

CDAlert

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MEASLES : PERSPECTIVES & ISSUES

Measles remains a leading cause of death due to Vaccine Preventable Diseases amongst young children. Despite the availability of safe and potent vaccine, globally more than half a million people, mainly children, died of the disease in 2003 alone. While measles is now rare in many industrialized countries, it still remains a common illness in many developing countries. More than 30 million people are affected every year globally. Data on estimated measles death globally in different WHO regions (2003) is given in Table-1.

Table-1 WHO Region-wise measles deaths, 2003	
WHO Region	Measles deaths
African region	2,52,000 (48%)
South East Region	1,82,000 (34%)
Eastern Mediterranean region	69,000 (13%)
Western Pacific Region	22,000 (4%)
European region	5,000 (1%)
American region	0 (0%)

The main reason for countries having high measles morbidity and mortality is the failure to deliver at least 1 dose of measles vaccine to all infants at the age of 9 months under the routine immunization policy. Secondly, when given at 9 months of age the efficacy of the vaccine is 85%; therefore, some children will not develop the immunity even after vaccination, and this leads to build up of a susceptible population over a period of time and results in outbreaks. In India about 50,000 cases of measles have been

reported annually. (See Table 2)

Table-2 Year-wise measles case, India, 2000-2004	
Year	Measles cases
2000	38,835
2001	51,780
2002	38,927
2003	46,736
2004	51,546

Source: CBHI

CAUSATIVE AGENT

Measles is caused by an RNA paramyxovirus, of the genus *Morbillivirus*. There is only one serotype of measles virus. Measles virus is rapidly inactivated by heat, sunlight, and extremes of pH, ether, and trypsin. It has a short survival time (<2 hours) in the air, or on objects and surfaces. Measles is a human disease. There is no known animal reservoir, and an asymptomatic carrier state has not been documented.

MODE OF TRANSMISSION

Mode of transmission is through the airborne route, by droplet spread, direct contact with nasal or throat secretions of infected persons. The infective material includes secretions from nose, throat and respiratory tract of a case of measles during the prodromal period and the early stages of rash. **Period of communicability ranges from 1 day before the beginning of the prodromal period (usually about 4 days before rash onset) to 4 days after rash appearance; minimal after 2nd day**

of rash. A person vaccinated with the measles vaccine cannot transmit the virus to another person.

The virus can spread in any season. Epidemics are common in India during winter and early spring (January to April). In temperate areas, measles disease occurs primarily in the late winter and spring.

Isolation of the patient for a week from the onset of rash covers more than the period of communicability.

Infants are generally protected by maternal measles antibody until 5-9 months of age. This is the reason why most countries recommend measles vaccination starting from the age of 9 months only. Natural infection produces lifelong immunity. Measles vaccination produces long-term (probably lifelong) immunity in most individuals.

CLINICAL FEATURES

Incubation Period

The incubation period is about 10 days, but may range from 7 to 18 days from exposure to onset of fever.

The Prodromal Stage:

The prodrome lasts 2–4 days (range 1–7 days). It is characterized by fever, which increases in stepwise fashion, often peaking as high as 103°–105°F. This is followed by the onset of cough, coryza (running nose), and/or conjunctivitis. Koplik's spots on oral mucous membranes, are considered to be pathognomonic for measles. They occur 1–2 days before the onset of rash to 1–2 days after the appearance of rash, and appear as punctate blue-white spots on the bright red background of the buccal mucosa.

Eruptive Phase

The eruptive phase is characterized by a typical, dusky-red, macular or maculopapular rash, which begins behind the ears

and extends down the body taking 2 to 3 days to progress to the lower extremities. The rash may remain discrete, but often it becomes confluent and blotchy. In the absence of complications, the lesions and fever disappear in another 3 to 4 days signaling the end of the disease. The rash fades in the same order of appearance leaving a brownish discoloration that may persist for 2 months or more.

POST MEASLES COMPLICATIONS

Post-measles stage presents with weight loss and weakness is observed in the affected child for a number of days. There may be failure to recover and a gradual deterioration into chronic illness – due to increased susceptibility to other bacterial & viral infections, nutritional and metabolic effects and tissue destructive effects of the virus. There may be growth retardation, diarrhoea, pyogenic infections and reactivation of pulmonary tuberculosis etc.

An individual with severe or complicated measles may have one or more of the following signs and symptoms:

- Diarrhoea (three or more loose stools a day)
- Otitis media characterized by ear pain, draining pus, red immobile ear drums
- Pneumonia characterized by rapid-breathing, chest indrawing
- Croup characterized by a harsh cough and breathing problems
- Encephalitis characterized by altered sensorium and decrease in the level of consciousness.
- Malnutrition characterized by wasting, recent severe weight loss
- Dehydration (thirst, sunken eyes, skin pinch goes back slowly)
- Eye disease characterized by pus; corneal ulcer, perforation and clouding. It is often due to vitamin A deficiency

- Stomatitis characterized by sore/red mouth
- Convulsions or coma

Though measles can be easily diagnosed clinically, a number of other illnesses can be mistaken as they have signs and symptoms similar to measles. Therefore, it is important to confirm the diagnosis of measles through laboratory investigations especially to confirm an outbreak. Illnesses that are accompanied by fever and rash and can sometimes be confused with measles include:

- Dengue fever
- Rubella
- Scarlet fever
- Roseola
- Herpes
- Chicken pox (although the rash is vesicular)

Mortality

Death within one month of onset of rash is considered to be associated with measles. The proportion of measles cases that die, i.e. the case-fatality rate, in developing countries is estimated to be in the range of 3-5% but may reach 10-30% in certain situations. The major causes of death in a measles infection that contribute to the high case-fatality rate are:

1. Pneumonia
2. Diarrhoea
3. Croup
4. Encephalitis

Outcome of the disease is adversely affected by malnutrition, younger age at infection, overcrowding, higher fertility patterns, non availability of health care and increased rate of intercurrent infection.

CLINICAL CASE DESCRIPTION

Any person with

- ◆ Fever; AND
- ◆ Maculo-papular rash
- ◆ Cough or coryza or conjunctivitis

Laboratory criteria for diagnosis

- ◆ Presence of measles specific IgM antibodies OR
- ◆ Isolation of measles virus; OR
- ◆ At least a four fold increase in the IgG antibody titre in two serum samples collected at an interval of at least 2 weeks

Case classification

Suspect case: Any case with fever and rash

Probable case: Any suspect case that is diagnosed as measles by medical officer on the basis of clinical case description

Confirmed case: A case that meets the clinical case definition and which is laboratory confirmed or linked epidemiologically to a laboratory confirmed case.

WARNING SIGNALS FOR AN OUTBREAK

Trigger Level – 1

- ◆ Single case of measles/fever with rash reported from a tribal area
- ◆ More than 2 cases of fever with rash in a village/ geographical area of 1,000 population in one week

Trigger Level – 2

- ◆ More than 4 cases of fever with rash in a geographical area of 1000 population in one week
- ◆ Similar illness in more than 1 village reported in the same week

LABORATORY DIAGNOSIS

Laboratory diagnosis of measles is established by

- a) Serological assay
- b) Virus isolation
- c) PCR

Table-3 Laboratory diagnosis of measles

Type of test	Purpose of test/source material	Method
Serological assays	Demonstration of measles specific antibody	Indirect IgM ELISA
		IgM capture ELISA
		Enzyme Immuno-assay (EIA) for detection of IgM antibody in oral fluids
	Demonstration of measles specific four fold rising IgG antibody in two samples collected at an interval of at least 15 days	IgG ELISA
Virus isolation	From urine, nasopharyngeal swabs, or peripheral blood lymphocytes	Cell culture and immunofluorescence
		RT/nested PCR & nucleotide sequence analysis
Detection & characterization of genomic viral RNA	On clinical material – Nasopharyngeal swab, urine or peripheral blood lymphocytes or viral isolates	Virus neutralization tests (VN)
		Haemagglutination inhibition test (HAI)

The details of the above mentioned tests are summarized in the Table-3.

Sample collection & transportation

Right time for sample collection and its transportation to the laboratory is the key point in the diagnosis of measles from clinical samples. The same is summarized in Table-4.

CLINICAL MANAGEMENT

Significant morbidity and mortality are associated with measles, particularly during an outbreak. Proper case management must be encouraged and facilitated through the provision of necessary support.

Clinical assessment should initially be carried out in the health centre. Any child with rash and fever, or suspected for other reasons of being a case of measles, should be kept in isolation away from other children, particularly the young ones. Children must be examined for the signs and symptoms of severe or complicated measles to ensure that those with severe complications are properly treated. Child should not be allowed to attend school.

Case management of uncomplicated measles

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

Table-4 Specimen Collection & Transportation

Specimen	Collection time	Transportation
Blood for serology (Serum)	Within 28 days of rash onset	Cold chain (4°–8°C)
Nasal Swab/Aspirate	-Do-	In VTM & Cold chain
Throat Swab	-Do-	-Do-
Urine	0-7 days after onset of rash	Cold chain (4°–8°C)
Serum (IgG, HAI, PNT/SNT)	Acute phase } Paired sample Convalescent }	-Do-
IgM EIA	Acute phase after 3 days of onset	-Do-

(VTM – Viral Transport Media; HAI – Haemagglutination inhibition test; PNT – Plaque Neutralisation Test; SNT – Serum Neutralisation Test; EIA – Enzyme Immuno Assay)

- Administer Vitamin A : It should be given in all cases regardless of vitamin A supplement administration status.
- 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.
- Treat mouth ulcers
- Control fever by keeping the child cool
- Vaccinate close contacts within 72 hours of exposure
- Complete rest

- ⇒ High grade fever persists
- ⇒ The eyes become painful, cloudy, or there is a change in vision
- ⇒ There is deep mouth ulcer
- In uncomplicated measles, the fever will decline within one week and the rash will fade within 10-14 days.
- The child may be vulnerable to other diseases such as diarrhoea, acute respiratory infections and other infections in the weeks following measles. Consequently, the mother should bring the child to a health facility as early as possible to seek medical advice.

Table-5 Recommended Vitamin A schedule for measles cases		
Age	Immediately on diagnosis	Next Day
Infants < 6 months	50 000 IU	50 000 IU
Infants 6-12 months	100 000 IU	100 000 IU
Children 12 months plus (upto 5 years)	200 000 IU	200 000 IU

Case management of complicated measles

Actions to be taken in case of complications include:

Communicate the following advice to mothers of children with measles:

- Continue breast-feeding, or give as much weaning foods and fluids as the child will take.
- Yellow fruits and vegetables and dark green leafy vegetables are important for recovery,
- Give ORS, if there are any signs of dehydration (ensure the mother knows the signs of dehydration and explain how to mix and give the child ORS)
- Control the child's fever with paracetamol to reduce the risk of febrile convulsions. Monitor the temperature regularly which should be kept as near to normal as possible.
- Bring the child for treatment if:
 - ⇒ The general conditions worsens
 - ⇒ Breathing becomes rapid or difficult
 - ⇒ Diarrhoea continues or there are signs of dehydration
 - ⇒ The child is not able to drink

- Refer to health facility for further management
- Follow the above recommendations for case management of uncomplicated measles.
- Ensure that two doses of vitamin A are given.
- Clean eye lesions and treat with antibiotic eye dropper ointment three times a day for 7 days (for corneal lesions, cover the eye with a pad) – vitamin A administration is particularly important to minimize the risk of potentially blinding eye lesions; in this case, a third dose of vitamin A should be given four weeks later using the same dosage and age as given in table 4.
- Clean ear discharge and treat with antibiotics
- Refer suspected encephalitis cases to the hospital
- Treat malnutrition and diarrhoea with sufficient fluids and a high quality diet
- Treat pneumonia with antibiotics
- Treat mouth ulcer with gentian violet paint 0.25%

MANAGEMENT & CONTROL OF OUTBREAK

Detecting an outbreak

A surveillance system needs to have its objective defined as:

- Detecting and investigating outbreaks so as to ensure proper case management and determining why outbreaks have occurred (e.g. vaccination status, vaccine failure, accumulation of susceptible persons).
- Identify high-risk groups or areas
- Monitor and evaluate the program through monitoring incidence and vaccination coverage
- Describe the changing epidemiology of measles in terms of age and vaccination status and intervals between outbreaks.

If surveillance is not functioning in all areas, it may be difficult to detect small outbreaks. However outbreaks can be suspected if:

- Large numbers of cases are suddenly occurring in an area.
- If health clinic attendance or admission to hospitals due to febrile rash illnesses are increasing
- If media reports suggesting an outbreak appear.

Guidelines for measles immunization during outbreak

- Effective case management should be a priority.
- Strengthen routine immunization and raise awareness of vaccination

Supplementary vaccination activities in the course of an outbreak are not recommended if there is a delay in identification of the index case beyond 72 hours. There is one exception to this

recommendation i.e. 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.

Use of laboratory testing in diagnosis

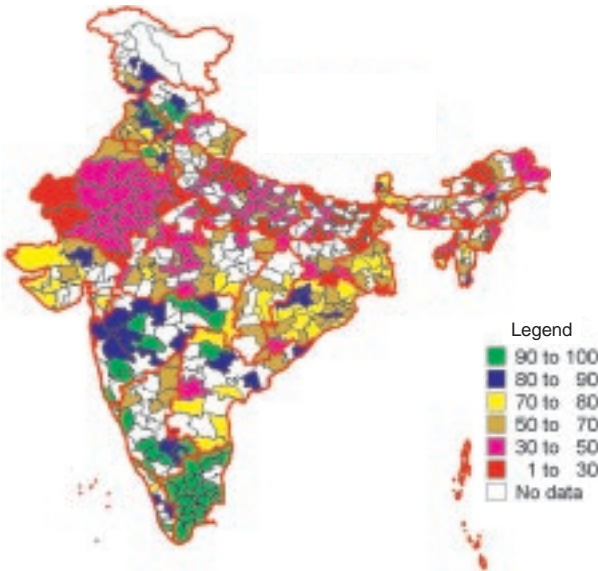
Measles can be clinically diagnosed in most of the cases. Laboratory testing can be performed to confirm the diagnosis. During an outbreak, testing of initial 5 to 10 cases suspected of having measles should be performed. This testing is to be done only in the initial phase of an outbreak to confirm the disease. The presence of measles-specific IgM antibodies in blood (serum) specimen confirms the diagnosis. An IgM negative case that does not meet the case definition can be considered as not measles. Once the outbreak is confirmed, it is not necessary to collect specimens from each and every suspected case reported in the outbreak.

Once the outbreak has been Laboratory confirmed, additional cases can be confirmed if they meet the clinical case definition, or are epidemiologically linked to another case that is confirmed with a positive IgM antibody to measles virus. Epidemiological linkage means that the person had direct contact with confirmed IgM positive measles case that had rash onset 7-18 days before the present case.

Routine measles immunization

Routine measles immunization was introduced under UIP in 1995. Since then, single dose of vaccine is being given to every child in age group of 9-12 months. Currently, vaccine manufactured using Edmonston Zagreb strain is being used and

Fig. I District-wise measles vaccination evaluated coverage, India, 2002-03



Source: EPI, Govt. of India

0.5 ml of reconstituted vaccine is given in upper arm of the vaccinee.

Measles vaccine coverage

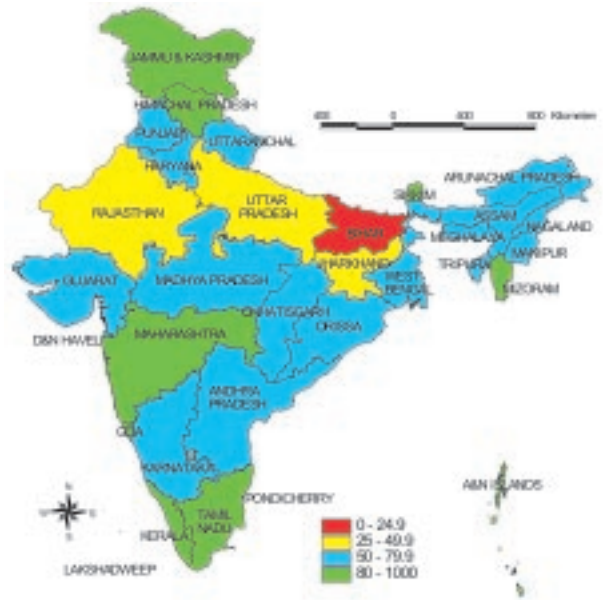
Different measles vaccine coverage evaluation surveys have been carried out to monitor the measles immunization programme. The findings of the same have been depicted in Figs. I & II.

Strategies for administering measles vaccination during disasters

As per national immunization schedule measles vaccine is to be given between 9-12 months of age. However, following any disaster, there is high risk of getting measles infection due to poor nutritional status of children and overcrowding in relief camps. To prevent measles outbreak, initiate the following activities immediately :

- ❖ Administer one dose of measles vaccine to all children between 6 months to 5 years of age irrespective of previous immunization. Children who received vaccine at 6 months age must be re-immunized after completing 9 months of age.

Fig. II Measles vaccination evaluated coverage, India, 2001



- ❖ Auto-disable syringes for injection and disposable syringes for reconstituting the freeze-dried vaccine are mandatory.
- ❖ Orient/train all vaccinators regarding –
 - The use & disposal of auto-disable syringes.
 - Maintenance of cold chain
 - Use of reconstituted measles vaccine within four hours of reconstitution.
 - Adverse events following immunization

Strengthen the surveillance system for vaccine preventable diseases including measles for early detection of cases/ clustering of cases/ early identification of outbreaks.

Strengthen routine measles vaccination in disaster affected and surrounding areas.

MEASLES ERADICATION POLICY

Since the inception of Expanded Programme of Immunization in 1974, the number of cases and deaths attributed

world-wide due to measles have declined substantially from an estimated hundred million cases and 5.8 million deaths to an estimated 44 million cases and 1.1 million deaths in 1995. Despite these achievements, measles remain one of the leading causes of mortality in developing countries and is responsible for approximately 10 per cent of all the deaths amongst children below 5 years of age. The impact of measles vaccination has varied among six WHO Regions. Of these regions, the most substantial progress has been achieved in the American Region where most countries have implemented only one time mass immunization campaign across a wide age group. The main aim of this strategy is to reduce the number of susceptible children in the population and interrupt the transmission of measles virus in the community. A laboratory-based surveillance as in the case of polio should be developed for the elimination of the disease globally. India is still in stage of developing policy for measles elimination programme.

Under the National multi year strategic plan for Immunization, the Government of India has set the objective to reduce measles mortality by two-thirds by 2010, compared to 2000 estimates.

The plan emphasizes on achieving at least 80% coverage in 80% of the districts of the country by 2009 and collection and use of good quality epidemiological data from active surveillance and outbreak investigations to guide further action.

The key strategies to achieve the goal of measles mortality reduction are:

- Achieving high routine measles vaccination coverage of infants at 9-12 months of age.
- Establish effective measles surveillance that provides information at at least regarding number of cases and deaths by month, age and vaccination status of cases and deaths, conducts outbreak investigation supported by laboratory confirmation.
- Improving management of measles cases, including vitamin A supplementation and adequate treatment of cases.
- Based on evaluated measles immunization coverage and surveillance data, providing a second opportunity for measles immunization to appropriate age groups of children through a second routine dose of measles vaccine or through supplemental immunization activities.

Laboratories engaged in diagnosis of measles in India:

1. National Institute of Virology, Pune (Maharashtra).
2. National Institute of Communicable Diseases, Delhi.
3. King Institute of Preventive Medicine, Guindy (Tamil Nadu).
4. Pasteur Institute of India, Coonoor (Tamil Nadu).
5. Central Research Institute, Kasauli (Himachal Pradesh).

...about CDAlert

CDAlert is a monthly newsletter of the National Institute of Communicable Diseases (NICD), Directorate General of Health Services, to disseminate information on various aspects of communicable diseases to medical fraternity and health administrators. The newsletter may be reproduced, in part or whole, for educational purposes.

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