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Special Articles

Appropriate strategy for immunisation of children in India IV : Measles and its control, priority number one

Mark C. Steinhoff, M.D., F.A.A.P. and T. Jacob John, F.R.C.P., F.A.A.P., PhD.

Although a hidden health problem, measles is the commonest vaccine-preventable disease and the most common preventable cause of death among our underfives. These facts, plus the availability of a safe and effective vaccine make measles vaccination the highest priority in the control of communicable disease in India. The use of the pulse vaccination strategy will result in better coverage rates than the conventional strategy of immunisation in fixed health centres. India's annual requirement of measles vaccine is 20 million doses. For economy and uninterrupted supply, measles vaccine must be manufactured in India without any further delay.

Key words : Measles ; measles vaccine ; immunisation strategy.

In our review of the priorities of vaccines in the Indian context, we suggested that the highest priority should be given to measles vaccine.[1] Although measles immunisation has been an integral component of routine childhood immunisation in most developed countries for nearly two decades, it is not yet part of our national programme of immunisation in that the vaccine is not procured and distributed by governmental agencies. An expert study group, reporting recently on an alternative strategy for health for all, listed 10 communicable diseases to be controlled or eradicated in India by the year 2000, but measles was not included.[2] This state of affairs may be partly due to the failure of many experts to perceive the public health importance of measles, which remains hidden because popular beliefs prohibit seeking medical attention for this disease[3,4]. Since only a very small proportion of children with measles are brought to clinics or hospitals, most physicians have not been aware of the high frequency of this illness or the magnitude of its effects. We will review information from several community studies in India to show that measles is the *most common vaccine-preventable illness*, as well

From the Department of Child Health and The ICMR Centre of Advanced Research in Virology, Christian Medical College and Hospital, Vellore

Reprint requests : Dr. T. Jacob John

The opinions expressed here are those of the authors and not necessarily of the supporting institutions.

as the *most common vaccine-preventable cause of death* in pre-school children.

The Indian Academy of Pediatrics accepted the recommendations of early investigators and included measles vaccine in their routine immunisation schedule.[5-7] Subsequently, measles vaccine has been included in the list of vaccines under the Expanded Programme of Immunisation (EPI), but no steps have been taken to make it available for general use in the community. This may be due to the belief that the vaccine is too expensive and has too stringent cold storage requirements to be included in a national programme. In contrast, we believe that measles immunisation is a simple and relatively cheap public health measure for improving health and reducing mortality of children in India. We will discuss below why measles should be controlled and a strategy by which this may be achieved.

Epidemiology

The epidemiology of measles in India has been delineated by investigations of outbreaks, retrospective and longitudinal studies and serological surveys.[8-22] These studies show that *virtually all children are infected during childhood* and a large majority develop clinical measles. In rural areas measles tends to occur as periodic epidemics every 2,3 or 4 years, whereas in urban areas annual outbreaks may occur[11,17]. Epidemics usually occur in the cooler months of the year in most parts of India.[11]

During outbreaks the highest attack rate (upto 50%) is seen in 1 to 3 years old, while younger and older children are less often affected. In most outbreaks 10-15% of all cases occur in infants under 12 months[8-10], although in one retrospective survey in rural Maharashtra, nearly 30% of all cases were reported in infants.[12]

Seroepidemiological investigations have been reported from Bombay, Vellore, Chandigarh, Delhi and Pondicherry.[18-22] The data from Vellore and Bombay are displayed in Figure 1 to show the range of these results. The survey results of Vellore, Chandigarh, Pondicherry and Delhi, a retrospective study in Maharashtra[12] and prospective surveillance in Delhi[17] all show a median age of measles

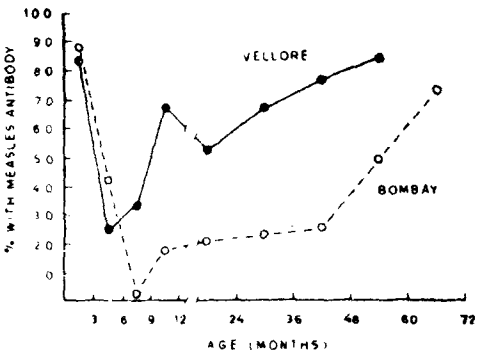

Fig. 1 : The percentage of children with measles antibody in Vellore (HAI>8), and Bombay (HAI>10) (Adapted from Ref. 19 and 18)

infection between 12 and 24 months. The serological study in Bombay demonstrated a higher median age of infection, namely 48 months.[18]

Among the vaccine preventable diseases of importance in India, measles appears to be the one with the highest overall attack rate, with whooping cough as a close second[23]. Although *polioviruses*[24] and *Corynebacterium diphtheriae* may also infect virtually all children, diseases due to them are much less frequent. Measles is the single most com-

mon vaccine-preventable disease of childhood in our country.

Since only a small proportion of measles cases are admitted to hospital, we will not review the data from hospital studies. As stated earlier there are several community-based studies on the epidemiology, sequelae and mortality of measles.[8-22] Selected data from Vellore area, derived from studies of outbreaks in 7 villages with a total of 1198 Pre-school children,[8,9] are presented in Table 1. Attention is drawn particularly to the case-fatality rates of 3 to 16 per cents. Reports from other parts of India also show that about 30 per cent of affected children develop serious complications and that the case fatality rate is 1-3 per cent.[8-17] In general, the case fatality rate is low in communities with adequate nutrition and health care, but it may reach 20 per cent in rural communities without ready access to medical care.[9,10,13] In one epidemic, measles killed 9% of all the children under 2 in the Village.[9]

Table 1 : Measles Epidemics Near Vellore

Attack rate	:	20-40% of the unimmunized children became ill
Complications	:	of those who were ill : 14-50% developed diarrhoea 7-50% developed severe respiratory disease 87% Lost weight 3-16% died
Case fatality rate : Measles mortality rate	:	0.7-4.2% of unimmunized preschool children died of measles

An important sequela of measles is the weight loss which occurs in a majority of cases. Most children take two months or more to regain the lost weight[8,15]. In some children the weight loss leads to gross protein-energy malnutrition and its complications. Other long-term consequences include the activation of tuberculosis, the development of bronchiectasis, and the rare instances of subacute sclerosing panencephalitis. These sequelae may lead to death at a time remote from the measles episode and may not be recognised as measles-related by the family or the physician. Such late deaths are not included either in calculating the case fatality rates mentioned earlier or in estimating mortality figures.

The proportions of deaths caused by measles as reported in a national survey of causes of death and in longitudinal surveillance in rural areas in Tamil Nadu and Punjab are presented in Table 2 [14,16,25]. Using the all-India data, approximately two per cent of infant deaths and about 10 percent of pre-school deaths are caused by measles, which is thus the third most frequent cause of death in under-fives, & probably, the most common cause of vaccine-preventable death in Indian children.[25] The Tamil Nadu data also

Table 2 : Proportion of All Deaths Caused by Measles

Region	Under 1 year	1-4 years
All India — 1979[25]	1.9%	9.4%
Tamil Nadu— 1972[16]	2.3%	10.3%
Punjab — 1959[14]	3.6%	8.3%

shows measles to be the most common vaccine-preventable cause of death. In the Punjab study, tetanus was the most common account of the high incidence of neonatal tetanus. Although respiratory and diarrhoeal diseases are the most common causes of death, they are multifactorial in aetiology and are not preventable by vaccines available today. Using the figures in Table 2 and current estimaters of the child population and childhood mortality rates in India, it can be conservatively estimated that measles kills over 200,000 children under five, annually. In other words, of the more than 20 millions infants born each year, one in 100 will die of measles before age five. This estimate of the measles mortality rate is similar to the rate published 20 years ago.[5] In the intervening years the estimated annual measles mortality has increased from 85,000 to 200,000 due to population growth without a measles immunisation programme.

The above data shows that measles is a serious public health problem in India. Fortunately it is a problem for which a solution is readily available, namely measles vaccine, which has been proven both safe and effective.

Measles Vaccine and Seroconversion

The live attenuated measles virus vaccine has been in use in many parts of the world for two decades, and has a very high protective efficacy.[6] Table 3 displays seroconversion rates in American, Kenyan and Indian children and the protective efficacy rates in American children[27-31]. It is evident that seroconversion (development of antibodies) and efficacy (protection from disease when exposed) are related to the age of the child at vaccination. This is because maternal antibodies in the infant prevent infection and seroconversion.[32] These antibodies are catabo-

Table 3 : Seroconversion and efficacy rates of measles vaccination

Age at Vaccination (Months)	% Seroconversion US	% Seroconversion Kenya	% Seroconversion India	% Efficacy US
6	32	43	85	56
7	58*	93*		
8	71	90		
9	72		94	
10	85			64
11	95	100		
12	95		98	91
13	96			94
14	95			
15	93			95
16	100			

* Difference significant by x^2, $P<0.01$.

lised at a steady rate: therefore, as age increases the maternal antibody level declines and the likehood of seroconversion increases. In American children both seroconversion and efficacy rates are greater than 90 per cent when they are vaccinated at 12 months, and these rates exceed 95 per cent if vaccination is at 14-15 months. It appears that Kenyan children may seroconvert earlier as their seroconversion rate is over 90 per cent at 7 months[28] Indian children seem to fall between American and Kenyan children in their age specific seroconversion rates.

Other studies in Indian children have reported discordant results. Two groups have reported 60-70 per cent seroconversion rates in infants of 6-12 months.[21,33] A recent study showed 85 per cent seroconversion in infants over 10 months.[34] One well-conducted study reports a rate of 95 per cent seroconversion in children aged 6 to 18 months, but no age-specific rates were given. [35] An investigation of an outbreak of measles in villages near Vellore demonstrated 100 per cent protective efficacy of the vaccine when given to children at or after 12 months of age.[9]

In short, the seroconversion rates and proctective efficacy are very high in Indian children given measles vaccine at 12 months or later. Further studies are awaited to define age specific seroconversion rates at earlier ages. The principles for successful vaccination against measles are, 1) Vaccinate before the age of occurrence of the disease 2) Vaccinate at ages when seroconversion and efficacy are high 3) Vaccinate as high a proportion of susceptible as possible

Age of Vaccination

There has been discussion regarding the optimum age for measles immunisation in India [6,7,34]. The first principle above argues for early immunisation, perhaps at six months. The second principle indicates immunisation at an older age, say fifteen months. A balance must be struck between these two optima.

One approach is to use estimates of age-specific incidence and seroconversion rates and to calculate the number of measles cases prevented by immunisation at specified ages. This has been done in Table 4, using the serological data from

Table 4 : Reduction of measles cases by vaccination at various ages

Age	Estimated % previously infected	Estimated % seroconversion	Estimated % Measles cases prevented*
6 months	1-3	30-50	29-50
9 months	4-9	70-90	64-86
12 months	10-40	95-100	57-90
15 months	15-50	100	50-85

*100—(% previously infected) $\times \frac{\%\ \text{seroconversion}}{100}$ = % Cases prevented.

figure 1 to estimate incidence rates and assuming that Indian children will seroconvert at rates between those of Kenyan and US children. Note that immunisation between 9 and 12 months of age will prevent the greatest number of cases. This supports the recommendations of the Indian Academy of Pediatrics and the Ministry of Health and Family Welfare[7]. The table shows that the optimal age of immunisation depends on the local pattern of disease. During epidemics and in communities with a high proportion of cases before 1 year of age, 9 months is the best age for immunisation. Vaccination at the first birthday or later is more appropriate for inter-epidemic periods and for communities with few cases before 1 year. An effective immunisation progrom will likely shift the median age of infection upwards, and the optimal age for immunisation could also be moved upwards to take advantage of the higher seroconversion rate.

Strategy of Immunisation

The means of obtaining as high an immunisation coverage rate as possible is the strategy discussed here. If a high proportion of susceptibles are vaccinated: the number of susceptibles remaining will be too low to sustain transmission within the community, and the periodic epidemics of measles should not occur.

Two strategies for measles immunisation have deen described. Conventional *immunisation of children in clinics* as they reach the recommended age is the first strategy. It requires that highly motivated and well-informed parents bring their children for immunization at the correct time, and that clinics have a constant supply of properly stored vaccine. This strategy has not been successful in achieving high coverage rates with DPT or OPV in India. Even if all children attaining the optimal age are vaccinated in clinics, this technique will reduce susceptibles relatively slowly and lead to the interruption of epidemics only after a few years.

We have suggested an alternative trategy, the annual immunization of children near their homes by mobile teams [36]. We feel this *pulse immunisation* is better suited to our conditions. Because vaccine is brought to neighbourhoods after publicity, parental motivation is less important. The difficulty of cold chain management is reduced since there are fewer steps between producer and the child. The first immunisation pulse should include all children under five who have not had measles. Assuming a high coverage during this initial pulse, the eqidemic pattern will be interrupted. After this first pules, annual immunisation of children over one year will immunise new susceptibles. The availability of central vaccine storage and mobile teams allow quick intervention to stop measles epidemics if they develop. Other advantages in the utilization of resources and in the further development of primary health care delivery have been discussed [36].

Conclusions and Recommendations

As a means to reduce the mortality and improve the health and nutrition of our children, measles immunisation should become a part of the national immunisation programme, and receive the highest priority. The pulse immunisation strategy is better suited to India than the conventional strategy of year-round, clinic based

immunisation. As India's requirement of measles vaccine will be over 20 million doses annually, it must be manufactured within the country as a priority in the control of communicable diseases. As the nation with the third largest group of scientists and technicians and with the present state of rapid advances in technology, India should achieve this with no further loss of time.

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