CYTOMEGALOVIRUS AND CHILD DAY CARE

Evidence for an Increased Infection Rate among Day-Care Workers

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Abstract To determine whether day-care workers acquire cytomegalovirus infection from the children they care for, we studied 610 women employed at 34 day-care centers over two years.

Forty-one percent of the caretakers were seropositive for cytomegalovirus. After adjustment for the effects of race, marital status, and age on seropositivity, the women who cared for children younger than two years of age had a significantly higher seropositivity rate (46 percent) than the women who cared for children older than two years of age (35 percent) (relative risk, 1.29; 95 percent confidence interval, 1.05 to 1.57; $P<0.02$).

Of 202 initially seronegative caretakers (observed for an average of 305 days per woman), 19 seroconverted, for an annual seroconversion rate of 11 percent. This rate was significantly higher than the 2 percent annual rate of seroconversion among 229 seronegative women (11 of whom seroconverted) in a comparison group of female hospital employees observed for an average of 781 days per woman (relative risk, 5.0; 95 percent confidence interval, 2.4 to 10.5; $P<0.001$). At three day-care centers in which the children were also studied, seven of the nine women shed isolates of cytomegalovirus in their saliva or urine that had *Eco*RI and *Bam*HI DNA-digestion patterns identical to the DNA patterns of isolates shed by one or more children in their care.

We conclude that workers in day-care centers may acquire cytomegalovirus infection from the children in their care and that this risk is significantly greater among those who care for children less than two years of age. (N Engl J Med 1989; 321:1290-6.)

BETWEEN 25 and 60 percent of preschool children cared for in group day-care centers shed cytomegalovirus (CMV) without apparent symptoms.[1-4] These high rates of infection with CMV are due to child-to-child transmission of the virus.[5] The mothers of preschool children attending group day-care centers also have higher rates of CMV infection than women without children in day care.[6,7] CMV-seronegative mothers frequently acquire primary CMV infection from their children, who have acquired the virus from day-care contacts.[5] Infants born to mothers who acquired a primary CMV infection during the first half of pregnancy have the greatest risk of permanent neurologic damage.[8] This risk, along with the high rate of maternal infection that results from the frequent transmission of CMV within day-care centers and the increased use of day care, suggests that caring for children in day-care centers may enhance the incidence of congenital disease due to CMV.

Susceptible caretakers of young children in day-care centers also risk the acquisition of CMV during pregnancy. Three reports indicate that professional day-care workers do not have a higher rate of CMV-seropositivity than groups of women without frequent contact with young children.[9-11] However, we observed that two women employees at one day-care center shed isolates of CMV with DNA patterns identical on restriction-endonuclease analysis to each other and to the isolates shed by numerous children in their care.[5] This observation suggested that these women had acquired CMV infection from the children. To determine the frequency of CMV infection among women caring for young children in group day-care centers, we undertook a prospective study of women day-care workers.

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METHODS

Subjects

The subjects were women employed at 34 day-care centers in the Richmond, Virginia, metropolitan area. Twenty-eight of the day-care centers, which enrolled children ranging from birth to school age, made up all the licensed day-care centers in the area that enrolled children two years of age or younger. The remaining six centers enrolled only children older than two years of age. These six centers asked to participate in the study after they learned about it. Twenty-five of the centers were commercial enterprises, and nine were nonprofit. The average number of caretakers per center was 17 (range, 7 to 30). The average number of children two years of age or younger enrolled in 28 day-care centers was 15 (range, 7 to 41). The average number of children more than two years of age enrolled per center was 84 (range, 20 to 200).

Protocol

Between August 1986 and July 1988, each day-care center was visited approximately every six months; at these visits, all full- and part-time employees were invited to participate in the study. The participants completed a questionnaire recording age, race, family income, educational level, ages of the children cared for, length of day-care employment, marital status, and number and age of children in the household. At each visit, samples of serum, saliva, and urine were obtained from each participant. Women found to be seropositive for CMV provided only urine and saliva samples at subsequent visits.

For each of the four six-month periods of the study, the number of women participating at each center was divided by the number of caretakers employed there to determine the testing rate for that center for that period. The average testing rate for all day-care centers for the total study period was 0.68 (range, 0.41 to 1.00).

At three centers, each with a daily census of 37 to 49 children, samples of the urine and saliva of all but 14 of the children were obtained for culture at each visit. During the study, specimens for culture were collected from 271 children; of these 271 children, 160 were found to shed virus.

Women employed by the Medical College of Virginia Hospitals between 1983 and 1988 constituted an additional group of subjects. Each woman provided a serum sample when she was first employed, and seronegative women were retested annually until the

end of their employment. Most hospital employees provided personal data similar to those obtained from the workers in the day-care centers.

This study was approved by the University Committee for the Conduct of Human Research. Written consent was obtained from the subjects or their parents.

Laboratory Methods

IgG antibody to CMV was measured by enzyme immunoassay as previously described.[12] Seroconversions (the development of IgG antibody to CMV in previously seronegative subjects) were confirmed by testing paired serum samples simultaneously. Saliva and urine were cultured for CMV as previously described.[1] *Eco*RI and *Bam*HI restriction-endonuclease analysis (using ^{32}P-labeled DNA) was performed as previously described.[5]

Statistical Analysis

Statistical analysis was performed using the SAS computer program (SAS Institute, Cary, N.C.) and logistic regression analysis. The SAS Logist (PROC LOGIST) procedure was used to test the significance of the independent variables predicting seropositivity. Relative risk and 95 percent confidence intervals were calculated as described by Kleinbaum et al.[13]

Results

Seroprevalence

Of 610 women day-care workers, 41 percent were seropositive. This rate of seropositivity did not differ significantly from the 47 percent rate for 565 female hospital employees matched with the day-care workers for age and race. The mean age (±SD) of the day-care workers was 29±11 years, and 75 percent were white. The mean age of the hospital employees was 29±8 years, and 67 percent were white.

For the women employed in day-care centers, seroprevalence was not significantly associated with family income, educational level, or the presence of young children in the home (Table 1). Seroprevalence was, however, significantly associated with race, marital status, day-care employment for more than one year, and the care of children two years of age or younger (Table 1). It was also significantly associated with age (data not shown). The mean age of 251 seropositive women was 32±12 years. This figure differed significantly from the mean age of 26±9 years for 357 seronegative women ($t = 6.8$, $P = 0.001$).

Three of the variables that were associated with an increased rate of seropositivity (age, length of day-care employment, and marital status) were correlated with one another ($r \geq 0.4$, $P < 0.0001$).

Of the 147 women who cared only for children two years of age or younger, 71 were seropositive for CMV. The 48 percent seropositivity rate for these women was similar to the 44 percent rate for the 206 women who cared both for children two years of age or younger and children over two years of age. However, the seropositivity rate for all women who cared for children two years of age or younger was significantly higher than that for those who cared only for children more than two years of age (46 vs. 35 percent; Table 1).

To determine whether caring for children two years of age or younger was an important independent predictor of seropositivity, we first compared the characteristics of women who cared only for children older than two years of age with those of the women who cared for children two years of age or younger, whether they also cared for older children or not. Both groups were similar in terms of mean age, marital status, race, and the percentage of women with children at home (Table 2). When the women were grouped according to the length of their day-care employment, the women who cared for children two years of age or younger had consistently higher rates of seropositivity than those who cared for older children.

We also used logistic regression (the SAS Logist procedure) to determine the most efficient predictor of seropositivity. On the basis of stepwise regression, the final predictive model ($P<0.0001$) included the women's age ($P<0.0001$), their race ($P<0.0004$), and the ages of the children cared for ($P<0.026$). The best predictive equation for seropositivity among the day-care employees is shown in Figure 1.

Seroconversion

Two or more consecutive serum samples were obtained from 202 initially seronegative caretakers (a total of 595 specimens). The average interval between the first and last serum sample was 305 days. Nineteen of the women were found to have seroconverted; the annual seroconversion rate for the day-care workers was thus 11 percent. This seroconversion rate was significantly higher than the 2.2 percent annual rate observed among 229 initially seronegative women employed at the Medical College of Virginia Hospitals (Table 3). The relative risk of seroconversion for the caretakers was 5.0 (95 percent confidence interval, 2.4 to 10.5).

The seronegative hospital employees were similar in age and race to the seronegative day-care workers, but a higher percentage of the seronegative day-care workers were married (Table 3). Seronegative day-care workers and hospital employees also differed in educational background and family income. Ninety-five percent of the seronegative hospital employees had had some college or vocational training after high school, but only 48 percent of the day-care workers had had any training after high school. This educational difference was reflected in family incomes. Thirty-nine percent of the seronegative day-care workers had annual family incomes under $20,000; 39 percent had incomes between $20,000 and $40,000; and 22 percent had incomes over $40,000. Of the seronegative hospital employees, 11 percent had annual family incomes under $20,000; 66 percent had incomes between $20,000 and $40,000; and 23 percent had incomes over $40,000.

None of the 19 caretakers who seroconverted was pregnant. Their mean age was 33 years (range, 15 to 60). The 183 women who remained seronegative had a

Table 1. Seroprevalence of CMV among Day-Care Workers.*

VARIABLE	No. of Women			P Value†	Relative Risk (95% Confidence Interval)
	CMV-positive	CMV-negative	Total (% CMV-positive)		
Age of children cared for					
≤2 yr	161	192	353 (46)	0.015	1.29 (1.05–1.57)
>2 yr	91	166	257 (35)		
Years of day-care employment					
<1	140	243	383 (37)	0.005‡	1.34 (1.10–1.62)‡
1 to 3	61	76	137 (45)		
>3 to 5	13	14	27 (48)		
>5	29	18	47 (62)		
Marital status					
Single	90	179	269 (33)	0.01§	1.42 (1.15–1.73)§
Married	135	158	293 (46)		
Previously married	26	20	46 (57)		
Race					
White	173	287	460 (38)	0.001	1.44 (1.19–1.75)
Black	77	65	142 (54)		
Annual family income					
≤$20,000	59	116	175 (34)	>0.1	1.20 (0.93–1.55)
>$20,000	99	146	245 (40)		
Children at home					
≤3 yr of age	25	43	68 (37)	>0.1	1.12 (0.79–1.59)
None	103	211	314 (33)		
Education					
High school	91	117	208 (44)	>0.1	1.17 (0.94–1.45)
≥1 yr college	98	165	263 (37)		

*Not all women provided all the information requested.

†P values were determined by chi-square tests with Yates' correction.

‡Women who had worked less than one year were compared with women who had worked more than one year.

§Single women were compared with married and previously married women.

mean age of 27 years (range, 16 to 63). Other characteristics of the caretakers who seroconverted were similar to those of the women who remained seronegative (Table 4).

Because only 17 caretakers were employed, on average, at each day-care center, a statistically valid comparison of variables associated with either seropositivity or seroconversion among or within day-care centers was not possible. However, no clustering of high rates of seropositivity, seroconversion, or any of the variables listed in Table 2 was observed at any single day-care center or group of centers. The 19 women who seroconverted were employed at 17 different day-care centers. Two day-care centers each employed two women who seroconverted.

Table 2. Characteristics of Day-Care Workers According to the Age of the Children Cared for.

CHARACTERISTIC	Ages of Children	
	≤2 yr	>2 yr
Mean age ±SD	29±11	28±10
No. white/total no. (%)	273/352 (78)	187/250 (75)
No. married/total no. (%)	172/353 (49)	121/255 (47)
No. with children/total no. (%)	178/353 (50)	117/257 (46)
No. with young children at home*/ total no. (%)	41/353 (12)	27/257 (11)
No. seropositive/total no. (%)		
Employed <1 yr†	83/205 (40)	57/178 (32)
Employed 1 to 3 yr	44/93 (47)	17/44 (39)
Employed >3 to 5 yr	11/22 (50)	2/5 (40)
Employed >5 yr	17/25 (67)	12/22 (55)

*"Young children" were defined as children ≤3 years of age. Not all women provided all the information requested.

†The seropositivity rate (0.37) for all women employed in day care less than one year was significantly lower (χ^2 = 8, 1 df; P<0.01) than the rate (0.49) for all women employed longer than one year, regardless of the ages of the children cared for.

Viral Excretion

Two hundred thirty-nine seropositive day-care workers provided 815 sets of urine and saliva samples for viral isolation (an average of 3.4 culture sets per woman). Of the 239 caretakers, 27 were found to be shedding CMV. For 16 of the 27 women, the first samples contained CMV. For 11 of the 27 women, no virus was excreted in the first sample but virus was shed in subsequent samples. Four of the 19 day-care workers who seroconverted shed CMV in urine, saliva, or both. For the women who seroconverted, the average interval during which seroconversion occurred was 300 days. This interval probably accounted for the low rate of recovery of virus from the samples collected from the caretakers who seroconverted.

At three of the 34 day-care centers, the children were included in the study. Samples of urine and saliva were obtained from 95 percent of the children in attendance at the time of each visit (five visits per center over the course of the study). Each of these three centers enrolled children two years of age or younger. Seventy-seven caretakers at these three centers participated in the study. Six of the 77 women declined to provide serum samples but provided samples of urine and saliva. Of the 71 day-care workers who provided serum samples, 32 (45 percent) were initially seropositive. This seropositivity rate did not differ from the 41 percent rate for the entire study group of 610 women. The average testing rates for the three centers where the children were tested were 0.88, 0.65, and 0.44. The average rate at which caretakers were tested at these three centers (0.66) did not differ from the 0.68 average testing rate for all the centers.

Of the 32 seropositive women evaluated at the three centers where the children were tested, seven excreted CMV during the study. Two of these seven women have been described previously.[5] These two women (E1 and E2 in Fig. 2) worked at the same day-care center. The *Eco*RI and *Bam*HI restriction-endonuclease patterns of the viral DNA in these two women's

samples were identical to each other and to the DNA patterns of the isolates shed by 29 children at that center (Fig. 2). The majority of these children were younger than two years of age and were cared for by both caretakers who were shedding CMV.

At the second center at which children were tested, two seropositive women were found to be excreting CMV (E3 and E4 in Fig. 2). Each woman shed an isolate the DNA pattern of which was identical to that shed by 47 children at that center. Thirty of these children were younger than two years of age, and both women cared for many of these children.

At the third center where the children were tested, three seropositive caretakers were found to be excreting CMV. The DNA patterns of the isolates shed by two of these three women (E6 and E7 in Fig. 2) were identical to each other and to the DNA pattern of the isolate shed by a 34-month-old child in their care. The third woman (E5 in Fig. 2) shed an isolate whose DNA pattern differed from that of the isolate shed by the other two caretakers. This isolate, however, had a DNA pattern identical to that of an isolate shed by a 13-month-old child at the center.

One woman working at the first center shed CMV but did not provide a serum sample. Her isolate had a DNA pattern that was different from the patterns of the isolates shed by the children at that day-care center.

Of the 39 seronegative caretakers at the three centers at which children were tested, four women seroconverted. Two women seroconverted during a six-month period, and neither was excreting virus when the second serum sample was obtained. A third woman who seroconverted did not provide specimens for culture. A fourth woman who seroconverted was shedding CMV when the second serum sample was obtained. The isolate had a DNA pattern that differed from those of all the isolates shed by the children in her care at that day-care center.

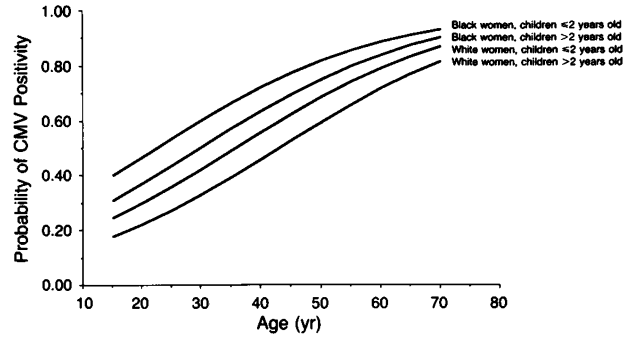

Figure 1. A Graph of the Equation of the Predictive Model of Cytomegalovirus (CMV) Positivity Generated by Logistic Regression, According to Age, Race, and the Age Group of the Children Cared for.

The predictive equation was as follows: probability of CMV positivity = $1/[1 + EXP(1.6055 - 0.544 \times \text{age} - 0.3992 \times \text{group} + 0.7229 \times \text{race})]$, where age was a value between 15 and 70. Group was scored 1 for children ≤2 years of age and 0 for children >2 years of age, and race was scored 1 for white women and 0 for black women. EXP denotes e to the indicated power.

Discussion

That women who cared for children two years of age or younger had a higher seroprevalence than women caring for older children was anticipated. Children younger than two years of age have the highest rates of viral excretion in both urine and saliva, and they usually excrete CMV for 12 to 24 months.[1-5] Children in this age group also require more "intimate contact" — diaper changing, feeding, bathing, and so on.

We did not determine the variables (such as age, race, or marital status) that may have contributed to the fact that the seropositivity rate was lower among women who cared for children more than two years of age (35 percent) than among hospital employees (47 percent). The 29 percent increase in the rate of seropositivity that we observed for women caring for children two years of age or younger — as compared with women caring for older children — is only an estimate. On the basis of the 95 percent confidence limits, the actual increase in the rate may vary from 5 to 57 percent. Thus, we cannot assume that women who care for older children will not acquire CMV from the children in their care, but only that they have a lower risk of infection. The positive association between the length of day-care employment and seropositivity may reflect the older ages of women employed for longer periods, rather than the continued acquisition of CMV from the children in their care.

The annual seroconversion rate of 11 percent for the 202 initially seronegative day-care workers provides a quantitative measure of the magnitude of the occupational risk for CMV-seronegative women and is consistent with the data on seroprevalence. Thirteen of the 19 women who seroconverted cared for children two years of age or younger.

Annual seroconversion rates higher than 10 percent have been observed previously among women who were in frequent contact with young children excret-

Table 3. CMV Seroconversions among Initially Seronegative Day-Care Workers and Hospital Employees.

Characteristic	Women	
	Day care	Hospital
Total no.	202	229
No. of seroconversions	19	11
Days observed	61,580	178,938
Mean age ±SD	29±10	28±6
Range (yr)	16–68	20–51
% White	81	87
% Married	45	34
Annual seroconversion rate (%)	11*	2.2

*Significantly different from the rate for hospital employees ($\chi^2 = 20.4$, 1 df; $P<0.0001$).

Table 4. Characteristics of the Day-Care Workers Who Seroconverted and Those Who Remained Seronegative.*

Characteristic	No. of Women			P Value†	Relative Risk (95% CI)
	Seroconverted (N = 19)	Remained Seronegative (N = 183)	Total (% Seroconverting)		
Age of children cared for					
≤2 yr	13	103	116 (11)	>0.1	1.61 (0.64–4.06)
>2 yr	6	80	86 (7)		
Years of day-care employment					
<1	13	107	120 (11)	>0.1‡	1.48 (0.59–3.74)‡
1 to 3	2	48	50 (4)		
>3	4	28	32 (13)		
Age of children at home					
<3 yr	2	19	21 (10)	>0.1§	1.01 (0.25–4.10)§
≥3 yr	6	54	60 (10)		
None	11	110	121 (9)		
Race					
White	14	148	162 (9)	>0.1	1.65 (0.64–4.29)
Black	5	30	35 (14)		
Unknown	0	5	5 (0)		
Marital status					
Single	9	90	99 (9)	>0.1	1.067 (0.45–2.52)
Married or previously married	10	93	103 (10)		

*CI denotes confidence interval.

†P values were determined by chi-square tests with Yates' correction.

‡Women who had worked less than one year were compared with women who had worked more than one year.

§Women with children less than three years of age were compared with women without children or with children more than three years of age.

ing CMV. Yeager observed that 7 of 15 seronegative mothers of 15 children with transfusion-acquired CMV infections seroconverted within one year.[14] Over three years, Taber et al. observed an annual seroconversion rate of 11 percent for 50 seronegative mothers with young children in Houston.[15] Pass et al. reported an annual seroconversion rate of 15 percent for 67 parents of children attending day care (46 had children who were shedding CMV).[7] As reported previously, we observed that of 18 seronegative mothers with children who were shedding CMV, 6 acquired CMV from their children within seven months.[5]

For seronegative women without infected children — including pediatric nurses and low- and middle-income pregnant women — reported annual seroconversion rates have been below 10 percent. In Minneapolis, Balfour and Balfour observed an annual seroconversion rate of 1.84 percent for 519 nurses and blood donors.[16] In 1983 Dworsky et al. reported annual seroconversion rates of 3 percent for 61 nurses and 2.3 percent for 1549 middle-class pregnant women.[17] Annual seroconversion rates for pregnant women range from 1 to 4 percent.[18]

Extremely poor women have high rates of seropositivity, and seronegative women in such socioeconomic groups have high annual seroconversion rates. In Birmingham, Stagno et al. observed an annual rate of infection with CMV of 6.8 percent for low-income women, as compared with a 2.5 percent annual rate for middle- or upper-income women.[8] Because the day-care workers we studied were poorer and had less education than the hospital employees, it is possible that the high seroconversion rate for the day-care workers reflects their exposure to CMV in the community or at home rather than at work. This seems unlikely, however. The women in the low socioeconomic group studied by Stagno were younger (mean age, 21 years), were more likely to be black (89 percent), and had a higher rate of seropositivity (77 percent) than the day-care workers we studied. The higher rate of seropositivity for the women of low socioeconomic status studied by Stagno reflects their frequent exposure to CMV and probably accounts for the high annual rate of primary infection among the initially seronegative women. The low initial seroprevalence we observed among the day-care workers (41 percent) and hospital employees (47 percent) suggests that their rates of exposure outside the workplace were similar. The occupational acquisition of CMV by hospital employees, including pediatric nurses, has not been demonstrated.[16,17,19]

We observed a fivefold increase in the occupational risk of CMV infection among seronegative day-care workers as compared with hospital employees (95 percent confidence interval, 2.4 to 10.5). The actual increase in the occupational risk for individual day-care workers may depend on many factors, including the prevalence of CMV infection in a particular area or population, the proportion of children who excrete CMV, the ratio of caretakers to children in a particular classroom or center, and the frequency and type of "intimate contact" between child and caretaker. Pass and Hutto reported a 20 percent annual seroconversion rate among 82 initially seronegative caretakers — a rate that was significantly higher than the 4 percent observed among 45 office workers.[20]

A high percentage (11 percent) of seropositive day-care workers shed CMV. This rate of viral shedding is similar to the rate of cervical excretion among seropositive women but higher than the 1 to 3 percent rate expected for viral excretion from other sites.[21] Previous studies from our laboratory demonstrate that the digestion of CMV DNA with *Eco*RI and *Bam*HI is adequate to identify epidemiologically related strains of CMV.[1,5,6,19] At the three day-care centers where the children were tested, nine women shed CMV. Of these nine women, seven shed strains with DNA patterns identical to those of the strains of virus isolated from the children in their care. This observation suggests that these workers acquired CMV from the children in their care. The day-care workers might have

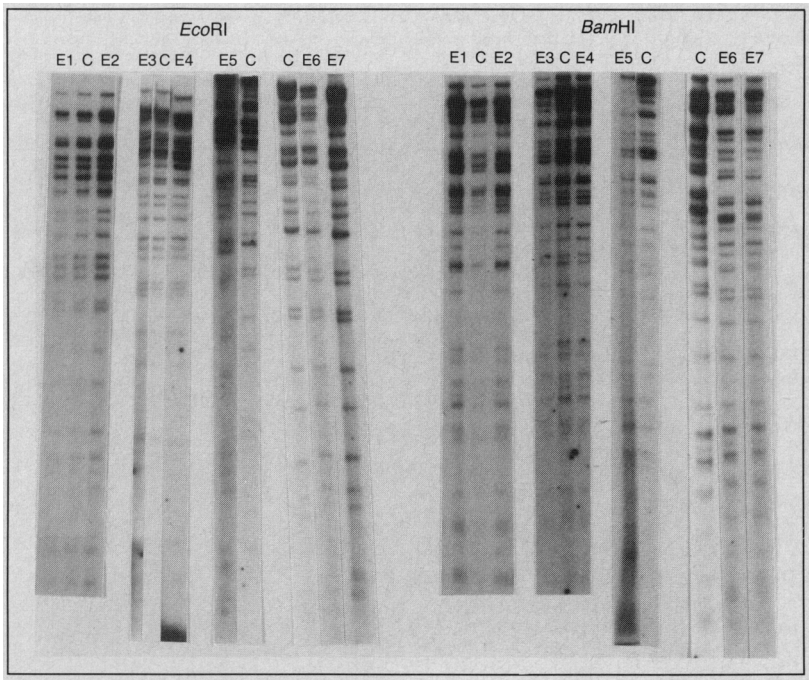

Figure 2. Restriction-Enzyme Digestion of the DNA of CMV Isolates Shed by Seven Day-Care Workers (E1 to E7) and by the Children In Their Care (C).

E1 and E2 were employed at the same day-care center, where 29 children shed this strain. E3 and E4 were employed at the same day-care center, and 47 children at this center shed this strain. E5, E6, and E7 were employed at a single center; a single child shed each strain shown.

acquired CMV from one another, however, or even have transmitted the virus to the children.

Primary maternal infection with CMV during the first 24 weeks of pregnancy places the fetus at greatest risk (approximately 15 percent) for permanent damage.[8] Nationally, an estimated 3000 infants each year have mental retardation, a hearing deficit, or both as permanent sequelae of congenital CMV infection. Because only a small fraction of pregnant women are employed as child-care workers, an increase in the national rate of symptomatic congenital infection due to this occupational risk will be difficult to detect.

Day-care workers, particularly those who care for children younger than two years of age and who are pregnant or anticipating pregnancy, should be given the option to be tested for immunity to CMV. Seronegative women may decide not to care for children during the first half of the pregnancy. If they continue caring for young children, they should be counseled to avoid "intimate contact" with children during this period. Such counseling should recommend frequent hand washing and, if feasible, the use of gloves, especially when handling diapers or respiratory secretions, and the avoidance of mouth-to-mouth contact and unnecessary or excessive kissing of children. Whether such practices would reduce the risk of acquiring CMV infection is unknown. If rigorously maintained, however, they should be successful.

Retesting of all seronegative caretakers for seroconversion during pregnancy is probably inadvisable. Determining when in pregnancy infection occurred requires the testing of paired serum samples. Seroconversion should be confirmed by the detection of IgM antibody to CMV or isolation of the virus. IgM assays have not been evaluated for mass screening, and laboratories capable of viral isolation are not always readily available. Moreover, when a primary maternal infection during early pregnancy is confirmed, counseling is difficult. No prepartum tests will determine whether an infant has been infected in utero or whether neurologic damage will occur. The risks during a given pregnancy are low, and the spectrum of neurologic damage is broad, ranging from unilateral hearing loss to severe mental retardation.[8]

None of the three methods used in this study — determination of seroprevalence, identification of seroconversion, or restriction-endonuclease analysis — is sufficient alone to prove that young children in day care frequently transmit CMV to their caretakers. Taken together, however, the findings based on these three means of observation reinforce one another and strongly suggest that these women have a significant occupational risk for the acquisition of CMV. Additional data are required to confirm these observations and to define the magnitude of the problem nationally. If these findings are confirmed, the most effective solution will be the development of a vaccine that provides immunity against the acquisition of CMV, fetal damage, or both.

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CORRELATION BETWEEN PREOPERATIVE ISCHEMIA AND MAJOR CARDIAC EVENTS AFTER PERIPHERAL VASCULAR SURGERY

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Abstract Patients who undergo peripheral vascular surgery are at increased risk for postoperative cardiac events and are difficult to assess preoperatively because of limitations on their activity. We prospectively studied 176 consecutive eligible patients undergoing elective vascular surgery to determine the value in predicting a postoperative cardiac event of preoperative electrocardiographic monitoring to detect myocardial ischemia.

Of the 176 patients, 32 (18 percent) had 75 episodes of monitored ischemic ST-segment depression preoperatively (of which 73 were asymptomatic), and 13 (7 percent) met strict criteria for major postoperative cardiac events, including 1 with a fatal myocardial infarction, 3 with nonfatal infarctions, 4 with unstable angina, and 5 with ischemic pulmonary edema. Of the 32 patients with ischemia before their operations, 12 had postoperative events (univariate relative risk, 54; 95 percent confidence interval, 7.2 to 400). Only 1 postoperative event occurred among 144 patients who did not have preoperative ischemia. The sensitivity of preoperative ischemia was 92 percent, the specificity 88 percent, the predictive value of a positive result 38 percent, and the predictive value of a negative result 99 percent. In multivariate analyses, preoperative ischemia was the most significant correlate of postoperative cardiac events and remained a statistically significant independent correlate even after we had controlled for all other preoperative factors (multivariate relative risk, 24.4; 95 percent confidence interval, 6.8 to 88).

These preliminary data suggest that preoperative electrocardiographic monitoring to detect episodes of myocardial ischemia is a useful method for assessing cardiac risk in patients who undergo elective vascular surgery. In particular, the absence of ischemia during monitoring indicates a very low risk. (N Engl J Med 1989; 321:1296-1300.)

PATIENTS who undergo peripheral vascular surgery are at increased risk for postoperative cardiac complications,[1] presumably because of the high prevalence of important coronary artery disease.[2] However, assessing cardiac risk is difficult because these patients often have problems, such as claudication and stroke, that limit their physical activity and decrease the likelihood that underlying coronary artery disease will be symptomatic or that conventional exercise testing will be helpful. Dipyridamole–thallium scintigraphy shows promise in these patients, but the technique is costly and not widely available.[3-5]

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Ambulatory electrocardiographic monitoring is a reliable method for detecting myocardial ischemia,[6] and preliminary evidence suggests that ischemia detected by ambulatory monitoring independently predicts the risk of cardiac events in patients with stable and unstable angina pectoris.[7-10] The goal of our study was to determine whether preoperative myocardial ischemia, as revealed by ambulatory electrocardiographic monitoring, provides independent, incremental information to improve risk prediction in patients undergoing elective peripheral vascular surgery.

METHODS

Two hundred seventy-four consecutive patients who were scheduled to have vascular operations — except thoracic or upper-extremity procedures, portal–systemic or peritoneal–venous shunting, and the repair of trauma — at Brigham and Women's Hospital from September 1987 to July 1988 were screened. Ninety-eight patients were excluded because they did not consent (n = 54) or because they had emergency surgery (defined as procedures undertaken within 24 hours of their diagnosis) (n = 16), base-line