

Hepatitis B Virus Immunization Among Young Injection Drug Users in San Francisco, Calif: The UFO Study

Paula J. Lum, MD, MPH, Kristen C. Ochoa, BA, Judith A. Hahn, PhD, Kimberly Page Shafer, PhD, MPH, Jennifer L. Evans, MS, and Andrew R. Moss, PhD

Hepatitis B virus (HBV) infection is common (44%–80%) in injection drug users (IDUs),^{1–8} and younger IDUs are at high

risk.^{9–11} Although a safe and effective vaccine is available, high vaccine completion rates in IDUs (70%–86%) have been achieved primarily in drug treatment settings.^{12–15} Among street-recruited young injectors in San Francisco, Calif, only 13% had serological evidence of prior immunization, and 28% had been infected with HBV.¹⁶

We combined cash incentives and street outreach with flexible immunization schedules to improve HBV vaccine completion in young injectors in San Francisco. We examined factors associated with vaccine completion and observed postvaccination antibody responses in completers.

METHODS

Subjects were recruited in a San Francisco study of HIV and viral hepatitis (the UFO Study) described elsewhere.¹⁷ Four hundred four IDUs younger than 30 years were interviewed and underwent counseling and serological testing for HIV, HBV, and hepatitis C virus (HCV). Persons without evidence of acute infection, a chronic carrier state, or immunity conferred by antibody to hepatitis B surface antigen (anti-HBs) were recruited. Those declining participation in the study were offered free immunizations.

A 20- μ g intramuscular dose of recombinant DNA hepatitis B vaccine was administered at enrollment. Participants were instructed to return in 1 to 2 months for the second dose and then at 4 to 6 months for the third dose; they received \$10 cash each time. Street-based outreach workers began delivering follow-up reminders 3 weeks after the first vaccine dose and again 11 weeks after the second dose.

We measured postvaccination anti-HBs seroconversion at 4 weeks after the third dose. We measured vaccine series completion and conducted bivariate analyses of variables associated with vaccine completion. We conducted a multiple logistic regression analysis of significant variables ($P < .10$) and other variables of interest or potential confounders.

RESULTS

Of the 404 persons screened, 265 (66%) were eligible for immunization. Of the

TABLE 1—Bivariate Associations of Selected Demographic Factors and Baseline Serology With Hepatitis B Vaccine Completion Among Young Injectors in San Francisco, Calif (N = 170)

	No. of Completers/n (%)	OR (95% CI)	P
All participants	80/170 (47.1)		
Age, y (median = 21; interquartile range = 19–24)			
15–19	26/54 (48.1)	1.00	.40
20–24	31/74 (41.9)	0.78 (0.36, 1.67)	
25–29	23/42 (54.8)	1.30 (0.54, 3.17)	
Sex			
Male	57/120 (47.5)	1.00	.86
Female	23/50 (46.0)	0.94 (0.46, 1.92)	
Race (n = 169)			
White	64/142 (45.1)	1.00	.32
Non-White	15/27 (55.6)	1.52 (0.62, 3.77)	
Education (n = 169)			
< High school	40/85 (47.1)	1.00	.94
High school graduate	26/53 (49.1)	1.08 (0.51, 2.28)	
Some college	14/31 (45.2)	0.93 (0.37, 2.29)	
Months lived in San Francisco			
< 3	31/86 (36.0)	1.00	< .01
≥ 3	49/84 (58.3)	2.48 (1.28, 4.84)	
Prior HIV test			
No	7/30 (23.3)	1.00	< .01
Yes	73/140 (52.1)	3.58 (1.35, 9.87)	
HIV antibody (n = 169)			
Negative	79/168 (47.0)29
Positive	1/1 (100.0)		
Hepatitis B antibody			
Negative	75/163 (46.0)	1.00	.19
Positive	5/7 (71.4)	2.93 (0.46, 31.45)	
Hepatitis C antibody (n = 169)			
Negative	46/112 (41.1)	1.00	.04
Positive	33/57 (57.9)	1.97 (1.03, 3.77)	

Note. OR = odds ratio; CI = confidence interval.

vaccine-eligible persons, 211 (80%) returned for their test results, and 170 of the 211 (81%) participants consented to enrollment. Participants did not differ from nonparticipants by demographics, serology, or injecting and sexual behavior (data not shown). Median age was 21 years, 84% were White, and 71% were male (Table 1). Most were new to San Francisco and unstably housed. During the prior year, 57% had been incarcerated. HIV-positive test results were found in 0.6%; 34% were anti-HCV positive. Most were frequent heroin injectors, and 76% attended syringe exchange programs in the last

30 days (Table 2). Thirty percent were gay or bisexual, and 8% had traded sex for money or drugs in the last 30 days.

Vaccine Completion

Of the 170 participants, 128 (75%) received the second vaccine dose, and 80 (47%) completed the series. The median time to the second dose was 5 weeks (interquartile range [IQR]=4–8 weeks) and the median time to the third dose was 21 weeks (IQR=17–26 weeks).

Vaccine completers were more likely to have lived in San Francisco for 3 or more

months, to have received prior HIV testing, and to have anti-HCV-positive test results (Table 1). Completers were more likely to inject drugs daily, to attend syringe exchange programs, and to have had sex with another IDU (Table 2). They were less likely to receive new needles from friends (“kickdowns”) or to purchase needles from a pharmacy. Completers also were more likely to report that they could rely on outreach workers for social support and marginally more likely to report that they could rely on syringe exchange program staff (Table 3).

On multivariate analysis, vaccine completion was associated with living in San Francisco for 3 months or longer (adjusted odds ratio [OR]=2.41; 95% confidence interval [CI]=1.20, 4.82), with prior HIV testing (adjusted OR=2.79; 95% CI=1.05, 7.41), and with outreach worker social support (adjusted OR=2.49; 95% CI=1.23, 5.05). Vaccine completion was less likely in persons receiving “kickdowns” (adjusted OR=0.43; 95% CI=0.21, 0.87).

Vaccine Response

Protective vaccine responses (anti-HBs ≥ 10 mIU/mL) were observed in 38 of 49 (78%) completers, including 12 of 17 (71%) completers who were anti-HCV positive and 26 of 32 (81%) who were anti-HCV negative (OR=0.55; 95% CI=0.12, 2.82).

DISCUSSION

With street-based outreach and \$10 incentives, 75% of the young injectors received their second vaccine dose, and 47% completed a flexible HBV immunization schedule. These figures compare favorably with completion rates among street-recruited IDUs elsewhere: 27% in Washington¹⁸ and 31% in Alaska.¹⁹ Completion rates in non-IDUs are comparably low: 11% at a teenage clinic,²⁰ 17% to 38% at sexually transmitted disease clinics,^{21–26} and 30% at correctional facilities.²⁵

Geographic stability, HIV testing, reliance on outreach workers, and syringe sources were independently associated with vaccine completion. Young IDUs residing longer in San Francisco may have more stable

TABLE 2—Bivariate Associations of Injecting and Sexual Behavior With Hepatitis B Vaccine Completion Among Young Injectors in San Francisco, Calif (N = 170)

	No. of Completers/n (%)	OR (95% CI)	P
Injecting behavior			
Years injecting (median = 4; interquartile range = 1-7)			
0-1	18/49 (36.7)	1.00	.07
2-3	15/29 (51.7)	1.85 (0.66, 5.21)	
4-5	13/32 (40.6)	1.18 (0.43, 3.24)	
6-7	16/26 (61.5)	2.76 (0.93, 8.29)	
8-9	6/16 (37.5)	1.03 (0.28, 3.82)	
≥ 10	12/18 (66.7)	3.44 (0.97, 12.63)	
Frequency of injection			
< Daily	48/116 (41.4)	1.00	.03
Daily	32/54 (59.3)	2.06 (1.02, 4.19)	
Ever borrowed a used syringe			
No	25/57 (43.9)	1.00	.55
Yes	55/113 (48.7)	1.21 (0.61, 2.42)	
Exchanged syringes, last 30 days			
No	21/63 (33.3)	1.00	<.01
Yes	59/107 (55.1)	2.46 (1.23, 4.96)	
Exchanged at established SEP, last 30 days			
No	40/102 (39.2)	1.00	
Yes	40/68 (58.8)	2.21 (1.13, 4.35)	.01
Exchanged at underground SEP, last 30 days			
No	41/100 (41.0)	1.00	
Yes	39/70 (55.7)	1.81 (0.93, 3.52)	.06
Exchanged with outreach worker or friend, last 30 days			
No	50/101 (49.5)	1.00	.44
Yes	30/69 (43.5)	0.78 (0.40, 1.52)	
Received new syringes from friends, last 30 days (n = 169)			
No	58/107 (54.2)	1.00	
Yes	22/62 (35.5)	0.46 (0.23, 0.93)	.02
Purchased new syringes on street, last 30 days			
No	53/117 (45.3)	1.00	.50
Yes	27/53 (50.9)	1.25 (0.62, 2.53)	
Sexual behavior			
Sexual orientation (n = 168)			
Heterosexual	51/117 (43.6)	1.00	.26
Gay or bisexual	27/51 (52.9)	1.46 (0.71, 2.97)	
Years sexually active (n = 161)			
≤ 5	24/59 (40.7)	1.00	.17
> 5	53/102 (52.0)	1.58 (0.78, 3.18)	
Ever diagnosed with a sexually transmitted disease (n = 165)			
No	58/126 (46.0)	1.00	.77
Yes	19/39 (48.7)	1.11 (0.51, 2.43)	
Traded sex for money or drugs, last 6 mo			
No	70/156 (44.9)	1.00	.06
Yes	10/14 (71.4)	3.07 (0.84, 13.91)	

Continued

lifestyles, making a 6-month intervention more feasible. Had this intervention been limited to those living in San Francisco for 3 months or more, completion would have been 58%. Young IDUs who can rely on outreach workers may have greater engagement with social service agencies. Their vaccine adherence underscores the important work of these organizations. Immunizations also may be more acceptable to injectors, who identify with a drug culture and engage in other prevention activities, such as HIV testing and syringe exchange programs. Indeed, 30 of 36 (83%) syringe exchange program–recruited participants in New York completed the vaccine series.¹⁹ Less established injectors may not recognize their high risk of infection and may think that immunizations are unwarranted.

Only 78% of the vaccine completers underwent anti-HBs seroconversion, compared with 99% reported by vaccine manufacturers.²⁷ These figures raise concerns about blunting of young injectors' immune responses. Suboptimal responses (58%–76%) have been noted among IDUs elsewhere.^{28,29} Although higher immunogenicity is associated with younger age, young IDUs are more likely than other young people to have poorer health and altered immunity. We observed a lower vaccine response among participants who were anti-HCV positive, but numbers were too small for significance. Other studies, however, have suggested that HCV infection may diminish the HBV vaccine response.^{30–32}

Strategies to improve HBV vaccine completion and response in young IDUs are urgently needed, given the high incidence of co-infection with HBV and HCV^{10,17,33–35} and of accelerated liver damage in co-infected subjects.^{36–40} Higher vaccine doses (40 µg) and accelerated schedules have been used successfully among hemodialysis patients⁴¹ and alcoholic patients⁴² and may be effective for young IDUs. Young injectors are a challenging population in which to implement interventions aimed at preventing blood-borne infections. We suggest that a combination of street outreach and financial incentives may be important components of immunization programs for young injectors in other cities. ■

TABLE 2—Continued

	No. of Completers/n (%)	OR (95% CI)	P
Sex with another injector, last 6 mo			
No	15/44 (34.1)	1.00	.05
Yes	65/126 (51.6)	2.06 (1.01, 4.21)	
No. of sexual partners, last 6 mo			
0	11/21 (52.4)	1.00	.81
1	33/71 (46.5)	0.79 (0.27, 2.32)	
>1	36/78 (46.2)	0.78 (0.27, 2.26)	
<100% condom use for vaginal or anal sex, last 6 mo			
No	14/31 (45.2)	1.00	.85
Yes	56/119 (47.1)	1.08 (0.46, 2.57)	

Note. OR = odds ratio; CI = confidence interval; SEP = syringe exchange program.

TABLE 3—Bivariate Associations of Social Supports With Hepatitis B Vaccine Completion Among Young Injectors in San Francisco, Calif (n = 160)

	No. of Completers/n (%)	OR (95% CI)	P
Can rely on family			
No	37/65 (56.9)	1.00	.04
Yes	38/95 (40.0)	0.51 (0.26, 1.02)	
Can rely on main sexual partner or spouse (n = 159)			
No	33/70 (47.1)	1.00	1.00
Yes	42/89 (47.2)	1.00 (0.51, 1.97)	
Can rely on friends (n = 159)			
No	10/24 (41.7)	1.00	.56
Yes	65/135 (48.1)	1.30 (0.50, 3.42)	
Can rely on outreach worker (n = 159)			
No	22/63 (34.9)	1.00	.01
Yes	53/96 (55.2)	2.30 (1.13, 4.67)	
Can rely on SEP staff (n = 159)			
No	27/69 (39.1)	1.00	.07
Yes	48/90 (53.3)	1.78 (0.90, 3.54)	

Note. OR = odds ratio; CI = confidence interval; SEP = syringe exchange program; no response = not much, none, or not applicable; yes response = some, very much, totally.

About the Authors

Paula J. Lum is with the Positive Health Program, Department of Medicine, University of California, San Francisco, and the San Francisco General Hospital. Kristen C. Ochoa, Judith A. Hahn, Jennifer L. Evans, and Andrew R. Moss are with the Department of Epidemiology and Biostatistics, University of California, San Francisco. Kimberly Page Shafer is with the Center for AIDS Prevention Studies, Department of Medicine, University of California, San Francisco.

Requests for reprints should be sent to Paula J. Lum, MD, MPH, Box 0874, University of California, San Francisco, San Francisco, CA 94143-0874 (e-mail: plum@php.ucsf.edu).

This brief was accepted February 9, 2002.

Contributors

P.J. Lum designed and conducted the study, analyzed and interpreted the data, and wrote the brief. K.C. Ochoa participated in the design and execution of the study and the interpretation of the data. J.A. Hahn and J.L. Evans participated in the statistical analysis and interpretation of the data. K. Page Shafer and A.R. Moss participated in the design of the study, the interpretation of the data, and the revision of the brief.

Acknowledgments

This research was conducted with the support of grants from the Universitywide AIDS Research Program

(PC97-SF-2016S), the National Institute of Mental Health (T32 MH-19105-10), and the National Institute on Drug Abuse (1R01 DA12803-01).

We gratefully acknowledge the dedication of the UFO Study field staff and the street outreach efforts of Rachel McLean, Ivy McClelland, and Ben Sizemore from the Haight Ashbury Youth Outreach Team. We are also indebted to Drs Susan Fernyak and Mitch Katz of the San Francisco Department of Public Health for their generous contribution of hepatitis A and B virus vaccines. This brief is dedicated to the memory of Jennifer Hopkins.

Human Participant Protection

The study was approved by the Committee on Human Research at the University of California, San Francisco.

References

- Seeff LB, Zimmerman HJ, Wright EC, et al. Hepatic disease in asymptomatic parenteral narcotic drug abusers: a Veterans Administration collaborative study. *Am J Med Sci.* 1975;270:41–47.
- Cherubin CE, Schaefer RA, Rosenthal WS, et al. The natural history of liver disease in former drug users. *Am J Med Sci.* 1976;272:244–253.
- Mangla JC, Kim YM, Brown MR, Schwob D, Hanson SE. Liver tests, HB-Ag and HB-Ab in asymptomatic drug addicts. *Am J Gastroenterol.* 1976;65:121–126.
- Blanck RR, Ream N, Conrad M. Hepatitis B antigen and antibody in heroin users. *Am J Gastroenterol.* 1979;71:164–167.
- Kunches LM, Craven DE, Werner BG. Seroprevalence of hepatitis B virus and delta agent in parenteral drug abusers: immunogenicity of hepatitis B vaccine. *Am J Med.* 1986;81:591–595.
- DeCock KM, Jones B, Govindarajan S, Redeker AG. Prevalence of hepatitis delta (delta) virus infection: a seroepidemiologic study. *West J Med.* 1988;148:307–309.
- Zeldis JB, Jain S, Kuramoto IK, et al. Seroepidemiology of viral infections among intravenous drug users in northern California. *West J Med.* 1992;156:30–35.
- Levine OS, Vlahov D, Koehler J, Cohn S, Spronk AM, Nelson KE. Seroepidemiology of hepatitis B virus in a population of injecting drug users: association with drug injection patterns. *Am J Epidemiol.* 1995;142:331–341.
- Garfein RS, Vlahov D, Galai N, Doherty MC, Nelson KE. Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. *Am J Public Health.* 1996;86:655–661.
- Van Ameijden EJ, Van den Hoek JA, Mientjes GH, Coutinho RA. A longitudinal study on the incidence and transmission patterns of HIV, HBV and HCV infection among drug users in Amsterdam. *Eur J Epidemiol.* 1993;9:255–262.
- Doherty MC, Garfein RS, Monterroso E, Brown D, Vlahov D. Correlates of HIV infection among young adult short-term injection drug users. *AIDS.* 2000;14:717–726.

12. Borg L, Khuri E, Wells A, et al. Methadone-maintained former heroin addicts, including those who are anti-HIV-1 seropositive, comply with and respond to hepatitis B vaccination. *Addiction*. 1999;94:489–493.
13. Rodrigo JM, Serra MA, Aparisi L, et al. Immune response to hepatitis B vaccine in parenteral drug abusers. *Vaccine*. 1992;10:798–801.
14. Mezzelani P, Venturini L, Turrina G, Lugoboni F, Des Jarlais DC. High compliance with a hepatitis B virus vaccination program among intravenous drug users [letter]. *J Infect Dis*. 1991;163:923.
15. Lugoboni F, Migliozi S, Schiesari F, et al. Immunoresponse to hepatitis B vaccination and adherence campaign among injecting drug users. *Vaccine*. 1997;15:1014–1016.
16. Lum PJ, Ochoa K, Hahn J, Page-Shafer K, McLean R, Moss AR. Low rates of hepatitis B vaccination among young injectors in San Francisco. Paper presented at: 127th Annual Meeting of the American Public Health Association; November 7–11, 1999; Chicago, Ill.
17. Hahn JA, Page-Shafer K, Lum PJ, Ochoa K, Moss AR. Hepatitis C virus infection and needle exchange use among young injection drug users in San Francisco. *Hepatology*. 2001;34:180–187.
18. Hepatitis B vaccination for injection drug users—Pierce County, Washington, 2000. *MMWR Morb Mortal Wkly Rep*. 2001;50:388–390, 399.
19. Des Jarlais DC, Fisher DG, Newman JC, et al. Providing hepatitis B vaccination to injection drug users: referral to health clinics vs on-site vaccination at a syringe exchange program. *Am J Public Health*. 2001;91:1791–1792.
20. Wong VK, Woodruff C, Shapiro R. Compliance of hepatitis B vaccination in patients presenting to a teenage clinic. *Pediatr Infect Dis J*. 1994;13:936.
21. Asbel L, Hodges V, Abakporo E, Goldberg M. Hepatitis vaccination in a busy inner city STD clinic. Paper presented at: National STD Prevention Conference; 1998; Atlanta, Ga. Abstract P68.
22. Dal-Ré R, González A, Ramirez V, Ballesteros J, del Romero J, Bru F. Compliance with immunization against hepatitis B: a pragmatic study in sexually transmitted disease clinics. *Vaccine*. 1995;13:163–167.
23. Farmer G, Adelakun A, Olthoff G, van Blerk G. Hepatitis B vaccine at Prince George's County STD Clinic. In: National STD Prevention Conference—Untapped Opportunities: Connecting Science With Solutions; December 4–7, 2000; Atlanta, Ga. Abstract P98.
24. Sellors J, Zimic-Vincetic M, Howard M, Chernesky MA. Lack of compliance with hepatitis B vaccination among Canadian STD clinic patients: candidates for an accelerated immunization schedule? *Can J Public Health*. 1997;88:210–211.
25. Lane P, Jenkins H, Rose M, et al. An evaluation of hepatitis B vaccinations for high risk adolescents in Connecticut. In: National STD Prevention Conference—Untapped Opportunities: Connecting Science With Solutions; December 4–7, 2000; Atlanta, Ga. Abstract P97.
26. Finley C, Zimmerman R, Rabins C, McMahon K, Renier E, Bornstein S. STD clinic client risk and vaccination acceptance and compliance rates for hepatitis B in two Illinois STD clinics. In: National STD Prevention Conference—Untapped Opportunities: Connecting Science With Solutions; December 4–7, 2000; Atlanta, Ga. Abstract P103.
27. West DJ. Clinical experience with hepatitis B vaccines. *Am J Infect Control*. 1989;17:172–180.
28. Minniti F, Baldo V, Trivello R, et al. Response to HBV vaccine in relation to anti-HCV and anti-HBc positivity: a study in intravenous drug addicts. *Vaccine*. 1999;17:3083–3085.
29. Rumi M, Colombo M, Romeo R, et al. Suboptimal response to hepatitis B vaccine in drug users. *Arch Intern Med*. 1991;151:574–578.
30. Navarro JF, Teruel JL, Mateos M, Ortuno J. Hepatitis C virus infection decreases the effective antibody response to hepatitis B vaccine in hemodialysis patients [see comments]. *Clin Nephrol*. 1994;41:113–116.
31. Navarro JF, Teruel JL, Mateos ML, Marcen R, Ortuno J. Antibody level after hepatitis B vaccination in hemodialysis patients: influence of hepatitis C virus infection. *Am J Nephrol*. 1996;16:95–97.
32. Wiedmann M, Liebert UG, Oesen U, et al. Decreased immunogenicity of recombinant hepatitis B vaccine in chronic hepatitis C. *Hepatology*. 2000;31:230–234.
33. Hagan H, McGough JP, Thiede H, Weiss NS, Hopkins S, Alexander ER. Syringe exchange and risk of infection with hepatitis B and C viruses. *Am J Epidemiol*. 1999;149:203–213.
34. Garfein RS, Doherty MC, Monterroso ER, Thomas DL, Nelson KE, Vlahov D. Prevalence and incidence of hepatitis C virus infection among young adult injection drug users. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1998;18(suppl 1):S11–S19.
35. Crofts N, Aitken CK. Incidence of bloodborne virus infection and risk behaviours in a cohort of injecting drug users in Victoria, 1990–1995. *Med J Aust*. 1997;167:17–20.
36. McCrudden EA, Hillan KJ, McKay IC, Cassidy MT, Clark JC. Hepatitis virus infection and liver disease in injecting drug users who died suddenly. *J Clin Pathol*. 1996;49:552–555.
37. Ilan Y, Ashur Y, Tur-Kaspa R, Shouval D. Chronic hepatitis C virus infection with exposure to hepatitis B virus. *Isr J Med Sci*. 1994;30:259–263.
38. Tsai JF, Jeng JE, Ho MS, et al. Effect of hepatitis C and B virus infection on risk of hepatocellular carcinoma: a prospective study. *Br J Cancer*. 1997;76:968–974.
39. Cacciola I, Pollicino T, Squadrito G, Cerenzia G, Orlando ME, Raimondo G. Occult hepatitis B virus infection in patients with chronic hepatitis C liver disease. *N Engl J Med*. 1999;341:22–26.
40. Zarski JP, Bohn B, Bastie A, et al. Characteristics of patients with dual infection by hepatitis B and C viruses. *J Hepatol*. 1998;28:27–33.
41. Stevens CE, Szmunes W, Goodman AI, Weseley SA, Fotino M. Hepatitis B vaccine: immune responses in haemodialysis patients. *Lancet*. 1980;2(8206):1211–1213.
42. Rosman AS, Basu P, Galvin K, Lieber CS. Efficacy of a high and accelerated dose of hepatitis B vaccine in alcoholic patients: a randomized clinical trial. *Am J Med*. 1997;103:217–222.