

- **Background:** We examined the prevalence of and risk factors for current and past viral infections in a large cohort of women.
- **Methods:** 871 HIV-infected and 439 high-risk HIV-uninfected women aged 16-55 from four US cities were enrolled in the HIV Epidemiology Research (HER) study from 1993 to 1995. Serum antibody tests were done for cytomegalovirus (CMV), hepatitis B core antigen (HBV) and hepatitis C virus (HCV), human herpesvirus 8 (HHV-8), and herpes simplex virus types 1 & 2 (HSV-1, HSV-2). Human papillomavirus (HPV) was detected by PCR from cervicovaginal lavage specimens. Data were analyzed using X^2 tests and logistic regression.

- **Results:** The prevalence of viral infections was higher among HIV-infected women (Table 1), of whom 60.4% had at least 4 of the other infections and 39.2% had at least 5. After controlling for demographics, injection-drug use (IDU), and sexual behavior, women with evidence of having had more infections (≥ 5 vs. < 5) were more likely to be HIV-infected ($OR_{adj}=2.0$, 95% CI 1.4-2.9). HPV had the strongest association with HIV ($OR_{adj}=6.3$, 95% CI 3.8-10.5). Increasing age was strongly associated with HBV ($OR_{crude}=1.5$, 95% CI 1.3-1.6) and HCV ($OR_{crude}=1.5$, 95% CI 1.4-1.6), moderately associated with HSV-2 ($OR_{crude}=1.2$, 95% CI 1.1-1.3) and CMV ($OR_{crude}=1.2$, 95% CI 1.0-1.4), and inversely related to HPV ($OR_{crude}=0.9$, 95% CI 0.8-0.99). Other factors significantly associated with infection in univariate analyses are shown in Table 2.

Table 1. Prevalence of Infection by HIV Status

	CMV	HBV	HCV	HHV-8	HSV-1	HSV-2	HPV (by PCR)
HIV+	94.6%	58.9%	60.8%	17.8%	74.6%	67.7%	63.8%
HIV-	88.7%	42.4%	48.0%	12.6%	74.6%	56.5%	27.4%

Table 2. Major Risk Factors for Infection Odds Ratio (95% Confidence Intervals)

	CMV	HBV	HCV	HSV-1	HSV-2
<HS Education	2.2 (1.4-3.6)	1.7 (1.3-2.1)	1.7 (1.4-2.2)	1.8 (1.4-2.4)	1.5 (1.2-1.9)
Commercial Sex	2.7 (1.6-4.7)	2.3 (1.8-2.9)	2.1 (1.6-2.6)		1.5 (1.2-1.9)
Black Race	4.1 (2.6-6.5)	1.4 (1.1-1.8)			1.8 (1.4-2.2)
IDU		12.3 (9.4-16.1)	74.5 (51.8-107.1)		

- **Conclusions:** The prevalence of current and past viral infections in these women was much higher than in the general population, and being infected with HIV was significantly associated with having more infections. Evidence of sexually transmitted infections was found more often at an earlier age than IDU-related infections, implying that sexually transmitted infections occur more frequently than IDU-transmitted infections among younger women. Disadvantaged women and women engaging in high-risk behaviors were more likely to have additional current or past viral infections.

Viral coinfections in HIV-infected individuals can cause significant morbidity and mortality. To better understand viral infections in HIV-infected and high-risk uninfected women, we examined the prevalence of and risk factors for several viral infections in a large cohort of women.

Study Participants

The HIV Epidemiology Research Study (HERS) enrolled 1310 (871 HIV-infected & 439 uninfected) women aged 16-55 from 1993-95 in 4 US cities: Baltimore, Detroit, New York, Providence (RI).

The objective was to study the physical, social and psychological effects of HIV on the health of women in the US.

The women were matched on demographic characteristics, with about half reporting injection drug use (IDU) and half reporting sexual risk behaviors only.

Laboratory testing

Serum antibody tests were done for cytomegalovirus (CMV), hepatitis B core antigen (HBV), hepatitis C virus (HCV), human herpesvirus 8 (HHV-8), and herpes simplex virus types 1 & 2 (HSV-1, HSV-2).

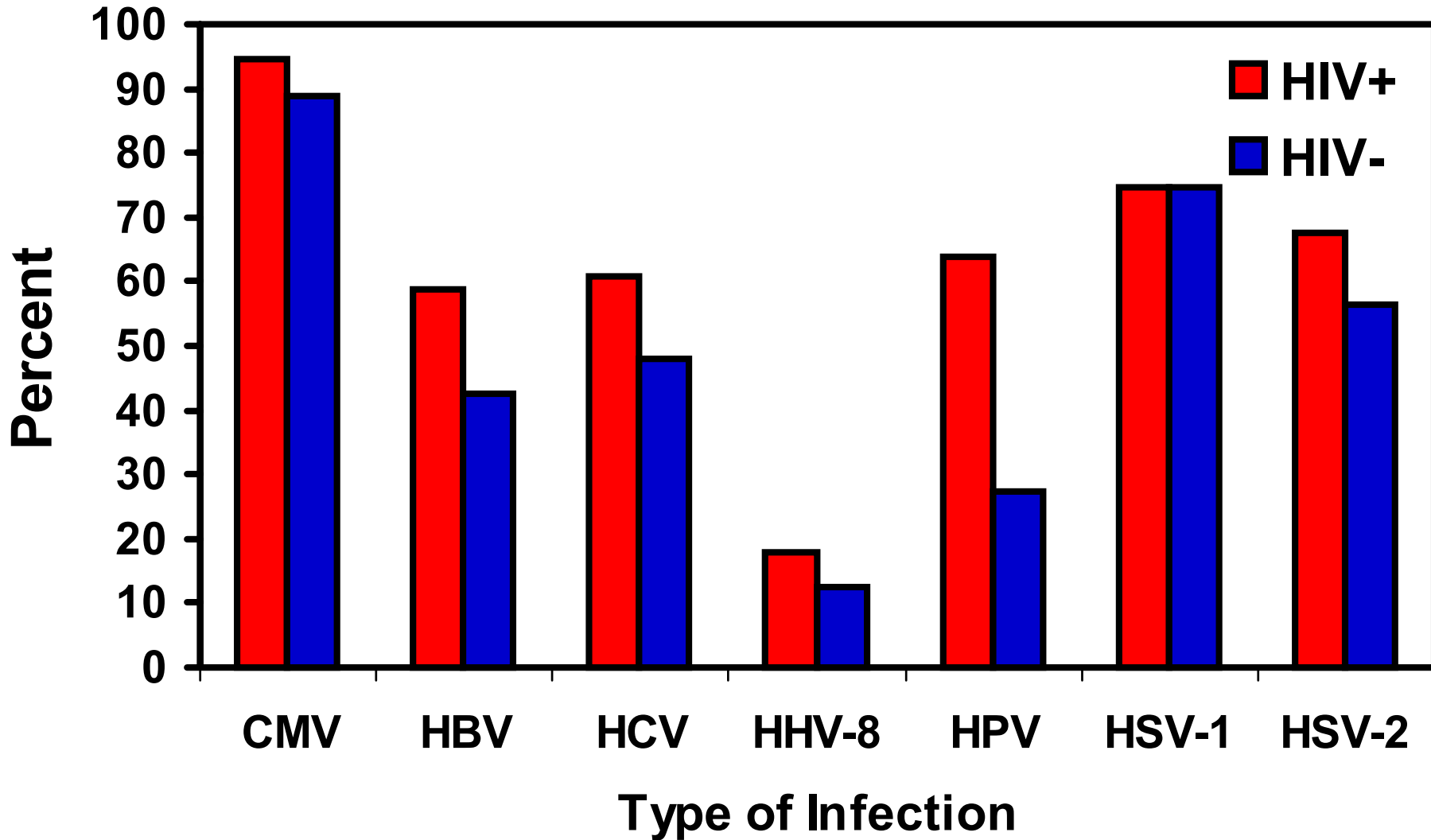
Human papillomavirus (HPV) was detected by a generic probe and PCR amplification from cervicovaginal lavage specimens.

Statistical Methods

Data were analyzed using Chi-square tests and logistic regression.

Multivariate models included demographic variables, data-based confounders (i.e. inclusion changed odds ratios by >10%) and variables found significant in previously published data.

Percentage of Women Testing Positive by Type of Infection



Prevalence of Infection by HIV Status

	HIV-infected	Non-infected	
	% (No.)	% (No.)	OR (95% CI)
CMV	94.6 (800)	88.7 (378)	2.2 (1.5 - 3.4)
HBV	58.9 (505)	42.4 (182)	2.0 (1.5 - 2.5)
HCV	60.8 (520)	48.0 (205)	1.7 (1.3 - 2.1)
HHV-8	17.8 (153)	12.6 (55)	1.5 (1.1 - 2.0)
HPV	63.8 (489)	27.4 (107)	4.6 (3.6 - 6.1)
HSV-1	74.6 (630)	74.6 (317)	1.0 (0.8 - 1.3)
HSV-2	67.7 (572)	56.5 (240)	1.6 (1.3 - 2.0)

% Testing Positive for Each Infection (Comparing HERS and the General Population)

	General Population	HIV-uninfected (HERS)	HIV-infected (HERS)
CMV¹	~70.0	88.7	94.6
HBV²	4.1	42.4	58.9
HCV³	1.8	48.0	60.8
HHV-8⁴	3.9*	12.6	17.8
HPV⁵	1.8**	27.4	63.8
HSV-1⁵	64.4	74.6	74.6
HSV-2⁶	21.9	56.5	67.7

* Among blood donors

** Seroprevalence

1 Stewart J, unpublished data.

2 McQuilan GM, Coleman PJ, Kruzson-Moran D, et al. Prevalence of Hepatitis B Virus Infection in the United States: The National Health and Nutrition Examination Surveys, 1976-1994. American Journal of Public Health. 1999; 89: 14-18.

3 Alter MJ, Kruzson-Moran D, Nainan OV, McQuilan GM, et al. The prevalence of hepatitis C virus in the United States, 1988-94. New England Journal of Medicine 1999 Aug 19; 341 (8); 556-62.

4 Pellett PE, unpublished data.

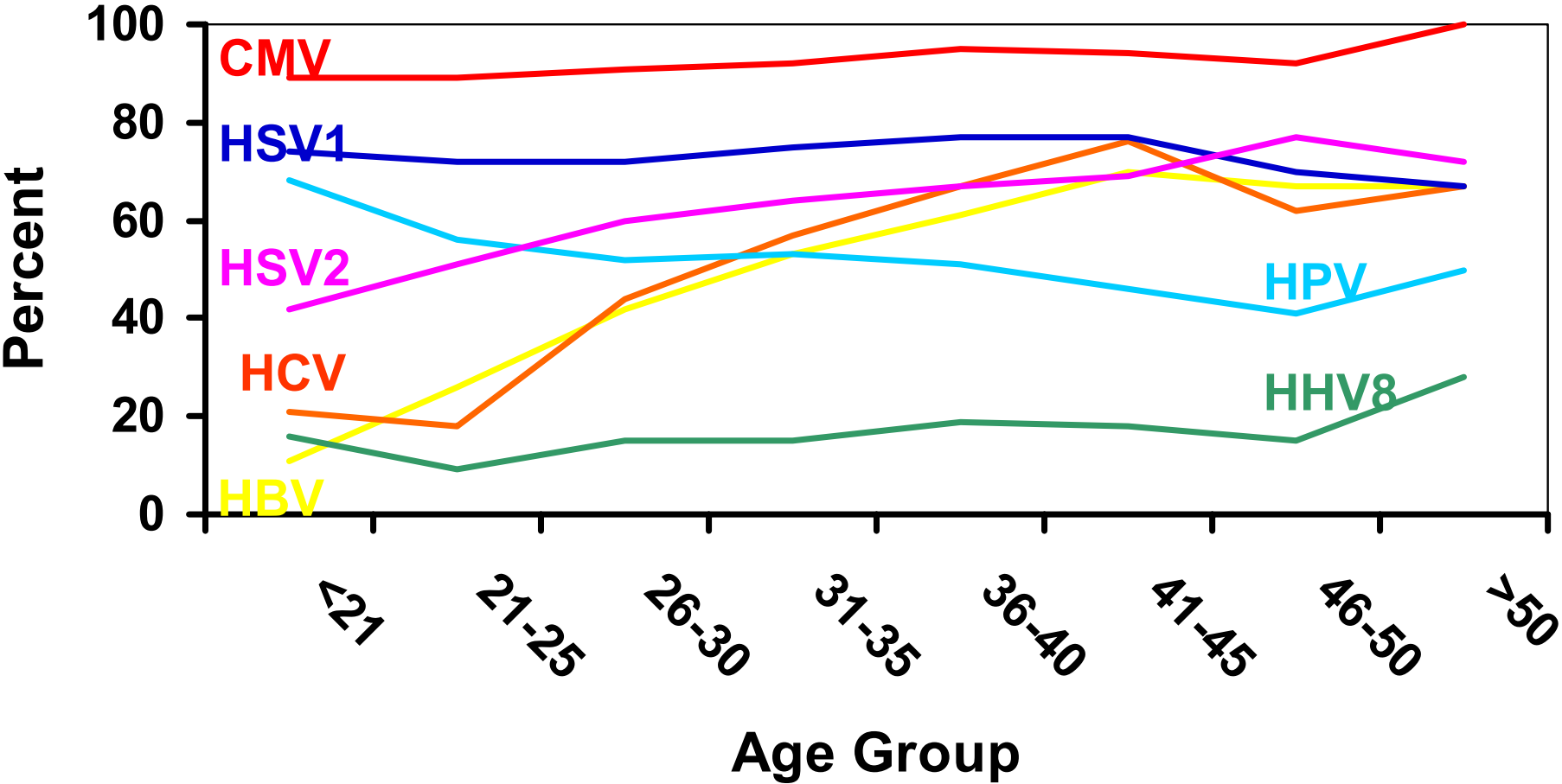
5 Division of STD Prevention. Sexually transmitted disease surveillance, 1996. Atlanta, GA: Centers for Disease Control and Prevention, September, 1997.

6. Fleming, DT, et al. Herpes simplex virus type 2 in the United States, 1976-1994. New England Journal of Medicine 1997; 337:1105

HIV Status and Multiple Infections

Number of co-infections	HIV infected	HIV uninfected	OR (95% CI)
At least 4	60.4%	43.5%	1.8 (1.3 - 2.5)
At least 5	39.2%	22.6%	2.0 (1.4 - 2.9)

Percentage of Women Infected by Age Group and Type of Infection



Crude Association between Infection & Risk Factors

(Crude OR)

	CMV	HBV	HCV	HHV8	HPV	HSV-1	HSV-2
Age*	1.2	1.5	1.5	1.1	0.9	1.0	1.2
Black Race	4.1	1.4	0.9	1.3	1.3	0.9	1.8
Education <HS	2.2	1.7	1.7	1.3	1.2	1.8	1.5
Income <\$12,000	1.4	1.1	1.3	1.0	1.1	1.2	1.1
Smoked Crack	1.4	0.8	0.8	0.8	0.9	0.9	1.3
IDU	1.6	12.3	74.5	1.5	1.1	1.3	1.2
Lifetime sex partners	1.1	1.1	1.0	0.9	1.0	0.9	1.1
Age at 1st sex	1.8	1.5	1.4	0.8	1.1	0.9	1.2
Commercial sex	2.7	2.3	2.1	1.2	1.0	1.0	1.5

p < .05

*** ORs compare prevalences of adjusted 5-year categories (e.g. 26-30 vs. 21-25)**

Selected Multivariate Models

After controlling for potential confounders, we observed the following associations:

*** Each variable was adjusted for all other variables in the table.**

Association between HSV-2 and Other Variables

Risk Factor	OR (95% CI)	P-value
HSV-1 —seronegative	1	
seropositive	0.6 (0.4 - 0.8)	0.003
HIV —seronegative	1	
seropositive	1.4 (1.0 - 1.9)	0.03
Age —≤25	1	
26-35	1.8 (1.1 - 2.9)	0.02
36-45	2.3 (1.4 - 3.8)	0.002
>45	3.6 (1.7 - 7.7)	0.0009
Race —Non-black	1	
Black	2.3 (1.6 - 3.3)	<.0001
Site —New York	1	
Detroit	0.6 (0.4 - 0.9)	0.01
Baltimore	0.5 (0.3 - 0.7)	0.0008
Providence	0.7 (0.5 - 1.0)	0.04
Education — ≥High School	1	
<High school	1.7 (1.2 - 2.2)	0.0005
Age at 1st Intercourse —≥16	1	
<16	1.1 (0.9 - 1.5)	0.36
Lifetime sex partners —<5	1	
5-10	1.1 (0.8 - 1.6)	0.64
11-20	0.9 (0.6 - 1.5)	0.79

Association between HPV Shedding and Other Variab

Risk Factor	OR (95% CI)	P-value
HIV —seronegative	1	
seropositive	4.6 (3.3 - 6.5)	<.0001
Age —≤25	1	
26-35	0.5 (0.3 - 1.0)	0.06
36-45	0.6 (0.3 - 1.1)	0.10
>45	0.5 (0.2 - 1.2)	0.13
Race —Non-black	1	
Black	0.9 (0.6 - 1.4)	0.57
Site —New York	1	
Detroit	1.3 (0.8 - 2.2)	0.26
Baltimore	1.2 (0.8 - 1.9)	0.39
Providence	1.0 (0.8 - 1.6)	0.87
Education —≥High School	1	
<High School	0.9 (0.7 - 1.3)	0.62
Crack use —No	1	
Yes	1.0 (0.7 - 1.4)	0.96

Association between CMV and Other Variables

Risk Factor	OR (95% CI)	P-value
Race —Non-black	1	
Black	3.2 (1.6 - 6.3)	<.0001
HIV —seronegative	1	
seropositive	1.7 (1.0 - 2.9)	0.04
Age —≤25	1	
26-35	1.1 (0.4 - 3.0)	0.79
36-45	1.4 (0.5 - 3.8)	0.52
>45	1.2 (0.3 - 5.0)	0.77
Site —New York	1	
Detroit	1.5 (0.5 - 4.0)	0.44
Baltimore	1.1 (0.4 - 2.8)	0.87
Providence	0.4 (0.2 - 0.8)	0.01
Education —≥High School	1	
<High School	0.5 (0.3 - 0.9)	0.01
Crack use —No	1	
Yes	1.1 (0.7 - 1.9)	0.60

Association between HBV and Other Variables

Risk Factor	OR (95% CI)	P-value
Ever Injected Drugs —No	1	
Yes	5.9 (4.4 - 8.0)	<.0001
HIV —seronegative	1	
seropositive	2.4 (1.8 - 3.3)	<.0001
Age —≤25	1	
26-35	1.5 (.09 - 2.6)	0.15
36-45	3.0 (1.7 - 5.6)	0.0003
>45	7.4 (3.1 - 18.1)	<.0001
Race —Non-black	1	
Black	1.7 (1.2 - 2.4)	0.004
Site —New York	1	
Detroit	0.8 (0.5 - 1.2)	0.22
Baltimore	0.9 (0.5 - 1.4)	0.51
Providence	1.0 (0.6 - 1.5)	0.87
Education —≥High School	1	
<High School	0.8 (0.6 - 1.0)	0.08
Creek use —No	1	

- **Prevalence of current and past viral infection among women in this cohort was much higher than in the general population.**
- **Being infected with HIV was significantly associated with having more infections.**
- **Women at highest risk for additional infections were those with less education, lower income, black race and engaging in high-risk behaviors.**
- **Evidence of sexually transmitted infections was found at an earlier age than IDU-related infections, implying that sexually transmitted infections occur more often than IDU-related transmission among younger women.**

After controlling for potential confounders, we observed the following associations:

- HBV was strongly associated with IDU and HIV infection.**
- HPV shedding was strongly associated with HIV infection.**
- CMV was associated with black race, although absolute prevalence differences were modest (96.5% Black, 87.1% Non-black).**
- HSV-1 & HSV-2 were inversely related, suggesting that antibodies to one protected against infection by the other.**