should be centrifuged at 1000xg for 10 minutes to separate the serum
- Blood can be stored at 4-8⁰C for up to 24 hours before the serum is separated
- **Do not freeze whole blood**
- If there is no centrifuge, blood should be kept at room temperature (4-30⁰C) until there is complete retraction of the clot from the serum
- Carefully remove the serum, avoiding extracting red cells, and transfer aseptically to a sterile labelled vial
- Store serum at 4-8⁰C until it is ready for shipment. The serum can be stored in refrigeration for a maximum period of 7 days. Serum must be frozen at -20⁰C if it is going to be stored for longer periods
- Fill in case investigation forms completely (Annex 8). Three dates are very important:
 - ⇒ Date of last measles vaccination
 - ⇒ Date of rash onset
 - ⇒ Date of collection of sample.

1.2. Second blood samples

A second sample may occasionally be required under the following circumstances:

- the first sample submitted for IgM was collected within 3 days of rash onset and is negative on ELISA. The laboratory may request a second sample for repeat IgM testing, given the probability of false negatives in early samples
- the measles IgM capture ELISA gives an equivocal result
- the clinician needs to make a definitive diagnosis on an individual patient with an initial negative result.

Timing

A second sample for IgM testing may be collected anytime between 3 and 28 days after rash onset. Collection of a second sample 10 - 20 days after the first will permit the laboratory to test for an increase in IgG antibody level, as well as re-testing for IgM. However, this is not recommended on a regular basis since additional information obtained will be limited.

1.3 Urine for virus isolation

Ten to fifty millilitre samples are adequate, collected within 7 days of rash onset. Early morning specimens are preferable. Urine samples are the most convenient specimen to collect in field conditions.

Collection procedures

- Urine must be collected into a sterile container
- The sample must be placed at 4 -8°C prior to centrifugation
- Centrifugation must be done within a few hours

1.4 Nasopharyngeal specimens for virus isolation

Nasopharyngeal specimens for virus isolation:

- must be collected as soon as possible after onset and not longer than 7 days after the appearance of the rash, when the virus is present in high concentration.
- must be placed in viral transport medium
- must be refrigerated (4-8°C) and transported to the laboratory within 48 hours.

Collection procedures

Nasopharyngeal specimens can be taken as follows, in order of higher yield of virus:

- **aspiration:** nasal aspirates collected by introducing a few millilitres of sterile saline into the nose with a syringe fitted with fine rubber tubing and collecting the fluid into a screw-capped centrifuge tube containing viral transport medium
- **lavage:** throat washes obtained by gargling with a small volume of sterile saline and collecting the fluid into viral transport medium.
- **swabbing:** nasopharyngeal swabs obtained by firmly rubbing the nasopharyngeal passage and throat with sterile cotton swabs to dislodge epithelial cells. The swabs are then placed in sterile viral transport medium (or Gelatron isotonic saline solution) in labelled screw capped tubes, refrigerated and transported to the laboratory on wet ice (4 - 8°C) within 48 hours.

1.5 Lymphocytes for virus isolation

Measles virus is present in peripheral blood lymphocytes in the early stages of the disease, especially within the first 72 hours.

Collection procedure

A five to ten ml volume of blood is drawn by venepuncture into a heparinized tube which is immediately and gently inverted several times to prevent clotting. Heparinized blood must be transported immediately to the laboratory at 4-8°C for lymphocyte separation and culture.

The laboratory and the epidemiologists must agree in advance on the number, type and locations most appropriate for the collection of samples for virus isolation. Ideally, samples for virus isolation should be collected simultaneously with the blood samples for serological diagnosis and confirmation of measles virus as the cause of the outbreak. Each type of sample has different requirements, and decisions on types of samples will depend on the local resources and facilities for transport and storage. Because virus isolation is more likely when specimens are collected within 3 days of rash onset, collection of specimens for virus isolation should not be delayed until laboratory confirmation has been obtained.

2. Specimen storage and transport

2.1 Blood for antibody detection

Storage of specimens outside the laboratory:

- whole blood may be held at refrigerator temperatures (4 - 8°C) if it can be transported to arrive at the testing laboratory within 24 hours.
- if this is not possible, the tube must be centrifuged to separate the serum, which is transferred to a sterile, labelled screw-capped tube for transport to the laboratory.
- sterile serum must be shipped on wet ice within 48 hours, or stored at 4-8°C for a maximum period of 7 days
- for longer periods, sera must be frozen at -20°C and transported to the testing laboratory on frozen ice packs. Repeated freezing and thawing can have detrimental effects on the stability of IgM antibodies.

Shipment of Specimens:

- specimens must 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.
- 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.

Storage of specimens in the laboratory:

At the testing laboratories, sera must be stored frozen at -20°C.

2.2 Nasopharyngeal specimens

- these must be transported in viral transport medium* and shipped on wet ice (4 to 8°C) to arrive at the testing laboratory within 48 hours.
- if arrangements cannot be made for rapid shipment, swabs must be shaken in the medium to elute the cells, and then removed.
- the medium or nasal aspirate is then centrifuged at 2500xg for 15 minutes at 4°C and the resulting pellet resuspended in cell culture medium.
- the suspended pellet and the supernatant are stored separately at -70°C and shipped to the testing laboratory on dry ice (-70°C)

*If viral transport medium is not available, Gelatron isotonic saline solution, tissue culture medium or phosphate buffered saline may be used.

2.3 Urine samples

- Whole urine samples may be shipped in well-sealed containers at 4°C but centrifugation within 24 hours after collection is preferable.
- Centrifugation must be done at 2500xg for 15 minutes at 4°C
- The supernatant must be discarded and the sediment resuspended in 1 millilitre of viral transport medium or tissue culture medium
- The resuspended pellet may be stored at 4°C and shipped within 48 hours or it may be frozen at -70°C in freezing medium and shipped on dry ice (-70°C) to the appropriate measles laboratory.

3 Specimen referral data

A case investigation form must be completed for each suspected measles case investigated. A separate laboratory request form must be completed at the time of specimen collection and accompany all specimens sent to the laboratory. The laboratory request form should include the following data:

- patient identification data (unique IDCODE, name, place of residence, age)
- basic clinical information (date of onset of rash, does the patient fulfil the case definition)
- immunization history (number of doses of measles containing vaccine, date of last dose)
- date of collection and type of specimen (date sent to the lab, date of arrival, date of results).

ANNEX 9: DATA ANALYSIS AND EPIDEMIOLOGICAL CALCULATIONS

During an epidemic, collected data should be analysed rapidly and locally to determine the extent of the outbreak, the impact of actions taken to date and problems with the routine immunization system. Any delay in reporting should be investigated.

Analysis of data will help:

Confirm the measles outbreak:

Is the number of reported greater than the number expected for this period? (e.g. threshold)

What proportion of cases fulfil the case definition?

Define the extent of the outbreak (time, place, person):

Time What are the dates of onset of cases ? (e.g. epidemic curve)

Place Where do cases live ? (e.g. spot map)

Person Who are they ? (e.g. tables of age, immunization status)

Measure the severity of the outbreak

How many confirmed cases were hospitalised ?

How many confirmed cases suffered complications ?

How many confirmed cases died as a proportion of all cases ? (case fatality rate)

Measure the effectiveness of vaccination

How many confirmed cases occurred in vaccinated individuals?

How many confirmed cases occurred in unvaccinated individuals?

How effective was the vaccine at preventing infection (vaccine efficacy)?

How many cases could have been prevented by the immunization programme?

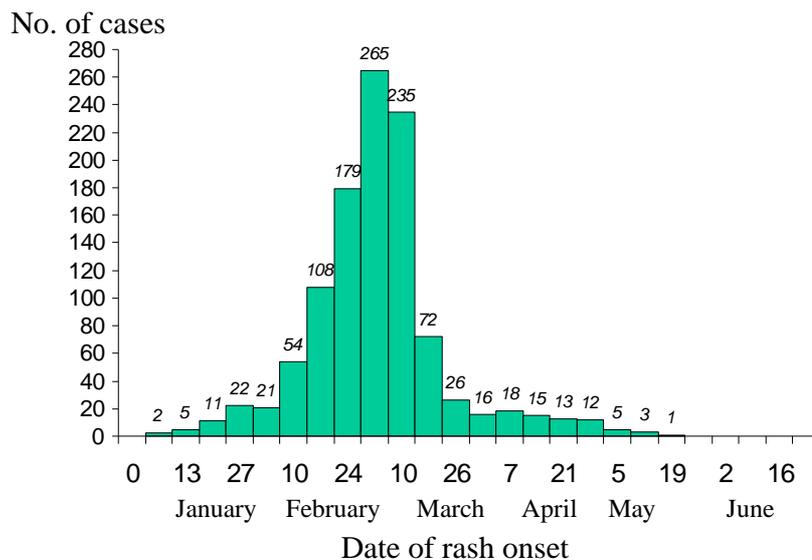
Basic analysis should include construction of an epidemic curve, graphing of the age distribution of cases⁴, and spot mapping of cases. Vaccine efficacy and the proportion of cases that were vaccine-preventable should be calculated. If population data are available, calculate age-specific attack rates.

Epidemic curve: a graph showing cases by date of onset or by date of report helps to demonstrate where and how an outbreak began, how quickly the disease is spreading, the stage of the outbreak (start, middle or ending phase), and whether control efforts are having an impact (Fig. 1)

Graph or table of age distribution and immunization status of cases: this should be constructed from the line listing of cases. This information is used for identifying the most affected age-groups and those cases which were not preventable (those developing measles before the scheduled age of immunization – see Fig. 2).

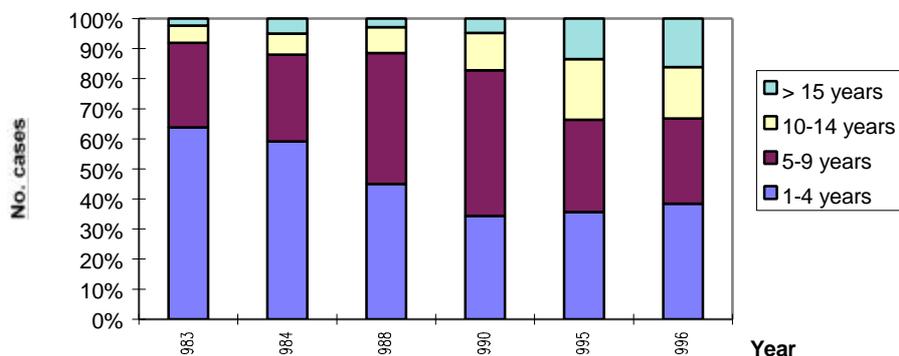
Estimation of vaccine efficacy: Using immunization history data one can tabulate those immunized but not protected (vaccine failures), and those who were not immunized.

Fig. 1: Reported cases of measles by date of rash onset, Kerman, Iran, January-June 1990



Source: Country Report to WHO

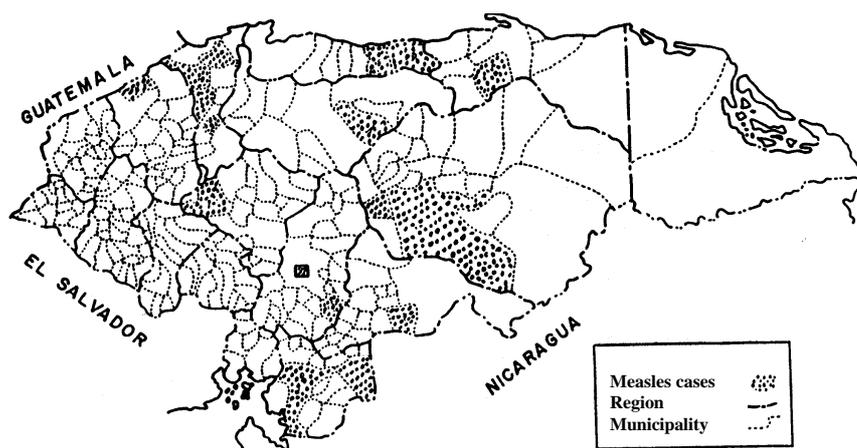
Fig. 2: Age distribution of reported measles cases Thailand, 1983-96



Source: Country Report to WHO

Spot map of confirmed cases: a map of the area of the epidemic should be marked with the location of all confirmed cases. Investigators can use this “spot map” to identify areas with clusters of disease. Further investigation of these areas may reveal weaknesses in the local immunization programme (Fig. 3).

Fig. 3: Confirmed measles cases by municipality during an outbreak, Honduras 1991



Source: Country report to PAHO/WHO

Map of incidence rates: at a national level, it may be helpful to map measles incidence per 100 000 population by district. Where surveillance is weak, however, it must be realised that variation in measles incidence rates may reflect variations in reporting reliability.

Age-specific Attack Rate (AR): If population data are available for the area of the outbreak, age-specific attack rates can also be calculated, for instance:

$$AR_{0-11 \text{ months}} = \frac{\text{number of cases in children age 0 to 11 months}}{\text{total number of children aged 0 to 11 months}}$$

Attack rates may also be calculated for other age groups. The denominator can be further refined to include only the population at risk (excluding those already vaccinated or who have suffered measles previously). This may give a more accurate attack rate among the susceptible population. The population included in the denominator should always be clearly stated (Table 1).

Case-fatality Rate (CFR)*: based on the case investigations and the total number of confirmed cases, this rate can be calculated as:

$$CFR = \text{number of patients who died of measles} / \text{total number of cases of measles}$$

CFRs should be estimated by age-group if possible.

* A further discussion on case-fatality rates can be found in WHO/EPI/GEN/93.3, *Generic protocol for estimating measles case-fatality rates in a community, either during an epidemic or in a highly endemic area*, available from WHO/EPI, Geneva.

**Table 1. Age-specific attack rates in a measles outbreak in
Utar Pradesh, India 1986**

Age	Population Surveyed	Reported Measles		Attack Rate %
		Number	%	
<5 months	29	4	0.5	13
6-8 months	19	4	0.5	21
9-11 months	10	5	0.6	50
1-4 years	512	279	36.2	54
5-9 years	628	290	37.6	46
10-14 years	447	158	20.5	45
15+ years	2 896	31	4.0	1
TOTAL	4 542	771	100	17

Source: Country Report to WHO

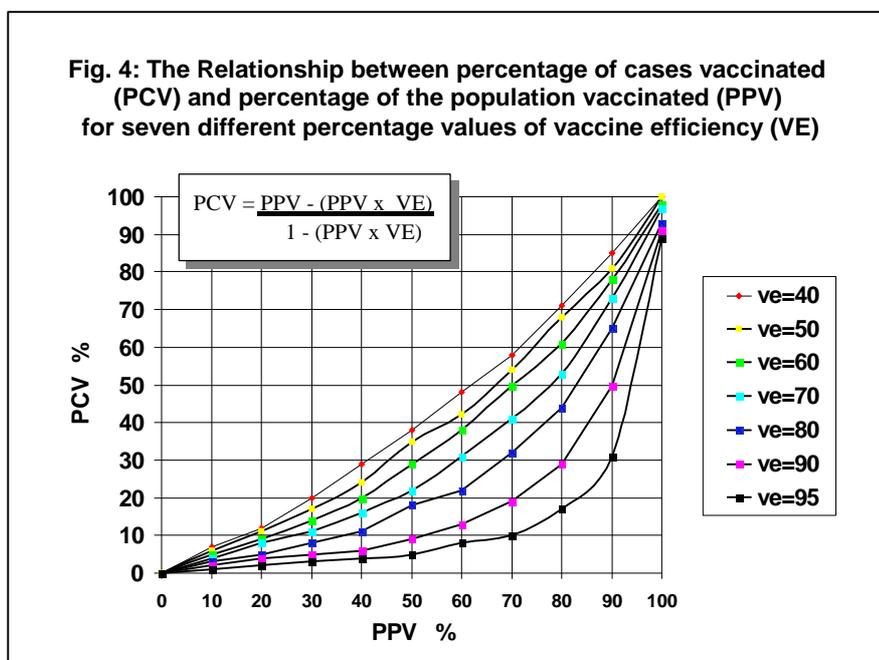
Vaccine efficacy (VE): can be estimated from the data collected during an outbreak investigation and from routine coverage data.⁵ The coverage must be known or estimated for the age group in which cases are occurring (Fig. 5).

This method is based on the difference between the attack rates among vaccinated persons (ARV) and those among the unvaccinated (ARU), expressed as a fraction of the attack rate among unvaccinated persons (ARU): The greater the proportional reduction of illness in the vaccinated group, the greater the vaccine efficacy.

$$VE = (ARU - ARV) / ARU$$

Vaccine efficacy can also be estimated by plotting the percentages of measles cases in vaccinated individuals (PPV) and the percentage of the population vaccinated (PCV%) on a nomograph which shows the relationship between PPV, PCV and VE (Fig. 4)*. For instance, if 20% of measles cases are from individuals vaccinated against measles and if vaccination coverage is 80%, vaccine efficacy is close to 95%; if 60% of measles cases are from individuals vaccinated against measles and if vaccination coverage is 80%, vaccine efficacy is close to 70%.

Fig. 4: The Relationship between percentage of cases vaccinated (PCV) and percentage of the population vaccinated (PPV) for seven different percentage values of vaccine efficiency (VE)



More accurate determinations of vaccine efficacy require intensive cohort or case-control studies. The method is beyond the scope of this paper, but is readily available⁵.

Proportion of vaccine-preventable cases (PVPC): It is also possible to estimate the proportion of vaccine-preventable cases. This is the number of cases occurring in children who were not immunized or who were immunized before the recommended age and not re-immunized at the correct age, as a proportion of the total number of cases. From case investigations and total number of cases, this rate can be calculated as:

$$PVPC = \frac{\text{number of vaccine-preventable cases}}{\text{total number of cases of measles}}$$

Table 2. Changes in the percentage of cases which occur in immunized children at different levels, for a hypothetical population of 100 000 children

	Coverage 40%	Coverage 80%
Total number of children	100 000	100 000
Number of unvaccinated children	60 000	20 000
Number of cases in unvaccinated children	30 000	10 000
Number of vaccinated children	40 000	80 000
Number of cases in vaccinated children	2 000	4 000
Total number of cases	32 000	14 000
% of all cases occurring in vaccinated children	6.3%	28.6%

Assumptions:

Disease incidence among unimmunized children: 50% per year

Disease incidence among immunized children: 5% per year (Vaccine efficacy: 90%)

As immunization coverage increases, a higher proportion of cases occurs among immunized children.

Source: Immunisation Policy, Global Programme for Vaccines and Immunization, WHO/EPI/GEN/95.03

ANNEX 10: EPIDEMIC RESPONSE TEAM - Roles and responsibilities

The epidemic response team may include representatives from:

- The Ministry of Health (communicable diseases, EPI, drug supply)
- Hospitals (clinicians and nurses)
- Laboratories
- NGOs
- Responsible persons of community health programmes
- Police and armed forces (when culturally and politically appropriate)
- Community leaders and/or representatives
- Others as appropriate

The responsibilities of the epidemic response team are to:

- Meet in the absence of an epidemic to predict and plan for epidemics
- Estimate and identify resources and procedures for preventive mass vaccination campaigns
- Estimate and identify additional resources needed for rapid epidemic response
- Ensure the availability of staff and training for epidemic response

- Analyse epidemiological information concerning the evolution of an epidemic
- Plan control and response strategies in the light of overall programme objectives
- Establish clear lines of responsibility for planned actions
- Meet regularly to review data and implemented measures
- Communicate with the general public and the media

- Evaluate the response
- Evaluate the immunization programme
- Produce a detailed report on outbreak response activities
- Make recommendations on changes to immunization strategy and programme

ANNEX 11: PREDICTION OF SEVERE DISEASE DURING OUTBREAKS

Severe disease with possible complications should be anticipated in high-risk areas or in high-risk groups.

As a matter of priority, the outbreak investigation team must reduce mortality and CFR by ensuring adequate case management of all cases, especially in high-risk groups and areas.

High-risk areas include those with:

- low immunization coverage
- poor socio-economic and educational status
- overcrowding, migration areas
- Poor access to health facilities
- vitamin A deficiency

High-risk groups include:

- the young, particularly those less than one year old
- the severely malnourished
- infants and children of HIV infected women
- other immuno-compromised children
- displaced populations such as refugees living in camps or population migrating to urban and peri-urban areas
- certain ethnic and religious groups who may have poor access to, or refuse immunization.

ANNEX 12: CAUSES OF MEASLES OUTBREAKS

The data collected during an investigation should be analysed to determine why the outbreak occurred. The data will help to identify in which group the susceptible individuals have accumulated. This will allow corrective measures to be taken. Although a measles outbreak may occur despite high levels of immunization, it is usually due to a failure to vaccinate.

The reasons for accumulation of susceptible individuals include:

1. Failure to give vaccine

Some children were not vaccinated: Despite the widespread availability of a safe and effective vaccine for over 30 years, failure to administer at least 1 dose of measles vaccine to all infants continues to be the main cause of measles mortality and morbidity. A high proportion of vaccine preventable cases (PVPC) in an outbreak would suggest that a failure to vaccinate children was a significant factor. Spot maps, demographic information and age-specific attack rates can help to identify reasons for a failure to vaccinate.

High-risk areas and groups can be identified with spot maps showing the location of cases. Maps should be examined for clusters of cases that reveal a failure of the programme to reach a specific geographic area or population subgroup. Spot maps of cases can be compared with those including coverage levels and other surveillance data to identify high-risk areas and focus future activities.

Surveys for missed opportunities may reveal why existing immunization services may not have been utilised. Education or motivation of health workers and guardians can be tailored to address these problems.

Some individuals were too old to be immunized at the onset of the programme : they were outside the target age group for vaccination when the vaccine was introduced, and the vaccination programme reduced the measles incidence to lower levels (thus reducing their chances of acquiring natural immunity).

The age distribution of cases and the age-specific attack rates should be examined to determine whether certain age groups are particularly susceptible, and whether the scheduled age for immunization is appropriate. In countries with outbreak prevention or elimination goals, older children are targeted for supplemental vaccination activities.

2. Vaccine failure

The measles-containing vaccines currently in use are safe and effective. However, these vaccines are not 100% effective: in countries where immunization is undertaken at 12-15 months of age, measles vaccine efficacy is estimated to be between 90% and 95%. In countries where the first dose is given at 9 months, vaccine efficacy is estimated to be approximately 85%.

If the calculated vaccine efficacy (VE) is below 80% during an outbreak in any setting, immunization and cold chain practices should be examined.

If vaccine efficacy is found to be low across all age groups, it is likely that there has been a cold chain failure (see below), or that reconstituted vaccine has been kept in the refrigerator, or that there was a problem with the original potency of the vaccine (as opposed to inappropriate immunization practices).

Even if a high level of vaccination coverage is achieved among each new born cohort, susceptible individuals will accumulate: the age of the child at the time of vaccine administration is critical to the efficacy of measles vaccine and can be determined from cluster surveys. When vaccine is administered below nine months of age, efficacy is much lower than the 85% expected when vaccine is administered at nine months. The age of confirmed measles cases at immunization should be examined to see if they were immunized at the recommended age.

Cold chain failure: if the efficacy of the vaccine appears to have been low across all age groups, especially during a specific period of time, the cold chain should be reviewed to ensure that it has been functioning correctly. Factors contributing to a cold chain failure must be identified and rectified.

Vaccine potency problems: the initial potency of the vaccine rarely needs to be re-examined. This is an expensive process and should only be undertaken in special circumstances and when adequate samples of vaccine vials are available (e.g., low vaccine efficacy where cold chain and immunization practices are **proven** to be excellent and when large amounts of vaccine are concerned).

ANNEX 13: SUPPLEMENTARY IMMUNIZATION ACTIVITIES

In all measles outbreaks, the activities of strengthening **routine immunization**, raising awareness of vaccination and effective case management should be a priority. It is critical to recognise that supplementary immunization activities may not have a substantial impact on the course of a measles outbreak; and that, even when they are successful, the cost per prevented case can be very high. **If it is decided to implement supplementary vaccination campaigns, these should focus on areas not yet affected, but where the outbreak is likely to spread.** They should be started immediately (do not wait for completion of the outbreak investigation). Experience has shown that supplementary immunization activities do not usually begin until well after the onset of an outbreak onset when disease spread has already occurred¹. Immunization in these circumstances usually fails to reach those missed by the routine programme. There is a marked decline in efficacy of post-exposure prophylaxis when vaccine is administered more than 72 hours after exposure.

When supplementary immunization activities are planned, staff and parents must be reassured that it is safe to give an extra dose of measles vaccine to a child already immunized.

Each country must decide which situations justify supplementary immunization efforts. In some outbreaks, there may be great political or community demand for supplementary immunization activities, even though the above criteria may not be satisfied. Supplementary vaccination activities are not recommended for use in such situations, but the strategies presented below may be adapted if necessary.

Immunization strategies

If a decision is taken to undertake outbreak immunization, one of the following immunization strategies may be considered:

- 1) immunize all children in the target age group **in those neighbouring areas where the outbreak is most likely to spread** (e.g. all susceptible children in nearby villages), regardless of the children's previous immunization history
- 2) immunize all children in the target age-group (see below) **in the affected area**, regardless of their previous immunization history.

The first approach is the most likely to affect the spread of transmission in a cost-effective way, since children in the immediate vicinity of the outbreak are likely to be rapidly exposed to the virus. The nearest geographically susceptible populations are identified by reviewing the epidemiology of the current outbreak (age distribution, setting, population subgroup, etc.) and finding similar groups in the surrounding area, where no cases have been identified. These groups are then targeted for supplementary immunization activities.

Vaccinating children in the area of the outbreak may have little impact because most susceptible individuals in the immediate vicinity of the case will probably have been exposed to the virus by the time the response is initiated. However if it starts immediately after an outbreak is identified, and if it is sufficiently extensive and rapidly implemented, this may raise immunization levels to the point of arresting transmission. This is suitable for areas of high population density (e.g., outbreaks in the urban poor) and for countries attempting measles elimination.

Timing

Transmission during a measles outbreak is very rapid, the mean time lag between index and secondary cases being 12-14 days. Therefore, supplementary immunization activities should begin as soon after the identification of an outbreak as possible. If virus has been transmitted for more than two generations beyond the index cases or index generation (more than 28 days), it is likely that most susceptible individuals have been exposed and immunization in the immediate vicinity of the outbreak will be an expensive, ineffective measure. Thus, supplementary immunization activities should be completed within 7-10 days of onset of the outbreak. Even if a strategy of immunizing in the next geographically susceptible area is being used, immunization activities should be completed as rapidly as possible.

Target population

The age group and geographic location of the target population for supplementary immunization activities must be decided:

Target age group:

lower age limit: WHO recommends that vaccination against measles normally be undertaken at age 9 months; however, during a measles epidemic, if a large proportion of cases occur in children below nine months (i.e., the attack rate for children <9 months is high), the age of measles immunization should be temporarily lowered to 6 months. Because of the lesser efficacy of the vaccine at this age, these children must be re-immunized as soon as possible after 9 months.

upper age limit: this depends on the epidemiology of the outbreak. Given the higher morbidity of measles in young children, those up to the age of five years should always be included in supplementary immunization activities. If high attack rates are observed in children above 5 years of age, consideration should be given to immunizing older age groups (e.g. school-age children).

Geographic location

This will depend on the strategy used, the distribution of cases as shown by a spot map of cases, the means of communication between communities and the efficacy of immunization programmes. If reliable coverage data are available, they can be used to identify pockets of susceptible individuals (i.e., those living in areas of low coverage).

Immunization sites

Supplementary immunization can be delivered as an extension of the existing routine programme (fixed sites or outreach sessions), extra immunization sites, or door-to-door campaigns.

Existing immunization sites: ideally, information campaigns ensure that the target population is reached through the existing fixed and outreach immunization points, thus limiting the cost of the operation while encouraging use of routine services.

Extra immunization sites: the most effective way to reach some target groups rapidly, such as school age children or an inner city population, may be to establish

extra immunization sites.

Door-to-door campaigns: given the cost and complexity of door-to-door campaigns, these are best reserved for countries undertaking a measles elimination programme, or in special situations of extra high risk, such as highly urbanised areas or refugee camps.

Review of routine immunization programme

Countries that have achieved a high level of measles control may decide that a revision of existing immunization policies is more cost-effective than conducting large supplementary immunization campaigns during outbreaks. In revising policy, priority should be given to maintaining immunization coverage at greater than 90% in all communities. Review should particularly focus on the identification of high risk populations and the selection of appropriate activities to immunize those populations.

ANNEX 14: MEASLES IN EMERGENCY SITUATIONS

Measles control programmes in emergency settings have two major components

- measles prevention through routine immunization
- measles outbreak response

Immunization programme management

A measles immunization programme should be an early priority of emergency relief programmes⁷. Such a programme will require:

- trained personnel
- vaccine
- cold chain equipment (refrigerators, freezers, cold boxes, vaccine carriers, ice-packs etc.)
- other supplies (auto-destruct syringes, safety boxes, monitoring forms: vaccination cards, tally sheets etc.).
- vaccine administration sites
- surveillance system
- other activities (e.g. nutritional supplementation and Vitamin A, treatment of complications)
- health education and social promotion materials

It is important to involve the national EPI programme from start in any plan or activity

For all elective and emergency mass campaigns it is recommended that auto-destruct syringes and safety boxes be used.

Outbreak response and control

In the event of an outbreak the main strategy should be to:

- Immunize the population at risk as soon as possible.
- Ensure proper case management (see Annex 2)

The presence of several cases of measles in an emergency setting does not preclude a measles immunization campaign. Even among individuals who have already been exposed and are incubating the natural virus, measles vaccine, if given within three days of infection, may provide protection or modify the clinical severity of the illness.

- Isolation is not indicated
- Do not withdraw children from feeding programmes

All children 9 months to 5 years of age should be immune against measles once they are inside the camp

Treatment of complications (See Annex 2)

ANNEX 15: SAFETY OF INJECTIONS

To ensure the safety of injections, WHO and UNICEF have issued a joint policy statement which recommends that sufficient quantities of auto-destruct syringes (which cannot be re-used), and safety boxes are automatically provided, together with high quality vaccine, for all elective and emergency mass immunization campaigns, including measles control operations (WHO/EPI 1997).

If adequate quantities of auto-destruct syringes are not available and well distributed, then injections must not be given during the mass campaigns. Needles must not be recapped after use. Needles should remain uncapped and placed immediately into a designated container (puncture resistant) and disposed by burning, as soon as possible after use.

For further reading on this topic, refer to *Safety of Injections: WHO/UNICEF policy statement for mass immunization campaigns, WHO/EPI/HIS/97.04*¹⁰

Monitoring Injection safety during campaign

To evaluate this you need to train the supervisors and include relevant questions in their supervisory checklists during the implementation and after the campaign. The following table is for a rapid assessment on injection safety during mass immunization campaigns.

INJECTION SAFETY CHECKLIST FOR MASS CAMPAIGNS

The following questionnaire is limited to a series of observations of compliance with safety procedures, without seeking background information or causal relations. Depending on the result of the observation, each box should be marked with Y (YES) if the procedure is safe (i.e. according to recommendations) or N (NO). There is place for 5 observations for each indicator. An attempt should be made to apply this questionnaire to as many vaccination teams as possible, representing the various regions/districts and different types of health workers

Questionnaire**Compliance with safety procedure**

Province/Region: _____

District/Block: _____

Name of Supervisor: _____

<u>Q</u> BSERVE / <u>E</u> NQUIRE:		THE CORRECT WAY:
Preparation procedures		
<i>O</i>	What types of syringes are used for administration?	Auto-destruct syringes (which cannot be re-used) to be provided for all elective emergency mass immunization campaigns
<i>O</i>	Storage of syringes before administration and preparation of syringes for administration	Syringes to be filled immediately before administration (not pre-filled before session)
<i>O</i>	Administration technique by observing at least one injection administration in each vaccination team	Measles vaccine to be administered subcutaneously. The administration site is the right upper arm. One syringe to be used for each dose administered.
<i>E</i>	Knowledge on injection safety by asking team members some questions	Health workers to receive information on safety injection practices. Use “ <i>key ensure injection safety</i> ” at back of this form to formulate 4 questions. Write <i>Y</i> more correct answers.
<i>O</i>	Distribution of supplies and availability of syringes according to the target population in each team	Adequate amounts of syringes and needles for every dose of injectable vaccine provided. (auto-destruct syringes required = target population X 1.1) A disposable syringe for reconstitution to be available for each vial.
Vaccine handling		
<i>O</i>	Reconstitution of vaccine and the temperature of the diluent at the time of reconstitution	The diluent provided by the manufacturer should be used. The diluent should be refrigerated
<i>O</i>	Handling of reconstituted vaccine vials at the end of the working session	Reconstituted doses should be discarded at the end of the session or after 6 hours whichever comes first
Disposal of used syringes and needles		
<i>O</i>	Procedures followed with used syringes and needles after use	Used needles and syringes to be dropped in safety box or puncture resistant container immediately after use (needles not to be recapped after use). Each vaccination team to have sufficient safety boxes to dispose of all the sharps. The safety boxes should not be overfilled or wet
<i>E</i>	Existence of guidelines to transport, store and incinerate used sharps	Guidelines to transport and store used syringes and needles distributed and are followed by health workers (timing, supervision, storage sites).
<i>O</i>	Provisions for incineration/destruction of syringes: How syringes and other sharps were stored and transported after use? Whether or not the syringes were incinerated after the campaign?	Used syringes (auto-destruct for administration and disposable for vaccine reconstitution) should be stored in a safe place and protected from the public until collection/incineration There should be a designated site for destruction. Incineration should be conducted in a close place avoiding dispersion and protection from the public.

Please use this page to write any additional information that you found especially relevant.

ANNEX 16: REFERENCE ADDRESSES AND CONTACTS

For more information on EPI aspects of measles, contact:

Medical Officer, Measles Focal Point

Expanded Programme on Immunization

Global Programme for Vaccines and Immunization

CH 1211 Geneva 27

Switzerland

Fax +22 791 4192/93

Email: gpv@who.ch (For subject, insert: "For EPI Measles Focal Point")

Other information on measles activities within the Expanded Programme on Immunization is available on the Internet at:

<<<http://www.who.ch/gpv-dvacc/research/virus1.htm>>>

In addition, online documentation may be downloaded from

<<<http://www.who.ch/gpv-documents/>>>

For more information on WHO outbreak response activities and products, please contact Department of Communicable Diseases Surveillance and Response (CSR)

Integrated Surveillance and Response (ISR)

Outbreak Verification Team

World Health Organization

20 Avenue Appia

CH-1211 Geneva 27

Switzerland

Fax + 22 791 4198

E:mail outbreak@who.ch

Web: <http://www.who.ch/emc/>

ANNEX 17: REFERENCES AND FURTHER READING

1. Aylward RB, Clements J, Olivé JM. The impact of immunization control activities on measles outbreaks in middle and low income countries. *Int J Epidemiol* 1997; **26**(3): 662-669.
2. World Health Organization-Global programme for vaccines and immunization, *Using surveillance data and outbreak investigations to strengthen measles immunization programmes*. WHO/EPI/GEN/96.02.
3. Cutts FT. *The immunological basis for immunization: Module N° 7: Measles*. Global Programme for Vaccines and Immunization/World Health Organization, Geneva, 1993. WHO/EPI/GEN/95.03 Rev.2.
4. Clements, CJ, Strassburg M, Cutts FT, Torel C. The epidemiology of measles. *Wld Hlth statist Quart* 1992; **45**(2/3): 285-91.
5. Orenstein WA, Bernier RH, Dondero TJ et al. Field evaluation of vaccine efficacy. *Bull Wld Hlth Org* 1985; **63**(6): 1055-1068.
6. World Health Organization-Global Programme for vaccines and immunization, *Immunization Policy*. WHO/EPI/GEN/96.02.
7. Tools MJ, Steketee RW, Waldman RJ, Nieburg P. Measles prevention and control in emergency settings. *Bull Wld Hlth Org* 1989, **67**(4): 381-88.
8. Laboratory diagnosis of measles infection and monitoring of measles immunization. *Bull Wld Hlth Org* 1994, **72**(2): 207-11

9. *WHO/UNICEF Policy statement for mass immunization campaigns.*
WHO/EPI/HIS/97.04
10. *Safety of Injections: WHO/UNICEF policy statement for mass immunization campaigns, WHO/EPI/HIS/97.04*

Other guidance on outbreak response in measles outbreaks

Médecins sans Frontières. *Conduite à tenir en cas d'épidémie de rougeole*. MSF : Paris, 1996
