CYTOMEGALOVIRUS INFECTION: A SEROEPIDEMIOLOGIC COMPARISON OF NUNS AND WOMEN FROM A VENEREAL DISEASE CLINIC

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A seroepidemiologic study of prevalence of antibody to cytomegalovirus (CMV) was simultaneously done in four populations: group I, nuns working as nurses or school teachers; group II, women admitted to an upper socioeconomic private hospital; group III, women admitted to a lower socioeconomic county hospital; and group IV, women attending a venereal disease clinic. Groups II, III and IV were not statistically different and showed an abrupt rise in antibody prevalence during young adulthood. Group I, however, did not show the expected abrupt rise in antibody prevalence during young adulthood, and the prevalence in this group was significantly lower than that in the other three groups at all but the oldest age range. These differences could not be accounted for by race, socioeconomic status or respiratory exposure to CMV. The data suggest that there may be more than one mechanism of CMV transmission and that venereal or intimate salivary contact may be a significant mode of spread in adults.

INTRODUCTION

The modes of transmission of cytomegalovirus (CMV) are not completely understood. Exposure to droplets of infected respiratory secretions, saliva or urine is considered the principal route of transmission (1). Although this is especially true in

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Abbreviations: CMV, cytomegalovirus; IHA, indirect hemagglutination.

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children, some evidence suggests that a genital route may also exist in adults. CMV has been isolated from cervical secretions (2, 3) and semen (4), from the latter in high titers and for prolonged periods in asymptomatic individuals (5). CMV has been isolated from cervical secretions when other sources, such as urine, have been negative (6) and after sexual contact with a male with infected semen (5). In women suspected of having venereal disease, CMV cervical isolations were significantly more frequent than in a control population, and the prevalence of CMV antibody was also significantly higher (2). Studies of the prevalence of complement-fixing CMV antibody in the general population show that a major acquisition of antibodies occurs after puberty, especially during young adulthood (7–11). No satisfactory explanation for this infection pattern has been given.

Taxonomically, CMV is a herpesvirus and shares many properties with herpes
simplex virus (12). All herpes simplex strains can be separated into two biologically different types: type I, transmitted principally by the oral-respiratory route, and type II, transmitted by the genital route. Likewise, antigenic differences have been shown between established strains of CMV (7, 13, 14). But it has not yet been possible to define separate antigenic types because common antigens are shared in various degrees. However, two studies have suggested that CMV strains obtained from the uterine cervix may have distinct characteristics which distinguish them from strains isolated from throat or urine cultures (15, 16).

A seroepidemiologic study involving nuns, women from a venereal disease clinic and female controls from two hospital populations was undertaken to investigate the role of genital contact in the transmission of CMV.

**MATERIALS AND METHODS**

All women in this study lived in Kansas City, Missouri, and had their blood drawn during June 1970. Participants were divided into four groups. Group I comprised 172 nuns, all with active daily contact with the general population in their work as nurses or school teachers. Every nun who qualified voluntarily donated her blood. Group II comprised 191 women routinely admitted to Menorah Hospital, a private hospital with predominantly white patients from the upper socioeconomic group. Group III comprised 318 women routinely admitted to Kansas City General Hospital, a county hospital with predominantly black patients from the lower socioeconomic group. Sera from individuals in both hospital groups were obtained from amounts remaining after blood chemistry determinations were completed. Group IV comprised 68 women examined, because of known or possible venereal disease exposure, at the Venereal Disease Clinic, Kansas City, Missouri, Health Department; 16 were known to be prostitutes. Sera from the Group IV women were obtained from amounts remaining after syphilis serologic tests were completed.

**Serum antibody determinations**

Serum specimens were stored at -20 C until tested for antibodies against the standard AD-169 strain of CMV by the indirect hemagglutination (IHA) technique (17, 18). All serum titers were determined on the same day with a single lot of antigen. Serial threefold dilutions were made on each serum specimen, beginning at a 1:6 dilution. Specimens with no detectable antibody titer at a dilution of 1:6 were considered negative. The chi-square method was used to assess the significance of the difference between the percentage of individuals in each group with negative antibody titers.

**RESULTS**

Figure 1 shows that CMV antibodies in groups II, III and IV are moderately prevalent during the teens but rapidly become more prevalent during young adulthood and remain high thereafter. Group I, however, has a different pattern of antibody acquisition. No rapid rise in the percentage seropositive occurs during young adulthood, but a rather slow steady increase in the percentage seropositive occurs throughout adulthood.

Antibody prevalence rates for groups II, III and IV are not significantly different (chi-square test) from each other at any age range. However, figure 1 shows that the prevalence rate for group I is significantly lower ($p < 0.05$) for the majority of age ranges when compared to the rates for any of the other female groups. When groups II, III and IV are combined, the prevalence rate is significantly higher than that for group I at all age ranges except 60 or older.

Mean antibody titers of those who had detectable antibody were determined for each group at each age range. There was no
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FIGURE 1. Percentage of females with CMV antibody by 10-year age groups. Group I, 172 nuns, working as nurses and teachers; Group II, 191 women admitted to an upper socioeconomic hospital; Group III, 318 women admitted to a lower socioeconomic hospital; Group IV, 68 women seen at a venereal disease clinic.

significant difference in mean titer between any two groups, and the mean titer for each group remained almost constant through all of the age ranges studied.

DISCUSSION

Like the complement fixation test (7, 14) the IHA test appears to measure antibody formed to group-specific antigens. This is supported by unpublished findings in our laboratory that all sera obtained from patients with a variety of clinical states, who have yielded CMV isolates from multiple sites, react with the AD-169 strain by IHA testing. Our present data show that the mean antibody titer did not fall with advancing age, thus indicating that the antibody detected by IHA persists. Therefore, the prevalence rate reflects the percentage of individuals who have been infected by any strain of CMV that shares antigens with the broadly reactive AD-169 antigen.

In groups II, III and IV the overall percentage of persons with antibody and the abrupt rise in antibody prevalence are very similar to the percentages and rises reported in several other series (7–10). However, group I (nuns) follows a different epidemiologic pattern with significantly lower antibody prevalences at age ranges less than 60 and fails to show an abrupt rise in antibody prevalence during young adulthood. Several possible explanations to account for the differences are considered.

Socioeconomic status alone cannot account for the difference because the prevalence rates for both the upper and lower socioeconomic groups (II and III) are not significantly different, although both are significantly different from the rate for group I. Race is also an unlikely explanation. Although the identity of the race of each group member is not available, the similarity of rises in antibody for group II (predominantly white patients) and group III (predominantly black patients) tends to rule out major racial differences.

Group I’s lack of exposure to respiratory air-borne particles or urine infected with CMV is also an unlikely explanation of the differences. Only nuns who had normal daily contact with society as grammar school teachers or nurses were chosen for the study. In this way their opportunities for casual oral, respiratory or urinary contact with CMV should be the same, or even greater, than for the rest of the Kansas City population. Group I, however, differs from the other three groups in several ways, including amount of intimate salivary contact, amount of venereal contact and number of pregnancies. The last is probably not important, however, since both men and women of the general population show a similar rapid rise in antibody prevalence in young adulthood (10). Differences in venereal contact could largely account for the lower antibody rate in the nuns and the lack of a high infection rate during young adulthood.

Lack of intimate oral contact (kissing) in
the nuns could also be a factor, however, since both oral and venereal transmission generally are expected to be maximal during young adulthood. Exposure by other routes of infection, such as casual contact with urine and salivary-respiratory secretions (coughing), is probably similar for all women in this study and could lead to a gradually increased prevalence rate, as seen in group I.

This study suggests that CMV can be transmitted in more than one manner and that different transmission mechanisms may be important at different ages. In order for CMV transmission to be better understood, oral and cervical CMV isolates should be antigenically characterized and strain-specific serologic tests should be developed to determine whether different CMV strains have different epidemiologic properties.

REFERENCES