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Prevalence of and Risk Factors for Viral Infections among Human Immunodeficiency Virus (HIV)–Infected and High-Risk HIV-Uninfected Women

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Viruses that can persist in the host are of special concern in immunocompromised populations. Among 871 human immunodeficiency virus (HIV)–infected and 439 high-risk HIV-uninfected women, seroprevalences of cytomegalovirus, hepatitis B virus, hepatitis C virus, and herpes simplex virus types 1 and 2 and prevalence of human papillomavirus DNA in cervicovaginal lavage fluids were all >50% and were 2–30 times higher than prevalences in the general population. Prevalences were highest among HIV-infected women, of whom 44.2% had ⩾5 other infections, and were relatively high even among the youngest women (age 16–25 years). In multivariate analyses, viral infections were independently associated not only with behaviors such as injection drug use and commercial sex but also with low income, low levels of education, and black race. Disadvantaged women and women who engage in high-risk behaviors are more likely to be coinfected with HIV and other viruses and, thus, may be at high risk of serious disease sequelae.

The prevalence of human immunodeficiency virus (HIV) infection in the United States has been conservatively estimated to be 0.32%, or 461,000 people [1]. In the United States, 30,000–41,000 new HIV infections occur annually, and the burden of HIV infection is borne increasingly by women [2, 3]. In 2001, 129,000 AIDS cases were reported among women, compared with 30,000–45,000 in 1984 [3, 4]. In 1999, 18%–23% of all persons with AIDS in the United States were women, compared with 7% in 1986 [3].

In parallel with the HIV epidemic, ~15 million persons in the United States annually acquire other sexually transmitted diseases [5]. Although the incidence of bacterial infections such as syphilis and gonorrhea has decreased, the incidence of viral sexually transmitted in-

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fections has increased considerably in recent years [5]. Viral infections associated with injection drug use (IDU) also represent a major public health problem. For example, an estimated 30,000–35,000 new hepatitis C virus (HCV) infections occur annually in the United States [6]. Viral infections have always been a source of substantial disease burden, but the HIV epidemic has created a population of immunosuppressed persons in whom the clinical manifestations of these infections may be even more severe.

Among the clinically important viral infections are several that can persist within an individual. They include cytomegalovirus (CMV), hepatitis B virus (HBV), HCV, human herpesvirus 8 (HHV-8), human papillomavirus (HPV), and herpes simplex virus (HSV) types 1 and 2. CMV is a leading cause of brain damage and hearing loss in children and is a major opportunistic infection among persons infected with HIV, in whom it often causes blindness or disseminated disease [7, 8]. HBV and HCV cause chronic liver disease, which can lead to cirrhosis and liver cancer, and liver failure due to HCV infection is the most common reason for liver transplantation [6]. HHV-8 is essential to the development of Kaposi sarcoma, an AIDS-associated cancer [9]. HPV, the most common sexually transmitted viral infection in the United States, can cause cervical cancer [10]. HSV-1 and HSV-2 cause recurrent ulcerative lesions that may facilitate HIV transmission [11, 12].

Although much research has been done on HIV and opportunistic infections in men, these infections and their sequelae are not as well studied among women. The prevalence and long-term effects of certain infections may differ between women and men [13–16]. In addition, many of the HIV risk factors for men who have sex with men (e.g., unprotected receptive anal sex and intercourse at bathhouses or sex clubs) are less common among women, yet women are acquiring HIV and other sexually transmitted infections at increasing rates, which suggests that they have risk factors for infection that differ from those for men.

The goal of this study was to provide robust estimates of viral infection prevalences in an understudied, immunocompromised population and to determine the primary risk factors for infection. To achieve this goal, we examined 7 viral infections among HIV-infected and high-risk HIV-uninfected women enrolled in the HIV Epidemiology Research Study (HERS).

METHODS

Study design. HERS followed up a cohort of women over a period of 6 years (1993–1999) to examine the biological, psychological, and social effects of HIV infection on women's health [17]. The study enrolled 871 HIV-infected and 439 demographically matched (i.e., by age, race/ethnicity, and study site) HIV-uninfected women aged 16–55 years in 4 US cities. Study participants spoke English and/or Spanish, consented to HIV testing or had documented HIV status within the previous 60 days, and reported ⩾1 HIV risk behavior (by study design, one-half reported IDU since 1985; the other half reported only sexual behavior risk since 1985). Data collection occurred twice yearly and consisted of a personal interview; physical examination; collection of blood, urine, and cervicovaginal specimens; and abstraction of medical records to document HIV- and AIDS-related diagnoses. For the present study, we analyzed cross-sectional data collected during the enrollment visit (except for HHV-8 [see below]).

Laboratory methods. Antibodies to HIV were identified by ELISA, with a Western blot to confirm positive ELISA results. CMV antibodies were detected by ELISA [18]. Antibody to HBV core antigen was detected by a competitive RIA (CORAB; Abbott Laboratories). Antibody to HCV was assessed by Abbott HCV EIA 2.0 (Abbott Laboratories) or Ortho HCV version 3.0 ELISA (Ortho-Clinical Diagnostics). Repeatedly reactive samples were tested with a supplemental immunoblot assay (Matrix HCV [Abbott] or Chiron RIBA 3.0 SIA [Chiron]). Only samples verified as positive for antibody to HCV by a supplemental assay were considered to be positive. HHV-8 infection was measured by use of 2 serological assays that target peptides from open-reading frames 65 and K8.1 [19, 20]. Type-specific gpG-based serological testing for HSV-1 and HSV-2 was done by use of immunoblot IgG assays with baculovirus-expressed gpG [21]. HPV infection was determined by DNA amplification (polymerase chain reaction) of cervicovaginal lavage specimens, rather than by serum antibody tests. Cervicovaginal lavage specimens were tested with L1 consensus primers [22, 23]. The results of examination of HHV-8 and HPV infections in HERS have been reported in more detail elsewhere [22–24] but are included here for comparison purposes. All assays tested specimens from the participants' first available visit, except for the HHV-8 assays, which used specimens from the last available visit [24].

Definitions. For multivariate analyses, we defined variables as follows: age at enrollment (16–25, 26–35, 36–45, and >45 years), race/ethnicity (black vs. white and other), education level (less than high school education vs. high school education or higher education), site of enrollment (Detroit; Providence, RI; Baltimore; and New York), annual income (<$12,000 vs. ⩾$12,000), having ever smoked crack cocaine, having ever injected drugs, lifetime number of sex partners (⩽20 vs. >20 partners), age at first sexual intercourse (<15 vs. ⩾15 years), commercial sex (having ever exchanged sex for money or drugs), having ever smoked cigarettes, and being infected with ⩾1 of the other viral infections. For most infections, lifetime number of sex partners was used as a marker for sexual activity. However, because HPV DNA detection in immunocompetent women has been associated with numbers of recent sex partners

Table 1. Prevalence of viral infections among human immunodeficiency virus (HIV)–infected and high-risk HIV-uninfected women enrolled in the HIV Epidemiology Research Study.

Variable	Percentage (no.) of women with positive results of testing for indicated virus[a]						
	CMV	HBV	HCV	HHV-8	HPV	HSV-1	HSV-2
HIV status							
Seronegative	88.7 (378)	42.4 (181)	48.0 (205)	12.6 (55)	27.4 (107)	74.5 (315)	56.7 (240)
Seropositive	94.6 (800)	58.9 (504)	60.8 (520)	17.8 (153)	63.8 (489)	74.5 (629)	67.7 (571)
Age at enrollment, years							
16–25	88.8 (103)	23.7 (28)	18.6 (22)	10.2 (12)	57.8 (67)	72.2 (83)	49.6 (57)
26–30	91.5 (215)	41.6 (99)	44.1 (105)	15.4 (37)	52.3 (123)	72.5 (171)	59.8 (141)
31–35	91.7 (322)	52.7 (186)	57.2 (202)	15.1 (54)	52.9 (173)	74.5 (260)	63.6 (222)
36–40	94.8 (289)	61.4 (189)	66.9 (206)	18.5 (58)	51.1 (144)	76.8 (232)	66.6 (201)
41–45	94.2 (163)	69.7 (122)	76.0 (133)	17.8 (31)	46.0 (64)	77.5 (134)	69.4 (120)
46–55	93.5 (86)	67.0 (61)	62.6 (57)	17.4 (16)	43.1 (25)	69.6 (64)	76.1 (70)
Race/ethnicity							
Black	96.5 (718)	56.9 (428)	55.7 (419)	17.6 (133)	54.0 (362)	73.5 (544)	69.5 (514)
White	81.0 (247)	45.6 (150)	59.6 (183)	11.5 (36)	46.8 (130)	66.6 (203)	51.8 (158)
Other	95.2 (198)	50.7 (106)	53.6 (112)	17.7 (37)	49.2 (92)	90.3 (187)	62.3 (129)
Study site							
New York	93.1 (311)	54.6 (183)	55.2 (185)	19.7 (66)	47.7 (148)	78.8 (260)	69.4 (229)
Detroit	96.2 (276)	43.4 (128)	45.1 (133)	11.7 (35)	52.2 (132)	71.4 (205)	64.1 (184)
Baltimore	96.2 (306)	65.2 (208)	68.7 (219)	19.3 (62)	53.3 (155)	78.0 (248)	64.2 (204)
Providence, RI	85.6 (285)	49.7 (166)	56.3 (188)	13.5 (45)	53.1 (161)	69.6 (231)	58.4 (194)
Annual income							
>$24,000	83.8 (119)	44.8 (64)	43.4 (62)	13.7 (20)	48.5 (63)	61.7 (87)	59.6 (84)
$12,001–24,000	92.6 (187)	48.3 (97)	46.8 (94)	15.1 (31)	47.3 (86)	69.0 (138)	60.0 (120)
$6001–12,000	93.7 (400)	52.8 (227)	57.9 (249)	16.8 (74)	50.8 (200)	78.5 (332)	64.1 (271)
≤$6000	94.3 (447)	57.9 (279)	62.9 (303)	16.8 (80)	55.1 (234)	76.9 (366)	67.0 (319)
Education							
College degree or higher	73.3 (44)	32.8 (20)	32.8 (20)	11.5 (7)	41.8 (23)	50.8 (31)	59.0 (36)
Some college	91.0 (213)	48.7 (115)	52.5 (124)	12.0 (29)	44.9 (96)	66.7 (156)	62.0 (145)
High school or GED	92.5 (394)	49.7 (212)	52.5 (224)	16.4 (71)	54.1 (212)	74.1 (314)	59.0 (250)
Less than high school	95.4 (521)	60.2 (333)	63.8 (353)	18.2 (101)	53.7 (263)	80.8 (438)	69.0 (374)
Ever smoked crack cocaine							
No	91.7 (332)	64.2 (235)	68.6 (251)	18.3 (68)	52.1 (168)	75.5 (274)	61.7 (224)
Yes	94.0 (656)	59.4 (419)	63.7 (449)	15.9 (113)	49.8 (319)	74.4 (517)	68.1 (473)
Ever injected drugs							
No	90.6 (484)	21.1 (113)	10.5 (56)	13.2 (71)	49.8 (248)	71.8 (381)	61.2 (325)
Yes	94.0 (693)	76.7 (572)	89.7 (669)	18.2 (137)	52.7 (347)	76.5 (562)	66.1 (486)
Lifetime no. of sex partners							
≤5	92.3 (274)	48.7 (144)	55.1 (163)	15.9 (48)	47.0 (127)	81.4 (241)	59.8 (177)
6–10	90.8 (206)	54.2 (124)	55.5 (127)	17.2 (41)	48.6 (101)	74.3 (168)	65.9 (149)
11–20	94.5 (137)	47.2 (70)	54.4 (80)	14.4 (21)	51.5 (69)	68.0 (100)	61.9 (91)
21–50	93.0 (120)	55.8 (72)	54.3 (70)	9.2 (12)	57.9 (70)	63.8 (81)	71.7 (91)
>50	93.2 (124)	56.7 (76)	59.7 (80)	15.9 (22)	43.9 (50)	75.6 (99)	66.4 (87)
Age at first intercourse, years							
≥15	91.2 (589)	50.8 (330)	54.5 (354)	16.8 (111)	50.9 (299)	74.5 (479)	62.5 (402)
<15	95.0 (343)	61.0 (224)	61.9 (227)	14.4 (53)	53.5 (176)	73.1 (264)	67.3 (243)
Commercial sex							
No	90.2 (608)	45.4 (309)	49.5 (337)	14.8 (102)	51.1 (316)	74.6 (501)	60.3 (405)
Yes	96.2 (452)	65.4 (310)	66.9 (317)	17.3 (83)	51.3 (218)	74.2 (347)	69.4 (325)
Ever smoked cigarettes							
No	90.1 (137)	31.0 (48)	29.0 (45)	17.0 (27)	49.3 (73)	74.8 (113)	58.3 (88)
Yes	93.0 (1041)	56.5 (637)	60.3 (680)	16.0 (181)	51.8 (523)	74.5 (831)	64.8 (723)
Overall prevalence	92.6 (1178)	53.4 (685)	56.5 (725)	16.1 (208)	51.5 (596)	74.5 (944)	64.0 (811)

NOTE. Data were not available for all subjects for all variables. CMV, cytomegalovirus; GED, general educational development (high school equivalence); HBV, hepatitis B virus; HCV, hepatitis C virus; HHV-8, human herpesvirus 8; HPV, human papillomavirus; HSV-1, herpes simplex virus type 1; HSV-2, herpes simplex virus type 2.

[a] For CMV, HBV, HCV, HHV-8, HSV-1, and HSV-2, seropositivity indicated infection; for HPV, infection was defined by detection of DNA in cervicovaginal lavage specimens by polymerase chain reaction.

Table 2. Univariate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between infections and selected risk factors among human immunodeficiency virus (HIV)–infected and high-risk HIV-uninfected women enrolled in the HIV Epidemiology Research Study.

Variable	OR (95% CI) for association with positive results of testing for indicated virus[a]						
	CMV	HBV	HCV	HHV-8	HPV	HSV-1	HSV-2
Study site							
New York	1	1	1	1	1	1	1
Detroit	1.9 (0.9–3.9)	**0.6** (0.5–0.9)	**0.7** (0.5–0.9)	**0.5** (0.3–0.8)	1.2 (0.9–1.7)	0.7 (0.5–1.0)	0.8 (0.6–1.1)
Baltimore	1.9 (0.9–3.9)	**1.6** (1.1–2.1)	**1.8** (1.3–2.4)	1.0 (0.7–1.4)	1.2 (0.9–1.7)	1.0 (0.7–1.4)	0.8 (0.6–1.1)
Providence, RI	**0.4** (0.3–0.7)	0.8 (0.6–1.1)	1.0 (0.8–1.4)	0.6 (0.4–0.9)	1.2 (0.9–1.7)	0.6 (0.4–0.9)	0.6 (0.5–0.9)
Older age[b]	**1.2** (1.0–1.4)	**1.5** (1.3–1.6)	**1.5** (1.4–1.6)	1.1 (1.0–1.2)	0.9 (0.8–1.0)	1.0 (0.9–1.1)	**1.2** (1.1–1.3)
Black race[c]	**4.1** (2.6–6.5)	**1.4** (1.1–1.8)	0.9 (0.7–1.2)	1.3 (1.0–1.8)	1.3 (1.0–1.6)	0.9 (0.7–1.1)	**1.8** (1.4–2.2)
Less than high school education	**2.2** (1.4–3.6)	**1.7** (1.3–2.1)	**1.7** (1.4–2.2)	1.3 (1.0–1.8)	1.2 (0.9–1.5)	**1.8** (1.4–2.4)	**1.5** (1.2–1.9)
<$12,000 income	**1.9** (1.3–3.0)	**1.4** (1.1–1.8)	**1.8** (1.4–2.4)	1.2 (0.8–1.7)	1.2 (1.0–1.6)	**1.8** (1.4–2.4)	1.3 (1.0–1.7)
Ever smoked crack cocaine	1.4 (0.9–2.3)	0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.8 (0.6–1.2)	0.9 (0.7–1.2)	0.9 (0.7–1.3)	1.3 (1.0–1.7)
Ever injected drugs	**1.6** (1.1–2.5)	**12.3** (9.4–16.1)	**74.5** (51.8–107.1)	**1.5** (1.1–2.0)	1.1 (0.9–1.4)	1.3 (1.0–1.7)	1.2 (1.0–1.6)
Commercial sex	**2.7** (1.6–4.7)	**2.3** (1.8–2.9)	**2.1** (1.6–2.6)	1.2 (0.9–1.6)	1.0 (0.8–1.3)	1.0 (0.7–1.3)	**1.5** (1.2–1.9)
Infection							
HIV	**2.2** (1.4–3.4)	**1.9** (1.5–2.5)	**1.7** (1.3–2.1)	**1.5** (1.1–2.1)	**4.7** (3.6–6.1)	1.0 (0.8–1.3)	**1.6** (1.3–2.0)
CMV		**3.6** (2.2–5.7)	**2.3** (1.5–3.5)	**3.5** (1.4–8.8)	1.2 (0.8–1.9)	**2.3** (1.5–3.6)	**2.3** (1.5–3.5)
HBV			**12.7** (9.7–16.5)	1.4 (1.0–1.9)	1.1 (0.9–1.4)	**1.6** (1.2–2.0)	**1.7** (1.3–2.1)
HCV				**1.7** (1.2–2.3)	1.2 (1.0–1.5)	**1.4** (1.1–1.8)	1.3 (1.0–1.6)
HHV-8					1.2 (0.9–1.7)	1.5 (1.0–2.1)	1.1 (0.8–1.5)
HPV						1.0 (0.7–1.3)	1.3 (1.0–1.7)
HSV-1							**0.6** (0.5–0.8)

NOTE. Bold text indicates significant difference ($P < .05$). CMV, cytomegalovirus; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV-8, human herpesvirus 8; HPV, human papilloma virus; HSV-1, herpes simplex virus type 1; HSV-2, herpes simplex virus type 2.

[a] For CMV, HBV, HCV, HHV-8, HSV-1, and HSV-2, seropositivity indicated infection; for HPV, infection was defined by detection of DNA in cervicovaginal lavage specimens by polymerase chain reaction.

[b] ORs compare prevalences of adjacent 5-year categories (e.g., 26–30 vs. 21–25).

[c] Black race vs. white and other.

[25], the number of sex partners in the previous 6 months was also evaluated for this variable. Because results for HPV were similar for both sexual behavior variables, only the data for lifetime number of sex partners are presented.

Statistical analyses. In univariate analyses, we evaluated associations between pairs of infections and between infections and risk factors by use of the χ^2 test of independence. Trends in age group prevalences of viral infections were examined using a test for linear trend in proportions. To determine whether univariate associations could be explained by confounding, we assessed risk factors for viral infections in multivariate logistic models constructed using assessments of colinearity, interaction, and confounding [26]. There was no evidence of significant statistical interaction, and, in general, odds ratios (ORs) relating infections to other variables were not sensitive to the choice of model covariates. Therefore, for each viral infection, we used a model that included all demographic variables, the most influential measures of behavioral risk (IDU and commercial sex), and HIV seropositivity.

RESULTS

By design, approximately two-thirds (66.5%) of the women in the study were infected with HIV, and more than one-half (58.5%) reported having injected drugs. Black was the dominant racial group (58.2%), followed by white (24.2%) and other (17.6%). Almost one-half of the women (42.7%) had less than high school education, and approximately three-fourths (72.6%) had an annual income of <$12,000. Two-thirds (65.8%) reported having smoked crack cocaine. Approximately one-fourth of the women (28.1%) reported having had >20 sex partners in their lifetimes, and 41.1% reported having had commercial sex. One-third (35.7%) of the women began having sex before they were 15 years old. Nearly all of the women (87.9%) reported having smoked cigarettes.

The prevalences of viral infections categorized by study variables are shown in table 1, with relationships among variables shown in table 2. HIV infection was significantly associated with having each individual infection, except HSV-1 (figure 1).

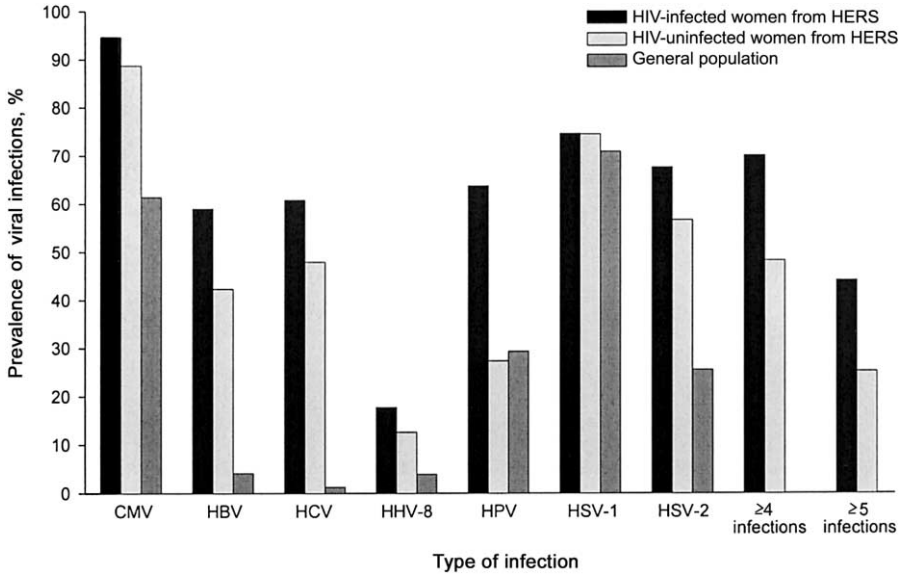

Figure 1. Prevalence of viral infections (cytomegalovirus [CMV], hepatitis B virus [HBV], hepatitis C virus [HCV], human herpesvirus 8 [HHV-8], human papilloma virus [HPV], and herpes simplex virus [HSV] types 1 and 2) among women in the HIV Epidemiology Research Study (HERS), by human immunodeficiency virus (HIV) status. Prevalence refers to seroprevalence, except for HPV, for which it refers to prevalence of DNA detection by polymerase chain reaction in cervicovaginal lavage fluids. Reported prevalences in the general population of women [7, 13–16, 27–29] are shown for comparison. The seroprevalence of HHV-8 in the general population is estimated from female blood donors and therefore is likely to be an underestimation (P. E. Pellett, D. J. Wright, E. A. Engels, D. V. Ablashi, S. C. Dollard, B. Forghani, S. A. Glynn, J. J. Goedert, F. J. Jenkins, T.-H. Lee, F. Neipel, D. S. Todd, D. Whitby, G. J. Nemo, and M. P. Busch, unpublished data). The prevalence of HPV in the general population was determined using similar assays in an age group comparable to the HERS population.

The association between HIV and HPV was especially strong (OR, 4.7; 95% confidence interval [CI], 3.6–6.1). HIV infection was also significantly associated with having multiple infections (figure 1). Among HIV-infected women, 70.1% had ⩾4 other infections, and 44.2% had ⩾5 other infections; among HIV-uninfected women, 48.3% had ⩾4 other infections, and 25.3% had ⩾5 other infections.

Across different age groups of HIV-infected women, the prevalence of most infections remained constant (figure 2). However, the seroprevalences of HBV and HCV increased with age and were nearly 4-fold higher among the oldest women than among the youngest. Among HIV-uninfected women, seroprevalence of HBV, HCV, and HSV-2 increased significantly ($P < .001$) with age. In the same group, HPV DNA was detected significantly less often in the genital tracts of older women.

In univariate analyses, CMV was strongly associated with black race, and HBV and HSV-2 were moderately strongly associated with black race (table 2). CMV, HBV, HCV, HSV-1, and HSV-2 were associated with less education, and CMV, HBV, HCV, and HSV-1 were associated with lower income. IDU was highly correlated with HCV and HBV infections and, to a lesser extent, with CMV and HHV-8. Among pairs of infections, findings of note included a strong association between HBV and HCV and an inverse association between HSV-1 and HSV-2.

Most univariate associations persisted in multivariate models (table 3). Significant positive associations included those of CMV with black race (adjusted OR, 2.8; 95% CI, 1.5–5.4); of HBV and HCV with IDU (for HBV, adjusted OR, 10.8, and 95% CI, 7.8–14.9; for HCV, adjusted OR, 63.4, and 95% CI, 41.2–97.7); and of HPV with HIV infection (adjusted OR, 4.2; 95% CI, 3.1–5.6). The negative association remained between HSV-2 and HSV-1 infection (adjusted OR, 0.6; 95% CI, 0.4–0.9). Controlling for HIV, age, race, site, IDU, and commercial sex attenuated the associations between socioeconomic factors and viral infections. However, lower level of education was still associated with CMV (adjusted OR, 1.6; 95% CI, 0.9–2.7), HBV (adjusted OR, 1.4; 95% CI, 1.0–1.9), HCV (adjusted OR, 1.5; 95% CI, 1.0–2.3), HSV-1 (adjusted OR, 1.7; 95% CI, 1.2–2.2), and HSV-2 (adjusted OR, 1.6; 95% CI, 1.2–2.1). Similarly, lower income level remained associated with HCV (adjusted OR, 1.7; 95% CI, 1.1–2.6) and HSV-1 (adjusted OR, 1.6; 95% CI, 1.2–2.2). HIV seropositivity remained associated with having multiple viral infections, even after we controlled for demographic and behavioral variables (for ⩾4 infections, adjusted OR, 2.4, and 95% CI, 1.9–3.1; for ⩾5 infections, adjusted OR, 2.4, and 95% CI, 1.8–3.2).

DISCUSSION

Although HIV has been identified as a serious problem among disadvantaged women and women with high-risk behaviors,

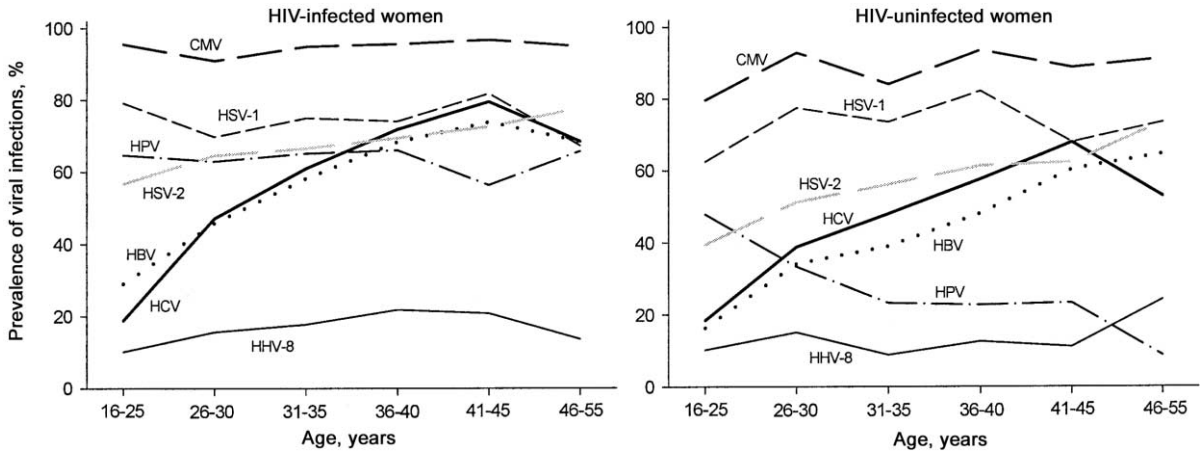

Figure 2. Prevalence of viral infections (cytomegalovirus [CMV], herpes simplex virus [HSV] types 1 and 2, human papilloma virus [HPV], hepatitis B virus [HBV], hepatitis C virus [HCV], and human herpesvirus 8 [HHV-8]), by age, among human immunodeficiency virus (HIV)–infected and HIV-uninfected women. Prevalence refers to seroprevalence, except for HPV, for which it refers to prevalence of DNA detection by polymerase chain reaction in cervicovaginal lavage fluids.

the overall burden of other viral infections in these women is not as clearly documented. Using data from one of the largest studies of women with or at risk for HIV infection (HERS), we examined prevalences of and risk factors for 7 additional viral infections. We found high prevalences of these viral infections among both HIV-positive and HIV-negative women, including prevalences of >50% for CMV, HBV, HCV, HPV, HSV-1, and HSV-2. Overall, the prevalences of viral infections among these women ranged from 2 to 30 times as high as previously reported prevalences among women from the general population [7, 13–16, 27–29]. Because HERS used a variety of recruitment modalities [17] in 4 different cities, these women are reasonably representative of the US population of HIV-infected women without AIDS and HIV-uninfected women at high risk for HIV infection.

Prevalences of viral infections were particularly high for HIV-infected women. This result is notable, because the consequences of viral infections may become increasingly grave and complex in the presence of HIV. CMV infection, for example, is usually asymptomatic in immunocompetent adults, but in persons coinfected with HIV, CMV can cause severe organ damage and blindness [7]. HHV-8, like CMV, has little effect on healthy persons but can cause Kaposi sarcoma when the immune system is deficient [9]. Coinfection with HIV increases the duration and severity of HPV infection, which may lead to increased risk for cervical dysplasia and cervical carcinoma if the HPV is an oncogenic type [10, 22]. Viral hepatitis complicates highly active antiretroviral therapy for HIV-infected persons, because the medications may exacerbate liver damage resulting from HBV or HCV infection [30–32].

We found that HIV was associated with multiple infections (e.g., ⩾4 and ⩾5 infections) even after we controlled for behavioral variables. This result suggests that, as has been shown for single infections [33, 34], HIV may facilitate the transmission of other viruses, and other viruses may facilitate the transmission of HIV. For example, genital HSV-2 lesions can facilitate transmission of HIV or other sexually transmitted agents [11, 12]. Conversely, in HIV-infected persons, HSV-2 lesions occur more frequently and tend to last longer, thus increasing the chance that an individual will acquire or transmit additional infections [11, 35, 36].

IDU was a strong risk factor for both HBV and HCV and was associated, to a much lesser extent, with HHV-8 and CMV. Nearly all HCV was acquired via IDU; HCV seroprevalence was 89.7% among injection drug users, compared with 10.5% among non–injection drug users, and IDU was by far the strongest risk factor for HCV infection in multivariate analyses. Women in HERS who did not inject drugs may have acquired HCV sexually [37]. The 10.5% HCV seroprevalence among non–injection drug users is much higher than that in the general population, which might be explained by higher numbers of sex partners and a higher prevalence of HCV infection in sex partners among women included in HERS.

HBV was associated with variables denoting high sexual risk in the HERS population, but most HBV infections were attributable to IDU. HBV seroprevalence was much higher among women who injected drugs than among women who did not (76.7% vs. 21.1%), and IDU was a stronger multivariate risk factor for HBV than was commercial sex (OR, 10.8 vs. 1.6). These results are consistent with the higher efficiency of bloodborne virus transmission by direct percutaneous exposures to blood than by sexual exposures; however, the high proportion of HBV infections attributable to IDU is also the result of the selection of a high proportion of injection drug users for par-

Table 3. Multivariate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between infections and selected risk factors among human immunodeficiency virus (HIV)–infected and high-risk HIV-uninfected women enrolled in the HIV Epidemiology Research Study.

Variable	OR (95% CI) for association with positive results of testing for indicated virus[a]						
	CMV	HBV	HCV	HHV-8	HPV	HSV-1	HSV-2
Study site							
New York	1	1	1	1	1	1	1
Detroit	1.3 (0.5–3.0)	**0.5** (0.3–0.8)	1.2 (0.6–2.1)	**0.5** (0.3–0.8)	1.2 (0.8–1.9)	1.1 (0.7–1.6)	**0.6** (0.4–0.9)
Baltimore	1.2 (0.5–2.9)	1.0 (0.6–1.6)	1.5 (0.8–2.7)	0.9 (0.5–1.4)	1.2 (0.8–1.8)	1.2 (0.8–1.9)	**0.5** (0.3–0.8)
Providence, RI	0.7 (0.4–1.3)	1.0 (0.7–1.6)	1.4 (0.8–2.5)	0.7 (0.5–1.2)	1.2 (0.8–1.8)	0.7 (0.5–1.0)	0.7 (0.5–1.0)
HIV status							
Seronegative	1	1	1	1	1	1	1
Seropositive	**2.4** (1.5–3.8)	**2.2** (1.6–3.1)	**2.3** (1.5–3.6)	**1.4** (1.0–2.0)	**4.2** (3.1–5.6)	0.9 (0.7–1.3)	**1.6** (1.2–2.0)
Age, years							
⩽25	1	1	1	1	1	1	1
26–35	1.1 (0.5–2.4)	1.7 (0.9–3.1)	**2.7** (1.2–5.9)	1.7 (0.8–3.7)	0.8 (0.5–1.2)	1.2 (0.7–2.0)	**1.6** (1.0–2.5)
36–45	2.1 (0.9–4.8)	**3.0** (1.6–5.8)	**5.6** (2.4–12.4)	**2.3** (1.1–4.9)	0.7 (0.4–1.2)	1.4 (0.8–2.4)	**2.1** (1.3–3.5)
>45	1.8 (0.5–5.8)	**4.7** (2.0–10.8)	**3.2** (1.1–8.7)	2.2 (0.8–5.7)	0.6 (0.3–1.2)	0.9 (0.4–1.7)	**3.6** (1.8–7.3)
Black race							
No	1	1	1	1	1	1	1
Yes	**2.8** (1.5–5.4)	**1.7** (1.2–2.5)	0.6 (0.4–1.0)	1.4 (1.0–2.2)	1.1 (0.8–1.6)	**0.6** (0.4–0.9)	**2.1** (1.5–3.0)
Education							
High school or above	1	1	1	1	1	1	1
Less than high school	**1.6** (0.9–2.7)	**1.4** (1.0–1.9)	**1.5** (1.0–2.3)	1.1 (0.8–1.6)	1.1 (0.8–1.4)	**1.7** (1.2–2.2)	**1.6** (1.2–2.1)
Income							
⩾$12,000	1	1	1	1	1	1	1
<$12,000	1.3 (0.8–2.1)	0.9 (0.6–1.3)	**1.7** (1.1–2.6)	0.9 (0.6–1.4)	1.1 (0.8–1.5)	**1.6** (1.2–2.2)	1.1 (0.8–1.4)
Ever injected drugs							
No	1	1	1	1	1	1	1
Yes	1.1 (0.7–1.8)	**10.8** (7.8–14.9)	**63.4** (41.2–97.7)	1.1[b] (0.8–1.6)	1.1 (0.8–1.5)	1.0 (0.8–1.4)	1.0 (0.7–1.3)
Commercial sex							
No	1	1	1	1	1	1	1
Yes	**2.4** (1.3–4.4)	**1.6** (1.2–2.3)	1.0 (0.7–1.5)	1.2 (0.9–1.7)	1.0 (0.8–1.4)	0.9 (0.7–1.2)	**1.4** (1.0–1.8)

NOTE. Multivariate model for each infection is adjusted simultaneously for all variables. Bold text indicates significant difference ($P < .05$). CMV, cytomegalovirus; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV-8, human herpesvirus 8; HPV, human papilloma virus; HSV-1, herpes simplex virus type 1; HSV-2, herpes simplex virus type 2.

[a] For CMV, HBV, HCV, HHV-8, HSV-1, and HSV-2, seropositivity indicated infection; for HPV, infection was defined by detection of DNA in cervicovaginal lavage specimens by polymerase chain reaction.

[b] For this multivariate model, ORs comparing categories of injection drug use with those who never used injection drugs are 1.0 for those who injected drugs, but not during the study; 1.1 for injection drug use at some point during the study; 1.8 for injection drug use during the 6 months preceding each visit, but not daily; and 6.2 for daily injection drug use during the 6 months preceding each visit.

ticipation in HERS. Among persons with acute hepatitis B in the overall US population, sexual exposures account for most HBV transmission, because persons who inject drugs represent only a small fraction of the total population [38].

High-risk sexual behaviors were only weakly associated with viruses with clearly sexual routes of transmission. For example, HSV-2, which is transmitted almost exclusively through sexual contact, was only weakly associated with younger age at first intercourse, having >20 sex partners, and commercial sex. Similarly, HPV, another sexually transmitted virus, was not significantly associated with sexual behavior variables. The lack of strong associations is probably due to study enrollment criteria. By design, nearly all HERS participants had relatively high levels of sexual risk, and, thus, a large proportion had acquired sexually transmitted viral infections. No low-risk comparison group was available, and therefore associations between sexual behavior and sexually transmitted infections were obscured.

Socioeconomic factors, such as lower level of education and income, were associated with all 7 viral infections. The strength of these associations was reduced after we controlled for be-

havioral variables, but, similar to previous reports for HBV and HCV [13, 15], several viral infections were independently associated with low socioeconomic level. These associations may have persisted in multivariate models because the behavioral variables incompletely described relevant behavioral risk or because women with low socioeconomic status are more likely to interact with virally infected persons.

We found age-related increases in prevalence for infections that were predominantly acquired through injection drug use (i.e., HBV and HCV). In contrast, there was an age-related decrease in HPV DNA prevalence among HIV-uninfected women, a decrease that has been noted by others [10, 39, 40]. In such women, HPV DNA is a marker for recent infection and thus is found more often in younger women, because they tend to have a higher prevalence of risky sexual behaviors. HPV DNA prevalence among HIV-infected women did not decrease with increased age, a finding that is consistent with previous reports suggesting that viral persistence is associated with immunodeficiency [22]. Despite varying age trends, most infections were highly prevalent, even in the youngest group, which suggests that behavioral interventions targeting sexual activity and IDU need to begin at a young age.

Even after we controlled for confounding, persons infected with one HSV type were less likely to be infected with the other type, which suggests that antibodies against one infection may protect against the other. Because HSV-1 infection usually occurs first via nonsexual routes in childhood, antibodies to HSV-1 may be partially protective against HSV-2. Several other studies also have found a protective effect [41–43], but in a large clinical trial [27] and a national survey [16], no such effect was found.

In conclusion, multiple viral infections are a common problem among women with or at risk for HIV infection. Although HIV infection and risky individual behavior are of key importance in the acquisition of viral infections, socioeconomic factors may also play an important role. We identified the scope of infection in this population, but a better understanding of consequences of viral diseases is still needed. Many of these infections have serious disease sequelae in immunocompromised persons, and therefore, as the number of women infected with HIV continues to increase, the number of women with serious sequelae from viral infections likely will increase as well.

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