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STUDIES ON LIVE ATTENUATED MUMPS VACCINE. II. FOLLOW-UP STUDY ON THE EFFICACY OF BIKEN VACCINE

SHIN ISOMURA, TAKAO OZAKI, TSUNEO MORISHIMA, SHOICHI NAGAYOSHI, SUNHON AN and SAKAE SUZUKI

Department of Pediatrics, Nagoya University, School of Medicine, Tsurumai, Showa-Ku, Nagoya

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SUMMARY Clinical and serological follow-ups were made on 18 children for 3 years and on another 18 children for 4 years, after immunization against mumps by attenuated mumps vaccine; Biken vaccine. To evaluate the protective efficacy of the vaccine, matched controls were studied during the same period. Serological examinations revealed that 77% of the vaccinees and 93% of the controls were infected with mumps after close contacts with mumps patients. Regular mumps was contracted by 88% of the controls, but none of the vaccinees. There was no substantial decrease in the antibody titers in unexposed vaccinees after vaccination.

INTRODUCTION

The preceding paper of this series (Isomura et al., 1973) reported comparative studies on clinical and serological responses after the administrations of two different live mumps vaccines; Biken vaccine and Jerlyl-Lynn strain vaccine. Both vaccines were safe, causing no clinical reactions and were highly immunogenic, resulting in nearly 100% seroconversion. However, the antibody titers after vaccination were considerably lower than those after natural infection.

In the present study, clinical and serological follow-ups were made on children three years and four years after a single injection of Biken vaccine. To evaluate the efficacy of the vaccine, the attack rate of mumps among vaccinees was compared with that among nonvaccinated, control children.

MATERIALS AND METHODS

1. *Vaccine schedules*

Two groups of seronegative children in Kasugai City, Aichi Prefecture were immunized against mumps with a single injection of Biken vaccine (Urabe strain of mumps virus; Yamanishi et al., 1970; Isomura et al., 1973): 18 children in the autumn of 1971 and 18 children in the summer of 1972. These children came from homes in almost all areas of the city and their socio-economical backgrounds were also widely different. In all, 31 of the 36 children showed successfull seroconversion by both the hemagglutination inhibition (HI) test and neutralization test (NT) after vaccination but in 5 children the HI antibody titers were below

$\times 5$ at 6 weeks after vaccination although seroconversion was demonstrated by the NT.

2. *Clinical follow-up on vaccinees*

Questionnaires were sent once a year to parents of vaccinees, to ascertain the frequency of contact of vaccinees with mumps patients and the incidence of mumps among the vaccinees. The extent of exposure and contraction of mumps were ascertained by interviewing the mothers, at the time of blood sampling.

3. *Nonvaccinated control group*

Healthy children of matched ages were randomly selected from the same residential areas in Kasugai City. They were asked whether they had come in contact with cases of mumps and whether they had contracted the disease during the period of this study. Children who had been exposed to mumps at before 3 years of ages were excluded, because (1) all the vaccinees were immunized at the age of 3 years old or more, (2) subclinical infections are frequently observed among young children (Isomura et al., 1975). Thirty eight children served as controls.

4. *Collection and examination of serum samples*

Serum specimens were obtained from samples of venous blood in the summer of 1975. The HI titers of sera were measured as described previously (Isomura et al., 1973).

5. *Grading of the extent of exposure to mumps*

The extent of exposure to mumps was carefully ascertained from mothers and classified as follows: (1) heavy, household contract group—children exposed to cases of clinical mumps in the family, (2) indoor contact group—children who had come in contact with cases of mumps in their class in kindergarten or primary school, or with indoor playmates who had contracted mumps, (3) outdoor contact group—children whose mothers reported mumps epidemics in their neighbourhood or in other classes at school, but who had apparently not been in direct contact with cases of mumps.

Children whose mothers reported two or more contacts with cases of mumps during the period were classified in a more heavy contact group.

RESULTS

1. *Heavy, household contact group*

Nine vaccinees and 10 control children were exposed to mumps in family during the period. Eight of the controls developed regular mumps, but none of the vaccinees did. Serological examination showed that all the vaccinees were infected with mumps virus, because their antibody levels increased to almost the same levels (geometric mean value (GMV) of HI antibody titer: $2^{8.2}$) as those of control children (GMV of HI antibody titer: $2^{8.6}$) (Fig. 1).

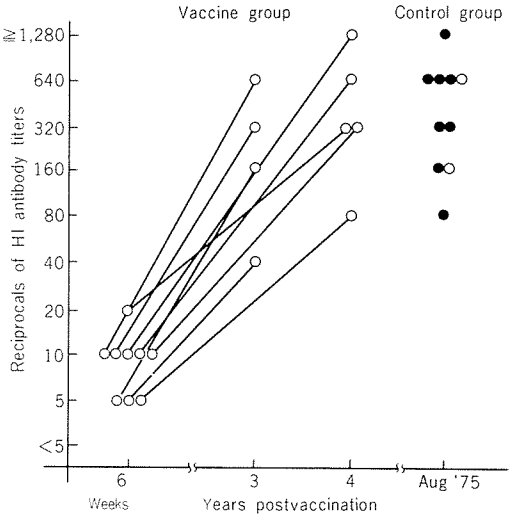

FIGURE 1. Results of clinical and serological examinations on children after intrafamiliar exposure. Symbols: ●, clinical infection after exposure; ○, no clinical infection after exposure.

2. *Indoor contact group*

Among the 13 vaccinees in this group, 10 showed increases in antibody without developing clinical mumps after exposure. Among the 15 controls, 14 exhibited increased antibody levels and 13 developed mumps after the contact. There was no difference in the antibody titers of the vaccinees (GMV of HI antibody titer: $2^{10.1}$) and controls (GMV of HI antibody titer: $2^{9.5}$) after exposure, irrespective of whether they developed clinical mumps or not (Fig. 2).

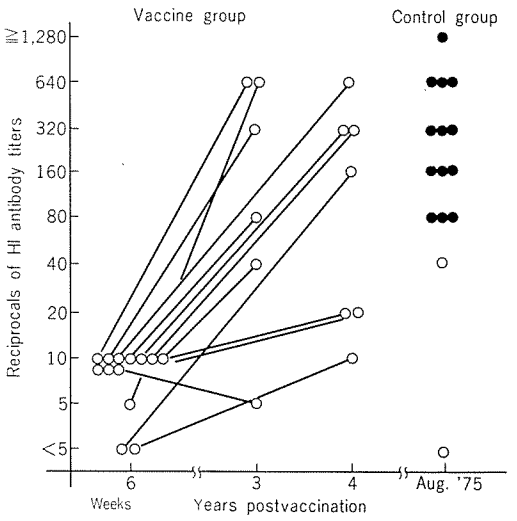

FIGURE 2. Results of clinical and serological examinations on children after indoor contact. Symbols: ●, clinical infection after exposure; ○, no clinical infection after exposure.

3. *Outdoor contact group*

Serological examinations showed that few children were infected with mumps as a result of slight outdoor contact (Fig. 3). No vaccinees developed clinical mumps. However,

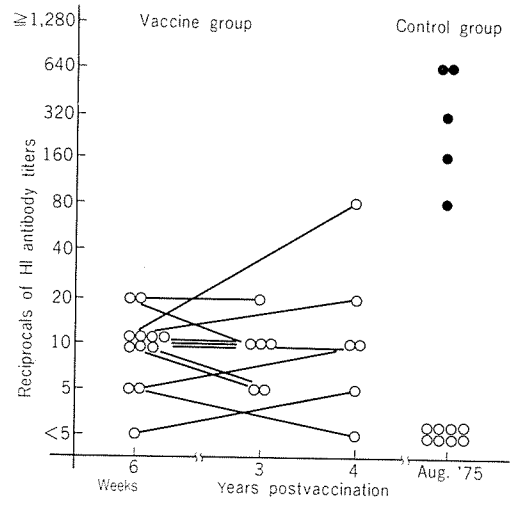

FIGURE 3. Results of clinical and serological examinations on children after outdoor contact. Symbols: ●, clinical infection after exposure; ○, no clinical infection after exposure.

it seems appropriate to exclude the children in this group in evaluating vaccine efficacy, because the rates of infection were low in both groups (1/12 in the vaccine group and 5/13 in controls).

4. *Unexposed group*

Two children had no contact with cases of mumps in the first 3 years after vaccination. Serologically, their antibody activities remained at the same level as those 6 weeks after vaccination.

5. *Relationship between extent of exposure and infection rate*

After intrafamiliar exposure, all the children in both groups experienced mumps virus infection. In the indoor contact group, serologically confirmed infection was recorded in 77% of the vaccinees and 93% of the controls. In contrast, very low infection rates were observed in the light, outdoor contact group. Thus, serological examination showed a direct correlation between the extent of contact and the infection rate (Table 1).

TABLE 1. *Relationship between extent of contact and infection rate*

	Serologically infected/Total
I. Intrafamilar contact	
Vaccinees	9/ 9 (100%)
Not vaccinated	10/10 (100%)
II. Indoor contact	
Vaccinees	10/13 (77%)
Not vaccinated	14/15 (93%)
III. Outdoor contact	
Vaccinees	1/12 (8%)
Not vaccinated	5/13 (38%)

DISCUSSION

The safety and high immunogenicity of Biken vaccine have been well documented (Yamanishi et al., 1970; Isomura et al., 1973).

Clinical and serological follow-up studies were carried out by Yamanishi et al. (Yamanishi et al., 1971) on vaccinees. They reported that (1) immunological studies showed no substantial decrease in the neutralizing antibody titers in 1 year and 3 years after vaccination, (2) answers to mail questionnaires revealed the high protective efficacy of the vaccine. The maintenance of antibody titers and low rate of clinical mumps among vaccinees were also reported by other investigators, using other strains of attenuated mumps viruses (Deinhardt et al., 1969).

To confirm this excellent protective efficacy of the vaccine, we examined the attack rates of mumps among vaccinated and nonvaccinated children after exposure to the disease. As seen in Table 1 and Fig. 1, serological examinations showed that all of susceptible siblings of cases of mumps were infected with mumps virus and 80% of the nonvaccinated children subsequently developed regular mumps. These findings are in good agreement with past reports on the intrafamiliar spread of mumps (Mayer, 1962; Isomura et al., 1975). This high communicability and high attack rate were also observed among susceptible children after indoor contact with extrafamiliar cases of mumps (Table 1 and Fig. 2).

In contrast, no vaccinees developed clinical infection after these types of contact (Table 2). Thus, Biken vaccine had a clear protective effect in these children.

TABLE 2. *Attack rate of mumps among seroconverted children after intrafamiliar and/or indoor contact(s)*

	Clinically infected/ Serologically infected
Vaccinees	0/19 (0%)
Not vaccinated	21/24 (88%)

Serologically, all the vaccinees showed increased antibody titers after close contact with cases of mumps. This high frequency of a booster effect may be due to the relatively low antibody titers developed after vaccination. No elevation of the antibody titers during the period was observed in 11 children in the outdoor contact group or two unexposed children. However, these children showed no appreciable decrease in their antibody level.

Further follow-up studies on these children are now in progress.

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