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ORIGINAL CONTRIBUTIONS

Syringe Exchange and Risk of Infection with Hepatitis B and C Viruses

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The authors utilized a cohort study among Seattle injection drug users (IDUs) to assess whether participation in a syringe exchange program was associated with incidence of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection. Susceptible IDU subjects (187 seronegative for antibody to HCV, and 460 seronegative for core antibody to HBV) were identified in drug treatment, corrections, and social service agencies from June 1994 to January 1996, and followed for seroconversion one year later. The subjects included in the analysis were Seattle-King County (Washington State) area IDUs enrolled in a larger multipurpose cohort study, the Risk Activity Variables, Epidemiology, and Network Study (RAVEN Study). There were 39 HCV infections (20.9/100/year) and 46 HBV infections (10.0/100/year). There was no apparent protective effect of syringe exchange against HBV (former exchange users, relative risk (RR) = 0.68, 95% confidence interval (CI) 0.2–2.5; sporadic exchange users, RR = 2.4, 95% CI 0.9–6.5; regular users, RR = 1.81, 95% CI 0.7–4.8; vs. RR = 1.0 for nonusers of the exchange; adjusted for daily drug injection). Neither did the exchange protect against HCV infection (sporadic users, RR = 2.6, 95% CI 0.8–8.5; regular users, RR = 1.3, 95% CI 0.8–2.2; vs. RR = 1.0 for nonusers; adjusted for recent onset of injection and syringe sharing prior to enrollment). While it is possible that uncontrolled confounding or other bias obscured a true beneficial impact of exchange use, these data suggest that no such benefit occurred during the period of the study. *Am J Epidemiol* 1999;149:203–13.

hepatitis B; hepatitis C; incidence; injection drug users; needle-exchange programs; needle sharing; prevention

Syringe exchange programs have been established in numerous communities throughout the United States, primarily for the purpose of prevention of blood-borne viral infections, but with the secondary purpose of gaining access to a hidden population with multiple health concerns. Evaluations of exchange programs have reported a reduced risk of HIV infection (1, 2), reduction in HIV risk behavior (3–6), and lower risk of infection with hepatitis B and C viruses (HBV and HCV) (7). This analysis addresses whether the risk of HCV and HBV infection in current injection drug users (IDUs) was associated with participation in the Seattle-King County Department of Public Health needle exchange program in Washington State.

MATERIALS AND METHODS

A cohort study design was used to address the relation between syringe exchange participation and HBV- and HCV-seroconversion. Subjects for this analysis were identified from IDUs enrolled in a larger multipurpose cohort study, the Risk Activity Variables, Epidemiology, and Network Study (RAVEN Study).

Beginning in June 1994, cohort study subjects were recruited from six drug treatment programs and from

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Abbreviations: anti-HBc, antibody to hepatitis B core antigen; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDU, injection drug user; RAVEN Study, Risk Activity Variables, Epidemiology, and Network Study; RR, relative risk.

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social service, corrections, and drug-use assessment agencies. In each setting, subjects were systematically selected by use of a random-number based scheme from 1) all agency clients present during recruitment hours (non-drug treatment settings), or 2) all newly enrolled drug treatment clients. Series of random numbers between one and nine were issued to interviewers who would select the *n*th client as he or she entered the agency, or appeared on client lists.

Those selected were screened for eligibility (drug injection during the previous one year, English or Spanish speaking, age 14 years or older, and not already in the study), and were also asked whether they were likely to be in the Seattle-King county area one year hence, when the follow-up interview would be completed. Participants were paid $10 to complete the baseline interview and blood draw, and $25 at the follow-up visit. To be included in the present analysis, participants needed to have been enrolled in the cohort study between June 1994 and January 1996 and to be seronegative for HBV or HCV infection at that time.

At the enrollment and follow-up visits, a standardized questionnaire was completed during a face-to-face interview. The interviews asked about sociodemographic characteristics, and injection and sexual risk behavior. Injection risk behavior included sharing of syringes, sharing of drug preparation equipment (drug-cookers and other items used to prepare for an injection), and dividing up drugs between two or more IDUs using a common syringe ("backloading"). Blood samples were tested at the Seattle-King County Department of Public Health Laboratory for antibodies to HCV and HBV. Sera were screened for anti-HCV using a third generation Enzyme Immunoassay (Abbott Laboratories, Chicago, Illinois). To determine susceptibility to HBV, sera were screened for anti-HBc using an Enzyme Immunoassay (Abbott). Seroconversion was determined by the appearance of anti-HCV or anti-HBc in a previously seronegative individual. All subjects were informed of their test results, were given risk reduction counseling, and were offered referral assistance in seeking medical care.

Classifications were created to characterize syringe exchange use during the follow-up period, to test the hypothesis that the syringe exchange would be able to prevent infection only if susceptible IDUs had access to the exchange during the follow-up period. In our primary analyses, we separated IDUs into four groups: 1) those who had never been to a syringe exchange by the follow-up interview (never exchangers); 2) IDUs who had been to the syringe exchange at some time before the baseline interview, but did not attend the exchange during the follow-up period (former exchangers); 3) current users of the syringe exchange who got most (half or more) of their syringes from sources other than the exchange ("sporadic" users); and 4) current users of the exchange who obtained most of their syringes from the exchange ("regular" users).

In this analysis, IDUs who did not inject during the follow-up period were removed, in order to estimate the effect of the exchange on risk of HBV or HCV in those who continued to inject. Because there was little variation in person-time, and time-to-event was not directly measured, cumulative HCV and HBV incidence and 95 percent confidence intervals were calculated. Demographic and risk behavior characteristics were examined in relation to syringe exchange use categories and HCV/HBV seroconversion, to identify factors that may have confounded the association between exchange use and seroconversion. Logistic regression analysis was performed, entering confounding factors and syringe exchange terms into the model. The confounding effect of a variable was assessed by first examining the distribution of subject characteristics in relation to syringe exchange and HBV/HCV incidence, to determine which needed to be evaluated in the multivariate analysis. If entering any of these in the logistic regression model changed the exchange-use coefficient by more than 10 percent, it was considered a confounder and retained in the final model. Relative risks and 95 percent confidence intervals were calculated for each category of exchange use, using IDUs who had never been to the exchange as the referent category. Because there were few former exchangers in the HCV-negative cohort ($n = 15$), this group was not included in the analyses of HCV infection.

RESULTS

Between June 1994 and January 1996, 2,728 injection drug users were systematically selected and asked to participate in the RAVEN study; 266 potentially eligible individuals (9.8 percent) refused (table 1). Of the 2,462 enrolled between June 1994 and January 1996, 353 were anti-HCV negative. Seven deaths occurred in this group (2 percent), and 241 (70 percent) of the remaining 346 returned for their follow-up visit. A total of 187 (78 percent) of the HCV-negative subjects reported any injections during the follow-up period. Enrolled subjects also included 780 anti-HBc-negative IDUs; 12 (1.5 percent) of these subjects died before the end of the follow-up period. Of the remaining 768 believed to have been alive at the end of the follow-up period, 565 (74 percent) completed their follow-up interview. A total of 460 (81 percent) of the HBV negatives injected at least once during the follow-up period.

There were no differences between IDUs lost versus those retained in the study with respect to baseline

TABLE 1. Injection drug users that were included in analysis of hepatitis C virus (HCV) and hepatitis B virus (HBV) seroconversion, RAVEN Study*, Seattle, Washington State, June 1994 to June 1997

	No.	%
RAVEN Study eligible subjects enrolled June 1994 to December 1995	2,462	
No. of subjects HCV-negative at enrollment	353	14.3
Deaths	7	2.0
Believed to be alive at the end of follow-up	346	98.0
Completed follow-up	241	69.7
Injected during follow-up period	187	77.6
No. of HCV cases (% per year)	39	(20.8)
No. of subjects HBV-negative at enrollment	780	31.7
Deaths	12	1.5
Believed to be alive at the end of follow-up	768	98.5
Completed follow-up visit	565	73.6
Injected during follow-up period	460	81.4
No. of HBV cases (% per year)	46	(10.0)

* RAVEN Study, Risk Activity Variables, Epidemiology, and Network Study.

interview characteristics, such as ever-use of the exchange prior to the baseline interview (74 percent and 72 percent of lost and retained, respectively), injecting once a day or more often (34 percent and 37 percent), reporting of any needle-sharing during the one month period prior to the baseline interview (67 percent and 66 percent), or sharing of cookers (42 percent and 45 percent). Neither were these risk behaviors related to exchange use reported at baseline among the IDUs who were lost to follow-up, with no differences observed in the characteristics of lost and retained exchange users and never-exchangers.

The study protocol allowed for a 12-month follow-up period to observe seroconversion; however, subjects could complete their second study visit beginning at 11 months after enrollment. For the HCV-negative cohort (n = 187), the mean follow-up time per subject was 408.9 days (standard deviation (SD) 81.1), with 209.5 person-years of observation contributed to the study. There were 39 cases of HCV infection, for a cumulative incidence of 20.8 percent per year. HCV-negative subjects included 47 who had never exchanged, 15 who stopped using the exchange (former exchangers), 35 current exchangers in the sporadic-use group, and 90 who were classified as current, regular exchange users.

The mean follow-up period for the HBV-negative cohort (n = 460) was 401.8 days (SD 81.8), with a total of 506.4 person-years of observation. Forty-six cases of HBV infection were detected, for a cumulative incidence of 10 percent per year. There were 102 never-exchangers in the HBV-negative cohort, 48 former exchangers, 95 current, sporadic exchangers, and 214 current, regular exchange users.

The annual incidence of HCV infection was relatively high in IDUs aged 24 years or younger (26 percent), and also elevated in 25–34 year olds (23 percent) compared with older injectors (14 percent, table 2). Although only 4 percent of blacks seroconverted to HCV-positive, the denominator was so small that the difference from the corresponding proportion of whites who seroconverted was well within the limits of chance. HBV infection was not associated to any appreciable degree with race/ethnicity or age; it was somewhat elevated in males (11 percent vs. 8 percent in females), in those who reported streets or shelters as their place of residence (17 percent vs. 9 percent for all others), and in heterosexuals (11 percent vs. 5 percent in gay or bisexual IDUs).

HCV incidence was particularly high among IDUs who had been injecting for one year or less at the baseline interview (31 percent), whereas HBV incidence was not associated with duration of drug injection. There was somewhat lower HCV incidence in subjects whose usual drugs were stimulants (~15 percent for cocaine or amphetamine users) compared with those who usually inject heroin alone (24 percent) or in combination with cocaine ("speedball", 20 percent). Only 2 percent of cocaine users seroconverted to HBV-positive compared with 9 percent of speedball users and 12 percent of those who usually injected heroin or amphetamines. Frequency of injection during the one month before baseline interview was not clearly related to HCV or HBV infection. However, other injection risk behaviors at the baseline and follow-up interviews (frequency of sharing syringes, the number of IDUs shared with, and indirect sharing via cookers and cottons or by backloading) were associated with a higher frequency of both HCV and HBV. For these subjects who continued to inject during the follow-up period, being in drug treatment at baseline or during the follow-up period was not associated with a lower risk of HBV or HCV.

Recency of sexual contact was associated with an increase in HCV incidence (22 percent vs. 16 percent depending on whether the last sexual contact was or was not within 6 months before baseline). Subjects who had sexual contact during the follow-up period had a somewhat lower incidence of HBV than those who did not. Women who had sexual contact with an IDU partner at baseline or follow-up had substantially higher incidence of HCV compared with other women. In general, sexual risk behavior was not associated

TABLE 2. Hepatitis C virus (HCV) and hepatitis B virus (HBV) seroconversion rates in injection drug users, by subject characteristics, RAVEN Study*, Seattle, Washington State, June 1994 to June 1997†

Characteristic	HCV-negative		HBV-negative	
	No.	% HCV converters	No.	% HBV converters
TOTAL	187	20.9	460	10.0
Demographic characteristics				
Sex				
Male	115	18.3	280	11.4
Female	72	25.0	180	7.8
Age group (years)				
≤24	50	26.0	81	9.9
25–34	78	23.1	184	8.7
≥35	59	13.6	195	11.3
Race/ethnicity				
White	143	23.1	344	9.9
Black	23	4.3	55	9.1
Other	21	23.8	61	11.5
Residence				
Lives in shelter/streets	38	15.8	71	16.9
Other	149	22.1	389	8.7
Sexual orientation				
Heterosexual	153	20.9	402	10.7
Gay/bisexual	33	21.2	56	5.4
Drug use characteristics				
No. of years injecting				
0–1	62	30.6	80	6.3
2–5	59	16.9	115	13.0
6–10	29	20.7	92	8.7
11–20	21	14.3	113	7.1
≥21	16	6.3	60	16.7
Drug injected most often				
Speedball	15	20.0	45	8.9
Heroin	102	23.5	293	11.6
Cocaine	26	15.4	57	1.8
Speed	28	14.3	34	11.8
Other	6	16.7	6	0.0
No. of injections/day				
0‡	33	15.2	84	9.5
0.1–1.0	43	23.3	106	5.7
1.1–3.9	70	18.6	171	11.7
≥4.0	41	26.8	99	12.1
Injection risk behavior				
Reported at the baseline interview				
Frequency that subject shared syringes				
Never	84	17.9	206	9.2
Rarely	27	29.6	78	7.7
Sometimes	24	25.0	50	8.0
Usually	8	25.0	23	26.1
Always	2	50.0	6	0.0

Table continues

with HBV infection in a pattern that would conform to substantial sexual transmission.

Characteristics associated with HCV infection were more prevalent in exchange users than nonusers. Current exchange users were somewhat younger than those who had never used the exchange, with twice as many less than 24 years old (table 3). Those who had been injecting one year or less (the group with highest

TABLE 2. Continued

Characteristic	HCV-negative		HBV-negative	
	No.	% HCV converters	No.	% HBV converters
Injection risk behavior (contd.)				
No. of IDUs* with whom subject shared syringes				
0	108	13.9	275	8.0
1	30	23.3	88	6.8
≥2	27	40.7	57	17.5
Shared cooker				
No	94	18.1	231	7.4
Yes	89	23.6	217	12.4
Shared cotton				
No	110	17.3	262	8.4
Yes	73	26.0	190	12.1
Backloaded				
No	90	17.8	244	7.8
Yes	64	26.6	136	14.0
In drug treatment				
No	96	21.9	189	11.1
Yes	91	19.8	271	9.2
Reported at the follow-up interview				
No. of IDUs with whom subject shared syringes				
0	102	12.7	235	9.8
1	65	30.9	198	10.3
≥2	7	28.6	27	18.5
Shared cooker				
No	54	9.3	138	8.7
Yes	125	26.4	305	10.5
Shared cotton				
No	69	10.1	163	8.6
Yes	110	28.2	277	10.8
Backloaded				
No	88	13.6	221	10.4
Yes	63	28.6	141	9.9
In drug treatment during follow-up				
No	48	27.1	94	10.6
Yes	136	19.1	363	9.9

Table continues

HCV incidence) were more likely to be never- or regular-users of the exchange. Both regular and sporadic exchange users were more likely to report sharing injection and drug preparation equipment during the follow-up period.

A substantially larger proportion of current exchange users reported that they usually injected four times per day or more often, a practice that was also associated with higher HBV incidence. In general, former exchange users had fewer HBV injection risk behaviors than did current users of the exchange. On average, regular users of the exchange injected more frequently than never- and sporadic users, and generally reported more high-risk behaviors (table 4).

IDUs who had never used the syringe exchange had a lower incidence of HCV than those who did use the exchange (15 percent vs. 21–26 percent, table 5). Compared with sporadic exchangers, the regular users had a slightly lower incidence. For HBV, never-exchangers and former exchangers had a lower risk of infection than current users of the exchange (4–6 percent vs. 11–14 percent).

For the association between use of the needle exchange and HCV infection, two factors were important confounders: direct syringe-sharing at the baseline period, and having begun to inject during the previous one year. Relative to nonusers of the exchange, regular users during follow-up had about a 30 percent increase in the rate of HCV infection (relative risk (RR) = 1.31), adjusted for these confounders. However, the confidence limits around this estimate were wide (95 percent confidence interval (CI)

TABLE 2. Continued

Characteristic	HCV-negative		HBV-negative	
	No.	% HCV converters	No.	% HBV converters
Sexual risk behavior				
Reported at baseline interview				
Last sexual contact				
>6 months before	25	16.0	60	15.0
1–6 months before	37	21.6	84	13.1
During last 1 month	125	21.6	315	8.3
How often usually uses condoms with steady sex partners				
Never–rarely	90	20.0	247	10.9
Sometimes–usually	34	32.3	56	3.6
Always	21	14.3	42	7.1
How often usually uses condoms with casual sex partners				
Never–rarely	29	10.3	68	10.3
Sometimes–usually	33	33.3	53	7.5
Always	51	25.5	94	7.4
Subject is a female who had sex with an IDU/1 month before baseline				
No	126	18.3	311	10.6
Yes	42	33.3	108	7.4
Reported at follow-up interview				
Last sexual contact				
Not during follow-up	24	10.3	62	19.6
During follow-up, not last month	51	23.1	120	9.2
During the month before follow-up	100	22.0	241	10.4
How often subject used condoms with casual sex partners				
Never–rarely	36	19.4	105	8.6
Sometimes–usually	45	24.4	106	11.3
Always	59	23.7	118	10.2
Subject is a female who had sex with an IDU/1 month before baseline				
No	78	19.2	197	11.6
Yes	30	24.3	73	5.5

* RAVEN Study, Risk Activity Variables, Epidemiology, and Network Study; IDU, injection drug user.
† Numbers may not sum to total because of missing values.
‡ These individuals did inject during the follow-up period and therefore were included in the analysis.

0.79–2.19), as were those around the even higher relative risk associated with sporadic exchange use (RR = 2.59, 95 percent CI 0.79–8.5). The analysis of the HBV cohort data adjusted for daily injecting at the baseline period. The adjusted relative risks (95 percent CIs) were 1.8 (0.69–4.77) for regular exchange use, 2.36 (0.86–6.47) for sporadic use, and 0.68 (0.19–2.46) for former use. Further analysis of the data did not reveal any subgroups in whom needle exchange use was associated with a particularly altered risk of HBV or HCV. However, the size of most of these subgroups was small, and so this analysis did not have much power to identify an across-subgroup difference in the impact of exchange use on infection rates even if one truly were present.

DISCUSSION

Particularly because our results were different from those of the case-control study that evaluated the impact of the Tacoma, Washington syringe exchange on hepatitis B and C (7), we assessed the possibility that the design or conduct of the present study might have affected our results. In a cohort study, selective losses to follow-up can lead to substantial bias. In this study, 26 and 30 percent of the initial cohort was not

TABLE 3. Subject characteristics in relation to needle exchange use in hepatitis C virus (HCV)-negative injection drug users, RAVEN Study*, Seattle, Washington State, June 1994 to June 1997†

Characteristic	Needle exchange use at follow-up					
	Never (n = 47)		Sporadic (n = 35)		Regular (n = 90)	
	No.	%	No.	%	No.	%
Age group (years)						
≤24	7	14.9	11	31.4	30	33.3
25–34	25	53.2	16	45.7	31	34.4
≥35	15	31.9	8	22.9	29	32.2
No. of years injecting						
0–1	18	38.3	6	17.1	35	38.9
2–5	11	23.4	15	42.9	28	31.1
6–10	8	17.0	8	22.9	11	12.2
11–20	6	12.8	3	8.6	7	7.8
≥21	4	8.5	3	8.6	9	10.0
No. of injections/day						
0‡	13	27.7	6	17.1	10	11.1
0.1–1.0	14	29.8	9	25.7	18	20.0
1.1–3.9	12	25.5	13	37.1	38	42.2
≥4.0	8	17.0	7	20.0	24	26.7
Injection risk behavior (follow-up period)						
No. of IDUs* with whom subject shared syringes						
0	31	78.1	21	70.0	44	55.0
1	2	6.7	6	20.0	19	23.8
≥2	7	17.1	3	10.0	17	21.3
Shared cooker						
No	16	36.4	10	28.6	23	26.4
Yes	28	63.6	25	71.4	64	73.6
Shared cotton						
No	22	50.0	9	25.7	33	37.9
Yes	22	50.0	26	74.3	54	62.1
Shared rinse water						
No	27	61.4	17	48.6	42	48.3
Yes	17	38.6	18	51.4	45	51.7
Backloaded						
No	30	75.0	15	55.6	35	47.9
Yes	10	25.0	12	44.4	38	52.1

* RAVEN Study, Risk Activity Variables, Epidemiology, and Network Study; IDU, injection drug user.
† Numbers may not sum to total because of missing values.
‡ These individuals did inject during the follow-up period and therefore were included in the analysis.

assessed for the incidence of HCV or HBV infection, respectively. We compared those who did complete the follow-up visit to those who did not return to the study, and did not note any important differences between the two groups in terms of age, sex, race, or injection or sexual risk behavior reported at baseline. Therefore, it is unlikely that selective losses to follow-up would have biased the association between exchange use and risk of infection.

Measurement error can be a problem in studies that rely on collection of self-reported risk behavior. In this study, behavioral information was used to classify subjects with respect to exposure, and to potentially confounding factors. Although most of the information on characteristics of study subjects was collected prior to the follow-up period, classification of exchange use was primarily determined by use during follow-up. If a person who became infected was more or less likely to report use of the exchange, the relative risks would have been under- or overestimated. However, few cases were aware that they had acquired infection at the time of the follow-up interview. Four of the 39 HCV cases (10 percent) reported that they had experienced symptoms of hepatitis, three of whom (8 percent) had jaundice during the follow-up. In the HBV cohort, seven cases (15 percent) had hepatitis symptoms, all of whom had jaundice. All of the symptomatic HBV cases and three of the four HCV cases with symptoms said they were current exchangers.

Our inability to measure a relevant confounding variable or misclassification of confounders that was measured could also have led to bias. The primary

TABLE 4. Subject characteristics in relation to needle exchange use in hepatitis B virus (HBV)-negative injection drug users, RAVEN Study*, Seattle, Washington State, June 1994 to June 1997†

Characteristic	Needle exchange use at follow-up							
	Never (*n* = 102)		Former (*n* = 48)		Sporadic (*n* = 95)		Regular (*n* = 214)	
	No.	%	No.	%	No.	%	No.	%
Age group (years)								
≤24	10	9.8	7	14.6	14	14.7	50	23.4
25–34	42	41.2	12	25.0	46	48.4	84	39.3
≥35	50	49.0	29	60.4	35	36.8	80	37.4
No. of years injecting								
0–1	20	19.6	5	10.4	11	11.6	44	20.6
2–5	17	16.7	12	25.0	30	31.6	56	26.2
6–10	21	20.6	14	29.2	21	22.1	36	16.8
11–20	26	25.5	10	20.8	27	28.4	50	23.4
≥21	18	17.6	7	14.6	6	6.3	28	13.1
No. of injections/day								
0‡	22	21.6	15	31.3	15	14.6	31	14.5
0.1–1.0	35	34.3	10	20.8	31	30.1	38	17.8
1.1–3.9	28	27.5	13	27.1	40	38.8	90	42.1
≥4.0	17	16.7	10	20.8	17	16.5	55	25.7
Injection risk behavior (follow-up period)								
No of IDUs* with whom subject shared syringes								
0	61	65.6	36	81.8	55	64.0	125	62.8
1	19	20.4	7	15.9	17	19.8	45	22.6
≥2	13	14.0	1	2.3	14	16.3	29	14.6
Shared cooker								
No	36	38.7	16	36.4	20	21.3	66	31.3
Yes	57	61.3	28	63.6	74	78.7	145	68.7
Shared cotton								
No	42	45.7	20	45.5	25	26.9	75	35.7
Yes	50	54.3	24	54.5	68	73.1	135	64.3
Shared rinse water								
No	56	60.9	24	54.5	35	37.6	105	49.8
Yes	36	39.1	20	45.5	58	62.4	106	50.2
Backloaded								
No	61	76.3	28	71.8	36	54.5	95	54.0
Yes	19	23.8	11	28.2	30	45.5	81	46.0

* RAVEN Study, Risk Activity Variables, Epidemiology, and Network Study; IDU, injection drug user.
† Numbers may not sum to total because of missing values.
‡ These individuals did inject during the follow-up period and therefore were included in the analysis.

needle exchange in Seattle is located in the drug/sex market area where there was a possible concentration of more compulsive drug users and those who risk exposure from unprotected sex to a greater degree. Indeed, this site was chosen for its proximity to a high-risk population. It is possible that non-exchangers who were able to obtain sterile syringes from pharmacies and other sources also may have been different from exchangers in other means of exposure to HBV and HCV beyond those we could measure and adjust for. Thus, retention in the needle exchange of higher-risk IDUs could have contributed to the observed higher HBV/HCV risk in current users of the exchange compared with nonusers and those who stopped exchanging. On the other hand, it is conceivable that participation in the exchange may have truly increased the risk of HBV or HCV among certain users by bringing them into regular contact with compulsive drug users and with those with a pattern of routine sharing of injection equipment. However, whether the exchange increased risk by association with higher risk IDUs could not be addressed by the data available because we did not ask about IDU-interactions stemming from exchange participation.

The design also limited the ability to examine any effects of participation in the exchange that extended beyond the one-year follow-up period. Examination of duration of exchange use in relation to exchange-category at follow-up indicated that more former exchange users had been using the exchange for more

TABLE 5. Relative risks (RR) of hepatitis C virus (HCV) and hepatitis B virus (HBV) seroconversion in relation to needle exchange use by injection drug users, RAVEN Study*, Seattle, Washington State, June 1994 to June 1997†

Needle exchange use	No	No. of cases	Risk/100/ year (%)	RR	95% CI	Adjusted RR	95% CI
			HCV seroconversion†				
Never	47	7	14.9	1.0		1.0	
Current–sporadic	35	9	25.7	1.72	0.71–4.19	2.59	0.79–8.5
Current–regular	90	19	21.1	1.42	0.64–3.13	1.31	0.79–2.19
			HBV seroconversion‡				
Never	102	6	5.9	1.0		1.0	
Former	48	2	4.2	0.71	0.15–3.38	0.68	0.19–2.46
Current–sporadic	95	13	13.7	2.32	0.92–5.87	2.36	0.86–6.47
Current–regular	214	24	11.2	1.9	0.8–4.52	1.81	0.69–4.77

* RAVEN Study, Risk Activity Variables, Epidemiology, and Network Study.
† The adjusted relative risk for HCV seroconversion was adjusted for onset of injection within the year prior to baseline interview and any sharing at the baseline.
‡ The adjusted relative risk for HBV seroconversion was adjusted for daily injection at baseline.

than one year (60 percent vs. 47 percent and 41 percent of regular and sporadic exchange users), and that sporadic exchange users were more likely to have begun using the exchange within the one month before baseline interview (33 percent vs. 10 percent of former users and 20 percent of regular users). This would be consistent with a gradual effect of needle exchange on development of safer injection skills, and with loss of more "successful" IDUs from the exchange as they acquire other, perhaps more convenient sources of syringes. Under the Prochaska "Stages of Change" behavior change model (8), new and inconsistent exchange users would tend to be in the contemplative or early action stages of risk behavior change, and former exchangers would include more IDUs who are able to maintain safe injection behavior even while not actively participating in the program. In this study, we did not collect data on risk behavior before 1994 or in relation to when subjects first began to use the exchange, so we could not explore whether behavior change was more substantial in earlier years. However, among exchange users, adjustment of the relative risks for duration of exchange use did not lead to an important change in the results.

There are several studies that have related risk of blood-borne viral infection to syringe exchange participation. Kaplan (9) tested all syringes returned to the New Haven syringe exchange and found that 50 percent of program syringes (originating from the exchange) tested positive for HIV, compared with 68 percent of non-program syringes. Assuming that non-program syringes were representative of those that IDUs had access to prior to the start of the exchange, Kaplan concluded from the difference in positivity in the syringes that there was a 25 percent decrease in the risk of HIV for exchange users. In an ecologic study, Hurley et al. (1) reported that HIV seroprevalence in IDUs increased an average of 6 percent per year in 52 cities without syringe exchange, but decreased 6 percent per year in 29 cities with an exchange program. The influence of the Amsterdam syringe exchange on HIV seroconversion was studied in a cohort of IDUs from 1986 to 1991 (10); after controlling for individual characteristics associated with seroconversion, no association with syringe exchange use could be found. However, the data suggested that calendar time modified the association, with a reduced risk (odds ratio = 0.4) in 1986–1987 but not in later years. A meta-analytic study design was used to estimate the effect of syringe exchange on HIV transmission in New York area IDUs (2); adjusting for other HIV risk factors, a threefold excess risk in those who did not participate in exchange programs was reported. Included in the meta-analysis were data from two current studies in New York, and historical controls (IDUs studied in the 1980s) who were classified as non-exchangers because exchange programs were not available when the studies took place. Another study examined hepatitis B and C incidence in relation to ever-use of the Tacoma syringe exchange during 1990–1993 (7); nonuse was associated with a six- to sevenfold greater risk of viral hepatitis. Most recently, an HIV outbreak occurred in IDUs in Vancouver, British Columbia, where there is a large-scale syringe exchange (11). In the investigation of the outbreak, 23 of 24 HIV seroconverters reported that the exchange was their main source of syringes. Even though no corresponding data were presented for persons who did not seroconvert, it is clear that the

presence of the syringe exchange program in Vancouver could not have prevented many IDUs from acquiring HIV infection. The tendency for the earlier studies, but not the later ones, to have shown a reduced risk of viral blood-borne infections among IDUs who used a syringe exchange program is compatible with the hypothesis that, over time, sterile needles are becoming increasingly available through means other than an exchange. The research also suggests that identification of a comparison group that is similar to exchange users regarding other risk factors for blood-borne viral infections may become increasingly problematic over time. For example, in Amsterdam in the early 1990s, the syringe exchange had become the primary source of safe injection equipment for a particularly high risk segment of the IDU population (10).

Our study suggests that the influence of needle exchange on risk of HCV infection may be affected by the high prevalence of infectious carriers in the underlying IDU population. During the period in which HBV/HCV infection was studied in the cohort, the incidence of HIV infection was quite low, with only four seroconversions among 1,651 study participants (0.2 percent). Thus, it would appear that high incidence of viral hepatitis can occur in the presence of low HIV incidence, presumably because of the higher prevalence of HCV carriers in the Seattle IDU population (70 to 80 percent, vs. 5 percent for HIV and HBV (12)) and perhaps because of higher transmission efficacy for HBV compared with HIV and HCV (13). Mathematical modeling of the ability of disinfectant bleach to prevent needle-borne HIV transmission indicates that predicted effectiveness of bleach may be highest in low-prevalence settings (14). Another study of more than 6,000 IDUs in 15 US cities (15) found that HIV seroprevalence modified the effect of individual risk factors for HIV seroconversion, with syringe-sharing being a significant risk factor in high-prevalence cities, whereas factors representing the likelihood that a needle-sharing partner was infected were associated with seroconversion in low-prevalence areas. In our study, the likelihood that another IDU was an HCV-carrier was at least 70 percent, and *any* syringe-sharing was an important risk factor for HCV infection.

The emphasis of risk reduction counseling in most needle exchange programs has been on direct sharing of syringes. Only recently has sharing of drug preparation equipment (drug cookers or cottons, or backloading) been recognized as an important risk factor for HIV, and an additional focus of HIV prevention education for IDUs (16, 17). In this study, we did not collect information regarding specific risk reduction advice given to subjects by needle exchange staff. However, if the primary effect of the needle exchange was to reduce direct sharing, then any infections that occur as a result of indirect sharing would tend to reduce the likelihood of detecting an association between exchange use and HBV/HCV. Both HBV and HCV infections occurred in some IDUs who reported that they did not share syringes, but shared cookers and cotton or backloaded. This would suggest that needle exchange users and other IDUs need to know that HBV and HCV might be transmitted by this route, and that the only safe way to inject is to not share any injection equipment whatsoever.

Conclusions

In this study, there was no indication of a protective effect of syringe exchange against HBV or HCV infection. Indeed, highest incidence of infection occurred among current users of the exchange, even after adjustment for confounding variables. Whether the excess incidence in exchange users is due to disproportionate retention of high risk IDUs in the exchange could not be directly addressed by the design of this study. Additionally, the incidence of viral hepatitis was high in the entire cohort, with 10 percent annual seroconversion rate among HBV-susceptible IDUs, and 20 percent among HCV negatives. In an era of HIV/AIDS, such high seroincidence of other blood-borne viral infections is troubling, and suggests that the goal of elimination or substantial reduction of risk behavior that may transmit HIV in IDUs has not been achieved. Clearly, risk factors for HBV/HCV infection such as syringe-sharing are still practiced by a substantial proportion of Seattle-area drug injectors.

Drug treatment programs that lead to cessation or reduction in drug injection may lower the risk of both HCV and HBV in current drug injectors (18, 19). Because only a small proportion of IDUs are in treatment programs at any point in time and treatment primarily attracts older IDUs, most of whom have already been infected with HBV and HCV, drug treatment may be expected to have a small net effect on HBV/HCV transmission (20). Additionally, programs to vaccinate IDUs against HBV have also been extremely limited, so this remains a possible but little-used HBV-control strategy.

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