CHAPTER IV

DISCUSSION

Cytomegalovirus infection of adults and children is almost always silent. It becomes importance mainly when the infection occurs in pregnant women and spreads to the fetus. CMV infection may cause mental retardation and deafness (Hanshaw et al., 1976, Reynolds et al., 1974). Preliminary data suggest that it may be most important cause of childhood handicap (Stern, 1977, Weller, 1971a, Weller, 1971b). The present study is initiated to provide further information on the frequency of primary and reactivation infections during pregnancy.

In studying 107 Thai pregnant women who attended the Antenatal Care Unit of Chulalongkorn Hospital and 75 married women who came for a routine check up at the National Cancer Institute, the characteristics of the two groups were no obvious differences. The mean of the age of the pregnant and married groups was 25.2 and 32, respectively. However, majority of the pregnant group had education at the level of primary and secondary school, while the education level of the control group was at college and university. The socioeconomic status of the pregnant women was in low and medium class. Majority of the pregnant women was primigravida. No evidence of syphilitic reactive was found in both groups.

In our study of cytomegalovirus isolation from cervical swab specimens, we found 14.9% (16 of 107) was positive, the same

frequency as it was recovered from the other study of oriental population in Japan (15%) by Numazaki et al. (1970), but was higher than the previous reports from Alabama, USA (9.5%) by Stagno et al. (1975b), from Pittsburg, USA (8%) by Montgomery et al. (1972), from Washington D.C., USA (3.5%) by Foy et al. (1970), and from London (1.8%) by Stern and Tucker (1973).

The possible explanation for the high incidence may be that crowding and living in depressed socioeconomic conditions (Table 6), including the residence in a tropical climate, has been shown to facilitate dissemination of CMV. Furthermore, it may also be that environmental conditions and attendant customs of daily life in some way play a major role in contributing to the much greater incidence of CMV infection, as compared to populations in temperate climates. Moreover, the differences in genetic make up which has been established to be a factor involving the susceptibility of many viral infections are yet to be seriously considerated. However, there is no evidence to suggest that CMV is shedding throughout the entire year, therefore it may be that the current study coincided with an epidemic of CMV in the community (Olson et al., 1970).

Another factor to be considered for the high or low incidence (CMV recovery rate) may be due to the virological procedures. Contamination during the collection of specimens could occur depending on the location where the specimens were handled, particularly the cervical swab specimens. Yeasts and bacteria, usually appear as contaminants, alter the metabolism and behavior of cell culture in subtle ways after inoculation and finally involve the

entire cells. These contaminants cause the failure of the virus to induce CPE and are the misleading of the viral detection. In addition, the contamination during the cell culture process also is the end result of the viral isolation. Virtually, the good sterile technique with reasonable precautions and maintenance of sterility are necessary.

Frequency of viral shedding also varied with age. Interestingly, CMV shedding decreased steadily with age. It was reported that the peak of the frequency were 15% and 8% at 11-14 years to undetectable levels at 31 years of age or older (Knox et al., 1979). In our study, the frequency of viral shedding between the younger age group and those who were over 30 years old were no difference. Infection rates of CMV from cervical excretions in pregnant women are related to the number of pregnancies of the subjects. It was found that CMV was recovered more often from the cervix of the women with two or less pregnancies, as shown in Table 8. Montgomery et al. (1972) found that CMV was recovered from cervical excretions in 11% of the women who had gravida three or less, but found in only 2% of those with gravida more than three times. Furthermore, Montgomery et al. (1972) also reported that the rate of CMV recovery from the cervix increased as the gestation progressed. It was 2%, 7%, and 12% in the first, the second and the third trimester, respectively. This observation was in agreement with the reports of Numazaki et al. (1970) who found 0%, 10%, and 28% infection rates during the first, second and third trimester, respectively. The results in our study showed some disagreement with that of Numazaki et al. (1970) and Montgomery et al. (1972) in the point that CMV was recovered most frequently in the second trimester.

The recovery rate in second trimester was 11.8% whereas 6.4% and 2.8% were found in the third trimester and the first trimester, respectively (Table 9). Among the CMV-positive culture pregnant women, only one subject had viral shedding in all three trimesters while the others had only one viral shedding in the same period. The reasons for this result may be due to the different factors. First, CMV can excrete from other body secretions such as saliva, tears, breast milk, and urine. Second, the level of cervical viral excretion is too low to be detected. Third, the excretion of the virus is intermittently.

Serological test for CMV-antibody will help to differentiate the primary infection, the reactivation of latent infection, and reveal the immune status of the subjects. By using a single serum, there is no precise cut-off of IgG-antibody titer that allow one to conclude that a recent infection occurred. A four-fold rise of the second or the third serum specimens, especially if the serum showed seroconversion, is the diagnostic of a current or a recent infection. The results in this study, performed by a Complement Fixation Test (CFT) which has long been established as a standard test for CMV-antibody detection, showed that 26.17% (28 of 107) of the pregnant women, whose gestational age was within 3 months, had antibody to CMV. This indicated that they might have a past history of CMV infection since the presence of IgG-antibody was a life long. However, the remaining 79 pregnant women (73.83%) had no CMV-CF-antibody. The characteristics of seropositive and seronegative groups were no statistically significant differences (Table 11). In 79 seronegative women; 37.97% (30 of 79) had seroconversion during the second or the third trimester, suggesting

that the subjects acquired primary infection while in gestation. Interestingly, 10 of the 30 seroconversion women had CMV-positive cultures. The seropositive rates of the pregnant women, within the first trimester, in this study were slightly low, compared with those of the same age group in Seattle studied by Chandler et al., 1985 (57%), including the other reports studied by Stagno et al., 1975a (52.7%) and by Montgomery et al., 1972 (58%). The reasons might have been due to history of pregnancy, race, sexual experience, or socioeconomic status. In addition, Puthavathana et al. (1983) showed 74.28% of CMV-antibodies in the first trimester among Thai pregnant women. This higher rate may be due to the differences in the characteristics of the subjects and the protocols. Majority (90%) of the seropositive pregnant women had antibody titer of 8 and 16.

Interestingly, there was one pregnant woman possessing CMV-positive culture had no CMV-CF-antibody while the remainders who had CMV-positive cultures showed seropositive evidence and 66.7% of them had seroconversion. The reason for this discrepancy may be due to the humoral immunity (HMI) of this individual. Osborn (1981) suggested that CMV infections were silent and apparently inconsequential. Furthermore, HMI was sometimes transient (Weller et al., 1973) and cellular immunity (CMI) was difficult to measure and assess. Including the transient depression of CMV-specific CMI during pregnancy (Gehrz et al., 1981) and the influence of the hormonal and emotional changes involved the pregnant state (Stagno et al., 1975b) could not be ruled out. However, this result was similar to the previously reported in Pittsburg by Montgomery et al. (1972) and in Seattle by Chandler et al. (1985).

The status of viral shedding without presence of antibody could be clarified if the sera from the mother and the infant were available for the serological test later after birth. Either or both serum should show the antibody. If not, then the immune status of the mother should be evaluated extensively for both HMI and CMI systems, to determine whether the mother had normal immune status. Also culture for CMV in the urine of the infants should be performed, including the follow-up of the infants to observe whether it would develop subsequent symptoms of CMV infection.

CMV infection during pregnancy is far more complex than other infections, such as rubella and toxoplasmosis, because of the ability of this virus to become frequently reactivated during the childbearing age and to be transmitted to the fetus in spite of maternal immunity (Schopfer et al., 1978, Stagno et al., 1977). Since epidemiological studies have shown that maternal antibody does not reduce the frequency of transmission of CMV to the fetus (Reynolds et al., 1978, Stagno et al., 1977). Therefore, antibody to CMV alone is not sufficient to prevent viral replication. Thus, there has been increasing concern about the association of asymptomatic infection with sensorineural hearing loss or other neurologic sequelae. Conceivably, reinfection with CMV could also be more problematic because of the large number of genetic variants of virus that circulate continuously in the general population (Huang et al., 1980). There is no doubt that CMV can have a devastating effect in an individual pregnancy. An obviously tragic event, although it occurs rarely, together with the ubiquitous nature of CMV and an increasing general interest in the ability of the virus to infect mothers and infants has lead to perhaps an unwarranted

concern regarding possible adverse pregnancy outcomes. More commonly, viral infection occurs silently or against a background of humoral immunity and therefore effects pregnancy and infant development. It is acknowledged that the outstanding of CMV and its effects on fetal development is incomplete. It is anticipated that additional knowledge will be fortcoming and further studies are needed to elucidate the role of CMV infection during pregnancy.