

## **Measles Control Strategies in India: Position Paper of Indian Academy of Pediatrics**

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Measles continues to be a major cause of childhood morbidity and mortality in India. Recent studies estimate that 80,000 Indian children die each year due to measles and its complications, amounting to 4% of under-5 deaths. Immunization against measles directly contributes to the reduction of under-five child mortality and hence to the achievement of Millennium Development Goal 4 (MDG 4). The live attenuated measles vaccines are safe, effective and provide long-lasting protection. The key strategies being followed globally for measles mortality reduction are high coverage of measles first dose, sensitive laboratory supported surveillance, appropriate case management, and providing second dose of measles vaccine. Prior to 2010, India was the only country in the world that had not introduced a second dose of measles vaccine in its National immunization program. We herein discuss the current status of measles vaccination along with the rationale and challenges of providing a second opportunity for measles vaccination, and the principles of measles catch-up campaigns.

**Key words:** *Catch-up campaign, Measles, Millennium Development Goal, Prevention, Vaccine.*

**M**easles is a highly infectious and potentially fatal viral infection mainly affecting children. Immunization against measles directly contributes to the reduction of under-five child mortality and hence to the achievement of Millennium Development Goal 4 [1]. Deaths from measles occur mainly in infants and young children and are primarily due to complications of the infection such as pneumonia and diarrhea. Measles continues to be a major cause of childhood morbidity and mortality in India. Although the true burden of measles in India is difficult to quantify, only a small proportion of cases seek treatment. Infection with measles virus is ubiquitous throughout the country.

A recent review of published literature from India shows the median case fatality ratio (CFR) of measles to be 1.63% (range: 0%-30.0%) [2]. Malnutrition and young age at infection are risk factors associated with measles mortality. Recent studies estimate that 80,000 Indian children die each year due to measles and its complications amounting to 4% of under-5 deaths [3]. The distribution of these deaths is not homogenous but is concentrated in states with the poorest performing immunization programs [4-6].

### **Global Goal for Measles Control**

The current global goal for measles control, as stated in

the Global Immunization Vision and Strategy (GIVS) 2006-2015 of the World Health Organization and United Nations Children's Fund, is to reduce measles deaths by 90% by 2010 compared to the estimated number in 2000. World Health Assembly (WHA) has also endorsed the same after the review by WHO's Strategic Advisory Group of Experts (SAGE) on immunization [7].

The key strategies being followed globally for measles mortality reduction are:

- High coverage of Measles 1<sup>st</sup> dose: Coverage for 1<sup>st</sup> dose measles vaccine must be  $\geq 90\%$  at national level and  $\geq 80\%$  for each district in routine immunization.
- Sensitive laboratory supported surveillance: Outbreak and case based surveillance fully supported by laboratories for serological and virological classification. An outbreak is considered confirmed if measles immunoglobulin M (IgM) is detected in serum from at least two suspected cases.
- Appropriate measles case management: Including administration of vitamin A to reduce mortality and complications.
- Providing 2<sup>nd</sup> dose of measles vaccine:
  - (a) Single dose in routine immunization - In India, states with  $\geq 80\%$  evaluated coverage for 1<sup>st</sup> dose of measles

vaccine in Routine Immunization (RI) (DLHS-3) will have the second dose of measles vaccine in RI with DPT booster [8].

- (b) Supplementary immunization activity (SIA) for measles through catch up immunization campaigns and or follow up immunization campaigns: States with <80% evaluated coverage of 1<sup>st</sup> dose of Measles vaccine in RI (DLHS-3) are conducting Measles Catch up campaigns since 2010 in a phased manner [9].

#### MEASLES VACCINES, EFFECTIVENESS AND DURATION OF PROTECTION

Live, attenuated measles vaccines are available, either as monovalent vaccine or as measles-containing vaccine (MCV) in combination with rubella or mumps vaccines. When using the combined measles-rubella vaccine or measles-mumps-rubella vaccine, the protective immune responses to each individual vaccine antigen as well as vaccine-associated adverse events remain largely unchanged. Available measles vaccines are safe, effective and may be used interchangeably within immunization programs.

Following vaccination, the long-term persistence of neutralizing measles antibodies (upto 33 years) and long-lasting protection against measles have been demonstrated. However, it is not definitively known whether a single dose of measles vaccine, without natural boosting by recurrent measles exposure, will result in lifelong protection. Studies using IgG avidity measurements to separate primary vaccination failures from secondary vaccination failures suggest that secondary failures may occur occasionally [10,11]. However, declining immunity has not been shown as an important risk factor [12].

*Indications, precautions and contraindications:* Mild illnesses are not a contraindication to vaccination, vaccination should be avoided if the patient is having high fever or having serious disease. Measles vaccine can be given to adolescent and adults if susceptible or travelling to endemic areas but should be avoided during pregnancy. Early stages of HIV infection is not a contraindication to measles immunization. People with a history of an anaphylactic reaction to components of the vaccine should not be vaccinated. Measles vaccine is also contraindicated in people who are severely immuno-compromised *e.g.* severe HIV infection, advanced leukemia or lymphoma, treatment with high-dose steroids [7].

Where no contraindications have been identified, measles vaccine should be given to all infants and young children as part of national immunization programmes. The vaccine may also be offered to teenagers and adults

likely to be susceptible and at risk of being exposed to measles virus – for example, to those who are travelling to areas where measles is endemic. The importance of vaccinating health workers is underlined by the numerous measles outbreaks occurring in health institutions, affecting both health workers and patients. Administration of immunoglobulins or other antibody-containing blood products may neutralize the effect of the vaccine for 3-11 months, depending on the dose of measles antibody. Following measles vaccination, receipt of such blood products should be avoided for 2 weeks if possible [7].

*Adverse Reactions:* Adverse reactions after measles vaccination are slight pain and tenderness at injection site and are transient. About 7 days after vaccination upto 5% children may experience fever, occasionally inducing febrile seizures (1:3000 children). Transient rash can occur in 2% and thrombocytopenic purpura in 1:30000 and anaphylactic reactions 1:100,000 following vaccination [13-15]. Extensive studies in different countries have demonstrated that there is no increased risk of permanent neurological sequelae and no evidence to support an increased risk of Guillain-Barré syndrome following administration of MCVs. There is also no scientific evidence to support reports that measles vaccination may be a risk factor for inflammatory bowel disease or for autism [16].

#### *Routine MCV1 Coverage*

In 1985, MCV1 was introduced in India's Expanded Program on Immunization, with a recommended age for vaccination of 9-12 months. Estimated national routine MCV1 coverage was 74% among children aged 12-23 months based on UNICEF sponsored national Coverage Evaluation Survey (CES) of 2009 [17]; state level MCV1 coverage ranged from 48% to 96%. District level data from the District Level Household and Facility Survey conducted during 2007-2008 (DLHS-3) indicated that MCV1 coverage was  $\leq 90\%$  in 26% of the evaluated districts [18].

#### SECOND DOSE OF MEASLES CONTAINING VACCINE (MCV2)

With 70% routine measles vaccination coverage and 85% vaccine effectiveness with a single dose given at 9 months of age, real protection to measles is only 60% ( $0.70 \times 0.85 = 0.60$ ) and thus approximately 40% of India's annual birth cohort of 26 million children remains susceptible to measles. At this rate, the accumulation of susceptible children in successive annual birth cohorts would reach the epidemic threshold level every 2-3 years [19].

The rationale for providing a second opportunity for

measles vaccination is two-fold [9]:

- *Immunological*: To immunize the primary vaccine failures; those children who failed to respond to the first dose
- *Programmatic*: To vaccinate those children who were missed by routine services for first dose of measles in routine immunization.

Most children who have failed to respond to the first dose of MCV respond well to a second dose [7]. MCV2 can be delivered either through existing routine services or through measles catch-up immunization campaigns, the choice is determined by the strategy that would attain the highest levels of coverage.

In weak program settings, organized catch-up vaccination campaigns that benefit from specific planning and intense communication and coordination efforts have been proven to effectively achieve high coverage levels in all socio-economic strata [5,20]. Furthermore, numerous studies from a range of development settings have found two doses of measles vaccine to be highly cost effective [7]. In settings of low immunization coverage, the campaign approach has also been found to be more equitable across wealth quintiles [21].

By 2008, the annual number of measles associated deaths occurring worldwide had reduced by 78% from 733,000 in 2000 to 164,000 [20]. Sub-Saharan Africa, in particular, has demonstrated the impact of increasing routine vaccine coverage while also providing a second opportunity for measles vaccination through measles catch-up campaigns [22]. From 2000 to 2008, measles deaths in Africa declined by 92%.

#### ***NTAGI Recommendations for India***

For reducing measles mortality in India, National Technical Advisory Group on Immunization (NTAGI) reviewed data on measles epidemiology and case fatality rate and has recommended the following [23]:

- A second dose of measles vaccine should be introduced in the UIP at the time of DPT booster dose (at 16-24 months of age) in states with  $\geq 80\%$  evaluated coverage with the first dose of measles vaccine.
- Catch-up measles vaccination campaigns should be implemented for children aged 9 months to 10 years in states with  $< 80\%$  evaluated coverage with the first dose of measles vaccine and that detailed action plans for these SIAs should be finalized immediately in states with low coverage and high measles mortality burden.

Indian Academy of Pediatrics endorses NTAGI recommendations.

#### ***India's Decision to Introduce MCV2***

Building on global experience and recognizing that measles represents a significant source of preventable child mortality, the Government of India announced in May 2010 its decision to implement the National Technical Advisory Group on Immunization (NTAGI) recommendation to introduce MCV2 [4,24]. As recommended by the NTAGI, the implementation strategy of MCV2 at the state level is determined by the underlying performance of the routine immunization (RI) program. In total, 14 states with measles vaccine coverage  $< 80\%$  (Arunachal Pradesh, Assam, Bihar, Chhattisgarh, Gujarat, Haryana, Jharkhand, Madhya Pradesh, Manipur, Meghalaya, Nagaland, Rajasthan, Tripura and Uttar Pradesh) will introduce MCV2 through catch-up vaccination campaigns. In the remaining 21 states with better performing routine immunization systems (i.e.  $\geq 80\%$  routine measles coverage) 17 will introduce MCV2 for children aged 16-24 months through the routine program. The remaining four States and Union Territories (Delhi, Goa, Puducherry and Sikkim) already use a second dose of measles vaccine in their RI program (as mumps-measles-rubella vaccine) financed with state resources [7]. After the campaigns in the districts of 14 states, those districts will start the MCV2 in routine immunization at 16-24 months after 6 months of completing the campaigns.

#### ***Supplementary Immunization Activities and Measles Catch-up Campaigns***

Measles catch-up campaigns are indeed SIAs just like polio SNIDs/NIDs. Supplementary immunization activities are mass campaigns targeting all children in a defined age group, with the objective of reaching a high proportion of susceptible individuals. Each campaign is conducted over a wide geographical area (e.g. province or country) in order to achieve a rapid reduction in the number of susceptible children. This is a one-time effort to vaccinate all children in a defined age group (based on the epidemiology of the country) irrespective of their prior immunization status (history or record). The goal is to rapidly reduce the susceptible proportion in a population and to rapidly enhance population immunity, i.e. the 'herd immunity'. It is not usual to conduct screening for vaccination status and prior disease history (i.e. the campaigns are usually 'non-selective'). Hence anyone who has already received measles vaccine (or MCV) or has history of measles disease in the past is also vaccinated [8]. During SIAs, many established principles of vaccination practices are not adhered to. For example, if a child has received a dose of measles or MCV just a day before the campaign is also targeted for a campaign dose. Even being a live vaccine, extra doses of measles vaccine do no harm, and in fact, may benefit few children with primary vaccine failure even after

booster doses. However, these campaign doses are not counted and routine vaccination is completed as per the schedule. The purpose is to rapidly reach a high coverage around 100% in a short span of time. Furthermore, SIAs also provide an opportunity to increase community awareness of immunizations and strengthen routine immunization programs [8].

### **Challenge for Routine Immunization**

Routine vaccination is a critical strategy for achieving high coverage with MCV1 and MCV2. The government of India is implementing measures to strengthen routine vaccination, especially in districts with low coverage. Nevertheless, substantial challenges exist, including the need for: increasing the number of trained staff at all levels; increasing public demand for and confidence in vaccines; improving vaccine stock and cold chain management; and developing a strong reporting and management system for AEFI [23].

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