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STUDIES ON LIVE MUMPS VIRUS VACCINE

IV. CLINICAL AND SEROLOGICAL FOLLOW-UP 1 YEAR AND 3 YEARS AFTER VACCINATION

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SUMMARY Clinical follow-ups were made for 1 year on 255 children vaccinated by one injection of the U-Am-4 strain (Group I), or two injections of the U-Am-6 strain with an interval of one month between injections (Group II) and for 3 years on 210 children vaccinated by inhalation of the T-All-16 strain (Group III). There were only two mild cases of mumps among these vaccinees, one in Group I and the other in Group II.

The protective efficacy was high in all three groups. Serological follow-ups were done 1 year after vaccination on the children in Groups I and II and 3 years after vaccination on those in Group III.

No substantial decline in the neutralizing antibody titers was found compared with those one month after vaccination.

INTRODUCTION

Preceding papers of this series (Hosai et al., 1970, Yamanishi et al., 1970), described results of vaccination by the inhalation method using the Towata strain in 1967 and by the injection method using the Urabe strain in 1969.

The immunogenicity achieved by the inhalation method using the Towata strain passaged 5 to 18 times in the chorioallantoic cavity was poor and so the seroconvertion rate was not satisfactory. On the other hand, the immunogenicity of the Urabe strain passaged 4 to 15 times in the aniotic cavity of chick embryos was not high, but the seroconversion rate was good.

In the present study, a follow-up was made by postal inquiry and by tests for mumps antibody in sera collected in 1970. Follow-ups were made on vaccinees three years after inhalation of the Towata strain and one year after injection of the Urabe strain.

This paper presents the results of these clinical follow-ups and analyses of serological findings on the vaccinees immunized with these two kinds of vaccines.

MATERIALS AND METHODS

1. *Vaccine schedules*

Three groups in Nishinomiya City, Hyogo and Suita City, Osaka, respectively, were vaccinated as follows:

Group I; 93 vaccinees in this group were injected once with the U-Am-4 strain (Urabe strain passaged 4 times in the amniotic cavity of chick embryos) in 1969.

Group II; 162 vaccinees in this group received two injections of the U-Am-6 strain (Urabe strain passaged 6 times in the amniotic cavity of chick embryos) with an interval of 1 month between injections in 1969.

Group III; Vaccinees of this group inhaled the T-All-16 strain (Towata strain passaged 16 times in the chorioallantoic cavity of chick embryos) for 30 to 60 seconds in 1967. (Hosai et al. 1970)

2. *Postal inquiry*

Questionnaires were sent to parents of vaccinees, who were in general well educated, asking whether there had been any cases of mumps in their neighborhood, whether their children had come in contact with cases of mumps, and whether their children had contracted mumps since being vaccinated.

If their children had contracted mumps, they were asked to report the doctor's diagnosis and the date of contraction of mumps and to describe the symptoms briefly.

3. *Serolgical examination*

The neutralizing antibody titers of sera were measured as described previously (Yamanishi et al. 1970).

RESULTS

1. *Contraction of mumps after vaccination*

1) Group I

As shown in Table 1, 43 answers to questionnaires were received and one vaccinee contracted mumps about 6 months after being vaccinated. However, his clinical symptoms were very mild, namely a slight swelling of the right parotid gland persisted for two days and there were no other symptoms.

2) Group II

Answers were received to 130 of the 162 questionnaires. (Table I) There were no cases of mumps in this group, although there were epidemics in the neighborhood.

3) Group III

Answers were received from the parents of 91 of the 210 vaccinees who had been vaccinated in 1967. (Table I)

One child contracted mumps 6 months after being vaccinated, but his symptoms were mild. No serological examination of this child could be made.

Forty-two of the other 90 vaccinees had been in contact with cases of mumps during the 3 years after the vaccination.

2. *Serological analysis*

1) Group I

As shown in Table 2, 92 children who were seronegative before vaccination were inoculated with the U-Am-4 strain in 1969 and all showed neutralizing antibody responses.

TABLE 1. *Protective efficacy against mumps for 1 and 3 years following vaccination*

Group	Method of inoculation	Years since vaccination	No. of questionnaires	No. of answers	No. of mumps cases cases/answers (%)	Mumps cases in neighborhood cases/answers (%)	Contact with patient with mumps cases/answers (%)
I	one injection	1	93	43	1/43 (2.3%)	17/43 (39.5%)	8/43 (18.6%)
II	two injections	1	162	130	0/130 (0.0%)	35/130 (26.9%)	19/130 (14.6%)
III	inhalation	3	210	91	1/91 (1.1%)	51/91 (56.0%)	42/91 (46.1%)

Of 21 children from whom blood specimens were taken, 19 (90.5%) had neutralizing antibody titers of over 1 : 2 one year after vaccination.

The geometric mean neutralizing antibody titer was 6.3 one month after vaccination and 9.1 one year after vaccination.

2) Group II

As shown in Table 3, children in this group received 2 injections of the U-Am-6 strain with an interval of one month between injections and all showed a neutralizing antibody response. The geometric mean neutralizing antibody titer one month after the first injection was 6.7 and that one month after the second injection was 15.1. All blood specimens from 35 vaccinees taken one year after vaccination had neutralizing antibody titers of over 1 : 2 and the geometric mean neutralizing antibody titer was 9.5. The geometric mean neutralizing antibody titer after the second injection was about twice that after the first injection and the antibody level induced by the vaccination did not decrease appreciably for at least 1 year. (Fig. 2)

3) Group III

Children in this group inhaled the Towata

TABLE 2. *Comparison of neutralizing antibody titers 1 month and 1 year after vaccination by injection*

Neutralizing antibody response 1 month after vaccination		Neutralizing antibody response 1 year after vaccination	
Seroconversion rate (%)	G. M.[b] titer (range)	Seropositive[a] rate (%)	G. M.[b] titer (range)
39/39 (100%)	6.3 (2–128)	19/21 (90.5%)	9.1 (2–64)

a neutralizing antibody titer of over 1 : 2
b geometric mean

TABLE 3. *Comparison of neutralizing antibody titers 1 month after the first and second injections and 1 year after vaccination by injection*

Neutralizing antibody response 1 month after the first injection		Neutralizing antibody response 1 month after the second injection		Neutralizing antibody response 1 year after vaccination	
Seroconversion rate (%)	G. M.[b] titer (range)	Seroconversion rate (%)	G. M.[b] titer (range)	Seropositive[a] rate (%)	G. M.[b] titer (range)
78/80 (97.5%)	6.7 (2–128)	54/54 (100%)	15.1 (2–128)	35/35 (100%)	9.5 (2–32)

a neutralizing antibody titer of over 1 : 2
b geometric mean

TABLE 4. *Compatison of neutralizing antibody titers 1 month and 3 years after vaccination by inhalation*

Neutralizing antibody response 1 month after vaccination		Neutralizing antibody response 3 years after vaccination	
Seroconversion rate (%)	G. M.[b] titer (range)	Seropositive[a] rate (%)	G. M.[b] titer (range)
25/37 (67.6%)	4.8 (2–32)	18/26 (69.2%)	5.6 (2–32)

a neutralizing antibody of over 1 : 2
b geometric mean

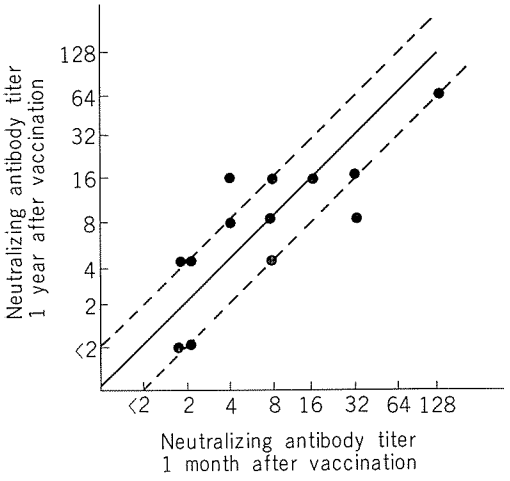

FIGURE 1. *Comparison of neutralizing antibody titers of paired sera obtained 1 month and 1 year after vaccination.*

strain for 30 to 60 seconds. As shown in Table 4, the seroconversion rate one month after vaccination was 67.6% and the geometric mean antibody titer was 4.8. Twenty-six blood specimens from vaccinees were collected about 3 years after the vaccination. Eighteen of the 26 had neutralizing antibody titers of over 1 : 2 (69.2%) and the geometric mean antibody titer was 5.6. As shown in Fig. 3, the antibody titers one month after the vaccination were similar to those 3 years after vaccination. Five children had neutralizing antibody titers of under 1 : 2 one month and 3 years after the vaccination, though the answers to the questionnaire revealed that these children had been in contact cases of mumps and had not yet contracted mumps.

DISCUSSION

The previous paper (Yamanishi et al. 1970), reported studies on inoculation of children without any history of mumps with live attenuated mumps virus which had been passaged in the amniotic cavity of developing chick embryos. All vaccinees showed an antibody response against mumps virus without any clinical manifestations of the disease. This showed that mumps virus was easily attenuated in the amniotic cavity of developing chick embryos. However, the antibody level following vaccination was lower than that following infection with natural mumps, and it was uncertain whether immnuity against mumps virus would persist.

As shown in Table 1, one child who had a neutralizing antibody titer of 1 : 8 one month after vaccination contracted mumps six months later, but his symptoms were very mild. Hilleman et al. (1967) reported that a neutralizing antibody titer of 1 : 2 or more was protective against challenge with natural mumps. A neutralizing antibody titer of 1 : 8 or more was also reported to be protective during an epidemic (Ennis, 1969, Meyer et al. 1966). On the basis of these reports, it seems that this child may have been wrongly diagnosed or that his neutralizing antibody titer may have dropped before he contracted mumps.

To increase the antibody level the effect of two injections of vaccine was examined. When the vaccine was injected into children twice with an interval of one month between injections, no vaccinees contracted mumps in the following year. The seroconversion rate after the second injection was 100% and the geometric mean titer increased from 1 : 6.7 to 1 : 15.1. A similar increase on antibody titer has been observed in most test subjects with pre-existing antibody who were vaccinated (Davidson et al. 1969, Furesz et al. 1970). The geometric mean neutralizing antibody titer of children who were inoculated twice with the vaccine decreased to 1 : 9.6 one year after vaccination. From comparison of the geometric mean neutralizing antibody titers of children in groups I and II one year after vaccination, there seems to be no difference in titers between the vaccination by one injection and by two injection. The seroconversion rate increased after the second injection, but the antibody induced by

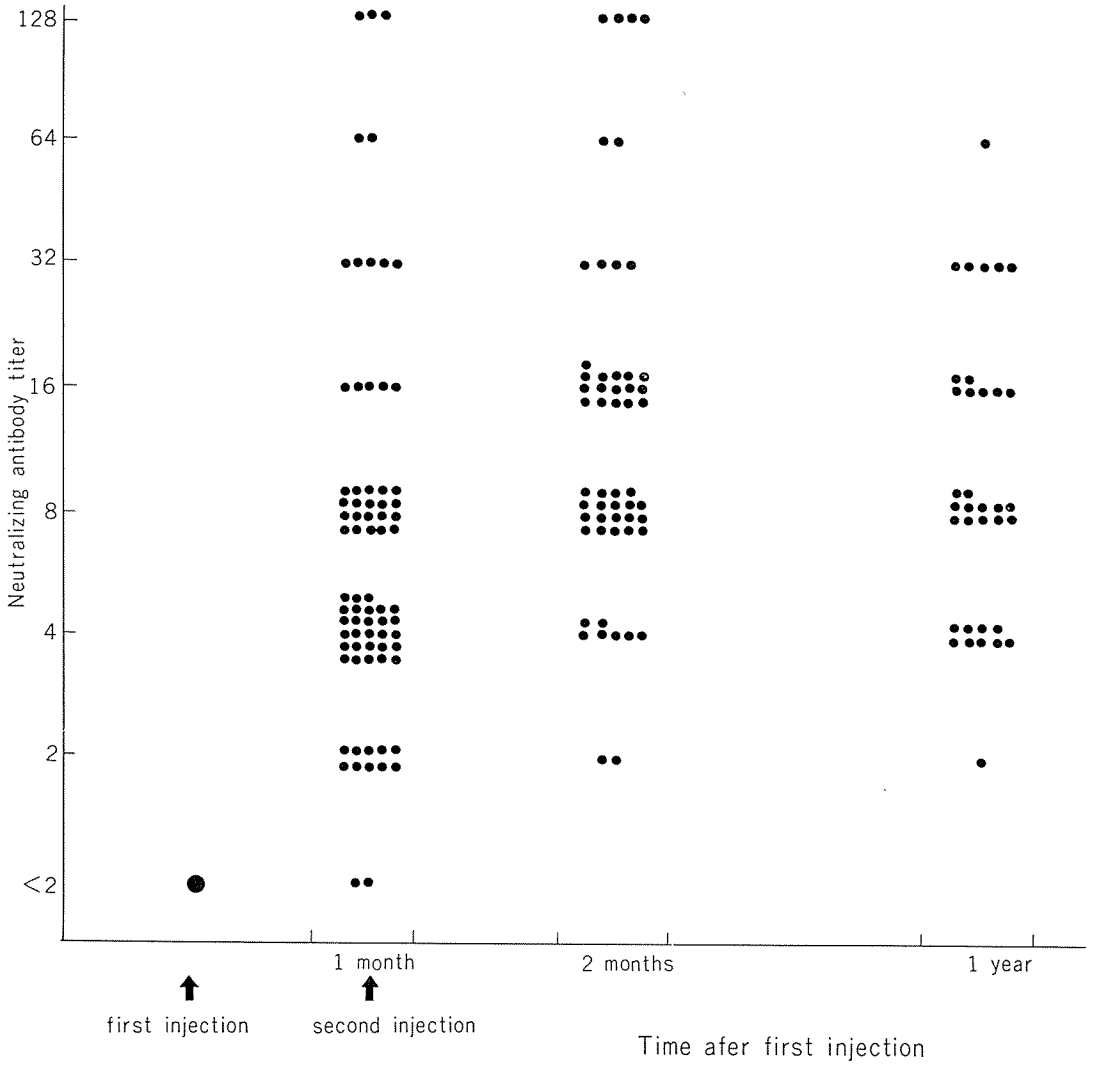

FIGURE 2. Neutralizig antibody titers after vaccination with Urabe strain live attenuated mumps virus vaccine.

the second injection did not persist at a high level but decreased to the same level as that induced by the first injection. This level will not decline for a long time. Thus, two injection are not neccessary to increase the antibody level.

As shown in Table 4, the seroconversion rate by the inhalation method was 67.6% one month after vaccination and 18 of the 26 vaccinees (69.2%) had a neutralizing antibody titer of over 1 : 2 3 years after vaccination. Answers to a questionnaire showed that 42 of 91 vaccinees (46.1%) had been in contact with cases of mumps during these 3 years. However, in spite of the low seroconversion rate, only one child contracted mumps (1.1%). Maynard

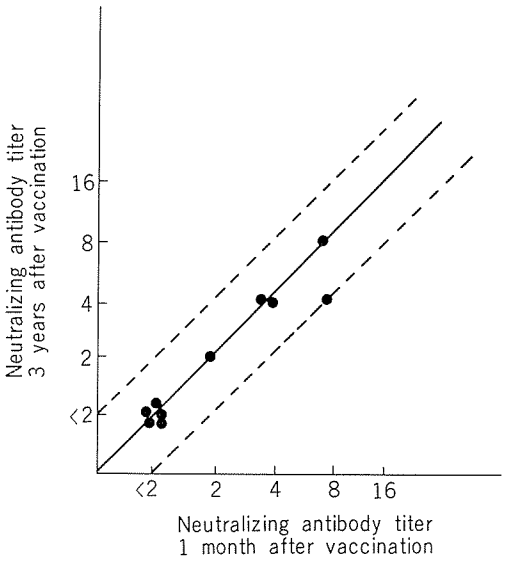

FIGURE 3. *Comparison of neutralizing antibody titerss of paired sera obtained 1 month and 3 years after vaccination.*

(1970) reported that the incidence of mumps among susceptible children on St. Paul Island was 35%. On the basis of this reports, protective efficacy of the mumps virus vaccine given by the inhalation method seems very satisfactory. Ten blood specimens from vaccinees collected 3 years after vaccination showed similar neutralizing antibody titers to those one month after vaccination (Fig. 3). It has been reported that the neutralizing antibody induced by live mumps vaccine persisted at essentially the same titer for at least 4 years (Weibel et al. 1970). We also found no substantial decrease in the neutralizing antibody titer for at least 3 years after vaccination by the inhalation method. Five vaccinees had neutralizing antibody titers of less than 1 : 2 both one month and 3 years after vaccination, although there were epidemics of mumps in this area (Fig. 3) Moreover, the younger brother of these 5 vac cinees contracted mumps, but her own neutralizing antibody titer did not increase. The 5 vaccinees in Group III were inoculated by the inhalation method, so this finding suggests that local immunity may contribute to protection against mumps.

From the above discussion it seems that though the antibody level induced by vaccination by the injection or inhalation method is not high, it remains unchanged at the raised level for a long time and seems to protect the vaccinee against challenge with natural mumps.

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