J. Hyg., Camb. (1982), **88**, 355
Printed in Great Britain

Antibody to cytomegalovirus in Malta*

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(*Received* 2 *September* 1981; *accepted* 12 *October* 1981)

SUMMARY

Antibody to cytomegalovirus (CMV) was sought in sera from Malta using immunofluorescence. Seven per cent of the infants, 36% of the school children, increasing to 100% of the adults aged over 40 years were found to have antibody. Most infection occurred in pre-school children and adults over 25 years of age. This pattern of antibody acquisition appears different from that described for other countries.

Cytomegalovirus has a world-wide distribution and is important both as the commonest intra-uterine virus infection and as a serious opportunistic infection in the immunologically compromised. Approximately 50% of the congenitally infected show some minor degrees of inco-ordination, slowness of development, etc. (Hanshaw *et al.* 1976; Collaborative Study, 1978), and a quarter of these have serious defects, including microcephaly, epilepsy, cerebral palsy, intracerebral calcification, retinitis, deafness and other symptoms. These infections are usually considered to be primary ones, but recently it has been suggested that maternal virus reactivation may also cause intra-uterine infection, but without obvious clinical signs (Stagno *et al.* 1977).

Acquired infection usually occurs early in life or in adolescence and young adulthood. Generally early infection is more frequent in tropical countries than in those with temperate climates and has been ascribed to neonatal transmission from the mother; it is commonly associated with a very high frequency of CMV antibody in the adult population (Krech, 1973). Acquired infection is usually subclinical, with the occasional case presenting as a Paul–Bunnell negative infectious mononucleosis, sometimes associated with hepatitis or polyneuritis. This

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Table 1. *Number and proportion of positive sera according to age and sex*

	Male		Female		Total	
Age	No.	Positive (%)	No.	Positive (%)	No.	Positive (%)
5–13 months	25	2 (8)	19	1 (5)	44	3 (7)
4–7 years	21	7 (33)	5	3 (60)	26	10 (38)
8–11 years	14	3 (21)	19	8 (42)	33	11 (33)
17–24 years	22	9 (41)	10	6 (60)	32	15 (47)
25–29 years	6	5 (83)	23	19 (83)	29	24 (83)
30–34 years	5	3 (60)	12	8 (67)	17	11 (65)
35–59 years	12	10 (83)	8	6 (75)	20	16 (80)

small study has been made to indicate the frequency of antibodies in Malta, to determine at which age infection is most common, and to compare data with those of other countries.

Blood samples in capillary tubes were taken between April 1978 and January 1979 from (*a*) 44 babies aged 5–13 months, (*b*) 30 normal school children aged 5–11 years and 29 mentally and physically handicapped children aged 4–11 years, (*c*) 45 male and 5 female healthy blood donors aged 18–59 years and (*d*) 48 pregnant women aged 17–43 years.

The presence of CMV IgG antibody was demonstrated by immuno-fluorescence (de Silva *et al.* 1977), the blood being tested at a dilution of 1/2 without separation of serum from the red blood cells.

Table 1 shows that the proportion positive for CMV antibody was higher in females than in males; this was so both among the children, 46% in females and 29% in males, and among the adults, where the proportions were 74% and 60% respectively. These sex differences, however, were not statistically significant ($\chi^2 = 1{\cdot}17$ in the children's group or 1·47 in the adult group). Seven per cent of the sera from those under one year of age were positive compared with 36% between the ages of 4 and 11 years ($\chi^2 = 10{\cdot}12$, $P < 0{\cdot}01$) with no evidence of any annual increase in new infections between the ages of 4 and 11 years. During adolescence and up to 25 years of age there was only a small increase in the antibody prevalence, 47% being positive among the 17–24 age group, as compared with 36% in the 4–11 age group ($\chi^2 = 0{\cdot}68$, not significant). Finally, there was a large increase in antibody prevalence after the age of 25 years among both men and women. The difference between the 17–24 (47%) and the 25–29 (83%) age groups was statistically significant at the 1% level ($\chi^2 = 7{\cdot}01$) but not between the 25–29 (83%) and 30–34 (65%) age groups ($\chi^2 = 1{\cdot}06$). All eight subjects over the age of 40 years had CMV antibody.

Table 2 shows the year of birth of the mothers of the children aged 4–11 years and the proportion of the latter with positive sera. The mothers born in 1949–53 and now in the high positive 25 to 29-year-old group did not have a higher proportion of children with positive sera than those of the younger age group. There is some evidence that mothers born in 1938 or earlier and now in the over-40 age group had more children with antibodies, and this appeared to be more marked among the children now 8–11 than those aged 4–7 years old.

https://doi.org/10.1017/S0022172400070200 Published online by Cambridge University Press

Table 2. *Number and proportion of positive sera according to year of birth of the mothers of the children aged 4–11 years in Table 1*

Year of birth of mother	Age of children: 4–7 years No.	4–7 years Positive (%)	8–11 years No.	8–11 years Positive (%)	Total No.	Total Positive (%)
1938 and earlier	4	1 (25)	8	5 (63)	12	6 (50)
1939–43	9	4 (44)	10	3 (30)	19	7 (37)
1944–48	8	3 (38)	7	1 (14)	15	4 (27)
1949–53	3	1 (33)	7	2 (29)	10	3 (30)
1954 and later	2	1 (50)	0	0 —	2	1 (50)
Unknown	—	— —	1	— —	1	— —

Fig. 1 shows the prevalence of antibodies in Malta by age compared with those in two areas in the U.K. analysed by one of us. There were two age peaks in the Maltese, but not in the U.K. subjects; one was between 25 and 29 years (83% of 29 subjects) and the other smaller one between 4 and 8 years, the rates among the other age groups, both younger and older, being lower. There is nothing to suggest that these two peaks are related, as the children whose mothers are now 25–29 years old did not have higher rates than those with younger mothers. Information was collected about the size of family, the parity of the antenatal mothers and the occupations of their husbands. None of these factors appeared to have any association with the proportion of positive results.

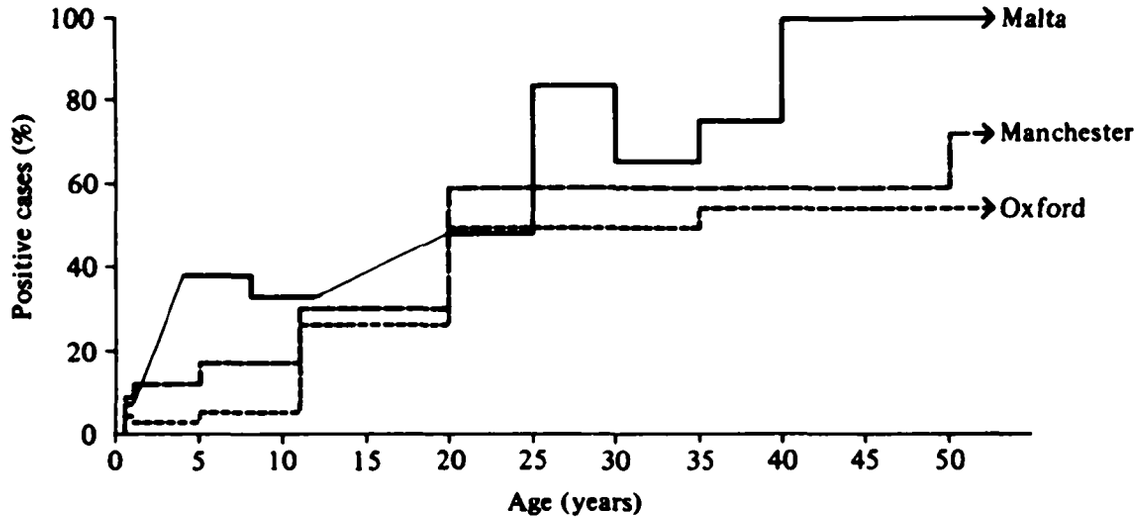

Fig. 1. Prevalence of CMV antibody by age in Malta and the UK.

The low rate of infection in the first year of life indicates very little vertical transmission from mother to baby and is similar to that found in Switzerland, the United Kingdom, North America and Australia (Krech, Jung & Sonnabend, 1971; Collaborative Study, 1970; Stern & Elek, 1965; Embil *et al.* 1969; Jack & McAuliffe, 1968), but different from that found in Japan, Central Africa and Singapore, where the proportion of infants infected in the first year of life ranged from 40 to 65% (Namasaki *et al.* 1970; Manube & Krech, 1972; Tobin, 1979).

The infection rate between 1 and 5 years is higher than that of the other

https://doi.org/10.1017/S0022172400070200 Published online by Cambridge University Press

European countries, with little evidence of spread in primary school children of 4–11 years. Most of the childhood infection in Malta is acquired during the second to fourth years of life, with only a slow increase in antibody frequency up to the latter part of the third decade, when it rises significantly. The adult prevalence is slightly higher than that of most European countries given in the WHO distribution table, with frequencies from 40 to 65% in Lyon, Freiburg, St Gallen, Albany and Manchester (Krech, 1973).

The increased infection rates in the Maltese pre-school children and in adults in their late twenties as compared with some other European areas suggests closer social contacts in these two age groups in Malta than at other ages. In Central Africa and other tropical countries those not infected in the first few months of life become so by the age of 5 years, the probable reservoir of infection being infants. This is unlikely in Malta, so the reservoir is probably in the young children themselves or possibly in the older age groups. After infancy infection is infrequent in pre-school children in European and North American cities with the marked exception of Anchorage; there antibody is present in 60% of 4-and 5-year-olds compared with 19% in those in the first year of life (Krech & Tobin, 1981). There is some evidence that mothers who are now 40 years old, i.e. in the age group which has a very high proportion of positive sera, are more likely to have children whose sera is positive to CMV than younger mothers.

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https://doi.org/10.1017/S0022172400070200 Published online by Cambridge University Press