—Short Communication—

Field work of rubella attenuated live virus vaccine in Thailand

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Rubella has serious implication when it occurs in a pregnant woman. The rubella virus can create an intrauterine infection and cause fetal death, spontaneous abortion, or a variety of congenital anomalies. For this reason, it is desirable to prevent rubella. The isolation of the etiologic agent in 1962 in tissue culture was followed by the development of diagnostic laboratory tests and live attenuated vaccine¹⁻⁴⁾.

In Thailand, a severe epidemic prevailed in 1984~1985, in which reported cases exceeded 9,000 and the crude morbidity rate was 18 and 5.5 per 100,000 pop. in 1984 and 1985, respectively⁵⁾. This report describes results of a field work on the immunization for Thai females in 1984 through 1986 with live attenuated rubella vaccine manufactured in Japan.

The vaccine used in this study was lyophilized product of Biken, Osaka University and of Chiba Prefectural Serum Institute. Biken-Vaccine contained attenuated Matsuura strain of virus grown in quail embryo cell culture⁶⁾ and Chiba-Vaccine contained attenuated TCRB 19 strain grown in rabbit kidney cell culture⁷⁾. A single 0.5 ml of the reconstituted vaccine was inoculated subcutaneously.

The vaccine was inoculated into children and young women whose HI antibody titers to rubella were not higher than 1:8. The investigated persons consisted of 228 females of students, teachers and their family of the Chiang Mai Drama School in 1984 (DH-1; 3 to 36 years old) and in 1986 (DH-2; 3 to 32 years old) and 71 children under the care of the Comprehensive Child Care Clinic (CCCC), Chiang Mai University (R-4C; 5 to 17 years old). Blood sera of these volunteers were collected before and two weeks to six months after the immunization and their HI titers were measured. The HI test was done according to the method of NIH, Tokyo⁸⁻⁹⁾. The geometric mean antibody titer was calculated with a formula, $(\log_2 X_1 + \log_2 X_2 + \dots + \log_2 X_n)/n$, where X was a reciprocal of an antibody titer.

Results are shown in **Table 1**. Seventy females without the positive antibody to rubella in Chiang Mai Drama School were immunized in 1984 (DH-1). Sixty-nine among them (98.6%) showed 1:16 or higher antibody titers six months after the immunization, and the geometric mean HI titer after the immunization was higher than 1:128.

Seventy-one children of CCCC without the positive antibody were immunized in 1985 (R-4C). After one month of the immunization, 66 (93.6%) of them acquired 1:16 or higher HI antibody

Table 1 Increase of HI titer after rubella vaccination

Immunized group		DH-1 '84		R-4 C '85		DH-2 '86	
HI titer before vaccination		<8	8	<8	8	<8	8
HI titer after vaccination	512	17		3	2		
	256	13		5	2	1	
	128	14	1	5	6	36	
	64	11	1	10	8	68	
	32	7	1	11	5	32	2
	16	4		8	1	13	
	8				2	3	1
	<8	1		2	1	2	
	Total	67	3	44	27	155	3
$\log_2$ GM HI titer $\pm \sigma_{n-1}$		7.029 $\pm$ 1.642		5.831 $\pm$ 1.690		5.734 $\pm$ 1.079	
Time of collecting sera after vaccination		6 month		1 month		2-6 weeks	

Table 2 Kinetics of increase of HI titer after rubella vaccination

Time after vaccination		2 weeks		4 weeks		6 weeks	
HI titer before vaccination		<8	8	<8	8	<8	8
HI titer after vaccination	256					1	
	128	6		8		27	
	64	5	1	12		56	
	32	21		6	1	24	1
	16	23		2		9	
	8	42		2		2	
	<8	27				2	
	Total	124	1	30	1	121	1
$\log_2$ GM HI titer $\pm \sigma_{n-1}$		3.640 $\pm$ 1.370		5.710 $\pm$ 1.131		5.770 $\pm$ 1.059	

Subject group is DH-2.

titers and the geometric mean HI titer was almost 1 : 64. Before immunization, the antibody titers to rubella virus of 44 children were lower than 1 : 8 and those of the rest 27 were 1 : 8. But after the immunization the geometric mean HI titer of the former 44 children was 1 : 53.8 and that of the latter 27 was 1 : 62.4, i.e., any significant difference was not detected between the two groups.

One hundred and fifty-eight females without the positive antibody titer to rubella in the Chiang Mai Drama School were immunized in 1986 (DH-2). One hundred fifty-five (92.6%) among them showed 1 : 16 or higher titer of the antibody two to six weeks after the immunization, and the geometric mean antibody titer of them was about 1 : 53. In this group, the HI titers were measured two, four and six weeks after the immunization. Results are shown in Table 2. The seroconversion to 1 : 16 or higher antibody titers was observed in 56/125 (43.8%) after two weeks, in 29/31 (93.8%) after four weeks and in 118/122 (96.7%) after six weeks, and the geometric mean HI titers were 1 : 12.5, 1 : 52.3 and 1 : 54.6, respectively. Thus the antibody titer was observed to have reached the maximum after four weeks of the immunization.

Periods of time between the immunization and the blood sampling are different among the three experimental groups of the volunteer, and the independent test of distribution¹⁰⁾ of HI titers

gave significant differences between each of the three groups. However, the differences of geometric mean HI titers after immunization was not significant between any groups, according to the analysis of variance (ANOVA)¹⁰ of our data. The independence test was done by using the frequency distribution table in **Table 1**. Many volunteers of DH-1 group acquired relatively high HI titers as 1:128 to 1:512 after six months of the immunization. They might have asymptomatic infection by natural contact to rubella virus during the six months which boosted the artificial immunization by rubella vaccine. Rubella epidemics were reported in Thailand in 1984 and 1985⁵.

Rubella attenuated liver virus vaccine was developed in 1960s⁴, and several Japanese products of the vaccine have been proved to be effective on the prevention of the disease¹¹⁻¹⁹. According to those reports, 99 to 100% of the vaccinees acquired the positive antibody five to six weeks after the immunization, the acquired geometric mean antibody titer was 1:32 to 1:158, the untoward effect was almost negative, any secondary infection of the vaccine virus to infants surrounding the vaccinees was not reported, and the immunity after the vaccination was stable for 10 years thereafter.

Results of our field survey concerning the effect of rubella vaccination in Thailand showed 93 to 99% seroconversion of the HI titer, and after the vaccination the geometric mean of HI titers of the inoculated increased to 1:53 to 1:131 from 1:8 or less. This results agreed well to the ones obtained with Japanese field survey. The problem of the reinfection of vaccinated persons²⁰ will be confirmed in the future.

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