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Risk Factors for Hepatitis B in an Outbreak of Hepatitis B and D Among Injection Drug Users

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ABSTRACT *During January–April, 2000, 12 cases of acute hepatitis B were reported in Pierce County, Washington, compared with seven in all of 1999. Seven (58.3%) case patients were injection drug users (IDUs), three of whom were coinfected with hepatitis D virus (HDV) and died of fulminant hepatitis. Vaccination clinics were implemented at the local health department and needle exchange program to control the outbreak. We investigated this outbreak to determine risk factors for hepatitis B virus (HBV) transmission among IDUs. Hepatitis B cases were ascertained through routine surveillance and prevaccination testing at vaccination clinics. We conducted a case-control study comparing IDU case patients with HBV-susceptible IDUs identified at the vaccination clinics. Fifty-eight case patients were identified during January–December, 2000, 20 (34.5%) of whom were coinfected with HDV. Thirty-eight case patients (65.5%) reported current IDU. In the case-control study, the 17 case patients were more likely than the 141 controls to report having more than one sex partner [odds ratio (OR) = 4.8, 95% confidence interval (CI) = 1.5–15.0], injecting more than four times a day (OR = 4.5, 95% CI = 1.2–15.6) and sharing drug cookers with more than two people (58.8% vs. 14.0%, OR = 14.0, 95% CI = 2.4–81.5). Results were similar after controlling for syringe sharing in multivariable analysis. IDUs should be vaccinated against hepatitis B and should be advised against sharing drug injection equipment.*

KEYWORDS *Hepatitis B, Hepatitis D, Intravenous drug abuse.*

INTRODUCTION

Injection drug use is a common mode of hepatitis B virus (HBV) transmission, accounting for 15–20% of reported cases of acute hepatitis B.[1] Up to 80% of injection drug users (IDUs) who have injected for five or more years have serologic evidence of exposure to HBV.[2–5] Although coinfection with HBV and hepatitis D virus (HDV) is rare in the general population of the United States, up to 20% of IDUs who are chronically infected with HBV also have evidence of HDV infection.[6]

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Although syringe sharing, a recognized risk factor for HBV infection among IDUs, declined during the 1990s, indirect sharing remains a common practice.[7–14] Indirect sharing refers to the injection practices other than reusing a syringe by which an IDU could come into contact with the blood of another IDU. These include the sharing of injection equipment such as drug cookers, filtration cottons, and syringe rinse water as well as the practice of using a syringe to distribute drugs to the syringes of other users, sometimes referred to as front- or back-loading. There is increasing evidence that indirect sharing practices can result in the transmission of viral pathogens.[13,15,16]

Between January and April, 2000, 12 cases of acute hepatitis B were reported in Pierce County, Washington, compared with seven cases in all of 1999. Seven of these 12 index case patients had injected drugs in the 6 months before the onset of illness, compared with one case in the previous year. In April 2000, three case patients died of fulminant hepatitis because of acute hepatitis B and D coinfection. To control the outbreak, HBV serologic testing and vaccination clinics for IDUs and other adults at risk for HBV infection were established at the local health department and syringe exchange program in May 2000.[17] In collaboration with the Washington Department of Health, we undertook an investigation to characterize the outbreak, determine risk factors for HBV transmission among IDUs, and develop recommendations to prevent further spread.

METHODS

Descriptive Epidemiology

A case of acute HBV infection was defined as detectable immunoglobulin M (IgM) antibody to hepatitis B core antigen (anti-HBc) in a serologic specimen obtained during 2000 from a resident of Pierce County, Washington. Cases were ascertained from reports collected as part of routine surveillance by the Tacoma Pierce County Health Department and review of prevaccination serologic testing results performed at hepatitis B vaccination clinics for IDUs.[17] Sera from cases of acute HBV infection were tested for hepatitis C virus (HCV) and HDV infection. A case of acute coinfection of HBV and HDV was defined as a person with acute HBV infection during 2000 whose serum tested positive for antibody to HDV (anti-HDV) or HDV RNA.

Laboratory Methods

Serologic testing was performed at the Hepatitis Reference Laboratory, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia. Serum samples were tested for hepatitis B surface antigen (HBsAg) (Auszyme Monoclonal), anti-HBc (Corzyme), IgM anti-HBc (Corzyme-M-EIA), and anti-HDV (HDV-EIA). All serological assays were manufactured by Abbott Laboratories (Abbott Park, Illinois) and performed per package insert. Serum samples were tested for anti-HCV by enzyme immunoassay (HCV 3.0. Ortho Dianostic Systems, Raritan, New Jersey), and repeatedly reactive results were confirmed using a third version recombinant immunoblot assay (RIBA™ Chiron, Emeryville, California).

HDV RNA was extracted from available serum samples that tested positive for IgM anti-HBc using methods described previously.[18] Samples that did not provide sufficient product after first amplification were reamplified using nested primers. Polymerase chain reaction (PCR) products were identified by electrophoretic separation in 2% agarose gels, followed by ethidium bromide staining for visualization.

Molecular techniques were used to evaluate the relatedness of HBV sequences from cases of acute HBV infection for which sera were available. HBV DNA was extracted using the MasterPure Complete DNA and RNA Purification Kit (Epicentre Technologies, Madison, Wisconsin) procedure for plasma per package insert. A 440 base-pair segment of the S region (encodes surface antigen) of the HBV genome was amplified by nested PCR using previously described methods.[19,20] HBV PCR products were purified (QIAquick spin columns, Qiagen, Valencia, California), and automated sequencing was performed (ABI Model 373 or 377, Applied Biosystems, Foster City, California), as previously described.[20] Sequencing reactions were done with a prism dye or dRhodamine terminator cycle sequencing kit according to manufacturer's protocol. Sequence data were further analyzed by Sequence Navigator (Applied Biosystems) and GCG Wisconsin Package software (Accelrys, San Diego, California).[21] The HBV phylogenetic tree was constructed using the neighbor-joining method.

Case-Control Study

A case-control study was conducted in May 2000 to determine risk factors for HBV infection among IDUs. For the case-control study, a case was defined as a positive IgM anti-HBc test performed during January–May 2000 in a Pierce County resident reporting injection drug use during the previous 6 months. Control subjects were all persons identified through prevaccination serologic testing at the hepatitis B vaccination clinics during May 2000 with a negative test for anti-HBc who reported injecting drugs in the previous 6 months.[17] Health department and CDC staff administered a standard questionnaire to collect information on demographic characteristics and sexual and injection practices from all persons attending the hepatitis B vaccination clinics and previously reported cases. Data from deceased case patients were collected by interview of family members or social contacts using the standard questionnaire and from medical record review.

This public health investigation was undertaken to control a communicable disease outbreak. It was reviewed by CDC Human Subjects Research staff and deemed to be primarily not research, and as such, did not require review by the CDC Institutional Review Board. Participants in the case-control study received a description of the outbreak investigation and gave oral consent before answering the questionnaire or undergoing serologic testing. Because the investigation was conducted over several months at a needle exchange program site that did not record identifying information from participants, we were unable to systematically track the participant refusal rate.

Statistical Analysis

All analysis was performed using STATA Statistical Software: Release 7.0 (College Station, Texas). Multivariable models were constructed using logistic regression. All variables significant to a P value of .15 or less in univariate analysis and the variable for syringe sharing were included in the multivariable model. Likelihood ratio testing was used to assess the effect of the removal of each variable from the model. Goodness of fit was assessed using Pearson's goodness of fit test and the Hosmer–Lemeshow χ^2.

RESULTS

Descriptive Epidemiology

Fifty-eight cases of acute hepatitis B were identified in 2000, 25 (43.1%) from routine surveillance and 33 (56.9%) from among the 1,755 people who underwent

prevaccination serologic testing at the vaccination clinics during May–December 2000 (Fig. 1). Case patients ranged in age from 18 to 57 years (median 36 years), and 39 (67.2%) were male. Thirty-eight (65.5%) of the case patients injected drugs in the 6 weeks to 6 months before the onset of symptoms or HBV testing, five had three or more sex partners in the previous 6 months, three had a sex partner who was an IDU, one was a man who had sex with men, and 11 reported no risk factors for HBV infection.

Twenty case patients (34.5%), all IDUs, also had evidence of coinfection with HDV. Eight case patients required hospitalization, six of whom were coinfected with HDV. Three HBV/HDV-coinfected case patients who were current IDU died in April 2000, for a case fatality rate of 15% among persons with acute HBV/HDV coinfection. Twenty-six of the cases had evidence of HCV infection, of whom 22 were IDUs. This includes the three IDU cases who died in April 2000. An additional 10 cases, all IDUs, were anti-HCV screening test positive but lacked adequate serum for confirmatory testing.

HBV DNA Sequence Analysis

Serum samples from 56 of the 58 acute hepatitis B cases identified during 2000 were available for HBV amplification and sequencing, of which 28 (50%) had detectable HBV DNA. Sequences from 22 of the cases were identical, one was 99.4% homologous and five differed by >9.7% (Fig. 2). Eighteen (78%) of the 23 cases with HBV DNA sequences that were ≥99.4% homologous were current IDUs, including the three deceased case patients, one (4%) was the sex contact of an IDU, and four (17%) did not report risk factors for HBV infection. All of the surviving IDU case patients with highly homologous sequences on whom the information was available reported knowing at least one of the deceased cases. Only one of the five cases with HBV strains that were <99% homologous reported injection drug use.

Case-Control Study

All 17 case patients who reported injection drug use and were identified during January–May 2000 were included in the case-control study, 11 ascertained from

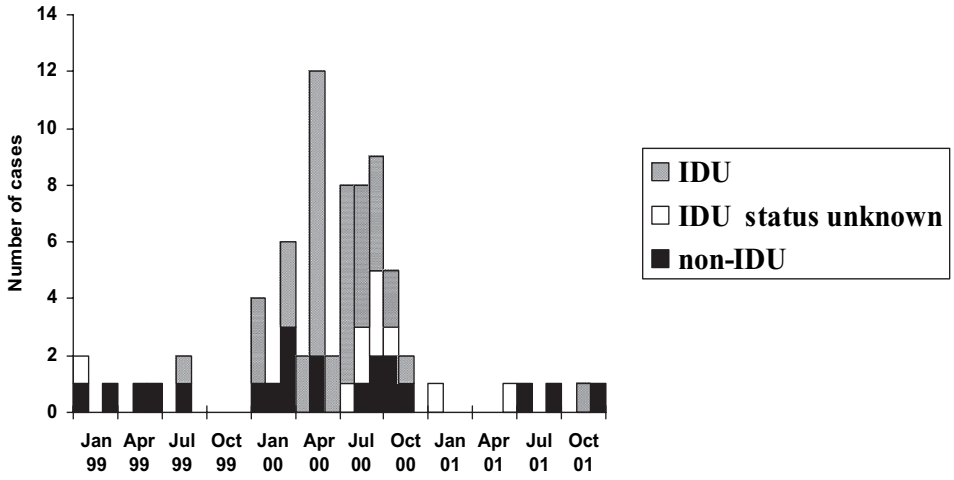

FIGURE 1. Cases of acute hepatitis B virus (HBV) infection by date of reporting or screening (n=74) and by injection drug use (IDU), Pierce County, Washington, January 1999–December 2001. Prevaccination screening, performed during May–December, 2000, resulted in identification of 34 cases.

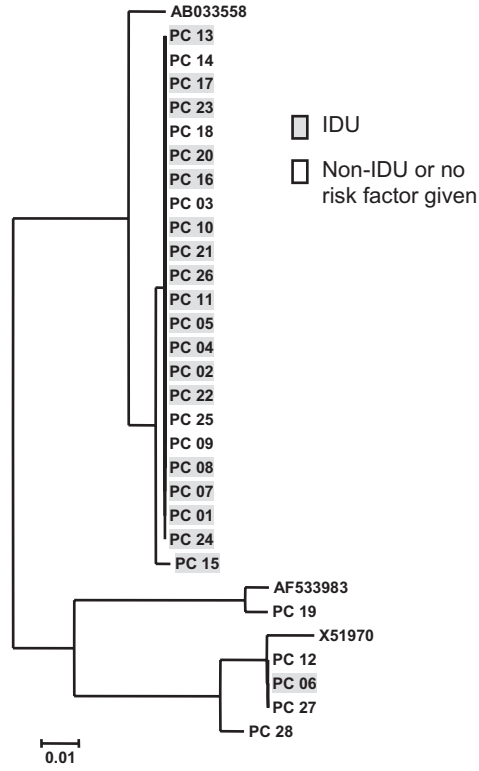

FIGURE 2. Phylogenetic distribution for 229 base-pair segments of the S region derived from serum collected from patients with acute hepatitis B virus (HBV) infection in Pierce County, Washington, during 2000. The horizontal line at bottom left represents 1% nucleotide substitution for that horizontal branch length. HBV genotype reference strains were obtained from GenBank (accession nos. X51970 for genotype A, AF533983 for genotype C, and AB033558 for genotype D). IDU, injection drug user.

case reports to the local health department during January–May, 2000, and six identified from prevaccination testing during May 2000. One hundred and seventy-eight (46.4%) of the 384 IDUs identified as potential controls from prevaccination screening in May 2000 were found to be susceptible to HBV. One hundred and forty-one (79.2%) reported injection drug use within the previous 6 months and were included in the analysis.

Cases and controls did not differ in age, race, education, homelessness, history of incarceration or sexually transmitted disease, proportion of women engaged in commercial sex work, or men who reported having sex with a man. Case patients were significantly more likely to report knowing one of the deceased cases [odds ratio (OR)=5.3, 95% confidence interval (CI)=1.8–15.7] and having more than one sex partner in the previous 6 months (OR=4.8, 95% CI=1.5–15.0) (Table 1). Heroin was the drug most frequently injected by the majority of both case patients and control subjects. There were no statistically significant differences between cases and controls in years of injection drug use, daily drug injection, or syringe sharing. Case patients were significantly more likely than control subjects to inject more than four times a day (OR=4.5, 95% CI=1.2–15.6) and to share drug cookers (OR=14.0, 95% CI: 2.4, 81.5) or filtration cottons (OR=6.4, 95% CI=1.6–26.3)

TABLE 1. Selected characteristics of case patients with acute hepatitis B virus (HBV) infection and controls, Pierce County, Washington, January–May 2000

Characteristics	Cases (N = 17)			Controls (N = 141)			Unadjusted odds ratio	95% Confidence interval
	N	Total response	%	N	Total responses	%		
Male sex	9	17	52.9	90	141	63.8	0.6	0.2–1.8
Age >35 years	8	17	47.1	75	141	53.2	0.8	0.3–2.1
Caucasian	14	17	82.4	101	141	71.6	0.9	0.5–6.8
Less than 12 years of education	8	16	50.0	49	140	35.0	1.9	0.7–5.3
Incarcerated during previous 6 months	8	17	47.1	66	138	47.8	1.0	0.3–2.7
Homeless	12	17	70.6	78	141	55.3	1.9	0.6–5.8
Knowing one of the deceased cases	10	14	71.4	30	141	21.3	5.3	1.8–15.7
Men who have sex with men	1	9	11.1	9	88	10.2	1.1	0.02–10.0
Commercial sex work* (females only)	4	5	80.0	16	51	31.4	3.7	0.6–25.8
Sex partners of the opposite sex*								
0–1 partner	5	17	29.4	94	141	66.7	Reference	
>1 partner	12		70.6	47		33.3	4.8	1.5–15.0
Years of injection								
<1 year	2	17	11.8	29	140	20.7	Reference	
1–4 years	6		35.3	50		35.7	1.7	0.3–18.6
5 or more years	9		52.9	61		43.6	2.1	0.4–21.5
Heroin as most frequently injected drug	13	17	76.5	104	139	74.8	1.6	0.3–5.2
Inject everyday	12	17	70.6	83	140	59.3	1.7	0.5–5.0
Obtains majority of syringes at syringe exchange program	12	17	70.6	119	139	85.6	0.4	0.1–1.3
Number of injections per day								
1–4	11	17	64.7	124	139	89.2	Reference	
>4	6		35.3	15		10.8	4.5	1.2–15.6
Number of people with whom share syringes in an average week*								
0	8	16	50.0	97	140	69.3	Reference	
≥1	8		50.0	43		30.7	2.7	0.8–8.9

TABLE 1. ***Continued***

Characteristics	Cases (N = 17)			Controls (N = 141)			Unadjusted odds ratio	95% Confidence interval
	N	Total response	%	N	Total responses	%		
Number of people with whom share drug cookers in an average week*								
0	2	17	11.8	59	140	42.1	Reference	
1–2	5		29.4	60		42.9	2.5	0.5–13.4
>2	10		58.8	21		15.0	14.0	2.4–81.5
Number of people with whom share filtration cotton in an average week*								
0	4	17	23.5	66	140	47.1	Reference	
1–2	6		35.3	56		40.0	1.8	0.5–6.6
>2	7		41.2	18		12.9	6.4	1.6–26.3
Number of people with whom share syringe rinse water in average week*								
0	9	17	52.9	81	139	58.3	Reference	
1–2	4		23.5	45		32.4	0.8	0.2–2.8
>2	4		23.5	13		10.7	2.8	0.7–10.5

*During the previous 6 months.

TABLE 2. Logistic regression models showing odds ratios (ORs) for sharing cookers or cottons, adjusted for sharing syringes, number of injections/day, number of sex partners, use of syringe exchange program, and contact with the deceased cases, Pierce County, Washington, January–May 2000

	Univariate analysis		Multivariable model	
Risk factors	Unadjusted OR	95% Confidence interval	Adjusted OR	95% Confidence interval
Share drug cookers with more than two people*	8.1	2.6–25.4	8.3	2.2–31.7
Share filtration cottons with more than two people*	4.7	1.5–14.6		
Shared syringes*	2.3	0.8–6.5	2.0	0.5–7.3
More than one sex partner in of the opposite sex*	4.8	1.5–15.0	4.6	1.5–26.8
Inject more than four times a day	4.5	1.4–14.4	6.3	1.5–26.8
Obtain the majority of new syringes from the syringe exchange program	0.4	0.1–1.3	0.1	0.03–0.7
Knew one of the deceased cases	5.3	1.8–15.7	8.1	1.9–35.1

Adjusted ORs are adjusted for other variables in the table.

*Sharing cookers, cottons, and syringes compares persons who shared with more than two people to those who shared with less than two people in an average week during the previous 6 months.

with more than two people in an average week. This association was also observed among the eight case patients and 97 control subjects who did not share syringes: 87.5% of case patients versus 10.3% of control subjects (OR = 60.9, 95% CI = 6.3–2773.2).

Because the variables for indirect sharing were found to be colinear, cooker sharing was the only indirect sharing variable included in the multivariable model. In the multivariable analysis, injecting more than four times a day, having more than one sex partner of the opposite sex in the previous 6 months, and knowing one of the deceased case patients were significantly associated with HBV infection (Table 2). Obtaining syringes through the syringe exchange program was associated with lower odds of infection. Sharing syringes was associated with increased odds of acute HBV infection but did not reach statistical significance. After adjustment for these risk factors, the OR measuring the association between sharing drug cookers and HBV infection remained statistically significant (OR = 8.3, 95% CI = 2.2, 31.7).

DISCUSSION

This is the first outbreak of hepatitis B among IDUs in which sharing drug injection equipment in the absence of syringe sharing has been identified as a risk factor for infection. Transmission of viral pathogens via shared drug injection equipment could occur under conditions that permit virus survival on blood-contaminated environmental surfaces. Factors affecting the survival of human immunodeficiency virus (HIV) in used syringes include the volume of residual blood, viral titers in the residual blood, storage temperatures, and length of storage.[22,23] HIV DNA has been recovered from drug cookers, cottons, and syringe rinse water contaminated with

HIV-infected blood.[24] Although HBV DNA has been detected in blood from syringes used by IDUs, we are unaware of any studies that have attempted to detect HBV DNA in cookers, cottons, or rinse water.[25] Currently, methods do not exist to determine whether HBV DNA detected in used injection equipment represents infectious HBV; however, previous studies suggest that HBV remains infectious in the environment at least as long as HIV.[26,27]

Most of the case patients from whom HBV DNA was isolated had highly homologous sequences and reported injection drug use and knowing at least one of the deceased cases. These findings are consistent with the results of the epidemiologic investigation and suggest that the outbreak resulted from the introduction of a single HBV strain into a community of susceptible IDUs. The cases infected with nonhomologous HBV strains most likely represent the baseline sporadic transmission seen in this community.

This outbreak was notable for the identification of HDV coinfection in over a third of the cases. Because the prevalence of HDV in the general population is low, health departments in the United States do not routinely collect data on cases of hepatitis D. Although HDV infection is more common among IDUs, with prevalence as high as 20%–53% among IDUs who are hepatitis B surface antigen positive,[28] outbreaks of acute HBV/HDV coinfection are infrequently reported, even among IDUs. In this outbreak, some cases that were infected with the outbreak strain of HBV did not have evidence of coinfection with HDV. It is unclear whether this finding resulted from a failure to detect markers for HDV in cases that actually were coinfected or whether there were cases in which HBV was transmitted without HDV.

Although several studies have demonstrated that IDUs who participate in syringe exchange programs engage in less syringe sharing, the effectiveness of these programs in reducing the transmission of HBV and other viral pathogens is less clear. In this outbreak investigation, as in several other studies, non–HBV-infected individuals were more likely to report participating in syringe exchange programs than infected individuals.[25,29–31] Two recent longitudinal studies reported increased HBV transmission among IDUs who participated in syringe exchange programs; however, these studies did not assess the prevalence of indirect sharing practices among study participants.[15,32] The results of our investigation suggest that transmission of HBV among syringe exchange users could be explained by the sharing of injection equipment other than syringes. Transmission of blood-borne pathogens by indirect sharing has been described only recently, and many IDUs, including those in syringe exchange programs, remain unaware of the potential risk that these practices pose. Prevention messages for IDUs should recommend avoiding contact with any piece of injection equipment used by another person, including cookers, cottons, and rinse water.

The results of this study are subject to several potential biases. There are many challenges to collecting accurate information about sensitive or illegal activities by self-report. From our pilot questionnaire, we found that many IDUs could not meaningfully report the number of individuals with whom they had shared injection equipment in the previous 6 months. Therefore, we chose to ask about injection practices over a shorter, representative time period of an "average week" to lessen the cognitive burden on the respondents. We recognize that injection practices during nonaverage weeks could differ substantially from those during "average weeks," and that this question format may have resulted in underreporting of risky practices. Information on drug use practices and number of sex partners was collected by self-report. Recall bias or probing by interviewers could have led to greater

reporting of risk factors by case patients compared with controls. This was controlled for to some extent by the identification and interview of potential subjects at the vaccination clinics before either the subjects or interviewers knew the results of serologic testing. Information on the deceased cases was collected by interview of friends and family members and may have been subject to overestimation of risk behaviors. To assess the magnitude of this potential bias, analysis of the case-control data was repeated after excluding the deceased cases. Results of the exclusion analysis did not differ substantially from the original analysis.

Hepatitis B vaccine provides the best protection against HBV and HDV infection. Until widespread hepatitis B vaccine coverage is achieved through aging of cohorts vaccinated as infants and adolescents, effective strategies for delivering hepatitis B vaccine to high-risk adults are needed. Vaccination programs for high-risk adults that have been successful have provided hepatitis B vaccine free of charge at accessible locations, such as syringe exchange programs and correctional facilities.[17,33–35] IDUs should be counseled against the sharing of all injection equipment, including cookers, cottons, and rinse water. Syringe exchange programs can serve as important access points for providing prevention messages to IDUs.

REFERENCES

1. Centers for Disease Control and Prevention. *Hepatitis Surveillance Report 57*. Atlanta, GA: CDC; 2000.
2. Garfein RS, Vlahov D, Galai N, et al. 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.
3. Murrill CS, Weeks H, Castrucci BC, et al. Age-specific seroprevalence of HIV, hepatitis B virus, and hepatitis C virus infection among injection drug users admitted to drug treatment in 6 US cities. *Am J Public Health*. 2002;92:385–387.
4. Dhopesh VP, Taylor KR, Burke WM. Survey of hepatitis B and C in addiction treatment unit. *Am J Drug Alcohol Abuse*. 2000;26:703–707.
5. Lopez-Zetina J, Kerndt P, Ford W, et al. Prevalence of HIV and hepatitis B and self-reported injection risk behavior during detention among street-recruited injection drug users in Los Angeles County, 1994–1996. *Addiction*. 2001;96:589–595.
6. Polish LB, Gallagher M, Fields HA, et al. Delta hepatitis: molecular biology and clinical and epidemiological features. *Clin Microbiol Rev*. 1993;6:211–229.
7. DesJarlais C, Perlis T, Friedman SR, et al. Behavioral risk reduction in a declining HIV epidemic: injection drug users in New York City, 1990–1997. *Am J Public Health*. 2000;90:1112–1116.
8. 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.
9. Cook PA, McVeigh J, Syed Q, et al. Predictors of hepatitis B and C infection in injecting drug users both in and out of drug treatment. *Addiction*. 2001;96:1787–1797.
10. McCoy CB, Metsch LR, Chitwood DD, et al. Parenteral transmission of HIV among injection drug users: assessing the frequency of multiperson use of needles, syringes, cookers, cotton, and water. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1998;18:S25–S29.
11. Thiede H, Romero M, Bordelon K, et al. Using a jail-based survey to monitor HIV and risk behaviors among Seattle area injection drug users. *J Urban Health*. 2001;78:264–278.
12. Hunter GM, Donoghoe MC, Stimson GV, et al. Changes in the injecting risk behaviour of injecting drug users in London, 1990–1993. *AIDS*. 1995;9:493–501.
13. Hagan H, Thiede H. Changes in injection risk behavior associated with participation in the Seattle needle-exchange program. *J Urban Health*. 2000;77:369–382.

14. Koester S, Hoffer L. "Indirect sharing": additional HIV risks associated with drug injection. *AIDS Public Policy J*. 1994;3:100–105.
15. Mansson AS, Moestrup T, Nordenfelt E, et al. Continued transmission of hepatitis B and C viruses, but no transmission of human immunodeficiency virus among intravenous drug users participating in a syringe/needle exchange program. *Scand J Infect Dis*. 2000;32:253–258.
16. Thorpe LE, Ouellet LJ, Hershow R, et al. Risk of hepatitis C virus infection among young adult injection drug users who share injection equipment. *Am J Epidemiol*. 2002;155:645–653.
17. Centers for Disease Control and Prevention. Hepatitis B vaccination for injection drug users – Pierce County, Washington, 2000. *MMWR Morb Mortal Wkly Rep*. 2001;50:388–390, 399.
18. Nakano T, Shapiro CN, Hadler SC, et al. Characterization of hepatitis D virus genotype III among Yucpa Indians in Venezuela. *J Gen Virol*. 2001;82:2183–2189.
19. Nainan OV, Cromeans TL, Margolis HS. Sequence-specific, single-primer amplification and detection of PCR products for identification of hepatitis viruses. *J Virol Methods*. 1996;61:127–134.
20. Nainan OV, Stevens PE, Taylor PE, et al. Hepatitis B virus (HBV) antibody resistant mutants among mothers and infants with chronic HBV infection. In: Rizetto, M, Purcell, RH, Gerin, JL, Verme, G, eds. *Viral Hepatitis and Liver Disease*. Turin, Italy: Edizioni Minerva Medica; 1997:132–134.
21. Devereux J, Haeberli P, Smithies O. A comprehensive set of sequence analysis programs for the VAX. *Nucleic Acids Res*. 1984;12:387–395.
22. Abdala N, Reyes R, Carney JM, et al. Survival of HIV-1 in syringes: effects of temperature during storage. *Subst Use Misuse*. 2000;35:1369–1383.
23. Clatts MC, Heimer R, Abdala N, et al. HIV-1 transmission in injection paraphernalia: heating drug solutions may inactivate HIV-1. *J Acquir Immune Defic Syndr*. 1999;22:194–199.
24. Shah SM, Shapshak P, Rivers JE, et al. Detection of HIV-1 DNA in needle/syringes, paraphernalia, and washes from shooting galleries in Miami: a preliminary laboratory report. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1996;11:301–306.
25. Heimer R, Khoshnood K, Jariwala-Freeman B, et al. Hepatitis in used syringes: the limits of sensitivity of techniques to detect hepatitis B virus (HBV) DNA, hepatitis C virus (HCV) RNA, and antibodies to HBV core and HCV antigens. *J Infect Dis*. 1996;173:997–1000.
26. Bond WW, Favero MS, Petersen NJ, et al. Survival of hepatitis B virus after drying and storage for one week. *Lancet*. 1981;1:550–551.
27. van Bueren J, Simpson RA, Jacobs P, et al. Survival of human immunodeficiency virus in suspension and dried onto surfaces. *J Clin Microbiol*. 1994;32:571–574.
28. Alter MJ, Hadler SC. Delta hepatitis and infection in North America. *Prog Clin Biol Res*. 1993;382:243–250.
29. Vlahov D, Junge B, Brookmeyer R, et al. Reductions in high-risk drug use behaviors among participants in the Baltimore needle exchange program. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1997;16:400–406.
30. Hagan H, DesJarlais DC, Purchase D, et al. An interview study of participants in the Tacoma, Washington, syringe exchange. *Addiction*. 1993;88:1691–1697.
31. Hagan H, Jarlais DC, Friedman SR, et al. Reduced risk of hepatitis B and hepatitis C among injection drug users in the Tacoma syringe exchange program. *Am J Public Health*. 1995;85:1531–1537.
32. Hagan H, McGough JP, Thiede H, et al. Syringe exchange and risk of infection with hepatitis B and C viruses. *Am J Epidemiol*. 1999;149:203–213.
33. Hutchinson SJ, Goldberg DJ, Gore SM, et al. Hepatitis B outbreak at Glenochil prison during January to June 1993. *Epidemiol Infect*. 1998;121:185–191.
34. Stevenson J, Tannahill M, Biggs V. An outbreak of acute hepatitis B infection among injecting drug users in Inverclyde, Scotland. *Commun Dis Public Health*. 2001;4:60–63.
35. Streetly A, Perkins A, Tucker KM, et al. An outbreak of hepatitis B among intravenous drug users in Medway. *Community Med*. 1988;10:147–155.