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STUDIES ON LIVE ATTENUATED MUMPS VACCINE.

I. COMPARATIVE FIELD TRIALS WITH TWO DIFFERENT LIVE VACCINES

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SUMMARY One hundred and thirty five seronegative children were immunized against mumps with live attenuated vaccines: 35 with Mumpsvax and 100 with Biken vaccine. None of the children showed adverse clinical reactions after immunization. The neutralization test showed 97.1% seroconversion after Mumpsvax and 97% after Biken vaccine. The mean values of antibody in the neutralization test were 1 : 5.2 after Mumpsvax and 1 : 11.3 after Biken vaccine. The relation between the antibody titers after each vaccine estimated by the neutralization test and the hemagglutination inhibition test was studied. The neutralization test seemed more sensitive, especially for detecting low titers of seroconversion. Twenty eight seropositive children were also vaccinated and serological 'booster' effect was observed in some of them.

INTRODUCTION

Mumps is a common childhood disease that may be severely and permanently crippling when it involves the brain, testes, ovaries, auditory nerves or pancreas. Adult men may also be permanently sterilized by mumps.

Attempts have been made to reduce the spread of mumps and to prevent its development by immunization with attenuated mumps virus. Since 1965, field trials with live mumps vaccine have been made in the U.S.A., using the Jerlyl-Lynn strain of the virus (Weibel et al., 1967).

This paper reports comparative studies on immunization with the Jerlyl-Lynn strain and with a newly developed vaccine, "Biken mumps vaccine."

MATERIALS AND METHODS

1. *Vaccines*

"Biken mumps vaccine," containing $10^{7.0}TCID_{50}$/dosis of the Urabe strain of mumps virus (U-Am-10 virus; Yamanishi et al., 1970) was kindly supplied by Prof. Okuno, Research Institute of Microbial Dis-

eases, Osaka University. Lyophilyzed live mumps vaccine of the Jerlyl-Lynn strain (Lyovac Mumpsvax; Buynak and Hilleman, 1966) was generously provided from Nihon Merk Co., Tokyo.

2. *Vaccination*

Children with no history of mumps living in Toyota City or Kasugai City, Aichi Prefecture were vaccinated by subcutaneous injection in the autumn of 1971. Blood samples were taken from the children shortly before, and six weeks after vaccination.

Pharyngeal swabs for virus isolation were collected on the 4th, 6th, 9th and 14th day after vaccination.

3. *Serological tests*

The hemagglutination inhibition (HI) test was carried out as described by Yamanishi et al. (1970). Namely, after removal of nonspecific inhibitors by treatment with Kaolin and chick cells, the HI antibody titers of the specimens were determined using 4 units of HA antigen (kindly supplied by Dr. Yamanishi, Osaka University) and a 0.5% suspension of chick red cells.

Serum neutralization tests (NT) were performed by hemoadsorption inhibition in LLc-MK2 cells (an established line of monkey kidney cells) cultures, using the Miyake strain of mumps virus as described by Yamanishi et al. (1970). The cells and virus for the NT test were kindly given by Dr. Yamanishi.

4. *Virus recovery test*

Swab specimens were inoculated onto LLc-MK2 cells immediately after collection. After 7 days the cultured fluid was transferred to other LLc-MK2 cells and these were cultivated for one week. The result was judged by the hemadsorption method. Primary green monkey kidney cells were also employed in some cases for isolation of the virus, using the same method as with LLc-MK2 cells.

RESULTS

1. *Clinical and serological responses of seronegative children to vaccine*

One hundred children were immunized with Biken vaccine and 35 with Mumpsvax. A list of the vaccinees is shown in Table 1.

No specific clinical side effects, such as swelling of the parotic glands, were observed among these children within 4 weeks after vaccination.

The seroconversion rates after immunization with Biken vaccine were 97% by the NT test and 93% by the HI test. Following Mumpsvax administration, the seroconversion rates were 97.1% by the NT test and 85.7% by the HI test. The antibody titers of these 135 children are summarized in Table 2. The geometric mean NT and HI antibody titers

TABLE 1. *Children immunized with vaccine*

	Age (years)			
	1–2	3–4	>5	Total
Mumpsvax group:				
Initially seronegative	17	15	3	35
Initially seropositive	0	4	1	5
Biken vaccine group:				
Initially seronegative	49	46	5	100
Initially seropositive	1	7	15	23

TABLE 2. *Comparison of NT antibody and HI antibody titers after vaccination with Biken vaccine and Mumpsvax*

Reciprocal of titer	Biken vaccine	Mumpsvax
NT ($\log_2$)		
<1	3	1
≧1–<2	5	7
≧2–<3	14	9
≧3–<4	34	7
≧4–<5	25	8
≧5–<6	16	3
≧6–<7	3	0
GMT	1:11.3	1:5.2
HI		
<5	7	5
5	17	11
10	26	7
20	24	8
40	19	4
80	7	0
GMT	1:16	1:11.2

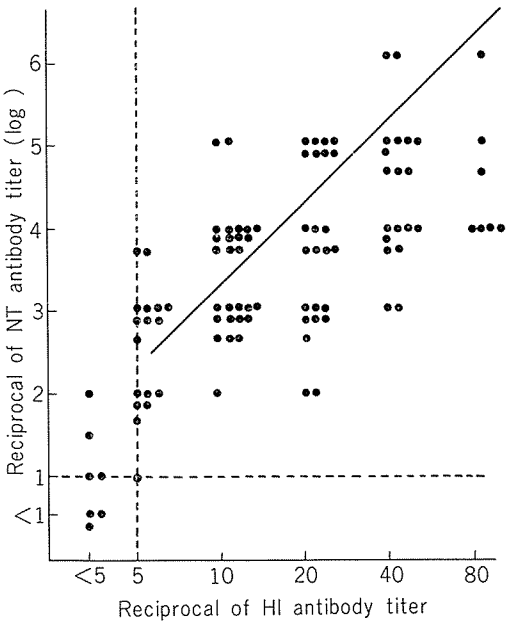

FIGURE 1. *Comparison of NT antibody and HI antibody titers after Biken vaccine. NT antibody conversion rate was 97% (GMV: ×11.3). (HI antibody conversion rate was 93% (GMV: ×16).*

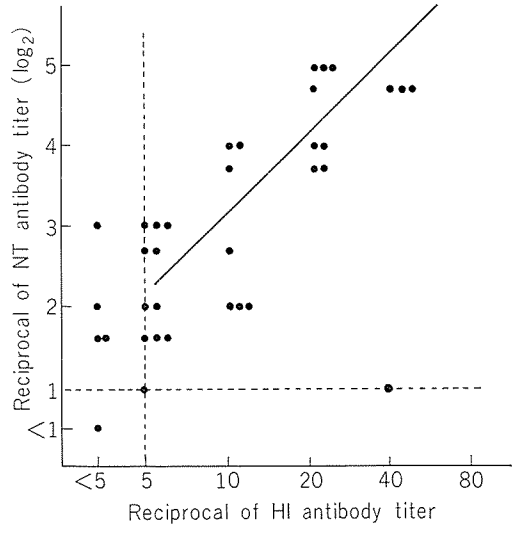

FIGURE 2. *Comparison of NT antibody and HI antibody titers after Mumpsvax. NT antibody conversion rate was 97.1% (GMV: ×5.2). HI antibody conversion rate was 85.7% (GMV: ×11.2).*

after immunization with Biken vaccine were 1: 11.3 and 1: 16, respectively, and those after immunization with Mumpsvax were 1: 5.2 and 1: 11.2, respectively.

The relations between the NT antibody and HI antibody titers after the two vaccinations are shown in Figs. 1 and 2. The NT test seemed more sensitive than the HI test for detecting a serological reaction.

2. *Communicability of the vaccine strains*

Throat swabs were collected from 10 children immunized with Biken vaccine and 5 children immunized with Mumpsvax. No mumps virus was isolated from these materials.

To confirm the lack of communicability of the vaccine virus, 32 members of the families of vaccinees were studied serologically: 23 were relations of children who received Biken vaccine and 9 were relations of children immunized with Mumpsvax. Blood samples were taken shortly before, and 10 weeks after

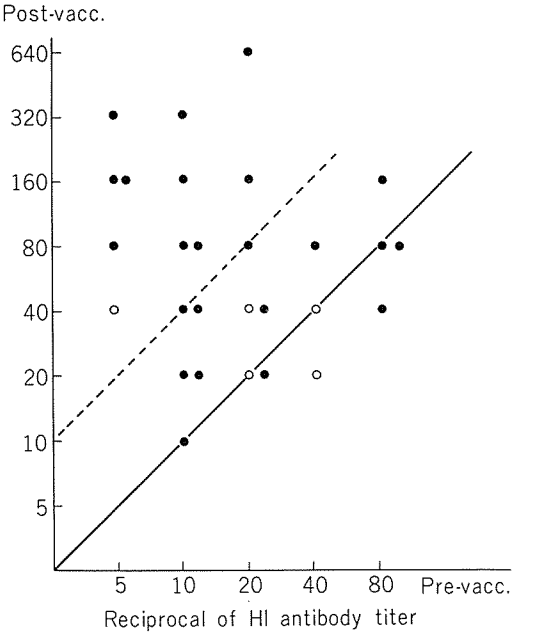

FIGURE 3. *HI antibody titers before and after vaccination of seropositive children. Mumpsvax, ○; Biken vaccine, ●.*

the time of vaccination. None of these relatives showed seroconversion.

3. *Serological response to vaccine of seropositive children*

Some children who were initially seropositive for mumps virus showed an increase in the serum HI antibody after vaccination, especially when their antibody activity was low before vaccination (Fig. 3).

DISCUSSION

Live mumps vaccines have been developed and used widely in the U.S.A. and U.S.S.R. It has been reported that only a low antibody titer is induced by vaccination but that it persists for years. Field trials showed that the vaccines gave excellent protection (Hilleman et al., 1967, Weibel et al., 1970).

In this work, 35 children were vaccinated with Hilleman's Mumpsvax and 100 children with a newly developed Biken vaccine.

None of the initially seronegative vaccinees who responded serologically after injection of either vaccine developed fever or other clinical reactions to the vaccine.

The seroconversion rates of these children by the NT test were 97% after Biken vaccine and 97.1% after Mumpsvax.

The Urabe strain of mumps virus seems to have been attenuated successfully for use as live mumps vaccine, since the seroconversion rate was high and the virus was not communicated to other members of the families of vaccinees.

The antibody titers following vaccination with either vaccine were low: the geometric mean titers by the NT test were 1: 11.3 after Biken vaccine and 1: 5.2 after Mumpsvax. However, from field trials on children Hilleman et al. (1967) reported that even a NT antibody titer as low as 1: 2 afforded immunity to mumps. It has been reported that the NT antibody induced by live mumps vaccine persists at essentially the same titer for at at least 4 years (Weibel et al., 1970). In their follow up studies on live mumps vaccine, Yamanishi et al. reported a high protective efficacy of Biken vaccine (Yamanishi et al., 1971). Further follow up studies on the two groups of the vaccines are now in progress.

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