

Seroepidemiology of rubella infection in Chinese and Caucasians in Hong Kong

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SUMMARY

The seroepidemiology of rubella infection in Hong Kong Chinese was examined by haemagglutination inhibition of normal sera and a comparison made where feasible with Caucasians living in Hong Kong. Taking reciprocal titre of 20 as a baseline, the incidence of maternally acquired antibody was 84% for Chinese and 90% for Caucasians. In babies up to 2 months this incidence was maintained in Caucasians but declined to 54% in Chinese. High titre antibody was more frequently detected in Caucasians generally, including women of child-bearing age. The detection of rubella-specific IgM in the Caucasian babies was suggestive of recent maternal infection. However, fewer Caucasian (20%) than Chinese (36%) women of child-bearing age (15–40 years) appeared unprotected against rubella. When all age groups were considered, 88% of Caucasians and 53% of Chinese were seropositive. The occurrence of a rubella outbreak during the study did not give rise to a significant increase in the incidence of seropositivity in Chinese 19–25 years, the only age group able to be evaluated in this manner. The ethnic differences in seroepidemiology are considered in the light of known HLA-1 and HLA-8 antigen distributions in Caucasian and Mongoloid people and the apparently low incidence of congenitally acquired rubella in Chinese.

INTRODUCTION

Congenitally acquired rubella infection is a significant problem in many western countries. Conversely, Japanese have a very low incidence although their serology suggests a similar pattern of postnatal infection (Kono *et al.* 1969). Though there is no specific information available for Chinese, it is generally felt that congenital disease is also rare in these people. We report here a seroepidemiological study which examines infection patterns in Chinese and Caucasians and suggest possible reasons for the lower incidence of congenital infection in Mongoloid people.

MATERIALS AND METHODS

Normal sera were obtained from Chinese and Caucasian members of the University of Hong Kong Health Service Panel. There are 9600 people on the Panel

comprising students and all grades of staff and their dependents, including children. The Chinese members represent all socioeconomic groups in Hong Kong whereas the Caucasians are generally expatriates of European extraction. Sera were collected from May 1976 to May 1978 and were frozen at -20°C on receipt. Assays for rubella virus antibody including control procedures were carried out by haemagglutination inhibition (HI) of freshly thawed sera, randomly collected and examined, after treatment with kaolin to remove lipoprotein non-specific inhibitors (Shortridge, 1977*a*). All titrations were performed once except those for sera of Caucasian children aged up to 2 months which were repeated because of their apparently high incidence of antibody (see Table 2). Representative pools of these sera each comprising 10 samples were examined for sensitivity to 2-mercaptoethanol (2-ME) following sucrose density gradient centrifugation for the presence of macroglobulin (IgM) antibody (Caul, Smyth & Clarke, 1974). The HI tests were performed in microplates using commercial rubella antigen (Flow Laboratories, Rockville, Md, U.S.A.) and trypsinized human group O erythrocytes (Shortridge & Hu, 1974). The rubella antibody patterns of Caucasians living in Hong Kong, and of cord and neonatal Ghurka sera were included for comparative purposes. The Ghurka sera were kindly provided by Dr H. Manuel, British Military Hospital, Hong Kong.

RESULTS

Taking reciprocal titre of 20 as a baseline, maternally acquired rubella antibody was present in 84% of Chinese and 90% of Caucasian infants at birth (Table 1). The detection of antibody of titre 320–1280 in 19% of Caucasian cord sera is suggestive of recent maternal infection. In the first year, contrasting behaviour between the two races was seen – the high incidence was maintained in Caucasians whereas the percentage of Chinese with evidence of antibody dropped to 29%. In Chinese it dropped further to 20% in the 1–5 years age group after which it began to rise, this rise continuing through childhood and adolescence until 79% in the 26–30 years age group showed evidence of infection; thereafter this order of incidence from 70 to 86% was maintained. In all age groups, more Caucasians were seropositive than Chinese, their titres were generally higher and showed a broader spread. As shown in Table 1, there was a steady rise in antibody to a maximum incidence of 70–90% for adults aged 25 years or more.

The effective biological half-life of IgG is around 3 weeks (Waldman, Strober & Blaese, 1971) and passive immunity tends to fade to insignificant levels after the fourth month. Closer examination of the first year data showed that for the first 2 months significantly more Caucasians (94%) than Chinese (54%) were seropositive (Table 2). In the case of Chinese, none of the sera of babies 2 months–1 year were seropositive, suggesting that maternally acquired antibody was absent or reduced to very low titre after 2 months. When pooled sera from the Caucasian infant were examined by centrifugation and 2-ME inactivation procedures as given in Materials and Methods, rubella specific IgM and IgG were detected, a finding seemingly in accord with the high titres observed in some cord sera (Table 1).

Table 1. Rubella virus antibody titres determined by haemagglutination inhibition in normal sera of Chinese and Caucasians in Hong Kong

Age (years)	Race	No. sera tested	Per cent positive	Per cent at titres							
				< 20	20	40	80	160	320	640	1280
Cord	Chinese	58	84*	16†	21	41	19	3	—	—	—
	Caucasian	60	90	10	7	32	17	17	15	2	2
< 1	Chinese	136	29	71	9	9	4	4	2	—	1
	Caucasian	66	94	6	11	18	36	12	12	5	—
1-5	Chinese	97‡	20	80	—	5	2	5	2	4	1
6-10	Chinese	101	27	73	5	4	9	4	2	3	—
11-14	Chinese	41	32	68	2	12	2	5	7	2	—
	Caucasian	44	73	27	7	18	11	16	9	11	—
15-18	Chinese	75	60	40	12	20	16	7	5	—	—
	Caucasian	44	73	27	7	18	11	16	9	11	—
19-25	Chinese	427	60	40	18	19	14	6	2	—	—
	Caucasian	40	85	15	13	18	18	15	18	3	3
26-30	Chinese	80	79	21	14	23	29	11	1	—	—
	Caucasian	44	82	18	7	18	23	16	14	2	2
31-40	Chinese	76	70	30	21	18	16	8	5	1	—
	Caucasian	103	89	11	10	19	22	18	13	4	3
41-50	Chinese	46	85	15	28	26	17	4	7	2	—
	Caucasian	81	93	7	20	23	20	17	11	1	1
51-60	Chinese	49	76	24	29	20	14	4	6	—	2
	Caucasian	42	90	10	12	21	26	21	10	—	—
< 60	Chinese	63	86	14	29	32	17	5	3	—	—
	Caucasian	33	94	6	12	24	30	24	3	—	—

* Approximately equal numbers of sera from males and females of each race were examined and the figures given are combined totals as the findings for both sexes of each race were essentially similar.

† Per cent values for each dilution expressed as nearest whole number.

‡ Insufficient sera were obtained from Caucasians aged 1-14 years for significant evaluation.

Table 2. Distribution of rubella virus haemagglutination inhibiting antibody in normal sera of Chinese and Caucasian infants up to 1 year of age in Hong Kong

Age (months)	Race	No. sera tested	Per cent positive
< 2	Caucasian*	66	94
< 2	Chinese	46	54
3-6	Chinese	28	0
7-12	Chinese	11	0

* Sera from Caucasians 3-12 months were unavailable.

It is of interest to note that Ghurka cord and neonatal sera were also examined and that 66% and 67% were seropositive, respectively.

The findings for females in the child-bearing ages 15-40 years are given separately (Table 3). The incidence of seropositivity was higher in Caucasians except in the important 26-30 years age group in which both ethnic groups were the same, namely 76%. Fewer Caucasians were sampled and this could account for the

Table 3. *Distribution of rubella virus haemagglutination inhibiting antibody in normal sera of Chinese and Caucasian females of child-bearing age in Hong Kong*

Age (years)	Race	No. sera tested	Per cent positive	Per cent at titres							
				< 20	20	40	80	160	320	640	1280
15-18	Chinese	35	54	46*	9	14	17	6	9	—	—
	Caucasian	23	78	22	9	30	9	17	4	9	—
19-25	Chinese	192	61	39	12	20	18	8	3	1	—
	Caucasian	22	78	23	14	14	18	14	14	—	5
26-30	Chinese	37	76	24	11	22	30	11	—	3	—
	Caucasian	17	76	24	6	24	12	12	18	—	6
31-40	Chinese	35	74	26	26	17	14	11	6	—	—
	Caucasian	48	83	17	10	27	10	15	8	6	6

* Per cent values for each dilution expressed as the nearest whole number.

Table 4. *Effect of a rubella outbreak on the incidence of rubella virus haemagglutination inhibiting antibody in normal sera of Chinese aged 19-25 years in Hong Kong*

Time of serum collection*	Sex	No. sera tested	Serum titre characteristics		
			Per cent positive	Positive titre range	Geometric mean titre of positive sera
Pre-Feb. 1977	M	213	59	20-320	32
Post-Feb. 1977	M	22	68	20-320	57
Pre-Feb. 1977	F	86	57	20-320	49
Post-Feb. 1977	F	106	64	20-640	57

* Normal sera were randomly collected from May 1976 to May 1978; the outbreak occurred from February to June 1977.

difference in incidence compared with cord sera which should reflect the antibody pattern of child-bearing women. However, one point of similarity emerges in the case of Caucasians for the two categories of sera in that high antibody titres were recorded in both providing further evidence of recent infection. The total incidence of antibody in women of child-bearing age was 64% and 80% for Chinese and Caucasians, respectively.

During the course of the study there was an outbreak of rubella which lasted from February to June 1977. Because the sera for the study were collected as they became available at the Clinic it was not possible to compare the same subjects before and after the outbreak. However, it was considered worthwhile to compare as a group sera collected before February 1977 with those collected afterwards. Only the samples for Chinese in the 19-25 years age group were numerically generous enough to permit assessment of its effect. Increases in seropositivity were marginal although the geometric mean titre for males increased by about 75% (Table 4).

A problem in diagnostic rubella serology is the adoption of a safe baseline and in this study titre 20 was used especially as it facilitates comparison with data from

Table 5. *Comparison of the incidence of rubella virus haemagglutinating inhibiting antibody in representative categories of sera at two baseline titres*

Serum category	Race	Sex	Per cent positive at titres	
			20	10
All ages	Chinese	M and F	53	72
	Caucasian	M and F	88	93
26-30 years	Chinese	F	76	92
	Caucasian	F	76	76
Cord	Chinese	—	84	91
	Caucasian	—	90	92

other regions. Provided adequate precautions are observed which do not lead to a deterioration of the sera (Shortridge, 1977a) a baseline of 10 may be used, 10 being the starting dilution of the titration. In a comparison of the two baselines, it is of interest that there is no appreciable difference in incidence in representative Caucasian sera whereas there is a marked increase using titre 10 in the case of Chinese (Table 5).

DISCUSSION

A rubella vaccination programme started in Hong Kong late in 1978 after the completion of this investigation. Taking titre 20 as a baseline the studies reported here show that the incidence of unprotected Chinese (36%) and Caucasian (20%) women in the child-bearing age of 15-40 years is about the same as that observed in many industrialized countries (see Banatvala, 1977). Approximately one-third of the Chinese births are to women 26-30 years and it was of interest that three-quarters of such women appeared to be protected against rubella, the same as their Caucasian counterparts in Hong Kong. However, when the incidence of seropositivity between the two races is considered, excluding children of 1-14 years, significantly more Caucasians (88%) than Chinese (67%) showed evidence of rubella infection and with a broader spread of antibody titres. When these children are included, the incidence for Chinese reduces to 63%. The antibody titres for Chinese were generally lower and approximately one-third of all the sera examined were of titre 10, indicating a lower immune response in these people.

These apparent ethnic differences were further exemplified by (1) high titre antibody in Caucasian women of child-bearing age suggesting greater susceptibility to infection, (2) the detection of rubella IgM activity in the sera of Caucasian babies less than 2 months old possibly as a consequence of maternal infection, and (3) the marked decline in antibody incidence and level in Chinese babies. In the case of the first point, the Caucasian women sampled had lived for many years in Hong Kong where rubella vaccination was not included as one of the immunization routines generally available. It may be that Caucasians, as a particular ethnic or socioeconomic group, are more susceptible to rubella in the Hong Kong environment.

The steady rise in percentage of seropositive Chinese from childhood up to 30 years of age suggests a relatively high rate of exposure to the virus. This is

further evidence that the apparent lack of congenital infections in Chinese is not merely due to a lower frequency of exposure. The significance of breast-feeding, practised by few Chinese women in Hong Kong today (Shortridge, 1977*b*), in the different behaviour patterns of the babies is unknown.

During the study there was an outbreak of rubella. Inasmuch as information is available for the 19–25 years Chinese age group, the absence of a significant increase in seropositivity after the outbreak suggests that there may be a maximum titre of naturally acquired immunity in the population. If so, this titre may be higher for Caucasians as evidenced by the greater incidence of high titre antibody in most age groups through to 60 years, presumably due to recent infection.

One possible reason for the contrasting behaviour between the two races could be different levels of serum lipoprotein non-specific inhibitors but kaolin treatment of randomly examined sera makes this unlikely (Shortridge, 1977*a*). Another reason could be a difference in the magnitude of the immune response to infection by rubella virus resulting in lower antibody production. Some support for this can be gained from the observed link between HLA-1 and HLA-8 histocompatibility genes and congenital rubella infection (Honeyman & Menser, 1974; Honeyman *et al.* 1975). There is recent evidence that virus infection modifies histocompatibility antigens on the cell surface and that immune responses are generated against modified 'self' antigen (Doherty, Blanden & Zinkernagel, 1976). Caucasians have been shown to have a much greater incidence of HLA genes 1 and 8 than do Mongoloids, including Chinese (Bodmer & Bodmer, 1973). It is thus tempting to speculate that the higher antibody titre, i.e. immune response, in Caucasians is due to the possession of HLA-1 and HLA-8 genes. Furthermore, the observed lack of congenital infection in Mongoloids generally could reflect a lower susceptibility of their fetal cells to infection by rubella virus.

All in all, a number of observations on the seroepidemiology of rubella in Hong Kong have been made and for some it was not possible to provide clear-cut explanations for their occurrence. Clearly, ethnic differences exist and, with the background information obtained in this study, it will be of interest to follow the immune response to rubella vaccination in the two ethnic groups in the coming years.

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