OBSTETRICS

The frequency of pregnancy and exposure to cytomegalovirus infections among women with a young child in day care

Beth C. Marshall, MD; Stuart P. Adler, MD

OBJECTIVE: The purpose of this study was to determine the frequency of pregnancy and exposure to cytomegalovirus (CMV) among mothers contemplating a possible additional pregnancy and with a child less than 2 years of age in group day care.

STUDY DESIGN: We performed a prospective observational study that included a demographic questionnaire and serologic and virologic monitoring of mothers and their children in day care.

RESULTS: Of 60 women, 62% were seronegative and 20% had a child shedding CMV. Of the 60 women, 23 women or 38% (95% CI, 0.27-0.51) became pregnant on average 10 months after enrollment. During pregnancy, 8 or 35% (95% CI, 0.19-0.55) of these pregnant women had a child in day care who shed CMV.

CONCLUSION: These results illustrate the potential magnitude of the public problem associated with exposure to a silent viral infection during pregnancy. Our data, when extrapolated to the US population, estimate that every 2 years between 31,000 and 168,000 susceptible pregnant women will be exposed to CMV by an infected child.

Key words: birth defects, cytomegalovirus, day care, pregnancy

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Following a primary maternal cytomegalovirus (CMV) infection during pregnancy, the transmission rate of CMV from a pregnant woman to her newborn is between 33% and 50%.[1,2] The frequency of hearing deficit and/or mental retardation for newborns who are congenitally infected following a primary maternal infection during pregnancy averages 28%.[2] Children in large group day care frequently acquire CMV infections from other children while children not in day care have very low rates of shedding CMV.[3,4] Once infected, children less than 2 years of age shed CMV in urine and saliva for between 6 months and 42 months (mean, 18 months).[5] The transmission rate of CMV for a child less than 2 years of age to a susceptible mother is approximately 50% within 1 year.[6-8] Since many women with a child in day care are planning to bear additional children, and potential interventions are available to prevent or treat women with congenital CMV infection during pregnancy, we sought to determine the frequency of pregnancy and exposure to CMV among mothers contemplating a possible additional pregnancy and who have a young child in day care.

From the Department of Pediatrics, Medical of College of Virginia Campus, Virginia Commonwealth University School of Medicine, Richmond, VA.

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Reprints: bmarshall@mcvh-vcu.edu.

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Materials and Methods

Subjects

Subjects were women recruited at 36 day care centers in the metropolitan areas of Richmond (18) and Norfolk, Virginia (18) between August 2005 and January 2007. The 36 day care centers enrolled 1394 children less than the age of 24 months, and of these, 912 mothers were approached at the day care center and asked to provide information about their plans for additional children. Information was provided by 696 (76%) women and of these: 81 (11.6%) stated they were pregnant or trying to become pregnant, 444 (63.8%) stated they planned no further pregnancies, and 171 (24.6%) were considering another pregnancy. Study participation was offered to women who had at least 1 child less than age 24 months attending day care at least 20 hours per week, and who were not pregnant or trying to become pregnant at enrollment, but did state they planned, were contemplating, or were undecided about a pregnancy within 5 years. Reasons for declining participation included lack of interest and/or knowledge about CMV, lack of paternal interest, the study appeared too time consuming, or plans to move or withdraw their child from day care. Women who stated they were definitely not planning an additional pregnancy were ineligible.

The protocol for enrolling subjects consisted of completion of a signed consent and demographic questionnaire and collection of serum, urine, and saliva specimens from mothers and children at enrollment and then every 6 months. If a woman became pregnant, specimens were obtained every 3 months until delivery and a urine specimen was obtained on all new-

TABLE 1
Characteristics of the study subjects by study location

Characteristic	Study location		Total
	Richmond (N = 32)	Norfolk (N = 28)	N = 60
Average maternal age (years + SD)	32 + 5	29 + 4	31 + 5
Percent of mothers seronegative	69[a]	54	62
Average number of children/household	1.1	1.3	1.2
Average day care child's age (months + SD)	14.3 + 6	12.5 + 5	13.5 + 6
Race			
No. white	30	22	52
No. African American	2	4	6
No. Hispanic	0	1	1
No. Asian	0	1	1
Mother's education (number by highest level attained)			
High school	1	3	4
College (no degree)	2	2	4
Associate's degree	3	4	7
Bachelor's degree	18	8	26
Post college graduate degree	8	11	19
Spouse's education (number by highest level attained)			
High school	3	4	7
College (no degree)	5	5	10
Associate's degree	3	0	3
Bachelor's degree	10	12	22
Post college graduate degree	11	4	15
No. of mothers with income			
< $20,000	1	1	2
$20,000-49,999	20	15	35
$50,000-74,999	5	8	13
$75,000-100,000	4	3	7
> $100,000	0	1	1
No. of spouses with income			
< $20,000	1	0	1
$20,000-49,999	9	10	19
$50,000-74,999	10	9	19
$75,000-100,000	7	3	10
> $100,000	3	2	5

[a] Not significantly different from women enrolled in Norfolk, $P = .2$.

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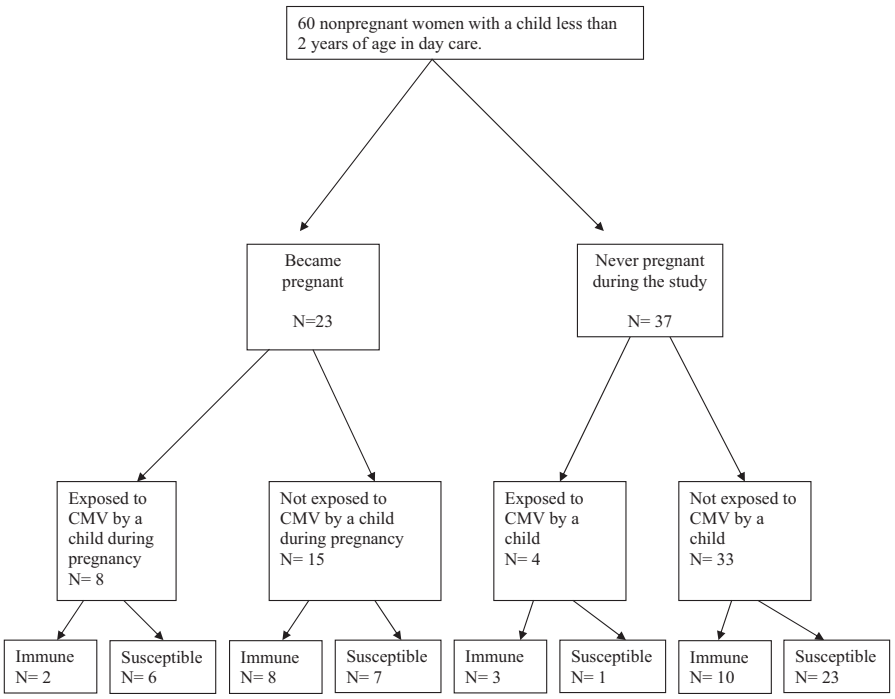
borns within 3 weeks of birth. To avoid altering the normal transmission of CMV, nonpregnant women were not told their serologic status or if their child was excreting CMV. Women who became pregnant notified the study nurses as soon as possible after conception. All women with a confirmed pregnancy were told their serologic status, and if seronegative, given detailed instructions for behavioral and hygienic precautions previously shown to be effective in preventing child-to-mother transmission of CMV among seronegative pregnant women.[7,8]

FIGURE 1
Enrolled subjects by pregnancy, shedding children, and serostatus



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Laboratory evaluation

Antibodies to CMV were measured in serum by an enzyme immunoassay (EIA) that used CMV glycoprotein B as the antigen.[9] Viral shedding was detected using conventional viral cultures on human fibroblasts.[10]

Statistical analysis

Fisher's exact test (2-tailed) was used for univariate comparisons. Confidence intervals were calculated using binomial proportions.[11]

This study was approved by the Virginia Commonwealth University Institutional Review Board.

RESULTS

Of 70 women enrolled, 10 were lost to attrition. Reasons for attrition were the subjects were unavailable for follow-up or withdrew their child from day care. The demographic features of the women not completing the study were similar to those who completed the study (data not shown).

Table 1 lists by study location the demographic makeup and serostatus of the 60 subjects included in the data analysis. Overall, the women from both locations were similar for ethnicity, level of education, family size, and income. The percentage of seronegative subjects enrolled from Richmond was not significantly different from those enrolled in Norfolk ($P = .2$). All of the women lived with a spouse or male companion.

Figure 1 summarizes the study results. Of the subjects, 62% were seronegative at enrollment (Table 1). Seropositive and seronegative mothers had similar average observation times and ages of their children at enrollment (Table 2). Of the women, 20% had a child who was or had begun shedding CMV during the study, with a similar rate for seropositive and seronegative women (Table 2). Among seronegative women, 4 of 7 had a child shedding CMV and seroconverted prior to becoming pregnant.

Pregnancy occurred for 23 women or 38.3% (95% CI, 27-51) an average of 10 months after enrollment (Table 3). Of the pregnant women, 8 or 34.7% (95% CI, 19-55) had a child who was shedding CMV at conception and during pregnancy. Although more of the seronegative pregnant women had a child shedding CMV (46%) as compared to seropositive women (20%), this difference was not statistically significant ($P = .39$). None of the seronegative pregnant women (all of whom received hygienic instructions on how to avoid CMV acquisition from their child) seroconverted during pregnancy.

TABLE 2
Characteristics of the study subjects by serostatus and CMV infection

Group	No. studied	Average time subject observed (months + SD)	Average age of child in day care at enrollment (months + SD)	No. of women with children shedding CMV (%) (95% confidence interval)	No. of women seroconverting before pregnancy
Seropositive	23	13.3 + 6	13.4 + 6.2	5 (22%) (9-42)	NA
Seronegative	37	13.8 + 5	13.4 + 4.8	7 (19%) (9-33)	4 (11%)
All subjects	60	13.5 + 5	13.4 + 5.7	12 (20%) (12-32)	NA

CMV, cytomegalovirus; *NA*, not applicable.

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TABLE 3
Characteristics of the study subjects by serostatus and pregnancy

Group	No. studied	No. who became pregnant (%) (95% confidence interval)	Average time after enrollment to becoming pregnant (months + SD)	No. of women pregnant with a shedding child	No. of women seroconverting while pregnant[a]
Seropositive	23	10 (43%) (25-63)	10.7 + 5	2	NA
Seronegative	37	13 (35%) (22-51)	9.2 + 5	6	0
All subjects	60	23 (38%) (27-51)	9.8+ 5	8	NA

CMV, cytomegalovirus; *NA*, not applicable.

[a] All pregnant women were instructed on behavioral techniques to avoid CMV acquisition from their child during pregnancy.[4]

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Comment

Among mothers with a young child in day care who were considering or planning additional children, we observed a very high pregnancy rate (38%) with conception occurring on average 10 months after enrollment. Further, among the seronegative pregnant women, approximately one half were exposed to CMV by a child shedding CMV after a probable day care–acquired infection. Although none of the seronegative pregnant women became infected during pregnancy, it is of note that 4 of 7 nonpregnant women seroconverted before conception. Although the numbers of women are small, this observation reinforces our previous studies with larger numbers of pregnant and non pregnant women indicating the effectiveness of behavioral intervention during pregnancy but its ineffectiveness for nonpregnant women.[7,8]

A possible limitation of this study is that relatively few women were studied and many declined to participate. However, we terminated the study after a planned interim data analysis indicated that enrolling additional subjects was very unlikely to alter the results or their implications. Another possible limitation of this study is that we did not determine the pregnancy rate for women who stated they were not planning additional children. Presumably some of these women did become pregnant, whether planned or unplanned. The rate of exposure to CMV during pregnancy, however, should be similar if not identical to that observed for women who were planning another pregnancy.

Another possible limitation of this study is that our subjects may not be representative of the entire US population that uses large group day care. This seems unlikely for 2 reasons. First, the women we observed were predominately white, college educated, of middle income, and with 2 parents working outside the home. Three quarters of births in the US are among whites and large group day care is expensive, so few lower socioeconomic status families can afford it. Recent estimates suggest that the greatest disease burden due to CMV acquisition during pregnancy occurs among whites and is attributable to the use of large group day care.[12]

A second reason our estimates are likely to extend to the US population is that they are similar to a recent report from the Centers for Disease Control that estimated that annually approximately 27,000 women ages 12-49 years have a primary CMV infection during pregnancy.[13] In the US, approximately 20% of children under the age of 5 years old are enrolled in day care.[14] For a US birth cohort of 4 million women, this means 1.6 million children less than 2 years of age are in day care. Nationally the average woman has 2.7 children, thus approximately two thirds of women (1 million nationally) with 1 child less than 2 years of age in day care will have additional pregnancies whether planned or not, and 60% of these women (600,000 nationally) will be seronegative. Our results, if applicable to the US population, suggest that in less than 2 years, at least 27% will become pregnant and of these, at least 19% or 31,000 seronegative women will be exposed during pregnancy to CMV by a child infected in day care. Our estimates and those of the Centers for Disease Control of the number of seronegative women exposed to CMV during pregnancy are sufficiently high to justify interventions for high-risk women to prevent or detect child-to mother transmissions during pregnancy.

A potential concern is the effect of CMV on the fetus among women who acquire a primary CMV infection just prior to conception. If maternal infection occurs in the 6 months before conception, transmission to the fetus and symptoms at birth may occur but at a low rate.[15] For this reason and because hygienic intervention is ineffective prior to conception, our study focused on exposure to CMV during pregnancy.

Without a vaccine, several interventions to prevent or detect primary CMV infection in pregnant women are still available. Enhanced public and obstetric awareness of CMV, which is currently low, would lead to women knowing their risk factors: serologic status, age of their child, and day care attendance. This awareness would in turn lead to enhanced vigilance and intervention by obstetricians for high-risk women during pregnancy.[16] Seronegative women with a child less than 2 years of age enrolled in group day care or who are employed caring for young children in day care could be instructed how to avoid acquiring CMV during pregnancy through behavioral

changes and hygienic practices, which should be effective.[7,8,17,18,19] Serologic monitoring during pregnancy of seronegative pregnant women with a young child in day care would allow for early detection of seroconversion and the option of either terminating the pregnancy or giving CMV hyperimmune globulin to prevent maternal-to-fetal transmission of CMV.

In summary, our results may reflect the magnitude of the public health problem associated with exposure to a silent viral infection during pregnancy. In the US every 2 years, at least 31,000 (an average of 80,000; range, 31,000-168,000) pregnant women will be exposed to CMV from an infected child, and of these, without a hygienic intervention, approximately half will become infected during pregnancy. Assuming a mother-to-fetus transmission rate of between 30% and 57%, and a rate of severe permanent neurological manifestations for infected fetuses of 28%, our observations estimate that every 2 years, group day care causes an average of between 6720 and 12,760 newborn infections with neurologic damage. Available data indicate the majority of these fetal infections are either preventable or treatable, and given the high financial costs associated with these infections, this estimate is sufficiently high to justify appropriate interventions.[20] ■

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