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## The Response of Children to a Reduced Dose of Measles Vaccine given with and without other Vaccines (Pilot Study)

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### INTRODUCTION

The cost of measles in terms of lives of children under five in developing countries has varied from two to 21 per cent. of cases in different surveys (Morley, 1969). The cost in terms of economics resulting from bed occupancy may make heavy inroads into strained budgets in even relatively well off countries (Saleh, 1970).

The introduction of live vaccines has grossly reduced both the morbidity and mortality of the disease — in some places by over 90 per cent each (reviewed by Naficy and Nategh, 1972). While therefore the achievement of a 100 per cent. vaccination amongst children is desirable, there are, in developing countries where much of the population is rural and widely scattered, certain practical difficulties which present themselves. Of these, time (the doctors' and nurses') and money have the greatest significance. To overcome these problems a pilot study was undertaken to determine whether sero-conversion would occur satisfactorily if a dose approximately 1/5 of that recommended was given hence saving both in vaccine and in time by virtue of the increase in the number of doses per syringe full. The dose was tested when given alone and at the same time as BCG, oral polio vaccine and smallpox vaccine.

### METHODS

The investigation was carried out in the course of the routine vaccination programmes in the Midlands province of Rhodesia. Children from four months to seven years from the well populated Nembudzia area attended the local clinic. Three groups of approximately 50 each were selected at random. Group I children were a little older (mean 3,3 years) than those in groups II and III who were matched for age and sex (mean 1,9 years). Group I received no vaccine (until the experiment was completed); Group II received 1/5 standard dose intradermally in the right deltoid region of Wellcovax measles vaccine; Group III received the 1/5 standard dose of measles vaccine and at the same time were inoculated with BCG (Behringwerke), oral polio vaccine (Sabin R.I.T.) and smallpox vaccine (Institut Vaccinal du Docteur Pourquier, Montpellier, France). All the children appeared well nourished and had no obvious concurrent illness.

After an interval of 29 days the children were bled by finger, thumb or heel prick and two or more capillary tubes were filled and sealed with plasticine. The tubes were kept at local ambient temperature (c 20°C) for 24 hours approximately until processed.

The tubes were spun in a haematocrit centrifuge for five minutes and the sera placed directly into cups of standard microtitre plates. Each was diluted with an equal volume of phosphate buffered saline. To remove non-specific inhibitors an equal volume of 50 per cent washed fresh vervet monkey red cells were added and left overnight at +4°C. The plates were then centrifuged and measured aliquots transferred to clean plates. Dilutions were made from one in 16 to one in 64 initially and standard haemagglutination inhibition tests performed according to the method given in Lennette and Schmidt (1964). Sera positive at one in 64 were further titrated to an end point if there was enough serum left to do so.

## RESULTS

## Group I

No vaccinations		
Total	50	
Titre	0=22	44%
"	16= 2	4%
"	32= 6	12%
"	64= 5	10%
* "	"over 64"=7	14%
"	128= 5	10%
"	256= 3	6%
		56%

## Group II

1/5 dose measles vaccine only

Total	31	
Titre	0= 4	13%
"	16= 1	3%
"	32= 0	—
"	64= 2	6%
* "	"over 64"=10	30%
"	128= 6	20%
"	256= 5	16%
"	512= 3	10%
		87%

## Group III

1/5 dose measles and other vaccines

Total	39	
Titre	0= 1	2,5%
"	16= 1	2,5%
"	32= 4	10%
"	64= 5	13%
* "	"over 64"=13	33%
"	128= 8	20%
"	256= 6	15%
"	512= 0	—
"	1024= 1	2,5%
		97,5%

\*insufficient serum to filtrate to end-point.

## DISCUSSION

There is a statistically significant difference between those with anti-measles antibody in group I and group II ( $P < 0,001$ ) and no such difference between groups II and III. Thus superficially it would seem that the 1/5 dose of vaccine achieves sero-conversion in a high proportion of cases and further the simultaneous administration of other vaccines did not affect this response — a finding already noted with vaccine in full doses (Froeschle & Casey, 1965, Gateff, 1972). Presumably the safety margin allowed by the manufacturers for natural inactivation and deterioration of vac-

cines accounts for the success of this reduced dosage. Morley (1973) has recommended the use of 1/5 dose measles vaccine provided certain technical precautions are taken and clinical trials in this country have suggested that the method gives adequate protection.

Following an attack of measles or the administration of vaccine, HAI antibodies appear first at about 12 days and reach a peak between 21 and 28 days. The HAI test equates with the neutralisation test and is the most satisfactory indicator of long term immunity against measles (Cutchins, 1962). Maximum levels vary a great deal (Krugman, Giles, Friedman & Stone, 1965). After a number of years residual levels may be quite low with apparent immunity and what is therefore important here is the rate of conversion rather than levels reached.

This study indicates that the use of the reduced dosage can be cautiously recommended and warrants further investigation. The small numbers and the lack of certain controls, i.e. a group immunised with the full dose are obvious features which make definitive conclusions impossible. However the results are distinctly promising and further long and short term studies should be undertaken with particular emphasis on clinical follow up.

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