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Association between Syphilis, Antibodies to Herpes Simplex Virus Type 2, and Recreational Drug Use and Hepatitis B Virus Infection in the Women's Interagency HIV Study

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Abstract

Background—Liver disease is a leading cause of death in human immunodeficiency virus (HIV)–infected women; however, risk factors for hepatitis B virus (HBV) infection in this population have not been well studied.

Methods—We describe the seroprevalence and predictors of HBV infection in a cross-sectional analysis of 2132 women with and at risk for HIV infection enrolled in the Women's Interagency HIV Study during the periods 1994–95 and 2001–02. Any test result positive for antibody to hepatitis B core antigen defined infection; those women with serological evidence of vaccine immunity were excluded from analysis. Women were stratified into those with a history of injection drug use (IDU), those with a history of noninjection drug use (non-IDU), and those with no history of illicit drug use.

Results—Of 1606 HIV-infected and 526 HIV-uninfected women, 7% and 12%, respectively, appeared to be vaccine immune. After exclusion of these women, 43% of 1500 HIV-infected and 22% of 461 HIV-uninfected women had HBV infection. HBV infection prevalence differed among the IDU, non-IDU, and no illicit drug use groups (76%, 30%, and 17%, respectively; $P < .0001$). HBV infection was strongly associated with herpes simplex virus 2 (HSV-2) seropositivity in the IDU group (odds ratio [OR], 2.9; 95% confidence interval [CI], 1.6–5.4) and with a history of syphilis in the non-IDU group (OR, 2.7; 95% CI, 1.4–5.0).

Discussion—We found a high prevalence of HBV infection in our cohort of women with and at risk for HIV infection. HSV-2 seropositivity and a history of syphilis appeared to be important correlates of HBV infection. Sexual transmission of HBV, particularly in those with a history of genital ulcer disease, should be a major focus of education in all high-risk groups.

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Since the advent of HAART, liver disease has become a leading cause of death in HIV-infected men and women [1, 2]. Death due to liver disease has been attributed to coinfection with hepatitis B virus (HBV), hepatitis C virus (HCV), or both HBV and HCV, as well as to other factors, including the use of alcohol and hepatotoxic medications. Even prior to the advent of HAART, coinfection with HIV and HBV (compared to infection with HIV alone) was associated with reduced survival [3]. In another study of men with chronic HBV infection [4], HIV coinfection was associated with a higher risk of HBV-related cirrhosis and decreased survival. As the clinical significance of coinfection with HIV and HBV becomes better understood, it is imperative to understand the prevalence and correlates of HBV infection in those with and at risk for HIV infection, especially because occult HBV infection (i.e., active HBV replication in the absence of HBV serological data suggestive of active disease) may be more common in this population.

HBV infection is highly prevalent in certain populations in the United States; the prevalence approaches 60%–80% in immigrants from areas of endemicity [5], men who have sex with men [4], injection drug users [6], and persons with multiple sexual partners [7]. HIV infection is also highly prevalent in the latter 3 groups, because HBV and HIV infections have similar sexual and parenteral modes of transmission. Users of noninjection drugs have also been identified as a group potentially at high-risk for HBV infection. In a recent study conducted in New York City [8], nearly one-quarter of 483 noninjection heroin users were HBV infected; sexual risk factors appeared responsible for the increased risk.

Epidemiologic studies of HBV infection have mainly involved men. The few studies involving women have been in predominantly HIV-uninfected women, and the prevalence of HBV infection has varied widely [7, 9, 10]. Women reporting injection drug use (IDU) and those reporting no history of IDU had prevalences of 74% and 38%, respectively, in a national multisite study conducted from 1986 through 1987 among 1368 female sex workers [7]. This study was conducted prior to the implementation of universal vaccination strategies to reduce HBV transmission and widespread strategies to reduce HIV transmission, which have likely impacted HBV transmission. Two subsequent studies [9, 10], both of which excluded women with a history of IDU, reported prevalences of HBV infection of 19% and 6%, respectively. The first study [9] was conducted from 1990 through 1991 and involved 599 inner city women in Brooklyn, New York; the other [10] was conducted from 1996 through 1998 and involved 1337 low-income young women in the San Francisco Bay area. Few if any studies have explored the prevalence and predictors of HBV infection in a cohort of predominantly HIV-infected women.

We determined the prevalence of and risk factors for HBV infection among the participants of the Women's Interagency HIV Study (WIHS). We performed a cross-sectional analysis of the predictors of HBV infection among women whom, at the time of their enrollment into the WIHS, reported either a history of IDU, a history of noninjection drug use (non-IDU) only, or no history of illicit drug use.

METHODS

From October 1994 through November 1995, 2628 women with or at risk for HIV infection were enrolled in the WIHS, an ongoing, prospective multicenter cohort study of HIV infection in women. From October 2001 through September 2002, an additional 1153 women were enrolled, primarily to increase the number of young, AIDS-free women in the cohort. As expected, given the evolution of the HIV epidemic, there was an increased proportion of Hispanic women and a decreased proportion of women reporting IDU, compared with the initial group. The study's recruitment, retention, enrollment, and quality assurance activities have been reported elsewhere [11, 12]. Two of the 6 WIHS sites did not

routinely perform all HBV serological tests and so were excluded from all analyses reported here.

Appropriate written and oral informed consent was obtained from all participants in this study. Guidelines for human experimentation in accordance with the US Department of Health and Human Services and the institutional review boards of each participating institution were followed in the conduct of the study.

Baseline HBV serological tests were performed for hepatitis B surface antigen (HBsAg), hepatitis B core antibody (anti-HBc), and hepatitis B surface antibody (anti-HBs) using Abbot Auszyme Microparticle EIA, Abbot Corzyme EIA, and Abbot Ausab EIA, respectively (Abbot Laboratories).

Subjects were considered to have HBV infection if they had a serological test result positive for anti-HBc. This included women who were previously infected with HBV and subsequently developed immunity to HBV (i.e., natural HBV immunity; defined as present in patients with serological test results positive for both anti-HBc and anti-HBs); those who had an isolated serological test result positive for anti-HBc, which most often indicates resolved infection without detectable anti-HBs, but which may also indicate chronic infection without detectable HBsAg; and those who had hepatitis B surface antigenemia, which indicates chronic HBV infection or acute HBV infection. Those with serological evidence of vaccine immunity (i.e., an isolated serological test result positive for anti-HBs) were excluded from the analysis.

In addition to the performance of HBV and HIV antibody assays at enrollment, the hepatitis C virus (HCV) EIA 2.0 or 3.0 (Abbot Laboratories) and the herpes simplex virus (HSV) type 1 and type 2 glycoprotein G-based EIA (Gull Laboratories) determined HCV and HSV-2 seropositivity. Self-reported data regarding any history of syphilis, gonorrhea, and/or chlamydia were obtained and were included in the analysis. Results from the rapid plasma reagin test, confirmatory microhemagglutination assay *treponema pallidum* (MHATP) test for syphilis, and ligase chain reaction test for chlamydia and gonorrhea were not used, because they determined current untreated infection, not whether the woman had ever been infected. Women were asked if they had ever used injection drugs, had used specific recreational drugs in the previous 6 months, had ever shared needles, and had ever had anal sex.

Fisher's exact test was used to compare the prevalence of HBV infection between HIV-infected and HIV-uninfected women and between the original cohort and the new cohort, by HIV infection status. Fisher's exact test and the χ_2 test were used to test risk factors for HBV infection for the combined old and new cohort.

Using logistic regression analysis, predictors of HBV infection were determined for the following 3 drug-use risk groups: those with a history of IDU involving heroin, crack cocaine, and/or cocaine (the IDU group); those who reported use of heroin, crack cocaine, and/or cocaine but not by injection (the non-IDU group); and those who reported no history of ever using these illicit drugs. Because there were numerous, substantial, and statistically significant interactions of this drug use categorization with other predictors, no pooled analysis of all 3 groups together was performed. Women with evidence of past vaccination were excluded, because it is impossible to know whether they would have been infected had they not been vaccinated. Sensitivity analyses that counted vaccinated women as HBV-infected or that counted them as HBV-uninfected produced results very similar to those of sensitivity analyses from which such women were excluded. Because interest here focuses on evaluation of risk factors and explanatory rather than predictive models, selection of variables for multivariate models favored inclusiveness. Demographic variables and

plausibly causal risk factors were included as candidates for multivariate models. Variables that were judged likely to be noncausal correlates of HBV infection or that did not reach $P < .10$ in the multivariate model for ≥1 drug use group were excluded. We did, however, examine the estimated effect of each excluded variable when added to the multivariate model for each group as a single additional predictor. Transfusion history was not included in the main models, because this was assessed only for women from the original cohort and only for years after 1977. Analyses that included this risk factor (and therefore excluded those subjects enrolled in 2001 and 2002) produced results similar to those shown. To facilitate comparison between the drug use groups, variables that qualified for inclusion in 1 group were also included in models for the other 2.

RESULTS

Of the 3781 women in the WIHS, 2132 (1606 HIV-infected women and 526 HIV-uninfected women) had data available for all 3 HBV serological tests, because 2 sites did not routinely perform serological testing for HBsAg. HIV-infected women had a higher prevalence of hepatitis B surface antigenemia, natural immunity to HBV, and an isolated anti-HBc pattern (i.e., anti-HBc alone), compared with HIV-uninfected women (table 1). HIV-infected women had a lower prevalence of vaccine immunity and, given the higher prevalence of HBV infection in this group, a lower prevalence of vaccine eligibility. Compared with newly enrolled HIV-infected women, those from the original cohort had a higher prevalence of hepatitis B surface antigenemia, natural immunity, and isolated anti-HBc pattern and a lower prevalence of vaccine immunity and vaccine eligibility.

In HIV-uninfected women, the prevalence of hepatitis B surface antigenemia was similar between those from the original cohort and those who were newly enrolled, but natural immunity to HBV infection showed a trend toward being more common among those from the original cohort, and the presence of an isolated anti-HBc pattern was more common in the original cohort. Vaccine immunity was less common in the original cohort of HIV-uninfected women, but there was no difference in the rate of vaccine eligibility between the original cohort and the newly enrolled cohort.

Of the 2132 women with complete serological data, 171 women with serological test results consistent with previous HBV vaccination were excluded from further analysis, resulting in a final group of 1961 women (1500 HIV-infected women and 461 HIV-uninfected women) who contributed data to the following analyses. After exclusion of the 171 women with vaccine immunity, 43% of HIV-infected women and 22% of HIV-uninfected women had serological evidence of HBV infection.

Prevalence of HBV infection by demographic characteristics and risk factors

Table 2 shows the prevalence of HBV infection among the 1961 women by demographic characteristics and common risk factors. Women who were older, were African American, had a lower education level, and had >10 sexual partners in their lifetime had a higher prevalence of HBV infection. The prevalence of HBV infection differed among those in the IDU group, those in the non-IDU group, and those who never used illicit drugs (76%, 30%, and 17%, respectively).

Univariate analysis of risk factors for HBV infection among 3 drug-use risk groups

In the univariate logistic regression analysis, history of syphilis and HSV-2 infection were predictive of HBV infection in all 3 drug-use risk groups (table 3). Exchanging sex for money, drugs, or shelter, a history of gonorrhea, and a history of chlamydia also were positively associated with HBV infection in the non-IDU group, whereas among those who

reported never using illicit drugs, having sex with an injection drug user was positively associated with HBV infection. Ever having anal sex appeared to be negatively associated with HBV infection in both the IDU group and the group of those reporting having never used illicit drugs. With regard to drug-use behaviors, crack cocaine use in the previous 6 months was positively associated with HBV infection in the IDU group, and amphetamine use in the previous 6 months was negatively associated with HBV infection in the IDU group.

Multivariate analysis of demographic and significant risk factors for HBV infection among 3 drug-use risk groups

Table 4 shows multivariate models for each drug use group. Serological evidence of HSV-2 remained strongly associated with HBV infection in the IDU group, after adjustment for other factors. Syphilis remained strongly associated with HBV infection in the non-IDU group and also had a substantial OR in the group of women reporting having never used illicit drugs. Exchanging sex for money, drugs, or shelter appeared to be associated with HBV infection in the IDU group; having had sex with an injection drug user appeared to be associated in the group of women reporting having never used illicit drugs—both based on substantial ORs. In the IDU group, not having graduated from high school and older age were associated with HBV infection.

Multivariate analysis of correlates of HBV infection among 3 drug-use risk groups

To understand the role of other factors associated with—but not necessarily causal of—HBV infection, we added each predictor separately to the multivariate models shown in table 4. The estimated effects of each predictor after addition to the multivariate model are listed in table 5 for each of the 3 drug-use groups. HIV infection and HCV infection were strong correlates of HBV infection, especially in the IDU group and in women who reported having never used illicit drugs. Gonorrhea and chlamydia no longer appeared to be strongly associated with HBV infection in the non-IDU group. However, a history of anal sex remained associated with a decreased risk of HBV infection in the IDU group. Use of crack cocaine in the prior 6 months did not appear to be associated with HBV infection in the IDU group.

DISCUSSION

These data are among the first to describe HBV seroprevalence in a large cohort of predominantly HIV-infected women in the United States. Not unexpectedly, given the similar modes of transmission of HIV and HBV infection, the 1500 women with HIV infection had a prevalence of HBV infection that was nearly twice that of HIV-uninfected women. However, our study suggests decreasing trends in HBV infection. The low prevalence of hepatitis B surface antigenemia in HIV-infected women enrolled from 1994 through 1995 (4%) was even lower in women enrolled from 2001 through 2002 (<1%). Another large multisite study reported a 4.6% prevalence of chronic HBV infection in HIV-infected women during the period from 1998 through 2001, using chart review and not serological evidence [13]. Overall, HIV-infected women have a lower prevalence of chronic HBV infection than the 8%–9% prevalence reported in men from 2 large multisite HIV cohort studies [4, 13]. However, our serological data has identified several areas of concern.

First, our cohort of high-risk women had a low prevalence of vaccine immunity, suggesting either a lack of vaccination, failure to complete the vaccination series, or an inability to develop an adequate immune response [14]. More than one-half of women appeared to be eligible for vaccination on the basis of negative serological test results. Although the raw prevalence of vaccine immunity was higher in the women who joined the cohort in 2001 and

2002, the proportion of HIV-infected women eligible for vaccination increased due to an overall decrease in HBV infection among newly enrolled women. The increased numbers of women eligible for vaccination may also reflect the fact that some women in our cohort were not recruited from clinics and thus may not have received routine primary care.

Second, 37% of HIV-infected women in our study with positive anti-HBc serological test results had an isolated anti-HBc pattern, which may be of concern in those with HIV infection because of the increased prevalence of detectable HBV DNA in HIV-infected patients with an isolated anti-HBc pattern, leading to an increased risk of cirrhosis and decreased survival time. Two studies [15, 16] found that 35%–60% of HIV-infected patients with anti-HBc alone had detectable HBV DNA levels. In a longitudinal study [15], 90% of 57 patients with an isolated anti-HBc pattern had HBV DNA detected at least once from an average of 3.5 samples during a median follow-up period of 31 months. In another study [16], 37 of 42 patients with anti-HBc alone had a persistent isolated anti-HBc pattern, and HBV DNA was detected in 35% of these 37 patients. However, another recent cross-sectional study [17] found that only 2% of HIV-infected patients with anti-HBc alone had detectable HBV DNA levels at baseline. A 10% prevalence of detectable HBV DNA among those with anti-HBc alone has been commonly reported in the general population [18]. Although our prevalence of isolated anti-HBc pattern is comparable to results reported in other studies involving groups mostly composed of HIV-infected men [15, 16], HIV-uninfected women in our cohort had a 32% prevalence of anti-HBc pattern, which is higher than the 10%–20% reported in HIV-uninfected persons with positive HBV markers from the United States and Europe [18]. Finally, small studies also suggest an increased risk of cirrhosis in those with the isolated anti-HBc pattern and concurrent HCV infection, regardless of HIV infection status [16, 19, 20]. Women in our cohort may be at particular risk of cirrhosis because of the high prevalence of concurrent HCV infection.

Our findings suggest that antibodies to HSV-2, a history of syphilis, and high-risk sexual behaviors are important risk factors that are associated with HBV infection, even among women with a history of IDU. Genital ulcers may facilitate the acquisition of HBV, have been demonstrated to facilitate the acquisition of HIV infection [21], and may also be associated with high-risk behavior. Nonulcerative STDs are more likely to only indicate high-risk sexual behavior than to play a causal role. In our multivariate analysis, chlamydia and gonorrhea no longer appeared to be associated with HBV infection in women reporting a history of non-IDU. In contrast to other studies involving men and women [7, 22, 23], anal sex was associated with a decreased risk of HBV infection in women with a history of IDU and was not strongly associated in the other 2 drug use groups. In a large multisite study of predominantly HIV-uninfected female sex workers [7], anal sex was associated with HBV infection only among women without a history of IDU. Our findings are difficult to interpret; perhaps the sexual partners of those with a history of IDU are more likely to use condoms, given the increased risk of disease transmission.

Limitations of the study include its cross-sectional design. It is not clear whether the high-risk behavior occurred before or after HBV transmission. Another limitation of our study is the possible underreporting of sensitive risk behaviors, as demonstrated in the strong correlation we found between infection with HIV, HCV, and HBV in women who reported never using illicit drugs. HCV is transmitted more efficiently via the parenteral than the sexual route [24]. The cross-sectional design also does not enable us to discern the temporal relationship between infection with HBV, HIV, and/or HCV. Use of self-reporting of STDs —particularly of chlamydia and gonorrhea, which are often asymptomatic in women—may also underestimate the effect of nonulcerative STDs on HBV infection.

Finally, data regarding frequency and duration of drug use, receptive sharing of needles, sharing of other drug-injecting equipment, and whether or not anal sex was protected was not obtained. Despite these limitations, our study represents one of the largest studies to investigate the prevalence and predictors of HBV in a cohort of predominantly HIV-infected women.

Reasons for the low prevalence of vaccine immunity in our cohort need to be studied, including whether HBV vaccine was administered, whether vaccination was completed, and, if completed, whether it was successful in developing immunity. The impact of occult HBV infection in our cohort of women, many of whom were also infected with HCV, must be further studied, including whether there is an accelerated progression to cirrhosis, as well as an increased risk of antiretroviral-associated hepatotoxicity.

HBV infection in injection drug users has been commonly attributed to risk behaviors directly associated with IDU, including the sharing of needles, but prevention of sexual transmission of HBV infection must not be overlooked. Preventing sexual transmission of HBV should be a major focus for all high-risk groups, and HBV vaccination should be routinely offered to those presenting with sexually transmitted diseases, especially genital ulcer disease [24].

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Table 1

Prevalence of hepatitis B virus (HBV) infection and vaccine immunity in women with and at risk for HIV infection

Serological status	All subjects, by HIV serostatus			HIV-positive subjects, by time of study enrollment			HIV-negative subjects, by time of study enrollment		
	HIV-positive (*n* = 1606)	HIV-negative (*n* = 526)	*P*[a]	1994–1995 (*n* = 1228)	2000–2001 (*n* = 378)	*P*[a]	1994–95 (*n* = 313)	2000–01 (*n* = 213)	*P*[a]
HBsAg-positive	46 (3)	2 (<1)	<.001	44 (4)	2 (<1)	<.001	1 (<1)	1 (<1)	1.0
HBsAb-positive and HBcAb-positive[b]	358 (22)	67 (13)	<.001	306 (25)	52 (14)	<.001	47 (15)	20 (9)	.027
HBcAb-positive only	238 (15)	33 (6)	<.001	214 (17)	24 (6)	<.001	26 (8)	7 (3)	.063
HBsAb-positive only[c]	106 (7)	65 (12)	<.001	41 (3)	65 (17)	<.001	19 (6)	46 (22)	<.001
All 3 HBV serological results negative[d]	858 (53)	359 (68)	<.001	623 (51)	235 (62)	<.001	220 (70)	139 (65)	.25
All subjects with HBV infection[e]	642 (43)	102 (22)	<.001	564 (48)	78 (25)	<.001	74 (25)	28 (17)	.047

NOTE. Data are no. (%) of subjects. HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen.

[a] All statistical comparisons were made using Fisher's exact test.

[b] Subjects with natural immunity.

[c] Subjects with vaccine immunity.

[d] Subjects who are eligible for vaccine.

[e] Excluding those subjects with vaccine immunity.

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Table 2

Seroprevalence of hepatitis B virus (HBV) infection, by demographic characteristics and risk factors

Characteristics	No. of subjects[a]	No. of subjects with HBV infection (% of subjects with the specified characteristic with HBV infection)	*P*[b]
HIV infection			
No	461	102 (22)	<.0001
Yes	1500	642 (43)	
Age, years			
<30	567	126 (22)	
30–34	460	140 (30)	
35–39	422	195 (46)	<.0001
≥40	498	274 (55)	
Race			
Black	1005	448 (45)	<.0001
White	334	123 (37)	
Hispanic	536	138 (26)	
Other	71	26 (37)	
Study site			
Brooklyn	528	228 (43)	<.0001
Los Angeles	673	156 (23)	
San Francisco	511	256 (50)	
Chicago	235	95 (40)	
Educational level			
Beyond high school	501	146 (29)	
High school graduation	528	229 (43)	<.0001
No high school graduation	676	311 (46)	
Drug use			
Injection drug use	581	440 (76)	<.0001
Noninjection drug use	512	153 (30)	
No illicit drug use	850	142 (17)	

Characteristics	No. of subjects[a]	No. of subjects with HBV infection (% of subjects with the specified characteristic with HBV infection)	P[b]
More than 10 lifetime sexual partners			
No	1042	289 (28)	<.0001
Yes	855	414 (48)	
Hepatitis C virus status			
Negative	1336	282 (21)	<.0001
Positive	593	442 (75)	
Blood transfusion (original cohort only)			
No	1244	511 (41)	.0003
Yes	198	109 (55)	
All subjects	1961	744 (38)	

NOTE. HBV infection was defined as any laboratory result positive for hepatitis B core antibody.

[a] Because of missing values, numbers may not add up to the total number of respondents.

[b] All statistical comparisons except those for race, site, and drug use group were made using Fisher's exact test.

Table 3

Univariate logistic regression models of associated factors for hepatitis B virus infection, by drug use category

	Injection drug use (*n* = 581)		Noninjection drug use only (*n* = 512		No illicit drug use (*n* = 850)	
Characteristic	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
More than 10 lifetime sex partners	1.28 (0.86–1.91)	.22	1.47 (0.98–2.20)	.061	1.32 (0.87–2.00)	.20
Sex with an injection drug user	1.25 (0.80–1.96)	.32	0.87 (0.59–1.30)	.51	1.70 (1.07–2.70)	.026[a]
Sex with an HIV-positive person	1.42 (0.93–2.19)	.11	0.74 (0.48–1.13)	.16	0.99 (0.67–1.46)	.96
Exchanging sex for food, money or shelter	1.44 (0.98–2.11)	.065	2.01 (1.37–2.95)	<.001[a]	1.48 (0.69–3.18)	.32
History of anal sex	0.48 (0.32–0.71)	<.001[a]	0.90 (0.61–1.33)	.60	0.54 (0.33–0.89)	.016[a]
Positive for herpes simplex virus 2 antibodies	3.79 (2.28–6.32)	<.001[a]	2.11 (1.15–3.88)	.016	2.24 (1.33–3.79)	.003[a]
History of syphilis	2.06 (1.21–3.51)	.007[a]	3.69 (2.35–5.78)	<.001[a]	1.89 (1.02–3.52)	.043[a]
History of gonorrhea	1.30 (0.88–1.91)	.18	1.82 (1.23–2.69)	.003[a]	1.32 (0.81–2.16)	.26
History of chlamydia	1.12 (0.66–1.90)	.66	2.34 (1.37–3.98)	.002[a]	0.86 (0.38–1.97)	.73
Cocaine use[b]	1.10 (0.71–1.69)	.67	1.24 (0.76–2.02)	.39	…	
Crack cocaine use[b]	1.55 (1.02–2.34)	.038[a]	1.50 (0.98–2.28)	.060	…	
Heroin use[b]	1.46 (0.94–2.26)	.089	1.07 (0.37–3.13)	.90	…	
Amphetamine use[b]	0.30 (0.16–0.55)	<.001[a]	0.29 (0.06–1.26)	.10	…	
Sharing of needles	0.82 (0.42–1.61)	.57	…	…	…	

[a] Statistically significant.

[b] Use in the 6 months before the baseline visit; data on lifetime use were not collected for individual drugs.

Table 4

Multivariate logistic regression models for hepatitis B virus (HBV) infection including demographic variables and plausibly causal risk factors by drug use category

	Injection drug use (*n* = 581)		Noninjection drug use only (*n* = 512)		No illicit drug use (*n* = 850)	
Characteristic (referent)	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Study site (San Francisco)						
Brooklyn	1.26 (0.53–2.98)	.60	2.69 (1.30–5.60)	.008[a]	2.62 (1.04–6.58)	.040[a]
Chicago	0.44 (0.22–0.91)	.027[a]	0.58 (0.23–1.49)	.26	1.42 (0.50–4.06)	.51
Los Angeles	0.20 (0.10–0.39)	<.00[a]1	0.88 (0.43–1.81)	.72	1.13 (0.43–2.96)	.81
Race (black)						
Hispanic	2.04 (0.97–4.29)	.061	0.63 (0.30–1.35)	.23	0.67 (0.34–1.30)	.23
Other	0.56 (0.15–2.07)	.38	0.91	.92	0.38 (0.08–1.77)	.22
White	1.34 (0.71–2.52)	.36	0.82 (0.37–1.78)	.61	0.47 (0.18–1.26)	.13
Education (beyond high school)						
No high school graduation	2.69 (1.42–5.09)	.003[a]	1.44 (0.72–2.87)	.30	1.58 (0.81–3.09)	.18
High school only	1.40 (0.75–2.63)	.29	1.56 (0.79–3.09)	.20	1.83 (0.97–3.47)	.064
Age, years (≤28)						
29–34	1.27 (0.55–2.95)	.58	0.85 (0.42–1.73)	.66	0.96 (0.47–1.96)	.92
35–39	2.48 (1.08–5.72)	.032[a]	0.92 (0.43–1.97)	.83	1.13 (0.57–2.26)	.72
≥40	3.80 (1.67–8.67)	.001[a]	1.35 (0.62–2.95)	.46	1.14 (0.58–2.25)	.70
More than 10 lifetime sex partners	1.49 (0.81–2.76)	.20	1.67 (0.93–3.01)	.087	1.31 (0.70–2.44)	.40
Exchanging sex for money, food, or shelter	1.73 (0.97–3.07)	.062	0.95 (0.52–1.73)	.87	0.89 (0.29–2.74)	.84
Sex with an injection drug user	0.70 (0.37–1.31)	.27	0.78 (0.46–1.31)	.35	1.78 (0.99–3.21)	.054
History of syphilis	1.38 (0.69–2.78)	.36	2.67 (1.44–4.97)	.002[a]	1.75 (0.81–3.79)	.16
Positive for herpes simplex virus 2 antibodies	2.93 (1.59–5.40)	<.001[a]	1.07 (0.53–2.16)	.85	1.53 (0.85–2.78)	.16

NOTE. Variables judged likely to be noncausal correlates of HBV infection or that did not reach *P* < .10 in table 3 for ≥1 drug use group are not included.

[a] Statistically significant.

Table 5

Estimated associations with hepatitis B virus (HBV) infection of predictors not necessarily causal of HBV infection, by drug use category

	Injection drug use (*n* = 581)		Noninjection drug use only (*n* = 512)		No illicit drug use (*n* = 850)	
Characteristic	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
HIV infection	5.84 (3.10–11.0)	<.001[a]	1.60 (0.83–3.07)	.16	7.41 (2.56–21.43)	<.001[a]
Positive for hepatitis C virus antibodies	3.89 (1.91–7.90)	<.001[a]	2.27 (0.98–5.26)	.056	3.08 (1.37–6.92)	.006[a]
Sex with an HIV-positive person	1.01 (0.57–1.78)	.97	0.89 (0.50–1.59)	.70	0.81 (0.46–1.42)	.46
History of anal sex	0.41 (0.23–0.71)	.002[a]	1.00 (0.57–1.75)	.99	0.73 (0.36–1.50)	.40
History of gonorrhea	0.77 (0.44–1.36)	.37	1.01 (0.57–1.80)	.97	0.71 (0.36–1.42)	.33
History of chlamydia	0.81 (0.36–1.79)	.59	0.84 (0.36–1.98)	.69	0.55 (0.17–1.84)	.33
Cocaine use[b]	1.14 (0.65–2.01)	.64	1.75 (0.92–3.32)	.086		
Crack cocaine use[b]	1.11 (0.64–1.95)	.71	1.50 (0.79–2.82)	.21		
Heroin use[b]	1.17 (0.66–2.06)	.59	1.43 (0.32–6.46)	.64		
Amphetamine use[b]	0.61 (0.23–1.63)	.32	0.98 (0.18–5.35)	.98		
Sharing needles	1.64 (0.64–4.19)	.30				

NOTE. Data were derived from multivariate logistic regression models that include all variables shown in table 4.

[a] Statistically significant.

[b] Use in the 6 months before the baseline visit; data on lifetime use were not collected for individual drugs.