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STUDIES ON MEASLES IN THAILAND. VI. A CLINICAL TRIAL OF "CAM 70" MEASLES VIRUS VACCINE IN HOME-DWELLING CHILDREN

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SUMMARY Two hundred home-dwelling children aged 1 to 5 years in Bangkok, Thailand were vaccinated with the CAM 70 further attenuated live measles virus vaccine (FAL) in September, 1972. Clinical reactions were surveyed in 116 of 125 initially seronegative children. The neutralizing antibody response was tested in 106 of the 116 children.

Febrile reactions were observed in 38 children (32.7%), but in most cases the fever dropped within 1 or 2 days. A sporadic and transient rash appeared in 4 children. Febrile convulsions occurred in 2 children, but there were no sequelae. A few children showed other symptoms such as catarrh and malaise. Neutralizing antibody titers of 1:4 or more were elicited in 103 children (97.2%). The geometric mean titer was 1:32.

INTRODUCTION

In tropical or developing countries measles is still one of the most common fatal diseases of children (Morley, 1969a; Naficy and Nategh, 1972), mostly due to malnutrition (Morley, 1969a) and insufficient medical care.

Naficy and Nategh (1972) reviewed the dramatic decrease in the number of cases and

mortality rate of measles as a result of mass campaigns against measles in African countries, Iran and South American countries. However, the vaccines used (Enders' B, Schwarz, Beckenham and Biken's CAM strains) caused rather high incidences of febrile reactions.

The CAM 70, a new FAL, was developed by Okuno and his associates in 1970 (Okuno et al., 1971), and licensed for general use in Japan in 1971. Clinical reactions due to the CAM 70 strain are milder than those to other FALs

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(Okuno et al., 1971), and the antibody titers elicited with it seem sufficiently high to result in long term protection (Ueda et al., 1971).

To see whether the CAM 70 strain could also be used safely and effectively in tropical countries where the mortality rate of children from measles is high, we tested it on home-dwelling children in Bangkok, Thailand in 1972. This paper presents results on the clinical reactions and neutralizing antibody responses of these children to vaccination with the CAM 70 strain.

MATERIALS AND METHODS

1. *Vaccinees*

Two hundred home-dwelling children aged 1 to 5 years in Bangkok were vaccinated with the CAM 70 strain in September, 1972. As shown in Table 1, 125 of the 200 children were seronegative. Initially immune children were excluded in analysis of the results.

TABLE 1. *Age distribution of children vaccinated with the CAM 70 strain*

Age	Suscep- tible no. (%)	Immune no. (%)	Total no. (%)
<1 year	2 (1.6)	1 (1.3)	3 (1.5)
1 "	42 (33.6)	7 (9.3)	49 (24.5)
2 years	31 (24.8)	18 (24.0)	49 (24.5)
3 "	27 (21.6)	15 (20.0)	42 (21.0)
4 "	14 (11.2)	25 (33.3)	39 (19.5)
5 "	9 (7.2)	9 (12.0)	18 (9.0)
Total (%)	125 (100) (62.5)	75 (100) (37.5)	200 (100) (100)

2. *Vaccine*

The CAM 70 strain of FAL (lot #320) was kindly supplied by the Research Foundation for Microbial Diseases of Osaka University (Handai Biken), Suita, Osaka, Japan.

The vaccine was lyophilized in one dose ampoules each containing more than 5,000 TCID₅₀ of the attenuated virus. The vaccine was injected subcutaneously immediately after being dissolved with 0.5 ml of the diluent.

3. *Survey of clinical reactions*

Parents of vaccinees were given clinical record cards on the day of vaccination. They were requested to examine the conditions of their children, and record the axillar temperature (4 times a day when the children had fever) and the presence of a rash and convulsions, if any, for 2 weeks after the vaccination. Health officers or nurses visited the vaccinees once a day for 2 weeks.

The clinical record cards were collected on the day when the second blood sample was taken one month after the vaccination.

4. *Test of antibody response*

Blood samples were collected on the day of vaccination and one month later. Initially seropositive children were screened by the HI test at a titer of 1:8. Children who had no detectable HI antibody were regarded as susceptible. The neutralizing antibody titers of serum specimens collected one month later were measured by the micro-neutralization test (Ueda, 1971).

RESULTS

1. *Fever*

Soon after the vaccination in September, 1972, an epidemic of influenza started which was antigenically similar to A/England/72 (H₃N₂) in Bangkok. Many of the vaccinees had fever from the first day after vaccination through the observation period (Table 2).

Usually the CAM 70 strain caused febrile reactions between days 5 and 12 after vaccina-

TABLE 2. *Fever of the 116 susceptible children during the observation period after vaccination*

Maximal temp (C)	Days after vaccination		
	1-4	5-12	13-14
37.1-37.5	37	11	23
37.6-38.0	6	10	4
38.1-38.5	9	9	1
38.6-39.0	3	7	2
39.1-39.5	3	1	0
39.6 or over	0	0	0
Total	58	38	30

tion (Okuno et al., 1971), so, the degree and duration of fever due to the vaccine were analysed between 5 and 12 days after vaccination.

Clinical reactions were surveyed in 116 of 125 initially seronegative children. As shown in Table 3, 38 of the 116 children (32.7%) had a fever of 37.1 C or over, and 80% of the maximal temperatures was under 38.5 C. No children had maximal temperatures of 39.6 C or over. In most cases the fever dropped within 1 or 2 days, and in no case lasted 4 days or more.

2. Other symptoms

Of the 116 children, 4 developed sporadic

and transient rash, and 2 had convulsions associated with fever. These febrile convulsions were over within seconds or minutes and left no sequelae. A few children showed other symptoms (Table 4), but these were so mild that no medical care was needed.

3. Neutralizing antibody response

Paired serum specimens were collected from 106 of the 116 children. As shown in Fig. 1, 103 children (97.2%) showed increase in measles neutralizing antibody titers of 1:4 or more one month after the vaccination, and 90% of them showed antibody titers of 1:16 or higher. The geometric mean titer was 2^{5.3}.

TABLE 3. *Fever of the 116 susceptible children from day 5 to 12 after vaccination*

Maximal temp (C)	Duration (days)				Total (%)	% to the 116 children
	1	2	3	4		
37.1-37.5	10	1	0	0	11 (28.9)	9.5
37.6-38.0	9	1	0	0	10 (26.3)	8.6
38.1-38.5	3	6	0	0	9 (23.7)	7.8
38.6-39.0	4	0	3	0	7 (18.4)	6.0
39.1-39.5	1	0	0	0	1 (2.6)	0.9
39.6 or over	0	0	0	0	0 (0)	0
Total (%)	27 (71.1)	8 (21.1)	3 (7.9)	0 (0)	38 (100)	32.8

TABLE 4. *Clinical reactions other than fever in the 116 susceptible children after vaccination*

Symptom	No. of cases
Rash	4
Convulsions	2
Weakness	3
Loss of appetite	3
Catarrh	2
Coughing	5
Diarrhoea	3
Vomiting	5
Abdominal pain	1

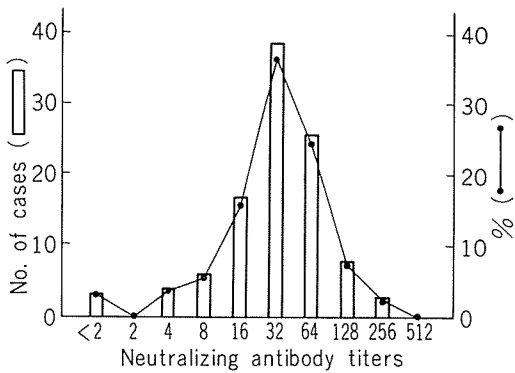


FIGURE 1. *Distribution of neutralizing antibody titers of the 106 initially seronegative children one month after the vaccination with the CAM 70 strain.*

DISCUSSION

In Thailand, we have done clinical tests on measles vaccines by the KL method and on FALs in institutionalized children since 1966. Vaccination by the KL method caused few clinical reactions and elicited a good antibody response, suggesting that it could be applied effectively in home-dwelling children without undesirable reactions despite the tropical climate (Tuchinda et al., 1967, 1968).

But, vaccination by the KL method had the disadvantages that two injections of killed and live virus vaccines, respectively, are needed and that atypical measles may develop (Fulginiti et al., 1967). Vaccination with FALs, CAM (Ueda et al., 1970a) and Moraten (Hilleman et al., 1968), caused febrile reactions in more than 50% of the children vaccinated and a high fever of 39.5 C or more in 17% of them (Sangkawibha et al., 1971).

The incidence of febrile reactions was similar to that described in an excellent review by Naficy and Nategh (1972), though it is difficult to make exact comparisons of results of vaccinations carried out in different countries. FALs have been recommended for use in tropical or developing countries (Morley, 1969b), but the incidence of febrile reactions following vaccination with FALs seems to be rather too high to make it satisfactory for use in campaigns against measles.

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- As reported in this paper, the CAM 70 strain caused febrile reactions in 33% of the children vaccinated. Moreover, it caused a fever of 39 C or more in only 1% of the children. There were two cases of convulsions among the 116 vaccinees, but these convulsions were febrile and had no sequelae. Other symptoms, such as a rash and catarrh, were so mild that they were not troublesome. Though the nutritional conditions of children in Bangkok may have been better than those in other tropical or developing countries, the mild clinical reactions observed in this test suggest at least that a tropical climate did not affect clinical reactions following vaccination. Judging from previous data (Ueda et al., 1970b, 1971), the antibody titers elicited seem to be sufficiently high to provide long term immunity.
- Thus, the CAM 70 strain can be used in campaigns against measles as effectively in tropical or developing countries as in Japan and without any troublesome side effects.
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- This work was partly supported by OTCA (Overseas Technical Cooperation Agency) of Japan based on the Medical Cooperation Program between Thailand and Japan under the Colombo Plan.
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