*Human Volunteers.*—Before vaccines 3C and 4A were used in children, three adult volunteers were injected subcutaneously with each batch. No untoward reactions occurred.

### Discussion

No specifications have yet been formulated for the preparation of measles vaccines. With few differences the procedures used for the vaccines described here are those described by Enders *et al.* (1960) for the clinical trial batches used in the United States in 1959 and 1960. Two techniques found to increase the yield of measles virus from the tissue cultures were used in the preparation of the two British vaccines: lowering the temperature of incubation of the tissue cultures to 32° C. during the period of virus growth, and freezing and thawing of the cultures to liberate cell-associated virus. The freeze-dried preparation appears to be stable under normal field conditions. Even after exposure of vaccine ampoules to strong sunlight little loss of titre occurred. The amount of virus in the preparation, together with the degree of stability shown, is sufficient to ensure a potent vaccine even when transported without refrigeration or subjected to adverse storage temperature.

In the absence of specifications for the testing of measles vaccine it was decided to test equally seed lots and final vaccine batches, following the principles established for yellow-fever vaccine and elaborated to include some tests necessary for poliovirus vaccine. The extensive testing of both seed and final vaccine is a necessity for attenuated live poliovirus vaccines because of the high risk of extraneous viruses in any individual monkey-kidney culture batch used for propagating the virus. Yellow-fever vaccine, on the other hand, is grown in chick embryos, a tissue with a very low incidence of viral contamination, and the burden of testing lies mainly on the seed lot. Since measles vaccine is also prepared from chick-embryo tissue, a similar principle may be held to apply in the future. However, for exploratory studies, such as those reported here, testing of both seed and final batch seems justified even to the extent of looking for known human pathogens never yet encountered in chick embryos. The inoculation of monkeys by the intracerebral route serves, for example, as a test for neurotropic viruses as well as an indicator of the virulence of the vaccine strain.

In respect of attenuation of the measles virus the monkey test has several difficulties. The animals may undergo natural measles infection prior to or at the same time as the actual carrying out of the test; the criteria of behaviour of virulent and attenuated measles strains are poorly defined; and the clinical symptoms not always easy to observe. While viraemia in inoculated monkeys is common with virulent strains and rare with attenuated, it is recorded in one monkey given attenuated virus by Enders *et al.* (1960), more frequently by Schwartz *et al.* (1960), and in one monkey in our series of tests. These findings might be regarded equally as indicating that viraemia is an unreliable index of attenuation or that the vaccine strain is insufficiently attenuated or that a variable incidence of wild infection was present in each group. In view of these difficulties it would appear a more reasonable and practicable objective to perform the monkey test only on seed lots on the model of yellow fever vaccine, at least when routine batch production is begun.

### Summary

Descriptions are given of the origin and preparation of four batches of measles vaccine used in the clinical trials described in Parts II and III. The method of preparation and testing of the two batches prepared in Britain are given in detail. Some problems arising from individual tests are outlined and the principles underlying testing are discussed.

The vaccines consisted of infected chick-embryo-tissue-culture fluids. All four were of similar potency with from $10^{2.7}$ to $10^{3.4}$ TCD50 per human dose. Three vaccines were freeze-dried and the fourth was stored frozen at −70° C. Freeze-dried vaccine was stable under field conditions and resisted exposure to sunlight.

We are indebted to Dr. V. Udall, of the Wellcome Research Laboratories, for histological examinations of inoculated animals; and to Dr. S. L. Katz for advice and strains of virus.

## PART II. CLINICAL TRIAL IN NIGERIAN CHILDREN

BY

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Clinical trials of measles vaccines prepared in the U.S.A. from the Edmonston strain of measles virus have been made in children in the United States (Katz *et al.*, 1960a, 1960b; Stokes *et al.*, 1960) and in Panama (Hoekenga *et al.*, 1960). Vaccination was followed by the formation of measles antibody and, in studies where exposure was demonstrated, by protection against the natural disease. The principal vaccination reactions consisted of pyrexia, which occurred in about four-fifths of the cases, and rash, which occurred in about half; children exhibiting these reactions were noticeably less ill than those with natural measles, and respiratory complications were minimal.

In the trial described here the clinical and antibody response to measles vaccine has been studied in children in Nigeria, among whom the mortality from measles is very high; the social and epidemiological circumstances in Nigeria differ greatly from those in the U.S.A. and Panama.

### Procedure

There were three studies, each of which included a control group of children vaccinated with Salk type poliomyelitis vaccine. Three measles vaccines were used.

Vaccine L (liquid, Enders type), vaccine 3C (dried, low-temperature type), and vaccine 4A (dried, Enders type). These vaccines are described in detail in Part I. All vaccines were injected subcutaneously.

*Study 1. Vaccination with Liquid Vaccine at Ibadan.*—The 24 children in this group were vaccinated on November 3, 1960. The first 18 who attended the clinic were given measles vaccine L and the next six who attended received poliomyelitis vaccine.

*Study 2. Vaccination with Dried Vaccine at Ibadan.*—The 44 children in this group were vaccinated between November 17 and December 1, 1960. The children were allocated randomly into three groups, and received either vaccine 3C or vaccine 4A or poliomyelitis vaccine.

*Study 3. Vaccination with Dried Vaccine at Ilesha.*—The 22 children in this group were vaccinated between November 23 and 30, 1960. As in Study 2, the children were allocated randomly into three groups and received either vaccine 3C or vaccine 4A or poliomyelitis vaccine.

The children were drawn from the infant welfare clinics of University College Hospital, Ibadan, and the Wesley Guild Hospital, Ilesha. The previous medical histories of these children were on record and parental consent for vaccination was obtained for each child. None of the children taking part had a previous history of measles. The majority had had B.C.G. at birth; those who had not were tuberculin skin-tested, and only tuberculin-negative reactors were included in the trial. The majority had also had regular malaria chemoprophylaxis. Where doubt existed about the efficacy of prophylactic antimalarials, a curative dose of chloroquine was given on the day of vaccination. All but one of the children were under 2 years of age.

Each child was medically examined. Children with pyrexia—rectal temperature over 99.6° F. (37.6° C.)—or with skin conditions that would interfere with interpretation of rashes, or with clinical signs of anaemia, or showing evidence of respiratory infection or otitis media, or with a "legitimate" complaint of diarrhoea were excluded from the trial. Only children in good health were vaccinated; immediately before vaccination a blood sample was taken.

After vaccination the children were examined daily for a minimum of 15 days. A second blood sample was taken three to six weeks after vaccination. The sera from all samples were separated and sent to England, where they were titrated for measles antibody. Thirteen children were found to have pre-vaccination antibody to measles and are excluded from the ensuing analysis. The number in each vaccination group and the age distribution are shown in Table III.

TABLE III.—*Number, Immune Status, and Age of Children Receiving Vaccines*

| Vaccine | No. of Children Vaccinated | Initially | | Children Initially Non-immune | | | | Average Age (Months) |
|---|---|---|---|---|---|---|---|---|
| | | | | Age Range (Months) | | | | |
| | | Immune | Non-immune | 6–12 | 13–18 | 19–24 | Over 24 | |
| *Ibadan Study 1* | | | | | | | | |
| L .. | 18 | 3 | 15 | 7 | 8 | 0 | 0 | 12·1 |
| Polio | 6 | 1 | 5 | 5 | 0 | 0 | 0 | 7·4 |
| *Ibadan Study 2* | | | | | | | | |
| 3C .. | 15 | 3 | 12 | 8 | 3 | 0 | 1 | 11·7 |
| 4A .. | 14 | 3 | 11 | 6 | 4 | 1 | 0 | 12·4 |
| Polio | 15 | 2 | 13 | 8 | 3 | 2 | 0 | 11·6 |
| *Ilesha Study 3* | | | | | | | | |
| 3C .. | 6 | 0 | 6 | 6 | 0 | 0 | 0 | 7·0 |
| 4A .. | 7 | 0 | 7 | 7 | 0 | 0 | 0 | 7·1 |
| Polio | 9 | 1 | 8 | 8 | 0 | 0 | 0 | 7·7 |

Many of the children at Ilesha failed to return each day during the follow-up and the record of the daily examinations in this study is incomplete. The comprehensive record at Ilesha has therefore been omitted, although the antibody levels and any noteworthy reactions are described.

## Methods

The vaccines were dispatched by air to Nigeria in dry ice. On arrival at Ibadan they were transferred to a −20° C. deep freeze until required.

The appropriate number of ampoules of vaccine were taken in an unrefrigerated container to the clinic at Ibadan immediately before each vaccination session, the contents of each ampoule of the dried vaccine being reconstituted immediately before injection. Vaccine was transported to Ilesha in vacuum flasks containing ordinary ice.

A numbered record card was made out for each child. In studies 2 and 3 the children were allocated to the appropriate group according to a table of random numbers, and the age distribution in the measles vaccinated and polio control groups was similar. In study 1 at Ibadan, where in contrast to the other two studies the allocation to vaccination groups was not made by random selection, the average age of those given the poliomyelitis vaccine was less than that of those given measles vaccine (Table III).

In all studies the physicians responsible for the follow-up were kept unaware of the vaccine given to each child.

## Results

The clinical disturbance observed during the follow-up was on the whole much less severe than that expected with natural measles.

### Pyrexial Response

The pyrexial response to vaccination at Ibadan is shown in Table IV. Of the 38 children vaccinated with

TABLE IV.—*Post-vaccination Daily Rectal Temperatures*

| Vaccine | Mean Temperature (°F.) before Vaccination | No. of Children | No. Without Pyrexia | No. with Pyrexia (≥ 100° F.) | Highest Temp. (°F.) after Vaccination | | |
|---|---|---|---|---|---|---|---|
| | | | | | 100–101·9° | 102–103·9° | >104° |
| Ibadan study 1: | | | | | | | |
| L .. .. | 98·6° | 15 | 0 | 15 | 9 | 5 | 1 |
| Polio .. | 99·2° | 5 | 5 | 0 | 0 | 0 | 0 |
| Ibadan study 2: | | | | | | | |
| 3C .. .. | 98·7° | 12 | 2 | 10 | 6 | 4 | 0 |
| 4A .. | 98·7° | 11 | 1 | 10 | 6 | 3 | 1 |
| Polio .. | 98·9° | 13 | 5 | 8 | 5 | 3 | 0 |
| All measles .. | | 38 | 3 | 35 | 21 | 12 | 2 |
| All polio .. | | 18 | 10 | 8 | 5 | 3 | 0 |

either vaccines 3C or 4A or L, 35 developed pyrexia of 100° F. (37.8° C.) or more during the course of the follow-up (Table IV). The principal pyrexial response began four to ten days after vaccination (average seven days) and persisted for one to nine days (average three and a half days) (Fig. 1). The pyrexia was generally continuous, although in occasional cases there was an intermission lasting for one day.

In three children a rise of temperature of more than 100° F. (37.8° C.) lasting for one day only was recorded on the day following vaccination.

In study 1 pyrexia of 100° F. (37.8° C.) or greater was not observed in the group given poliomyelitis

vaccine. In study 2, eight of the children in the control group developed various conditions associated with pyrexia (see below).

There was no evidence of an appreciable difference in vaccines 3C, 4A, or L with regard to pyrexia.

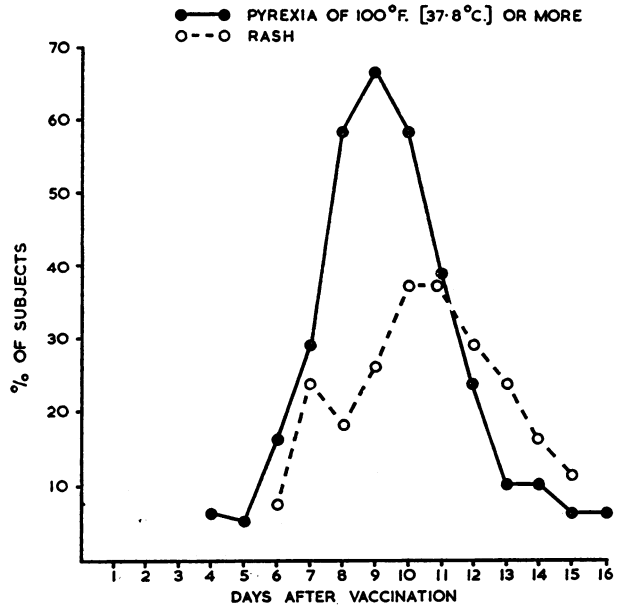


FIG. 1.—Pyrexia and morbilliform rash among 38 subjects at Ibadan (studies 1 and 2) after measles vaccination.

### Rash

Of the total of 38 children given either vaccines 3C, 4A, or L at Ibadan, 25 (66%) developed a morbilliform rash (Table V). In 22 cases the rash was much milder

TABLE V.—*Onset and Duration of Morbilliform Rash*

| Vaccine | No. of Children | No. of Children with Morbilliform Rash | Onset of Rash (Days after Vaccination) | | Duration of Rash (Days) | |
|---|---|---|---|---|---|---|
| | | | Range | Mean | Range | Mean |
| Ibadan study 1: | | | | | | |
| L .. .. | 15 | 12 | 7–10 | 9 | 1–6 | 3 |
| Polio .. | 5 | 0 | | | | |
| Ibadan study 2: | | | | | | |
| 3C .. .. | 12 | 6 | 6–11 | 9 | 2–5 | 3 |
| 4A .. | 11 | 7 | 6–14 | 11 | 2–8 | 3 |
| Polio .. | 13 | 3* 1† | 6–8 — | 7 14 | 2–3 — | 3 6 |
| Total measles vaccinated .. | 38 | 25 | 6–14 | 9 | 1–8 | 3 |

* Slight morbilliform rash but showed no rise in antibody titres.
† A case of measles which showed a rise in antibody titre.

than that associated with natural measles, with a limited distribution on the face, neck, and trunk. In one of the remaining cases the rash after vaccine 3C was florid and resembled actual measles, and in the other, given vaccine L, the rash was especially severe, involving the trunk and limbs with dark haemorrhagic areas. The onset of rash ranged from the sixth to the fourteenth day after vaccination. On average the rash persisted for three days before beginning to fade, but there was considerable variation in its duration.

Four of the 18 children vaccinated with poliomyelitis vaccine also developed morbilliform rashes. In three of these the rash was faint, in another it was pronounced and associated with the other symptoms of natural measles. The subsequent antibody estimations indicate that this child was the only one of the four who had sustained a measles infection.

Besides the morbilliform rashes described above, fine punctate rashes or erythema, diagnosed as sweat rashes, occurred in 26 of the 38 vaccinated children—in most cases these rashes immediately preceded the morbilliform rash. Non-morbilliform rashes were recorded in 7 of the 18 children given poliomyelitis vaccine.

### Further Clinical Findings

Fretfulness, mild conjunctivitis, and slight cough or coryza were recorded in many of the children (Table VI).

TABLE VI.—*Clinical Findings*

| Vaccine | No. of Children | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Vaccinated | No Symptoms | Pyrexia | Rash | Fretful for One or More Days | Conjunctivitis | Cough or Coryza | Diarrhoea |
| Ibadan study 1: | | | | | | | | |
| L .. .. | 15 | 0 | 15 | 12 | 12 | 13 | 10 | 6 |
| Polio .. .. | 5 | 4 | 0 | 0 | 0 | 0 | 0 | 1 |
| Ibadan study 2: | | | | | | | | |
| 3C .. .. | 12 | 1 | 10 | 6 | 6 | 7 | 4 | 3 |
| 4A .. .. | 11 | 0 | 10 | 7 | 5 | 10 | 8 | 3 |
| Polio .. .. | 13 | 3 | 8 | 4 | 4 | 8 | 7 | 6 |
| All measles .. | 38 | 1 | 35 | 25 | 23 | 30 | 22 | 12 |
| All polio .. | 18 | 7 | 8 | 4 | 4 | 8 | 7 | 7 |

These symptoms were most often found on the seventh to thirteenth days; they were not reported among the five children given poliomyelitis vaccine in study 1, but were common among the control group of study 2. During the period when study 2 was undertaken there was an outbreak of an upper respiratory infection of unknown aetiology in Ibadan, and many cases with symptoms similar to those observed in cases included in the trial were seen in the children's out-patient department, University College Hospital. Mild diarrhoea occurred in all vaccination groups.

TABLE VII.—*Hospital Admissions and Out-patient Chemotherapy*

| Vaccine | No. of Children | | Reason for | |
|---|---|---|---|---|
| | Vaccinated | Requiring Treatment | Hospital Admission | Out-patient Chemotherapy |
| Ibadan study 1: | | | | |
| L .. .. | 15 | 5 | Severe measles rash. Pyrexia 105° F. (40·6° C.) Otitis media.* Diarrhoea. Respiratory infection (one case of each) | Nil |
| Polio .. | 5 | 0 | Nil | ,, |
| Ibadan study 2: | | | | |
| 3C .. .. | 12 | 2 | Bronchopneumonia and severe measles rash | Otitis media* |
| 4A .. .. | 11 | 3 | Diarrhoea | Respiratory infection. Diarrhoea (one case of each) |
| Polio .. | 13 | 4 | Measles. Bulging fontanelle, admitted for observation only (one case of each) | Respiratory infection (two cases) |
| Ilesha study 3: | | | | |
| 3C .. .. | 6 | 0 | Nil | Nil |
| 4A .. .. | 7 | 1 | ,, | Otitis media* |
| Polio .. | 8 | 0 | ,, | Nil |
| All measles .. | 51 | 11 | 7 | 4 |
| All polio .. | 26 | 4 | 2 | 2 |
| Total vaccinated | 77 | 15 | 9 | 6 |

* Previous history of this condition.

Among the total of 51 children vaccinated with measles vaccine in all three studies, seven were admitted to hospital and four received specific treatment as out-patients during the course of the follow-up. Of the 26 children given poliomyelitis vaccine, two were admitted to hospital and two others received specific treatment as out-patients (Table VII).

### Antibody Response to Vaccination

Fig. 2 shows the antibody response to vaccination as estimated from the simultaneous titration of the 61 pairs of pre- and post-vaccination serum available. All

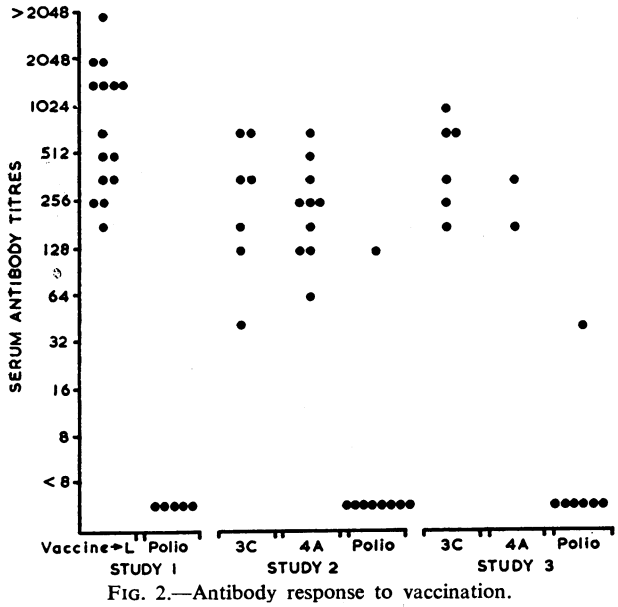


FIG. 2.—Antibody response to vaccination.

the sera examined showed a substantial rise in antibody titre after measles vaccination. All but two of the controls given poliomyelitis vaccine failed to form measles antibody; of the two exceptions, one exhibited manifestations of natural measles during the follow-up, but the other remained well throughout.

## Discussion

A safe and effective measles vaccine is of especial interest in Nigeria, where the mortality resulting from the disease is high. Accurate statistics are not available for the population at large, but among cases admitted to hospital for measles, and complications of measles, the mortality is about 20 to 25%. An estimate of the overall mortality from measles in the child population based on observations in a village study at Imesi, in Western Nigeria, is about 4% (D. Morley, 1961, personal communication). Reports from elsewhere in West Africa indicate a similar pattern.

In a trial of measles vaccine in Panama, involving both adults and children, the reaction to vaccination was on the whole satisfactory; but Hoekenga *et al.* (1960) reported that 70–80% of vaccinated children under the age of 5 years had some degree of fever; in some instances the rectal temperature reached 105° F. (40.6° C.). Nine children out of 245 vaccinated were hospitalized on account of reactions. It was thought possible that because of the high incidence of endemic infections prevalent in Nigeria reactions might be more severe. The investigation in Nigeria was on a small scale, but in general the types of reaction were similar to those reported elsewhere. The reaction rate was studied in children who were initially susceptible to measles and who all developed neutralizing antibodies subsequent to vaccination.

In assessing the significance of the frequency and character of the clinical disturbance after measles vaccination, it has to be appreciated that illness was frequent among the control group in study 2, the only control group which was both allocated by an effective method of random selection and closely followed up. In this study, during which upper respiratory infection was common at Ibadan, 20 of the 23 children vaccinated with measles vaccine developed pyrexia, 13 developed rash, and 11 were fretful for one or more days. Corresponding figures for the 13 children given poliomyelitis vaccine were 8, 4, and 4. By these criteria the experience of the children vaccinated with measles was similar to the poliomyelitis vaccinated group. In retrospect, however, the clinical impression gained by the follow-up was that children given measles vaccine were appreciably less well after vaccination than the control group. In the normal course of events the degrees of illness shown by some of the cases admitted to hospital would not have been regarded as serious enough to warrant admission. Ethical considerations, however, inclined us to offer optimal facilities to children who showed reactions of any degree of severity.

Seven of those admitted had been given measles vaccine. Three of these seven cases—two of diarrhoea and one of respiratory infection—may not have been due to measles vaccination, as the same conditions occurred in the control group and out-patient treatment was given. The four remaining cases—two with severe measles rash, one of hyperpyrexia, and one of otitis media—have been attributed to the vaccine. However, in view of the occurrence of a case of natural measles in the control group in study 2, the possibility of a concurrent infection with a natural measles virus in these cases cannot be excluded.

With the small number of children concerned, no substantial differences were apparent between the three batches of vaccine. Vaccine 3C had undergone a greater number of passages in an attempt at further attenuation, but the clinical reactions were similar to the other two.

The antibody response to all three batches of vaccine was satisfactory. None of the children from whom post-vaccination sera were obtained failed to respond; all the sera tested showed a high level of antibody. This suggests that the vaccines used would have a high protective effect against measles.

The current investigation was in the nature of a pilot study; further experience of the vaccine under close medical supervision is required in Nigeria.

## Summary

A clinical trial of measles vaccine in Nigeria is described. A total of 51 infants were vaccinated with one of three measles vaccines; the clinical and antibody response was compared with a control group given poliomyelitis vaccine. A satisfactory antibody response was produced by all the measles vaccines. About 92% of the children developed pyrexia and about 68% rash after vaccination. The reactions after vaccination were less severe than those which would be expected in natural measles. Reactions were similar after all vaccines.

We thank Professor Peter Armitage, Dr. S. L. Katz, and Dr. E. T. C. Spooner for their advice and help. Our thanks are also due to Dr. Norman-Williams, Chief Medical Adviser to the Federal Government, Nigeria, and to Dr. S. O. Franklin, Chief Medical Officer, Western Region, for their co-operation in the trial; to the medical and nursing staff of the children's department, University College Hospital, Ibadan; to the health sisters of the department of preventive and social medicine, University College Hospital, Ibadan; and to the health visitors of the School of Nursing, without whose assistance this investigation could not have been carried out.

# PART III. CLINICAL TRIAL IN BRITISH CHILDREN

BY

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The studies of measles vaccine in the United States reported by Katz *et al.* (1960a, 1960b) included children living in institutions. Vaccination against measles is likely to have a special application in these circumstances, where measles may be associated with serious morbidity and a high mortality.

In this investigation the clinical and antibody response to three vaccines has been studied among mentally deficient children at the Fountain Hospital, Tooting, London, and at Queen Mary's Hospital, Carshalton, Surrey. These hospitals together provide accommodation for 600 severely subnormal children in the imbecile and idiot range. They were especially suitable for the study since close medical supervision was possible throughout.

## Procedure

In December, 1960, samples of serum were taken from 107 children and examined for measles neutralizing antibodies. Eighty-five children were found to be non-immune and eligible for participation in the investigation; parental consent for the vaccination of these children was obtained. Eight of these children were subsequently excluded either because of intercurrent illness or because they had been exposed to chicken-pox between the time of allocation and vaccination. The remaining 77 children took part*; almost all were between 3 and 11 years of age (Table VIII).

TABLE VIII.—*Age of Children*

| Vaccine | No. of Children | Age Range (Years) | | | | | | Average Age (Years) |
|---|---|---|---|---|---|---|---|---|
| | | Under 3 | 3–5 | 5–7 | 7–9 | 9–11 | Over 11 | |
| 3C | 19 | 0 | 7 | 6 | 4 | 2 | 0 | 5 10·12 |
| 4A | 18 | 0 | 5 | 6 | 4 | 3 | 0 | 6 6·12 |
| 8 | 19 | 1 | 4 | 7 | 6 | 1 | 0 | 6 3·12 |
| Controls | 20 | 0 | 7 | 4 | 4 | 4 | 1 | 7 2·12 |
| Total | 76 | 1 | 23 | 23 | 18 | 10 | 1 | |

Three vaccines were used: vaccine 3C (dried, low-temperature type), vaccine 4A (dried, Enders type), and vaccine 8 (dried Parke, Davis type). All were given by subcutaneous injection. Details of these vaccines are given in Part I.

The children lived in self-contained wards each housing between 20 and 50. There was considerable inter-ward contact at the Fountain Hospital by virtue of attendance at the hospital school. To facilitate observation of vaccination reactions the children were vaccinated in groups at fortnightly intervals; at the Fountain Hospital 28 children were vaccinated on January 9, 1961, and 19 on January 23; at Queen Mary's Hospital all were vaccinated on February 6. The children were allocated to the vaccination groups independently by the Statistical Unit of the Wellcome Research Laboratories, as follows. The children were ranked by age in each ward and adjacent children in ranks were allocated randomly to one of three vaccination groups or to the unvaccinated control group. This procedure produced four groups of similar size and age composition (Table VIII). Each vaccine was used at each session.

Both vaccinated and unvaccinated children were closely observed for 21 days. Each child had an examination at least once a day by a physician kept unaware of the group to which the child had been allocated. The examination included an axillary temperature recording made in the late afternoon or evening and an examination for rash. On the twenty-first day a post-vaccination blood sample was taken. Thereafter, although the daily examinations were discontinued, the children were kept under observation within the hospital.

## Results

The commonest symptoms observed during the follow-up were pyrexia, rash, and fretfulness.

### Pyrexia

One child had a temperature of 100.4° F. (38° C.) on the day of vaccination, associated with a running nose and mild conjunctivitis. The remainder had temperatures of 98.6° F. (37° C.) or less (Table IX).

TABLE IX.—*Post-vaccination Daily Axillary Temperatures (°F.)*

| Vaccine | Mean Temperature before Vaccination | No. in Group | No. with No Pyrexia | No. with Pyrexia (99°+) | 99–99·9° | 100–101·9° | 102–103·9° | >104° |
|---|---|---|---|---|---|---|---|---|
| 3C | 97·7° | 19 | 4 | 15 | 0 | 8 | 6 | 1 |
| 4A | 97·3° | 18 | 3 | 15 | 6 | 6 | 3 | 0 |
| 8 | 97·6° | 19 | 3 | 16 | 3 | 9 | 4 | 0 |
| All measles vaccinated | | 56 | 10 | 46 | 9 | 23 | 13 | 1 |
| Controls | 97·5° | 20 | 16 | 4 | 2 | 2 | 0 | 0 |

Of the 56 vaccinated children, 10 (18%) had no appreciable rise in temperature throughout the follow-up period, and in a further nine the fever was slight. In the remaining 37 (66%) pyrexia was higher, and in one child reached 104.2° F. (40.1° C.). A similar degree of fever was found with all three vaccines. Pyrexia

*One child died during the follow-up period (see below) and has been excluded from the Tables.