Hepatitis B Virus Infection and Immunization Status in a New Generation of Injection Drug Users in San Francisco

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Summary and Introduction

Summary

Hepatitis B virus (HBV) infection is common among injection drug users (IDU). Younger IDU, however, may be less susceptible to infection due to the implementation of public health interventions, such as universal immunization programs and syringe exchange programs. To investigate the current epidemiology of HBV infection and control among a new generation of drug users in the United States, we conducted interviews and examined HBV serologic markers in a cross-section of street-recruited IDU under age 30 in San Francisco, CA. Of the 831 persons studied, 21% showed serologic evidence of current or past infection; 22% had isolated antibodies to hepatitis B surface antigen consistent with vaccine-mediated immunity; and 56% had no HBV markers. In multivariate analyses, HBV infection was associated with drug use behaviour in heterosexual males; sexual behaviour in males who have sex with males; and both drug use and sexual behaviour in females. Vaccine-mediated immunity was independently associated with female sex and younger age. In conclusion, HBV transmission persists among young IDU in San Francisco. Few young injectors show evidence of successful immunization and the majority remains susceptible to disease. Until the broad effects of universal vaccination are seen, targeted and innovative approaches to immunizing young IDU in the US are needed to prevent a substantial number of new HBV infections.

Introduction

Hepatitis B virus (HBV) has infected more than two billion people and is the tenth leading cause of death worldwide.[1] More than 350 million people are chronically infected, and they serve as reservoirs for continued transmission.[2] Chronic infection also results in significant morbidity and mortality, including cirrhosis and hepatocellular carcinoma, and reactivation of latent disease in immunocompromised hosts has raised new concerns.[3] Most newly-acquired HBV infections in the United States are among persons aged 25-45 years and associated with high-risk sexual activity or injection drug use.[2] Among injection drug users (IDU), years of injecting, frequency of injections, and syringe sharing are well known transmission risk factors.[4-7]

Younger IDU are at higher risk of HBV infection, because their young age is associated with riskier behaviour, including sharing injecting equipment and unprotected sex.[8,9] A new generation of IDU, however, also may be less susceptible to HBV transmission as a result of public health interventions to prevent new infections and reduce disease transmission. Among these are the approval of an effective preventive vaccine in 1982, the establishment of universal immunization programs for infants and children in the 1990s, and the dissemination of syringe exchange programs.

According to the Centers for Disease Control, the incidence of acute HBV in the United States declined 78% between 1990 and 2005, with the greatest declines (96%) among children and adolescents corresponding to an increase in hepatitis B vaccination coverage.[10] In California and other states, school-based immunization programs for adolescents were piloted as early as 1992.[11] In 1996, a routine health provider visit was established nationwide for catch-up immunizations among adolescents 11-12 years old.[12] In 1999, the national strategy was expanded again to include routine HBV vaccinations of all individuals aged ≤18 years. Thirty-two states now require proof of HBV immunization for children to enter middle school.[13]

Exposures to HBV also may be reduced among young IDU as a result of the growing public acceptance and availability of syringe exchange programs in the United States. Conceived first in the Netherlands in the 1980s, syringe exchange programs provide sterile needles and syringes in exchange for used injecting equipment to reduce the circulation time of

potentially contaminated equipment and prevent transmission of human immunodeficiency virus (HIV) and other blood borne infections.[14] Most current young IDU have initiated injecting drug use during the era of syringe exchange and therefore may have obtained the protective benefits that are intended. Of the several syringe exchange programs in San Francisco, the San Francisco Needle Exchange program focuses distinctly on serving young IDU in the Haight Ashbury district. Originating as an underground, roving outdoor exchange in 1997, this program has evolved into its present state: an "above ground" (legal), indoor, medically-supervised exchange with financial and political support from the San Francisco Department of Public Health and from several private foundations.

As many as one-third of the estimated 18 700 IDU in San Francisco in 2001 are age 29 years or younger.[15] Few studies, however, have evaluated current risk and the results of public health interventions that may benefit young IDU. Therefore, to investigate the current epidemiology of HBV infection and prevention in this high-risk population, we measured HBV serological markers in subjects participating in a large community study of young IDU in San Francisco, CA. We report on the prevalence of baseline serological markers and examine factors associated with past or current infection and with prior successful immunization.

Methods

Study Population

From January 2000 to January 2002, young IDU were recruited for a study of HIV and viral hepatitis (The UFO Study) to community field sites using street outreach worker-based convenience sampling in four neighbourhoods in San Francisco, CA. Eligible persons reported a history of injecting drug use in the last 30 days and an age of 29 years or under. Injection status was verified by field staff through visual inspection and questions about injection techniques that identified noninjectors. Potential participants, who demonstrated acute intoxication or behaviour impairing their ability to provide informed consent, were asked to return the following week. Participants were surveyed using a 40-min interviewer-administered questionnaire, which included questions on their demographics; health history; prior hepatitis immunization; drug practices, including use of syringe exchange programs; and sexual behaviour, including partner types, condom use, and sex exchanged for money. Participants then received client-centred risk reduction counselling prior to undergoing phlebotomy for viral testing. A $20 cash payment was offered at the initial visit and a $10 cash payment 1 week later, when subjects returned for results disclosure, post-test counselling, and health service referrals. At the follow-up visit, all participants were offered free hepatitis A immunizations. In addition, participants that tested seronegative for antibody to hepatitis B surface antigen (anti-HBs) were offered free hepatitis B immunizations. Informed consent was obtained from all participants and all study procedures were reviewed and approved by the Committee on Human Research at the University of California, San Francisco.

Individuals were defined as HBV infected by the presence of either hepatitis B suface antigen (HBsAg) or antibody to hepatitis B core antigen (anti-HBc). Vaccine-mediated immunity was defined as an anti-HBs titre ≥10 mIU / mL in the absence of other HBV serologic markers. Participants were considered HBV uninfected if they tested negative for all HBV markers.

Laboratory Testing

Hepatitis B surface antigen, anti-HBs, and anti-HBc were detected by standard commercial enzyme immunoassays (Abbott Laboratories, Abbott Park, IL, USA). Specimens testing positive for total anti-HBc underwent further testing for immunoglobulin M (IgM) antibody to anti-HBc. HIV testing was conducted using an enzyme immunoassay (Abbott Laboratories) and confirmed by Western blot. Antibody to hepatitis C virus (anti-HCV) was detected using a second-generation enzyme immunoassay (EIA-2.0; Ortho Diagnostics Systems, Raritan, NJ, USA).

Statistical Analysis

We estimated the prevalence of HBV serologic markers among all 831 participants and conducted separate analyses of variables associated with HBV infection and with vaccine-mediated immunity. Subjects demonstrating prior immunization were excluded from the first analysis comparing HBV-infected and uninfected individuals, because these individuals are

protected against infection. Study participants in this subset (n = 646) were stratified into three groups: females, males who have sex with males (MSM) and heterosexual males. Univariate associations between predictor and outcome variables were analysed using the chi-square test of association and the Fisher exact test for small cell sizes. The Mantel-Haenszel chi-square was used to test ordinal univariate associations. To determine whether stratified analyses by sex and sexual orientation were indicated, we examined the homogeneity of the odds ratios across the three strata using the Breslow-Day test, using a $P < .15$ cutoff. Because the null hypothesis of homogeneity of odds ratios across the three strata was rejected for age, prior sexually transmitted disease, exchanging sex for money, and the number of lifetime sexual partners, separate multivariate analyses were conducted for each stratum. In the analysis of variables associated with vaccine-mediated immunity, we compared HBV-uninfected individuals with those testing positive for only anti-HBs (n = 654); HBV-infected individuals were excluded. Using multivariate logistic regression, we examined the independent associations of the predictor variables on the two primary outcomes of interest. Variables selected for inclusion in multivariate models were those found to have a chi-square P value < .10 on bivariate analyses or those considered potential confounders based on expected biologic and behavioural inference. HIV and HCV status were excluded from the infection model to limit the analysis to plausible causal determinants. Variables were held in the models if they reached a significance level of 0.05 or less. Statistical analysis was performed using SAS version 8.0 (SAS Institute, Cary, NC, USA).

Results

Among the 831 young IDU screened, the median age was 22 years [interquartile range (IQR) 20-25 years], 80% were white, and 70% were male. Seventy-one percent of subjects had been homeless and one third had been incarcerated in the prior 3 months. The median number of years injecting was four (IQR 2-7), and 266 (32%) participants injected heroin daily or more often. Eighty-three percent of participants had ever used a syringe exchange program, and syringe exchange in the prior month was common (76%). Two hundred sixty-one (31%) reported never borrowing a used syringe, and 294 (35%) reported borrowing a used syringe in the last month. Nearly all (99%) participants were sexually active, and 657 (80%) reported having had sex in the prior 3 months. Among the sexually active, 404 (49%) identified lifetime sexual partners of the same or both sexes (39% of males, 72% of females); 159 (19%) reported more than 50 lifetime partners (20% of males, 17% of females); and 252 (31%) had ever traded sex for money (32% of males, 27% of females).

Serology

Twenty-one per cent of the total study population demonstrated serologic evidence of prior HBV infection, and 56% were nave for any HBV marker ( ). Thirty-six per-cent tested positive for anti-HBs: 118 (14%) in the setting of prior infection (anti-HBc + anti-HBs) and 185 (22%) from prior immunization (isolated anti-HBs). We detected isolated anti-HBs in six of 10 subjects who were ≤12 years of age on or after January 1, 1996, which was the year that catch-up immunizations for adolescents were instituted in the US. Isolated anti-HBs was found in 63 (38%) of the 168 subjects who were ≤18 years on or after January 1, 1999, the year routine HBV vaccinations were expanded to all children aged ≤18 years.

Table 1. Hepatitis B Virus Serologic Markers in 831 Young Injection Drug Users in San Francisco, 2000-2002

Serologic status	Total (N = 831)	HIV+ (n = 32)	HCV+ (n = 315)
HBV infection (past or current)	177 (21)	19 (60)	121 (38)
HBsAg only	4 (1)	0 (0)	1 (0)
Anti-HBc only	40 (5)	6 (19)	32 (10)
Anti-HBc + HBsAg	11 (1)	1 (3)	5 (2)
Anti-HBc + anti-HBs	118 (14)	11 (34)	80 (25)
Anti-HBc + anti-HBs + HBsAg	4 (1)	1 (3)	3 (1)
Vaccine-mediated immunity			

Anti-HBs only	185 (22)	4 (13)	56 (18)
HBV nave	469 (56)	9 (28)	138 (44)

Values are expressed as *n* (%).
anti-HBc, antibody to hepatitis b core antigen; anti-HBs, antibody to hepatitis B surface antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

Of the 32 (4%) persons testing positive for HIV-1 antibody, most (60%) had been infected with HBV and only 13% demonstrated vaccine-mediated immunity. Of the 315 (38%) persons that tested positive for anti-HCV, 38% had been infected with HBV and 18% showed vaccine-mediated immunity. Prevalence of HBV infection increased with duration of injecting drug use in a linear fashion; 9% were infected by their first year and 41% after 10 or more years (Figure 1).

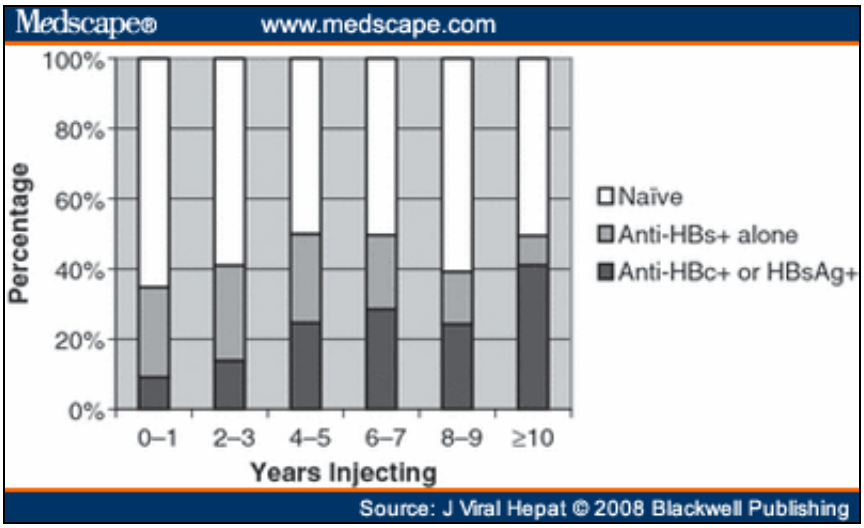

Figure 1.

Hepatitis B virus infection and vaccine-mediated immunity by years injecting in a sample of 831 young injection drug users in San Francisco, 2000-2002.

Factors Associated with Hepatitis B Virus Infection

Of the 646 subjects without evidence of prior immunization, past or current HBV infection was significantly associated with age, San Francisco residence greater than 1 year, presence of anti-HCV, and more than 10 years sexual activity for all three subject strata ( ). Among heterosexual males, HBV infection also was associated with the number of years injecting, daily or more frequent injection, and syringe exchange use in the prior month. Among MSM, HBV infection also was associated with nonwhite race, presence of HIV-1 antibody, daily or more frequent injection, syringe borrowing, and exchanging sex for money. Among females, HBV infection was associated also with the number of years injecting, incarceration, syringe borrowing, and more than 50 lifetime sexual partners. Infection in females was marginally associated with daily or more frequent injections ($P = .06$) and a prior sexually transmitted disease ($P = .08$). HBV infection was not associated in any of the three groups with education, condom use, or sharing cookers, cottons, or rinse water.

Table 2. Hepatitis B Virus Infection as a Function of Demographic and Risk Behaviours in 646 Unvaccinated Young Injection Drug Users in San Francisco

Variable	*N* anti-HBc or HBsAg / *N* (%)		
	Heterosexual males (*N* = 290)	**Males who have sex with males (*N* = 185)**	**Females (*N* = 171)**

All	65 (22.4)	71 (38.4)	41 (24.0)
Age			
15-19	3 / 40 (7.5)	0 / 12 (0)	9 / 54 (16.7)
20-24	25 / 133 (18.8)	37 / 101 (36.6)	17 / 78 (21.8)
25-29	37 / 117 (31.6)*	34 / 72 (47.2)*	15 / 39 (38.5)*
Race (*n* = 641)			
White	52 / 231 (22.5)	52 / 149 (34.9)	35 / 140 (25.0)
Nonwhite	12 / 57 (21.1)	18 / 34 (52.9)*	6 / 30 (20.0)
San Francisco residence			
<12 months	38 / 205 (18.5)	32 / 113 (28.3)	28 / 138 (20.3)
≥12 months	27 / 85 (31.8)*	39 / 72 (54.2)*	13 / 33 (39.4)*
Incarcerated, ever			
No	4 / 24 (16.7)	8 / 21 (38.1)	4 / 41 (9.8)
Yes	61 / 266 (22.9)	63 / 164 (38.4)	37 / 130 (28.5)*
HIV-1 antibody (*n* = 642)			
Negative	64 / 285 (22.5)	54 / 160 (33.8)	40 / 169 (23.7)
Positive	1 / 2 (50.0)	17 / 24 (70.8)*	1 / 2 (50.0)
Hepatitis C virus antibody (*n* = 644)			
Negative	19 / 175 (10.9)	19 / 95 (20.0)	18 / 115 (15.7)
Positive	46 / 115 (40.0)*	52 / 90 (57.8)*	23 / 54 (42.6)*
Years injecting			
<3 years	10 / 92 (10.9)	12 / 47 (25.5)	7 / 62 (11.3)
3-5 years	22 / 87 (25.3)	19 / 51 (37.3)	16 / 63 (25.4)
6-8 years	13 / 53 (24.5)	23 / 50 (46.0)	11 / 29 (37.9)
≥9 years	20 / 58 (34.5)*	17 / 37 (46.0)	7 / 17 (41.2)*
Frequency of injection, last 30 days			
Less than daily	29 / 175 (16.6)	34 / 110 (30.9)	20 / 105 (19.1)
Daily or more	36 / 115 (31.3)*	37 / 75 (49.3)*	21 / 66 (31.8)†
Borrowed a used syringe, ever			
No	18 / 103 (17.5)	15 / 63 (23.8)	5 / 40 (12.5)
Yes	47 / 187 (25.1)	56 / 122 (45.9)*	36 / 131 (27.5)*
Shared cookers, cottons, or rinse, ever (*n* = 644)			
No	8 / 41 (19.5)	9 / 19 (47.4)	2 / 12 (16.7)
Yes	57 / 249 (22.9)	62 / 166 (37.4)	39 / 157 (24.8)

Syringe exchange, ever (*n* = 646)			
No	4 / 51 (7.8)	9 / 27 (33.3)	5 / 35 (14.3)
Yes	61 / 239 (25.5)*	62 / 158 (39.2)	36 / 136 (26.5)
Syringe exchange, last 30 days (*n* = 645)			
No	8 / 76 (10.5)	9 / 29 (31.0)	8 / 48 (16.7)
Yes	57 / 214 (26.6)*	62 / 156 (39.7)	32 / 122 (26.2)
Years sexually active (*n* = 634)			
<10 years	23 / 142 (16.2)	24 / 86 (27.9)	22 / 118 (18.6)
≥10 years	41 / 142 (28.9)*	46 / 97 (47.4)*	17 / 49 (34.7)*
Lifetime number of sexual partners (*n* = 646)			
≥50	57 / 254 (22.4)	43 / 121 (35.5)	28 / 141 (19.9)
>50	8 / 36 (22.2)	28 / 64 (43.8)	13 / 30 (43.3)*
Sexually transmitted disease, ever			
No	59 / 252 (23.4)	57 / 137 (41.6)	22 / 111 (19.8)
Yes	6 / 38 (15.8)	14 / 48 (29.2)	19 / 60 (31.7)†
Inconsistent condom use, last 3 months (*n* = 497)			
No	13 / 50 (26.0)	19 / 62 (30.7)	10 / 36 (27.8)
Yes	32 / 154 (20.8)	31 / 81 (38.3)	26 / 114 (22.8)
Exchange sex for money, ever (*n* = 638)			
No	57 / 258 (22.1)	11 / 58 (19.0)	25 / 118 (21.2)
Yes	7 / 27 (25.9)	60 / 127 (47.2)*	15 / 50 (30.0)

anti-HBc, antibody to hepatitis b core antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus.
*χ^2, *P* value <0.05;
† X^2, *P* value <0.10.

In multivariate analyses stratified by sex and sexual orientation ( ) drug-use behaviour was independently associated with HBV infection in heterosexual men. The adjusted odds of infection (AOR) were significantly higher for heterosexual males who reported more years injecting [AOR = 1.14 / year of injecting; 95% confidence interval (CI) = 1.04, 1.16] and syringe exchange in the prior month (AOR = 2.9; 95% CI = 1.30, 6.48). In contrast, drug-use behaviour was not independently associated with HBV infection in MSM. The adjusted odds of prevalent infection were significantly higher for MSM of older age (AOR = 1.15 per year; 95% CI = 1.02, 1.30), nonwhite race (AOR = 2.89; 95% CI = 1.20, 6.96), San Francisco residence greater than 1 year (AOR = 2.14; 95% CI = 1.07, 4.30), and trading sex for money (AOR = 3.71; 95% CI = 1.64, 8.38). HBV infection in females was independently associated with both drug use and sexual behaviours. The AOR were higher for women with more years of injecting (AOR = 1.19 per year of injecting; 95% CI = 1.22, 7.60), ever borrowing a used syringe (AOR = 3.37; 95% CI = 1.07, 10.58), more than 50 lifetime sexual partners (AOR = 2.80; 95% CI = 1.15, 6.78), and San Francisco residence greater than 1 year (AOR = 3.05; 95% CI = 1.22, 7.60).

Table 3. Multivariate Predictors of Hepatitis B Virus Infection Among 641 Young Injection Drug Users in San Francisco,

2000-2002

	Adjusted odds ratio	95% confidence interval	*P* value
Heterosexual males			
Years injecting (per year)	1.14	1.06,1.22	<0.01
Syringe exchange, last 30 days	2.90	1.30,6.48	<0.01
Males who have sex with males			
Age (per year)	1.15	1.02,1.30	0.02
Nonwhite race/ethnicity	2.89	1.20,6.96	0.02
San Francisco residence (>1 year)	2.14	1.07,4.30	0.03
Ever traded sex for money	3.71	1.64,8.38	<0.01
Females			
San Francisco residence (>1 year)	3.05	1.22,7.60	0.02
Years injecting (per year)	1.19	1.06,1.33	<0.01
Ever borrowed a used syringe	3.37	1.07,10.58	0.04
Lifetime number of sex partners (>50)	2.80	1.15,6.78	0.02

Factors Associated with Immunization Status

Of the 654 subjects without serologic evidence of HBV infection, a significant and positive association was noted between isolated anti-HBs positive status and older age, female sex, San Francisco residence, history of mental health care, prior hepatitis testing, younger age of initiation into injecting drug use, sex with an IDU, sex with a male, and condom use (data not shown). In a multivariate model, vaccine-mediated immunity was independently associated with only younger age (AOR = 1.16 per year; 95% CI = 1.09, 1.23) and female sex (AOR = 1.55; 95% CI = 1.07, 2.25).

Discussion

In this study of more than 800 injectors under age 30 years in San Francisco, CA, we detected low vaccination coverage and a high prevalence of HBV infection. Despite the availability of an effective hepatitis B vaccine for the last two decades, a comprehensive US strategy to eliminate HBV transmission, and the evolution of syringe exchange programs, a large gap persists in the prevention and control of HBV infection among a new generation of IDU.

More than half of the participants in this study have not been effectively immunized against HBV infection. Vaccine coverage appears unacceptably low, particularly in the setting of HIV and HCV infection, where 28% and 44% of those with HIV and HCV, respectively, remain susceptible. Serologic evidence of successful prior immunization is evident among few young IDU, notably female and younger participants. However, in a sample with a median age of 22 years, a significant proportion of subjects were age-eligible to participate in universal vaccination programs for children and adolescents launched in the US in the 1990s.[16-18] The degrees of vaccine coverage detected among study subjects who were ≤12 years of age in 1996 (60%) and among subjects who were ≤18 years in 1999 (38%) are favourable compared with the proportion with vaccine-mediated immunity in the entire study population (21%). This difference suggests that the early effects of universal vaccination programs for school-aged youth may be demonstrable in high-risk populations. However, with estimates of the incidence of HBV infection among unvaccinated IDU ranging from 10 to 31 per 100 person-years,[19,20] it is unlikely that the long-term benefits of such programs will be evident among IDU for decades.[21]

We detected particularly high HBV prevalence in young MSM-IDU of whom 38% showed serologic evidence of prior or current infection, and which is significantly higher than the 10-25% prevalence reported in studies of young MSM

elsewhere.[2,22] Social context and sexual practice appear to play predominant roles in HBV transmission risk among the young MSM-IDU and female IDU in our study. Female participants with more than 50 lifetime sexual partners are nearly three times more likely to be infected than are female respondents with fewer partners. MSM subjects who trade sex for money are nearly four times more likely to be infected than MSM subjects who do not exchange sex for money. Prostitution, most often street-based, is common among young IDU in San Francisco. It is a frequently reported income-generating strategy for the purchase of drugs, food, and shelter; one third of the respondents in this study exchanged sex for money. Although the exchange of sex for money is not statistically associated with HBV infection among female subjects, sex for noncash benefits (e.g., drugs, shelter, protection, companionship) may be the more common mode of transaction for women reporting high numbers of sexual partners.

The stratification of infection status by sex and sexual orientation also is striking in its delineation of exposure risk behaviours and the possibilities these suggest for innovative immunization strategies. Female subjects demonstrate both sexual and drug use risk factors for HBV infection, compared with predominantly drug use factors among heterosexual males and sexual factors among MSM. In addition to the independent association between prevalent infection and numbers of sex partners reported by female respondents, women who borrow syringes are more than three times as likely to be infected as women who never borrow a syringe. Overlapping sexual and injection partnerships, which are significantly more common in females in this study population, may explain some of this two-pronged risk. In a prior analysis of the same study sample,[23] we found that young women who report syringe borrowing are significantly more likely to report an injecting partner who is a sexual partner. In addition, young female IDU are more likely to be injected by others,[23] to inject second when sharing syringes,[24] and to enter sexual partnerships with older men, who in turn have a higher pre-test probability of infection.[25]

Finally, we hypothesized that younger IDU in San Francisco would report fewer parenteral risk factors for HBV infection as most began injecting drugs in an era of growth and public acceptance of syringe exchange programs in the US.[14] In this study, more than 80% of respondents reported ever having used a needle exchange, but having ever used a syringe exchange was not associated in either direction with HBV infection status. Recent syringe exchange was reported more frequently by infected, heterosexual males, which may simply signify the appropriate use of syringe exchange programs by infected persons to discard their contaminated needles. Similar self-selection was observed in a prior study of HIV infection in San Francisco IDU, which found that syringe exchange programs reasonably attract HIV-infected IDU, who did not wish to infect others.[26] Our analysis suggests that syringe exchange programs in their current form do not eliminate the degree of syringe reuse that facilitates HBV transmission in young IDU in San Francisco. Indeed, needle borrowing is still common and was an independent predictor of HBV infection among female respondents. It is quite likely that structural barriers impair access to a sterile syringe for each injection. These barriers are modifiable, including limited hours of operation and ceilings on the numbers of sterile syringes that may be distributed. Most needle exchange sites in San Francisco are open for only 2 h each day and located only once weekly in most neighbourhoods. In addition, local paraphernalia laws discourage drug users from carrying sterile injecting equipment with them, and California law at the time of this study did not permit pharmacy sales of syringes without a prescription. On a national level, the US ban on federal funding for syringe exchange programs remains in effect and US global AIDS policies do not recognize the provision of access to sterile injecting equipment as an HIV prevention tool.

This report has a number of limitations. First, we recruited subjects by street-based convenience sampling. Our findings, therefore, may not be generalizable to all young, active IDU in San Francisco. Although many of our respondents have travelled widely throughout the United States, our findings also may not represent young IDU populations outside of San Francisco. Second, we collected sensitive self-reported data about sex, drug use, and illegal activities. Although street-recruited participants may engage in higher risk behaviour, they also may under-report risk in face-to-face interviews. Our risk estimates, therefore, may be conservative. Third, although more than 800 subjects were examined in this study, we conducted analyses with smaller subsets, resulting in lower precision of point estimates and the inability to detect other factors associated with HBV infection or immunity. This low precision is especially true for the analysis of infection in women (n = 171), who typically comprise only 30% of the young IDU population in San Francisco. Finally, cross-sectional studies such as this one can identify associations but are unable to determine causality or the directionality of these associations.

In conclusion, young active IDU comprise a generation that currently remains greatly susceptible to HBV infection and for which vaccination opportunities are often missed. Behavioural risk factors for infection vary significantly by sex and sexual orientation and can be utilized to guide targeted vaccination campaigns in nontraditional immunization settings for those at extreme risk. Publicly funded hepatitis prevention programs would do well to expand their efforts to identify and immunize young IDU, who, as a function of their illicit behaviour, occupy spaces outside the reach of traditional public health programs. Vaccine can be administered in convenient and familiar settings, such as syringe exchange programs, jails and prisons, and homeless drop-in centres. Our own experience immunizing young IDU achieved 47% completion rates by employing street-based reminders from outreach workers, flexible vaccine schedules, and modest cash incentives.[27] Des Jarlais *et al.* achieved 83% HBV vaccine completion with a stable clientele of older IDU in a syringe exchange program in New York.[28] Sexually transmitted disease clinics, sex clubs, sex work venues, and HIV test sites are other locales where vaccine may be administered to young MSM-IDU sex workers or female IDU with multiple sex partners. Accelerated immunization schedules, such as those offered to travellers, also may improve vaccine completion and achieve rapid immunity. Expanded access to sterile syringes, effective substance use treatment, improved condom use, and legal reform of paraphernalia laws are additional critical components in a multifaceted approach to HBV prevention and control for this high-risk group. Until the broad effects of universal vaccination programs are visible in a majority of high-risk youth, targeted prevention programs must immunize young IDU early to prevent a substantial number of new infections.

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Abbreviation Notes

AOR = adjusted odds ratio; CI = confidence interval; anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; IDU = injection drug users; IQR = interquartile range; MSM = males who have sex with males.

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