

Efficacy of measles vaccine

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In previous papers the incidence and severity of measles (Morley, 1962; Morley, Woodland & Martin, 1963) and the clinical reactions of Nigerian children to Enders 'B' live attenuated vaccine (Morley, Katz & Krugman, 1963) in West Africa, have been described. In this paper the results of the use of this vaccine in preventing measles are recorded.

Vaccination trials were made on two groups of children. The first consisted of 53 children from the village of Imesi, where a longitudinal child health study has been undertaken, and the second of 2000 children attending the 'under fives' clinic at the Wesley Guild Hospital in Ilesha.

THE IMESI VILLAGE GROUP

These children were involved in the preliminary trial of measles vaccine described under stage 1 of the preceding paper. They were paired as far as possible by sex, age and weight. Twenty-six children received live liquid measles vaccine; the 27 controls were given pertussis/tetanus vaccine. This was not a blind study, since the investigators knew which children had received measles vaccine. The children were followed for 18 months; during this period there was one minor and one major outbreak of measles in the village. The incidence of measles in the groups is set out in Table 1.

Measles was not seen in any of the children in the vaccine group, as opposed to 19 in the control group. The three deaths, of which two were due to measles, were all in the control group.

THE ILESHA HOSPITAL GROUP

This group was drawn from the 'under fives' clinic at the Wesley Guild Hospital, Ilesha, and included all the children in Stages 2 and 3 described in the preceding paper (Morley, Katz & Krugman, 1963), and a further 1000 on whom observations on the severity of the vaccine reaction were not made. The children have been followed through a period varying from 6 to 20 months. All have been exposed in one epidemic of measles, and some in two.

Vaccination was offered to children between the age of 6 months and 2 years. The mothers were warned that it would be effective in only half the children, but in spite of this over 2000 mothers brought their children for vaccination within

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14 months. By a system of random numbers, these children were divided into two equal groups. One group received measles vaccine, the first 120 without gamma globulin, and the remainder with gamma globulin at a dosage of 0.02 ml., equivalent to 40 units of measles antibody, per pound of body weight. It has been found that this dosage of gamma globulin represents approximately the amount needed to suppress post-vaccination reactions.

Table 1. *Incidence of measles in children receiving measles vaccine and in the control group*

	Number in group	Clinical measles	Deaths		Number observed for 18 months	Number that left the village
			Measles	Other causes		
Vaccine group (given liquid measles vaccine)	26	0	0	0	23	3
Control group (Given pertussis/tetanus vaccine)	27	19	2	1	22	2

The other group was a control one, receiving gamma globulin and inert material identical with that used in the culture of the virus; the children in this group only received temporary protection from the severe effects of measles.

In the follow-up period all children with 'measles-like' illness were seen, as far as possible, by one of us. The diagnosis of measles was at times difficult. Illnesses resembling measles were frequently seen; facilities for serological confirmation of the diagnosis were not available.

At the end of the trial period at the Ilesha Hospital 1962 record cards were available. Among these 272 showed a record of an illness suggestive of measles. Eighty of these illnesses were among the 991 children who had received vaccine, and 192 among the control 971 children. Successful vaccination against measles is believed to produce a life-long immunity, and there was no reason to believe that the vaccination was unsuccessful in a large proportion of the Ilesha children. It seems probable that the occurrence of so much 'measles-like' illness in the vaccinated children was a reflexion of the difficulty in making a firm diagnosis of measles in the African child at one visit. The problem of diagnosis also arose in the longitudinal study described in a preceding paper. The children in that study were, however, seen on many occasions during the illness, and there was less difficulty in deciding which illness was likely to be true measles. In the present study the follow-up had to be made in a crowded and over-worked clinic. Many of the children were seen only once and in the later stages of illness, and it was impossible to study each case individually and follow the illness through.

Among the children in this trial there were 17 known deaths. Six were due to causes other than measles, 5 of which were in the vaccinated group and 1 in the control group. Eleven deaths occurred during or immediately following measles. All of these were in the control group.

WEIGHT-GAIN FOLLOWING MEASLES VACCINATION

In a previous paper (Morley, Woodland & Martin, 1963) measles was shown to be responsible for a severe weight loss in a group of Nigerian village children. One-quarter of the children surveyed lost 10% or more of their weight. In 15% the weight lost was not recovered for more than 3 months. These findings were in a group of children under 3 years old, at a time when the normal child gains weight steadily. As a result of this experience an attempt was made to see whether the incidence of measles in the control group affected their weight-gain in the months following vaccination as compared with the group that were vaccinated and presumably were protected against measles. Mothers were encouraged to bring their children to be reweighed at the end of the trial. As the children had been followed for periods that varied between 6 and 20 months the average weight-gain per month for each child was estimated. The mean monthly weight in 283 vaccinated and 273 control children subdivided into age groups are set out in Table 2.

Table 2. *Mean weight-gain per month in children following measles vaccination compared with a non-vaccinated group*

Age in months	Vaccinated		Controls		Difference (vaccinated - control)
	Number	Mean gain (oz)	Number	Mean gain (oz.)	
6-8	69	8.82	78	7.88	0.94 ± 0.62
9-11	90	7.89	82	7.25	0.64 ± 0.47
12-14	71	7.81	54	6.47	1.34 ± 0.70
15-17	36	7.42	33	6.77	0.65 ± 0.97
18-20	17	7.76	26	6.90	0.86 ± 1.2

The mean gain in the controls was lower than in the vaccinated. The differences for each age group are not statistically significant, but if the consistency of the five differences is tested the probability is significant ($P = 0.006$). There is at least a suggestion that the mean gain in the control children was influenced by the occurrence of measles in some children in this group.

DISCUSSION

There is already good evidence that Enders 'B' vaccine will protect children against measles. This is based both on clinical observation, and laboratory studies of antibody titres (Krugman, Giles & Jacobs, 1960; McCrumb, Kness, Saunders, Snyder & Schleuderberg, 1961). The protection is known to last for two years and may be life-long (Krugman *et al.* 1960; Kempe, Ott, St Vincent & Maisel, 1960). When Enders 'B' vaccine alone was used, a serological conversion rate of 96.5% was achieved. If gamma globulin is given simultaneously at a level of 40 units per pound of body weight, there is a slight fall in the conversion rate to 90.5% (Krugman, Giles, Jacobs & Friedman, 1962).

The findings in this study further support the protective value of the vaccine. Information on the deaths of 11 children from measles was obtained; all 11 were

found to be in the control group. An attempt was also made to identify measles in the children in the out-patient clinic during 20 months after the start of the trial. As children were frequently only seen once and at any stage of the disease, they were broadly classified as having a 'measles-like' illness. The number with such an illness in the control group far exceeded that in the vaccinated group.

In this population measles is believed to be the most common infection to precipitate kwashiorkor (Gans, 1961; Morley, Woodland & Martin, 1963). In this trial the vaccinated children showed a better mean gain in weight subsequent to inoculation than the control children, many of whom are likely to have developed the disease. We believe that measles vaccination may well prove to be an important step in reducing the incidence of overt malnutrition in Nigeria.

Carrying out blind controlled trials in any community with a vaccine which may produce a severe reaction carries a considerable moral responsibility. The authors felt that, because of the difficulty of explaining the purpose of the trials to the people, these responsibilities are particularly heavy in an under-developed community. In justification of the trials, it may be pointed out that in Nigeria measles is a severe and often fatal disease held in awe by the people. It is the greatest single cause of child admission to the Wesley Guild Hospital, and, as stated in a previous paper, is a major hazard of Nigerian childhood with an overall mortality of around 5%. Reactions to the measles vaccine, which might be considered too severe in a community where measles has a low morbidity and a negligible mortality, are less important when they are an alternative to a dangerous illness. Moreover, the authors are confident that the vaccine saved the lives of a few children, and that measles in a number of children in the control group in whom naturally acquired measles occurred, was attenuated by gamma globulin.

In a recent editorial in the *British Medical Journal* (11 November 1961) doubts were expressed whether there was sufficient evidence to justify extensive trials of measles vaccine. Since this article appeared, an International Conference on Measles has been held in Washington D.C., the results of which have been published in the A.M.A. *Journal of Diseases of Children*. The experience from several sources of measles vaccine presented at this conference should go a long way to establish the safety of the vaccine and justify larger scale trials. Using a combination of vaccine and gamma globulin, or a more attenuated vaccine such as that described by Schwarz (1962), the health services of West Africa should have at their disposal an effective method of preventing measles with all the hazards that this disease brings to West African children.

SUMMARY

1. Approximately 1000 Nigerian children between the age of 6 months and 2 years were given Enders 'B' measles vaccine, combined with gamma globulin in all except 120 children. A control group of similar numbers received gamma globulin alone plus inert material.

2. In a preliminary village study the 26 vaccinated children remained free of measles, 19 of the 27 control children developed measles and 2 of these children died.

3. In a blind study among children attending the large child out-patient clinic at the Ilesha hospital, a follow up was also attempted but was more difficult. In all, 272 cases of 'measles-like' illness were seen, 192 in control children, and 80 in the vaccinated group. The number in the vaccinated group is believed to be a reflexion of the difficulties under which this diagnosis was made, rather than a failure of the vaccine to immunize. Eleven children are known to have died from measles. All these 11 were in the control group who had not had vaccine.

4. The control children showed a smaller mean gain in weight than the vaccinated in the months following inoculation. The difference may have been due to poor weight-gain among the control children who developed measles.

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