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## SHORT COMMUNICATION

### VACCINATION OF ADULT WOMEN WITH A JAPANESE RUBELLA VACCINE, QEF-PASSAGE BIKEN VACCINE

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Immunization with rubella was started on a nation-wide scale in Japan in the fall of 1977. The massive vaccination programs carried out in the U.S. and Europe, have shown that 1) clinical reactions, particularly joint symptoms, were observed more frequently than anticipated in a limited number of vaccinees in some field trials; and 2) the frequency of post-vaccination complaints, such as arthralgia, increased greatly with the age of vaccinees, though it varied depending on the kind of vaccine (Horstmann, 1971; Weibel et al., 1972). There are four kinds of vaccine licensed for use in Japan and they are recommended for general use on girls of 12 to 14 years of age and on susceptible adults (Shishido and Ohtawara, 1976). Many trials were made on these vaccines before they were licensed, but the trials were mostly done on the subjects of under 18 years of age.

This paper describes results on the antibody responses and clinical reactions of adult women with one of the licensed Japanese rubella vaccines and discusses the practical problems of vaccination.

The QEF-passage Biken vaccine, #102, prepared at the Research Foundation for Microbial

Diseases, Osaka University, Osaka, Japan (Minekawa et al., 1973), was used. Women susceptible to rubella were screened by the hemagglutination inhibition (HI) test. Fifty-nine susceptible women (HI titer <1: 8) of 18 to 24 years old (average age 19.2) agreed to receive vaccination with adequate precautions. Blood samples were taken 10 to 12 weeks after vaccination and their HI titers were measured by the microtiter technique using the standard method of N.I.H. of Japan (Japanese Rubella Vaccine Research Commission, 1971). The vaccinees were requested to record any symptoms, such as fever, rash, lymphadenopathy or joint pain, daily for 30 days on a self-evaluation chart. They were also asked to notify us if any symptoms developed, so that we could examine them clinically.

All of the vaccinees except two (96.6%) responded to the vaccine with a demonstrable HI antibody titer of 1: 8 to 1: 128, and the geometric mean titer (GMT) was  $2^{5.0}$  (Fig. 1). Twenty vaccinees (33.9%) developed low HI antibody titers of 1: 16 or less. Clinical reactions (fever, rash and cervical lymphadeno-

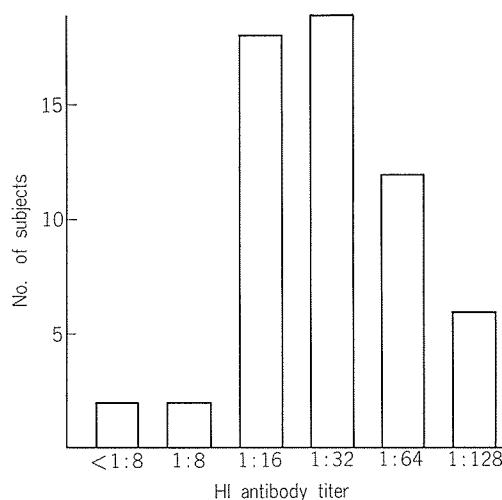


FIGURE 1. Distribution of HI antibody titers of 59 vaccinees

pathy) were observed in only 3 cases. In a case, fever up to 38°C developed 10 days after vaccination and continued for 2 days. In other cases, rash and cervical lymphadenopathy developed 2 or 4 days after vaccination, so they may not have been related to the vaccination. None of the vaccinees complained of joint symptoms which have been reported to develop frequently after rubella vaccination of adult women (Weibel et al., 1972).

The QEF-passage Biken vaccine has been reported to be clinically safe and immunogenically potent when given to adolescent girls and adult women (Minekawa et al., 1973; Minekawa et al., 1975). However, in field trials on children and young adults, the Biken vaccine gave a slightly lower sero-conversion rate and GMT than other vaccines (Shishido and Ohtawara, 1976). Our results also showed that the QEF-passage Biken vaccine was well tolerated by adult women and produced a rather low level of serum antibody.

A comparative trial of four kinds of vaccine currently used, Cendehill, HPV-77 DE-5, RA27/3 and TO-336 vaccines, was carried out in England by Best et al. (1974). They reported that TO-336 vaccine produced a slightly higher GMT than the other vaccines and caused fewer clinical reaction, although the difference was not statistically significant. We also tested the TO-336 vaccine, one of the licensed Japanese vaccines, on adult women of 18 to 29 years of age. All 50 vaccinees had developed HI antibody 6 to 8 weeks after vaccination, with titers of 1:16 to 1:128 and a GMT of  $2^{5.6}$ . But some clinical reactions, including joint symptoms, were observed in 34% of the vaccinees (Nakazono et al., 1977a). Our results show that QEF-passage Biken vaccine might be more attenuated than the currently used TO-336 vaccine.

The nation-wide rubella epidemic occurred in Japan in 1975 after 9 years interval. During this epidemic, at least 5 infants were born with congenital rubella, confirmed by virological and/or serological examinations, and some pregnant women exposed to rubella virus were given therapeutic abortions in Sapporo, which has a population of 1.3 million (Ishii et al., 1978). It is noteworthy furthermore that more than 20% of the unmarried women in Sapporo are still susceptible to rubella even after this large epidemic (Nakazono et al., 1977b). These women must be immunized as soon as possible and the antibody response after vaccination should be checked to confirm their immune status.

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