EXPERIENCE WITH A MEASLES VACCINE MANUFACTURED IN INDIA

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Five hundred and twenty seven children between 7 months and 2 years of age were vaccinated with measles vaccine manufactured by the Serum Institute of India. The sero-conversion rate in children who had no antibodies previous to vaccination was 98.4% as tested in HI. Ninety per cent of children who had pre-vaccination measles antibodies showed a two-fold or more rise in HI antibodies. The side reactions of the vaccine were negligible.

Key words: *Measles antibody, Immunization, Indigenous vaccine.*

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Measles, with its enormous morbidity, high frequency of complications and mortality in children, has drawn attention of the health planners all over the world. India being no exception, has introduced measles vaccine in the Universal Immunization Programmes since 1985. Several workers have reported the results of vaccination in India with vaccines obtained from abroad(1-8). The present communication reports the results of the studies of the immunization of children vaccinated with a vaccine manufactured in India.

Material and Methods

Healthy infants and children attending the Outpatient Immunization Clinic of the Pediatric Department of the Sassoon General Hospitals, Poona, were randomly selected for administration of the vaccine. The age of the children varied between 7 months and 2 years. Each child was subjected to clinical examination and children with history of fever and rash suggestive of measles were excluded. The vaccine was administered subcutaneously on the lateral side of the thigh by following usual precautions. It was manufactured by the Serum Institute of India Ltd. (Pune) prepared with the Edmonston-Zagreb strain grown on human diploid cells and contained "not less than 1000 TCID50 of the attenuated virus" as prescribed by the Indian Pharmacopoeia (1985).

Just before the administration of the vaccine, blood was collected by venepuncture. The parents were advised to report on days 3, 7, 14 and 30 after vaccination for any untoward effect and adverse reactions. Another sample of blood was collected 4-6 weeks post-vaccination. The sera was stored at –20°C till tested.

The sera were tested for measles virus antibody by Hemagglutination Inhibition

(HI) test(5). Briefly, the Edmonston strain of measles virus was grown in VERO cells and the tissue culture fluid harvested on the 5th day when the cells showed complete cytopathic effect. The tissue culture fluid was harvested, centrifuged and subjected to Tween 80 and ether treatment. The aqueous phase was collected and used as antigen. For the testing of the sera 4 hemagglutinating units were employed.

The test sera were inactivated at 56°C for 30 min. The sera were adsorbed with monkey erythrocytes as follows: to 0.1 ml of serum was added 0.025 ml of prewashed packed rhesus monkey erythrocytes and incubated overnight at 4°C. The mixture was centrifuged and the supernatant was diluted in PBS for hemagglutination inhibition test. Appropriate positive and negative controls were employed in each test.

Results

Blood samples collected previous to the administration of the vaccine as well as after the vaccination were available from 527 children for analysis. The age and genderwise distribution of the children are shown in *Table I*. Of these, 381 children did not have any detectable HI antibody in the prevaccination blood sample (Category "A"). The remaining 146 children (Category "B") had detectable antibodies in the prevaccination samples. There was no difference in the geometric mean titres of HI antibodies in any age group between the male and female children, therefore, for further analysis the difference in the genders was ignored.

Table II-A shows the further distribution of the 381 children who had no HI antibodies in the prevaccination blood sample (Category "A"). Of these, only 6 did not sero-convert, giving a percentage sero-conversion of 98.4. All children who sero-converted had HI titres 1:8 or more.

Of the 146 children in category "B", 143 had HI titre of 1:8 and 3 had titres of 1:16 (*Table II-B*) in their pre-vaccination serum samples. No rise in HI titre in post-vaccination samples was seen in 13 children. If two-fold rise in HI titre is considered as sero-conversion, then 90.9% children in this group responded to the vaccine. However, 68.5% children responded to develop 4-fold or more rise of antibody titre in this category.

The largest number of children in both the categories was in the age group 9-12 months. However, in both the categories there were enough children in the older age groups for statistical comparison.

TABLE I—*Distribution of Sera Tested*

Age (mo)	Pre-vaccination HI titre + ve		Pre-vaccination HI titre –ve		Total
	Male	Female	Male	Female	
<9	3	2	8	9	22
9-12	61	44	157	116	378
13-18	8	9	36	26	79
≥19	10	9	17	12	48
Total	82	64	218	163	527

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TABLE II-A— *Number of Sera Showing Sero-conversion in Different Age Groups: Category A (children who had no Detectable Antibodies in the Pre-vaccination Serial)*

Post vaccination HI titre	Pre-vaccination HI titre –ve				
	<9	9-12	13-18	≥19	Total
–ve	–	5 (1.83)	–	1 (3.45)	6
8	1(5.88)	39 (14.29)	12(19.35)	6 (20.69)	58
16	13(76.47)	177 (64.84)	40(64.52)	12 (41.38)	242
32	3(17.65)	46 (16.85)	8(12.90)	6 (20.69)	63
64	–	6 (2.20)	2(3.23)	4 (13.79)	12
Total	17	273	62	29	381

TABLE II-B—*Category B (Children who had Detectable Antibodies in the Pre-vaccination Sera)*

	Pre-vaccination HI titre = 8					Pre-vaccination HI titre = 16				
	<9	9-12	13-18	≥19	Total	<9	9-12	13-18	≥9	Total
No rise	–	8 (7.77)	3 (17.65)	–	11	–.	–	–	1	1
2 fold rise	–	24 (23.3)	5 (29.41)	5 (27.78)	34	–	2	–	–	2
4 fold rise	5	67 (65.05)	9 (52.94)	10 (55.56)	91	–	–	–	–	–
8 fold rise	–	4 (3.88)	–	3 (16.67)	7	–	–	–	–	–
Total	5	103	17	18	143	–	2	–	1	3

Figures in parentheses indicate percentages.

There were only 22 children below 9 months of age; of these 17 belonged to category "A" and 5 belonged to category "B". Of the 17 category A children, all responded well to the vaccine, the GM titre being 17.29 which was statistically not different from children of older age groups (*Table III-A*). Similarly, the 5 children who were less than 9 months of age in category B had developed GM titre 32.0, which was also statistically not different from the other age groups in the same category (*Table III-B*). In fact, the post-vaccination GM titres of different age groups within a category of the vaccinees were statistically

TABLE III-A— *Geometric Mean Titres in Vaccinees: Category A (Children who had no Detectable Measles Antibody in Pre-vaccination Sera)*

Age (mo)	Pre-vaccination GM	Post-vaccination GM
<9	ND	17.29 (17)
9-12	ND	15.96 (273)
13-18	ND	15.96 (62)
≥19	ND	17.61 (29)

ND: Pre-vaccination titres not detectable

TABLE III-B— *Geometric Mean Titres in Vaccinees: Category B: (Children who had Detectable Measles Antibody in Pre-vaccination Sera)*

Age (mo)	Pre-vaccination GM	Post-vaccination GM	
<9	8.0	32.0	(5)
9-12	8.11	25.23	(105)
13-18	8.0	20.43	(17)
≥19	8.3	28.68	(19)

Figures in parentheses indicate the number of vaccines in each group.

not different from each other (*Tables III A and B*).

Of the 527 children vaccinated, only one had high fever (102°F), rash was reported in one, diarrhea in one and local induration in two. None reported symptoms like incessant crying for more than 4 hours, convulsions, any other neurological manifestations or development of local abscess, *etc.*

Discussion

Several authors have reported the effect of measles vaccine in Indian children. In each study, the vaccine had been manufactured abroad. In a study at Vellore(1), which had administered "Attenuvax" (Merck, Sharp and Dhome: Moraten strain vaccine) the sero-conversion rates in normal children who were initially sero-negative was 92.8%. The 6-8 month group had 87.2% sero-conversion, 9-11 month group had 98% while the 12-15 month group had total sero-conversion. The malnourished children had less sero-conversion rates ranging from 81.8 to 94.1% in the different age groups, respectively. The number of malnourished children in the different age groups was quite small.

In a study carried out in Bombay, the overall sero-conversion rate was 95%(4). A study carried out at Delhi with Schwarz strain vaccine had sero-conversion rate of 82.8%(3). In another report with a vaccine imported from Belgium (Rimevax, Schwarz strain) the sero-positivity varied from 78.9 to 96.1% in different age groups but the assessment of the results was technically faulty(5). In a multicentric study(6) the sero-conversion rate was 90.27% for an imported vaccine. Follow up of the vaccinated children showed that the efficacy of the vaccine was 69%.

In the present study, the overall sero-conversion rate in children who had no previous antibodies, was 98.4%. In this category, children of different age groups sero-converted equally well, *e.g.,* in children <9 months the sero-conversion was 100%, 9-12 months 98.16%, 13-18 months 100% and ≥19 months 96.65% (considering 1:8 serum antibody titre as sero-conversion). It seems that all the age groups reacted almost equally well to the vaccine. In the category of children which had antibodies previous to vaccination, a 2-fold rise was seen in 90% and 4-fold or more rise was observed in about 69% of children after vaccination.

It has been postulated that even if 90% protection is achieved by effective immunization by 100% vaccine coverage, the unprotected 10% will be sufficient to maintain measles endemicity in a country(7). It can be assumed that if a vaccine gives higher sero-conversion rate, then measles endemicity can be further reduced. With the SII vaccine which could produce sero-conversion in 98.4% of children, the potential pool of susceptible children would be smaller.

Most of the above mentioned studies did not report about the side-reactions of

the vaccine. In a study reported with "Rouvax" (Schwarz strain vaccine manufactured by Institute Merieux, France, marked by SII, Pune), fever was reported in about 25% of children, local pain in 4.8%, excessive crying and irritability in about two-third (66%) of all cases, seizure in 0.46%, which was associated with high fever. Diarrhea was present in 5.6% of children and rash in 3.1%(8). In our group of children, mild fever which did not cause any concern to the mothers was reported in about 80% of children, while the incidence of other symptoms (which would alarm the mother) like high fever, convulsions, altered sensorium, irritability, incessant crying were absent. The occurrence of diarrhea and rash was also minimal. Therefore, in conclusion, it can be said that measles vaccine manufactured in India with the Edmonston-Zagreb strain has good immunogenicity and high degree of acceptability.

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