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Antibody response to measles immunization in India*

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Antibody response to measles vaccine was measured in 238 subjects aged 6–15 months. Seroconversion rates ranged from 74% at 6 months of age to 100% at 13–15 months; the differences in age-specific rates were not statistically significant. The postimmunization antibody titres increased with increasing age of the vaccinee. Seroconversion rates and antibody titres in 49 subjects with grades I and II malnutrition were not significantly different from those in the 189 normal subjects.

These results support the recommendation of 9 months as a satisfactory age for commencement of measles immunization in India. However, the highest antibody levels and seroconversion rates were obtained in children over 12 months of age.

In recent years, much discussion has centred on the issue of the optimum age for measles immunization in developing countries. While the recommended age in developed countries is 15 months (*1*), this might be inappropriate in areas where the prevalence of measles among infants is relatively high (*2*), and where the disease is often accompanied by serious complications (*3*) and significant mortality (*4*, *5*). The current recommendation in India is to commence measles immunization at 9 months of age (*6*). This study was conducted to record the age-specific antibody response to measles vaccine in order to evaluate this recommendation.

MATERIALS AND METHODS

The study population consisted of all children aged between 6 and 15 months who attended the immunization clinics of the Departments of Community Health and Child Health of the Christian Medical College Hospital, Vellore, during the period March–June 1981.

Consent was obtained from the parents of each subject. Children with any acute illness or fever at the time of presentation, or a history of prior measles or measles immunization, were excluded from the study. Age as given by the parent was confirmed for all but 3 children from records of dates of birth. Age refers to number of completed months at the time of immunization. Every child was weighed before immunization and nutritional status was assessed according to the recommendations of the Indian Academy of Pediatrics (*7*).

Before immunization, fingerprick blood samples were collected in heparinized capillary tubes from 278 children. A dose of measles vaccine was then administered. Four weeks later, 145 of the 278 children returned for a second visit, and a further sample of blood was collected. For those who did not return on the specified date, reminders were sent by post and home visits were made. The second sample was thus collected from a further 82 children by 6 weeks after immunization, and from 11 children by 10 weeks after immunization.

The vaccine used in this study was Attenuvax (Moraten strain).[a] Careful attention was paid to the maintenance of the cold chain and protection of the vaccine against exposure to light. The vaccine potency was tested at the beginning of the study and again towards the end of the study. Vaccine-virus infectivity assays were done in tube cultures of Vero cells using standard laboratory procedures.

All plasma samples were screened at a 1:4 dilution for the presence of measles haemagglutination-inhibition (HI) antibody using standard microtitration methods with appropriate precautions and controls (*8–10*). Samples with antibody were titrated in doubling dilutions from 1:4 to 1:512. Children whose sera showed no antibody activity at the 1:4 dilution were assumed to be seronegative. The proportion of initially seronegative children who acquired measles virus antibody after immunization was termed the seroconversion rate.

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[a] Merck, Sharp and Dohme.

RESULTS

Although 278 children were recruited into the study, postimmunization sera were obtained from only 238 children (120 male and 118 female). Of these, 230 were seronegative to measles virus prior to immunization. Their age-specific seroconversion rates are presented in Table 1. The lowest rate was seen in the 6-month age group, but the association between age and seroconversion rate was not statistically significant. The seroconversion rates were 87%, 94% and 98% in the age groups 6–8, 9–11 and 12–15 months, respectively (Fig. 1).

The postimmunization geometric mean titres (GMT) according to age are presented in Table 1. The GMT increased progressively with age at immunization, this association being statistically significant ($r = 0.81$, $P < 0.05$). In children immunized at 6–8, 9–11 and 12–15 months of age, the GMTs were 42.0, 50.2 and 66.0, respectively (Fig. 1).

Antibody response according to nutritional status and age is summarized in Table 2. As there were only 32 and 17 children with grades I and II malnutrition respectively, they were considered as a single group. Although seroconversion rates were higher in normal children, the difference was not significant. The variations in GMT were not consistent or significant.

The potency of the vaccine was measured twice, once at the commencement of the study and again at the end. The titres varied between 2000 and 3000 $TCID_{50}$[b] per dose.

DISCUSSION

Of the 278 children initially recruited, 238 (85.6%) completed the study. The distribution according to age, sex, place of clinic and nutritional status was not significantly different in those completing and not completing the study; thus the effect of non-compliance on the results is assumed to be negligible.

[b] Median tissue culture infective dose.

Table 1. Age-specific seroconversion rates and geometric mean antibody titres (GMT) following measles immunization

Age (months)	No. tested	No. initially sero-negative	No. showing sero-conversion	Sero-conversion rate (%)	GMT
6	32	31	23	74.2	37.2
7	38	38	33	86.8	40.3
8	29	28	28	100	48.7
9	37	37	36	97.3	47.9
10	25	24	21	87.5	50.8
11	28	27	26	96.3	53.1
12	20	19	18	94.7	54.9
13–15	29	26	26	100	75.1
Total	238	230	211	91.7	

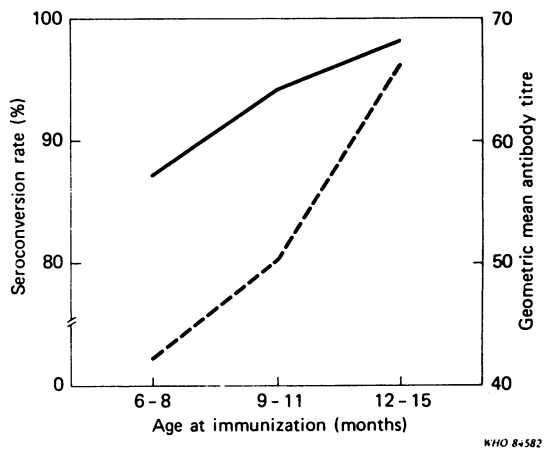

Fig. 1. Seroconversion rates (———) and geometric mean antibody titre (– – – –) following measles immunization, according to age.

Table 2. Seroconversion rates and geometric mean antibody titres following measles immunization according to nutritional status and age

Age group (months)	Normal children				Malnourished children			
	No. initially seronegative	No. showing seroconversion	%	GMT	No. initially seronegative	No. showing seroconversion	%	GMT
6–8	86	75	87.2	40.7	11	9	81.8	54.9
9–11	67	65	97.0	47.5	21	18	85.7	61.6
12–15	28	28	100	80.0	17	16	94.1	54.4

Table 3. Reported seroconversion rates after measles immunization in various areas

Area	Reference	Age group (months)	Seroconversion rate (%)
India	*16*	⩾6	95
India	Present study	6–8	87
		9–11	94
		12–15	98
Kenya	*13*	6–9	87
		12	100
Latin America	*15*	6–8	73
		9–11	91
		12	94
Nigeria	*14*	7–11	64
		⩾12	89
USA	*11*	7–11	79
		⩾12	100
USA	*12*	9–11	86
		⩾12	97

The potency of the measles vaccine ranged from 2000 to 3000 $TCID_{50}$. In many studies of measles virus antibody response in relation to age and the presence of maternal antibody, the role of the potency of vaccine has been ignored. For comparison of the results of different studies, it would be useful if the vaccine virus strain and potency were given.

A comparison of seroconversion rates according to age in different parts of the world is presented in Table 3 (*11–16*). In all studies, the highest seroconversion rates were seen in children aged 12 months or over. The rates seen in the 6–11-month age group in Kenya (*13*), Latin America (*15*), and in the present study were higher than those obtained in the USA (*11*, *12*). This geographic variation may also apply to other developing countries, enabling initiation of measles immunization at 9 or even 6 months of age with good seroconversion rates.

However, if epidemiological circumstances allow immunization to be delayed without significant risk of measles in the interim period, the maximum seroconversion rate would be obtained at or after 12 months of age. An added advantage in postponing immunization to this age is that a higher antibody level is also achieved. This finding is supported by several studies in which higher antibody levels were found in children immunized after 12 months of age as compared with those immunized at a younger age (*17*, *18*). It has been demonstrated by many workers that maternal antibodies may persist in infants and interfere with their response to measles vaccine even beyond the first 12 months of age (*19*, *20*). The epidemiological significance of this observation is not clear.

Low-level immune response in infants has been shown to interfere with subsequent reimmunization with measles vaccine (*21*). Furthermore, there have been reports of vaccine failure and consequent higher attack rates in those immunized before their first birthday than in those immunized later (*19*, *22*, *23*). It has also been postulated that high antibody titres may prove beneficial for long-term protection as well as in transplacental transmission of antibody to offspring (*21*).

There have been four earlier studies on serological response to measles vaccine in India (*16*, *24–26*). Three studies had an inadequate sample size or technical flaws that detracted from the reliability of the results (*24–26*). In the fourth study, which was technically satisfactory, antibody response was not assessed according to age: the overall seroconversion rate in 6–18-month-old children was 95% (*16*).

The nutritional status of the subjects did not significantly affect either seroconversion rates or GMT of measles antibody (Table 2). This observation has been corroborated by other authors (*15*, *27*). Far from being a contraindication, malnutrition is a strong indication of the urgent need for immunization, since in such children the disease is likely to be more severe, and more often associated with complications and mortality than in normally nourished subjects (*3*, *27*, *28*).

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RÉSUMÉ

RÉPONSE EN ANTICORPS À LA VACCINATION ANTIROUGEOLEUSE EN INDE

La réponse en anticorps au vaccin antirougeoleux vivant a été mesurée par inhibition de l'hémagglutination (HI) selon une méthode standard de microtitrage, chez 238 enfants âgés de 6 à 15 mois.

La proportion d'enfants séronégatifs (à la dilution 1:4) ayant acquis des anticorps antirougeoleux après vaccination (taux de séroconversion) allait de 74% chez les enfants âgés de 6 mois à 100% chez les enfants âgés de 13 à 15 mois; les différences de taux de séroconversion en fonction de l'âge n'étaient pas statistiquement significatives. Ces taux étaient respectivement de 87%, 94% et 98% pour les groupes d'âge 6–8 mois, 9–11 mois et 12–15 mois.

Le titre moyen géométrique (GMT) des anticorps mesurés par inhibition de l'hémagglutination après vaccination augmentait progressivement en fonction de l'âge à la vaccination, cette association étant statistiquement significative ($r = 0{,}81$; $P < 0{,}05$). Chez les enfants âgés de 6–8 mois, 9–11 mois et 12–15 mois, les GMT étaient respectivement de 42,0, 50,2 et 66,0.

Le taux de séroconversion et le titre d'anticorps chez 49 sujets souffrant de malnutrition de degré I ou II ne différaient pas de façon statistiquement significative de ceux observés chez les 189 sujets normaux.

Les résultats de divers travaux suggèrent que les taux de séroconversion observés dans le groupe d'âge 6–11 mois peuvent varier d'une région du monde à l'autre. Dans certaines régions, il serait ainsi possible de débuter la vaccination antirougeoleuse à 9 mois ou même à 6 mois avec des taux de séroconversion satisfaisants.

Toutefois, si les conditions épidémiologiques permettent d'attendre le temps nécessaire sans qu'il y ait de risque de rougeole, on obtiendra le meilleur taux de séroconversion et le meilleur titre d'anticorps avec une vaccination pratiquée à ou après l'âge de 12 mois.

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