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Persistence of antibody after subcutaneous vaccination with Wistar RA 27/3 rubella vaccine

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SUMMARY

After subcutaneous vaccination of rubella sero-negative children with Wistar RA 27/3 rubella vaccine, haemagglutination-inhibiting antibody titres were compared in sera taken 46 days and 2 years after vaccination. Antibody titres were well maintained in the absence of any known exposure to natural infection.

INTRODUCTION

Wistar RA 27/3 rubella vaccine has been licensed recently for general use in the United Kingdom and in the Republic of Ireland. However, since there is no clear evidence that available vaccines are free from the teratogenic and embryotoxic properties of the parent virus, mass vaccination of adult women against rubella is not recommended in any country. There is a risk that vaccine may be given to pregnant women in an adult mass vaccination programme. Thus in some European countries, including the Republic of Ireland and the United Kingdom, the prime group to whom the administration of rubella vaccine is recommended is 11- to 14-year-old girls, with the aim of securing immunity to rubella over their child bearing years. It is essential, therefore, that vaccine-induced immunity is maintained over a prolonged period of time. Booster doses might be indicated if immunity waned. However, even with careful timing some subjects will not be protected for a period before boosting, while others with a minimum level of fading immunity are unlikely to respond to revaccination and will become rubella susceptible later. Furthermore, booster doses may not be free from teratogenic effects. After vaccination with the Cendehill and HPV vaccines serum antibodies have been shown to persist without significant decline for periods up to 2 and 3 years respectively (Meyer *et al.* 1969; Prinzie *et al.* 1969), while Buser, Nicholas & Plotkin (1969) and Plotkin, Farquhar, Katz & Hertz (1969) have described antibody persistence 12 and 14 months after vaccination with Wistar RA 27/3 vaccine. This investigation describes the persistence of haemagglutination-inhibiting (HAI) antibody titres over a two year period in 20 children who took part in a previously reported study of Wistar RA 27/3 rubella vaccine (Hillary *et al.* 1969).

METHOD

In July 1970 samples of venous blood were collected from 20 of the 21 children vaccinated subcutaneously with Wistar RA 27/3 rubella vaccine in July 1968. Blood samples were also obtained from nine unvaccinated rubella seronegative children who served during the first study as sibling contacts for evidence of vaccine virus transmission. In 1968 post-vaccination samples were secured from all children at the 46th day after vaccination.

SEROLOGY

In 1968 rubella HAI antibody titrations were carried out on the 46th day post-vaccination sera by the method described by Stewart *et al.* (1967) which used acid-washed kaolin for the removal of non-specific serum inhibitors. Since then heparin and manganous chloride have replaced kaolin for this purpose (Mann, Rossen, Lehrich & Kasel, 1967; Plotkin, Bechtel & Sedwick, 1968). The original sera held at a temperature of $-20°$ C were therefore retitrated in parallel with the 2-year post-vaccination samples employing the revised techniques.

RESULTS

The modal, median and geometric mean rubella HAI antibody titres of 46-day and 2-year post-vaccination sera are shown in Table 1. Comparisons of the titres for individual sera titrated in parallel after heparin and manganous chloride pre-treatment, 46 days and 2 years after vaccination, are shown in Table 2. No dif-

Table 1. *Rubella haemagglutination-inhibiting antibody titres*

	Time after vaccination		
	46 days		2 years
	Kaolin treated	Heparin–$MnCl_2$ treated	Heparin–$MnCl_2$ treated
Modal titre	160	160	160
Median titre	160	160	80–160
Geometric mean titre	129·9	129·9	113·2

Table 2. *Comparison of haemagglutination-inhibition titres of* 20 *children in sera treated by the heparin–$MnCl_2$ method,* 46 *days and* 2 *years after vaccination.*

		Titres at 2 years				
		40	80	160	320	640
Titres at 46 days	40	–	–	1	–	–
	80	1	5	1	–	–
	160	2	2	5	–	1
	320	–	–	–	1	–
	640	–	–	1	–	–

The stepped lines enclose the area of not more than twofold change of titre.

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ference in titre is seen in 11 sera while in 15 the difference in titre was no more than twofold. Fourfold decreases in titre in the 2-year post-vaccination sera were seen in three children and fourfold increases in two children. Statistical comparison of 46-day and 2-year post-vaccination titres shows no significant increase ($P = 0{\cdot}05$). Minor differences are seen between the titres obtained after kaolin treatment and titres obtained after heparin and manganous chloride treatment of 46-day post-vaccination sera (Table 3). However, in no case was the difference between the titres more than twofold. It should be noted that the titrations were carried out almost 2 years apart by different technicians. None of the nine sero-negative unvaccinated sibling contacts had developed rubella HAI antibody in July 1970.

Table 3. *Comparison of haemagglutination-inhibition titres of* 20 *children* 46 *days after vaccination, in sera treated by the kaolin and heparin–$MnCl_2$ methods*

Titres, heparin–$MnCl_2$ method	Titres, kaolin method: 40	80	160	320	640
40	1	–	–	–	–
80	3	–	4	–	–
160	–	2	5	3	–
320	–	–	1	–	–
640	–	–	–	1	–

The stepped lines enclose the area of not more than twofold change of titre.

DISCUSSION

The present study demonstrates that rubella HAI antibody titres produced by subcutaneous administration of Wistar RA 27/3 rubella vaccine in July 1968 were maintained satisfactorily 2 years after vaccination. It is of course conceivable that the immediate post-vaccination sera may have lost some of their HAI antibody during two years storage at $-20°$ C but this seems unlikely, since rubella HAI antibodies are known to be heat-stable (Phillips & O'Brien, 1969). Detailed inquiries failed to produce evidence of any cases of natural rubella in the area concerned since July 1968. This is confirmed to some extent by the finding that nine sibling rubella seronegative contacts had not become seropositive during this period. It is clear therefore that the titres of the vaccinated children are unlikely to have been maintained by subclinical attacks of natural infection.

The relatively high average titres obtained in the first study (Hillary *et al.* 1969) are of some importance, since it has been shown that after vaccination with the Cendehill vaccine, groups with low geometric mean antibody titres are more likely to be reinfected than members of groups with higher titres. In fact, Horstmann *et al.* (1970) showed that reinfection rates were correlated in a general way with HAI antibody titres at the time of exposure, stating that if the titre was $\leqslant 1/64$ the risk of reinfection was considerably greater than if it was $\geqslant 1/128$. However, in the absence of a standard reference serum one cannot really compare antibody titres from different laboratories.

Persistence of antibody 2 years after vaccination is of course of short duration in

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comparison with the desirable period of several decades. Nevertheless, assuming that HAI antibody is an indication of immunity to infection, the finding that antibody titres did not significantly decline over the 2-year period indicates that immunity after Wistar RA 27/3 vaccine is likely to be prolonged.

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