A B S T R A C T

Objectives. This study investigated the sharing of drug preparation equipment as a possible route of hepatitis C virus (HCV) transmission.

Methods. HCV seroconversion was measured in a cohort of 317 injection drug users who tested negative for HCV antibody at recruitment.

Results. Cumulative HCV incidence was 16.7% per year. Among those who did not share syringes, HCV seroconversion was associated with sharing drug cookers and filtration cotton (adjusted risk ratio=5.9; 95% confidence interval=1.1, 31.7); 54% of HCV infections in injection drug users who did not share syringes were attributable to cooker/cotton sharing.

Conclusions. Among injection drug users who do not share syringes, an important proportion of HCV infections may be attributed to cooker/cotton sharing. (Am J Public Health. 2001;91: 42–46)

Sharing of Drug Preparation Equipment as a Risk Factor for Hepatitis C

Holly Hagan, PhD, Hanne Thiede, DVM, MPH, Noel S. Weiss, MD, DrPH, Sharon G. Hopkins, DVM, MPH, Jeffrey S. Duchin, MD, and E. Russell Alexander, MD

Hepatitis C virus (HCV) infection is very common among injection drug users. Studies of injection drug users in regions with a longstanding pattern of endemic injection drug use have reported prevalences of HCV antibody in the range of 65% to 90%, even where HIV prevalence is quite low. 1-5 The majority of HCV infections become chronic, resulting in a large reservoir of HCV infection among injection drug users. 6 Incidence of HCV infection in previously uninfected injection drug users ranges from 10 to 30 per 100 person-years at risk. 1-4,7-9 Prior studies have not observed a consistent pattern of risk associated with sex, duration or recency of injecting, or participation in a syringe exchange program. ^{3,4,7,10,11} Three incidence studies noted an association between HCV seroconversion and use of potentially contaminated syringes, 3,8,9 but in all but one8 the association was weak after control for other factors. Clearly, a great deal remains to be learned about the determinants and prevention of HCV infections in injection drug users.

Among the unexplored areas of HCV research is the importance to transmission of the shared use of drug preparation equipment in the absence of injection with a contaminated syringe. Because the prevalence of syringe sharing has declined since the appearance of HIV/AIDS, ¹² viral transmission associated with sharing equipment used to prepare drugs for injection may have risen in importance. In this study, we examined the risk of HCV transmission in relation to the sharing of cookers used to melt the drug into an injectable liquid, of cotton used to filter out particles as the drug is drawn into the syringe, and of water used to rinse the syringe. Injection with a syringe previously used by another injector, and use of a syringe to divide drug doses between users (backloading), ¹³ were also evaluated as potential means of HCV transmission.

Methods

Subjects were enrolled in a cohort study of health consequences and risk behaviors associated with injection drug use (the RAVEN Study). Recruitment occurred between June 1994 and May 1997 in 9 different locations in the Seattle area; a random-numbers table was used to select the nth client from among those present at each location. Eligibility criteria included having injected an illicit drug in the previous year, being English or Spanish speaking, being 14 years or older, and not being already enrolled in the study. After providing written consent to participate, subjects completed an interviewer-administered questionnaire and a blood draw. Follow-up 1 year later included an interview that asked about behavior during the follow-up period and a second blood specimen. Blood was tested for HCV antibody with a third-generation enzyme immunoassay (Ab-

Holly Hagan, Hanne Thiede, Sharon G. Hopkins, and Jeffrey S. Duchin are with the Seattle–King County Department of Public Health, Seattle, Wash. Holly Hagan, Hanne Thiede, Noel S. Weiss, Sharon G. Hopkins, and E. Russell Alexander are with the Department of Epidemiology and Jeffrey S. Duchin is with the Division of Allergy and Infectious Diseases, University of Washington Seattle.

Requests for reprints should be sent to Holly Hagan, PhD, Public Health—Seattle and King County, 106 Prefontaine Place South, Seattle, WA 98104 (e-mail: holly.hagan@metrokc.gov).

This brief was accepted May 15, 2000.

bott Laboratories, Chicago, Ill). HCV seroconversion was determined by the appearance of HCV antibody in a previously seronegative individual. Details of RAVEN methods are available elsewhere. Study protocols were approved by an institutional review board.

Baseline characteristics and risk behaviors during the follow-up period were evaluated as risk factors for HCV seroconversion by cumulative incidence. 14 The questionnaire asked about injection with a syringe previously used by another person, use of a cooker or cotton after another person had used it, use of rinse water another person had used, and use of a syringe to divide drugs. Throughout this report, these behaviors are referred to as syringe sharing, cooker and cotton sharing, sharing rinse water, and backloading, respectively. The magnitude of the association between these injection behaviors and HCV infection was estimated by means of the risk ratio and its 95% confidence interval. Shared use of cooker and of cotton were evaluated together, because among those who did not share syringes, all of the HCV seroconverters who shared cotton also shared a cooker.

Stratified analysis was carried out to separate the large effect of syringe sharing from the effect of other injection behavior. Logistic regression was used to estimate the risk of HCV infection associated with injection risk behavior among those who did not report sharing syringes during the follow-up period; this analysis obtained estimates of the association adjusted for confounding factors (adjusted risk ratio). Frequency of injection at the baseline interview was included in the model because it met databased criteria for confounding. 15 The attributable risk percentage is the proportion of disease in persons with a given behavior that is due to that behavior. 16 The attributable risk percentage was estimated by standard methods¹⁶ and as shown in Table 3. It was calculated for behaviors that were statistically significantly associated with HCV seroconversion, since some fraction of disease could reasonably be attributed to them. The attributable risk percentage in the underlying injection drug user population (population attributable risk percentage) was also calculated by standard methodology. 16

Results

During the recruitment period, 2879 injection drug users were enrolled in the RAVEN cohort; only 507 (17.6%) tested negative for HCV antibody. Follow-up was completed on 317 (62.5%) of the initially HCV-negative subjects; characteristics of these subjects in relation to cumulative HCV incidence are shown in Table 1. Fifty-three subjects seroconverted to HCV positive during the follow-up period (16.7%). The risk of HCV seroconversion was lower for African Americans than for others. but it was not associated with sex, age, or homelessness. Injection drug users whose first injection was in the previous 2 years, and those who reported at their enrollment interview that they injected at least once every day, were relatively more likely to become infected with HCV.

Also shown in Table 1, those who reported no injections during follow-up had the lowest risk of HCV seroconversion. All 3 seroconverters who did not inject during follow-up reported injecting in the month before enrollment, and only 1 of the 3 did not report any injection or sexual risk behavior during that period. Any syringe sharing was associated with a 3-fold higher risk of HCV infection (29% vs 10%; risk ratio [RR]=2.94; 95% confidence interval [CI]= 1.6, 5.3). Similarly, risk of HCV was 3-fold higher among those who shared a cooker or cotton (24% vs 7%; RR=3.39; 95% CI=1.4, 8.2). Risk of HCV seroconversion did not differ according to the frequency of sharing a cooker and cotton, but it was relatively higher among those who reported sharing syringes sometimes, usually, or always than among those who reported rare syringe sharing (χ^2 test for trend, P < .01). Among those who injected with a used syringe, there was no difference in HCV incidence between those who almost always used disinfectant bleach when they shared a syringe and those who never or inconsistently used bleach. None of the sexual risk behaviors analyzed were associated with HCV acquisition; these included number of partners, unprotected anal or vaginal sex, sex with another injection drug user, and exchanging money or drugs for sex.

Results of the analysis of HCV seroconversion stratified by syringe sharing are shown in Table 2. Among individuals who reported having injected at least once with a used syringe, sharing both a cooker and cotton was associated with a risk ratio of 1.7, sharing rinse water with a risk ratio of 0.9, and backloading with a risk ratio of 2.1 (all nonsignificant). Among those who did not inject with a used syringe, the risk ratio for cooker and cotton sharing was 3.8 (95% CI=1.1, 13.8), but sharing rinse water and backloading were not associated with much, if any, increased risk of seroconversion.

In a multiple logistic regression model that included only 123 injection drug users who injected but did not share syringes during follow-up, the adjusted risk ratio for cooker and cotton sharing was 5.9 (95% CI=1.1, 31.7). For injection drug users who shared rinse water or backloaded, risk of HCV seroconversion was not significantly different than for those

who did not share any equipment (for sharing rinse water, adjusted risk ratio [ARR]=0.6, [95% CI=0.1, 2.7]; for backloading, ARR= 1.1, [95% CI=0.2, 4.7]).

The attributable risk percentage for syringe sharing was 66% (Table 3). Since 77% of HCV seroconverters had shared syringes, the proportion of all HCV infections in the underlying population of injection drug users that was attributable to syringe sharing (the population attributable risk percentage) was 51%. Among those who did not share syringes but shared cookers and cotton, 74% of infections were due to cooker and cotton sharing. Because relatively few seroconverters shared cookers and cotton but not syringes (17%), the population attributable risk percentage for cooker and cotton sharing for all injection drug users was only 13%. However, in the underlying population of injection drug users who did not share syringes, the population attributable risk percentage for sharing cookers and cotton was substantially higher, 54%.

Discussion

The potential for blood-borne viral transmission via injection equipment other than syringes was reported in an earlier study of equipment collected in a Miami shooting gallery, where HIV-1 DNA was detected in rinses from cottons and cookers and in water used to clean paraphernalia and to dissolve drugs.¹⁷ A sterile syringe may become contaminated when the tip of the needle is inserted into a contaminated cooker or when the drug is drawn up through contaminated filtration cotton. This type of injection risk behavior appears to be quite common, and fewer injection drug users may recognize the hazard of sharing drug preparation equipment than recognize the hazard of sharing syringes. 18 The present study suggests that HCV may be transmitted via the shared use of drug cookers and filtration cotton even without injection with a contaminated syringe.

To our knowledge, there have been no prior published reports of incident blood-borne infections in injection drug users who shared equipment without sharing syringes. An association between backloading and prevalent infection with HIV was reported in a New York cross-sectional study; however, the magnitude of the association was small (adjusted odds ratio=1.65), and therefore a notable correlation between syringe sharing and HIV prevalence may have contributed to the observed relationship. 19 Another cross-sectional study reported an association between frequency of backloading and HIV and HCV seroprevalence, but the odds ratios were not adjusted for

TABLE 1—Hepatitis C Virus (HCV) Seroconversion in Seattle Injection Drug Users in Relation to Enrollment Characteristics and Risk Behavior During a 1-Year Follow-Up Period

	HCV-Negative Subjects at Baseline		No. of HCV	Seroconversio
	n	%	Seroconverters	Risk, ^a %
Total	317	100.0	53	16.7
Sex				
Male	191	60.3	29	15.2
Female	126	39.7	24	19.0
Race/ethnicity				
African American	56	17.7	3	5.4
White/other	261	82.3	50	19.2
Age, y	201	02.0	33	10.2
≤24	79	24.9	18	22.8
25–34	144	45.4	24	16.7
35–44	73	23.0	8	11.0
55–44 ≥45	73 21		3	
	21	6.6	3	14.3
ives on the street or in a shelter	0.4	10.0	4.4	40.0
Yes	61	19.6	11	18.0
No	251	80.4	42	16.7
Years since first injection				
<2	77	29.8	21	27.3
2–5	80	31.0	10	12.5
>5	101	39.1	19	18.8
njected every day during 1 month				
before enrollment				
Yes	156	49.2	34	21.8
No	161	50.8	19	11.8
Usual drug injected	101	30.0	19	11.0
	206	66.7	36	17.5
Heroin alone or with cocaine	206			
Cocaine alone	97	31.4	14	14.4
Other drugs	6	1.9	1	16.7
At follow-up interview, last injection was				
In last 1 month	158	49.8	34	21.5
Since study enrollment, but not in last month	101	31.9	16	15.8
Before enrollment	58	18.3	3	5.2
Among Those Who F	Reported Any Injection	ons During Follow-Up I	Period (n = 259)	
Injected with a syringe previously used	eported Any injection	nis burning i onow-op i	Feriod (11=259)	
by another injector	4.4	F F	F	05.7
Usually or always	14	5.5	5	35.7
Sometimes	27	10.5	13	48.1
Rarely	85	33.2	19	22.4
Never	130	50.8	13	10.0
Used bleach to disinfect syringe previously				
used by another injector				
Yes, always or usually	52	41.3	14	26.9
No, never or inconsistently	74	58.7	23	31.1
Shared a drug cooker	•			
Yes	174	69.6	42	24.1
No	76	30.4	6	7.9
Shared filtration cotton	10	50.4	U	1.9
	454	60.4	40	00.5
Yes	151	60.4	40	26.5
No	99	39.6	8	8.1
Shared cooker or cotton				
Usually or always	73	29.1	18	24.7
Sometimes	43	17.1	11	25.6
Rarely	64	25.5	14	21.9
Never	71	28.3	5	7.0
Shared rinse water			-	-
Yes	120	48.0	27	22.5
No	130	52.0	21	16.2
Backloaded	100	JZ.U	41	10.2
	116	46.0	0.4	00.0
Yes	116	46.2	34	29.3
No	135	53.8	14	10.4

Note. Numbers may not sum to total because of missing data.

syringe sharing.²⁰ In a Baltimore study of injection drug users aged 18 to 29 years, HCV antibody seropositivity at study enrollment was

associated with recent backloading and sharing of cookers, cotton, or rinse water, but not after adjustment for use of new syringes. 9

Potential sources of bias in the study were examined. Study retention was not associated with the injection risk behavior we examined, so

^aCalculated as number of HCV seroconverters per 100 HCV-negative subjects.

TABLE 2—Risk of Hepatitis C Virus (HCV) Seroconversion in Seattle Injection Drug Users Associated With Sharing Equipment During 1-Year Follow-Up, Stratified According to Syringe Sharing

	No. HCV Negative at Baseline	No. HCV Converted at Follow-Up	% Converted	RR (95% CI)
Injected With a Syringe	Already Use	d by Another I	njection Drug	User
	(n = 126)	(n=37)		
Shared both cooker and cotton		<u></u>		
Yes	95	31	32.6	1.7
No	31	6	19.4	(0.8, 3.7)
Shared rinse water				
Yes	78	22	28.2	0.9
No	48	15	31.3	(0.5, 1.6)
Backloaded				, ,
Yes	90	31	34.4	2.1
No	36	6	16.7	(0.9, 4.5)
Did Not Inject With a Syri	nge Already L	Ised by Anothe	er Injection Dr	ua User
2.a	(n = 123)	(n = 11)	,	ag 000.
Shared both cooker and cotton	(20)	<u>()</u>		
Yes	50	8	16.0	3.8
No	72	3	4.2	(1.1, 13.8
Shared rinse water	. –			(111, 1010)
Yes	41	5	12.2	1.7
No	81	6	7.4	(0.5, 5.1)
Backloaded		-		(, 5)
Yes	26	3	11.5	1.4
	20			

Note. Includes only those who injected during the follow-up period. RR=risk ratio; CI = confidence interval.

-Calculation of the Attributable Risk Percentage (AR%) and the Population Attributable Risk Percentage (PAR%) for Syringe Sharing and Cooker/Cotton Sharing and Hepatitis C Virus (HCV) Seroconversion in Seattle Injection Drug Users

	Syringe Sharing		Cooker/Cotton Sharing Without Syringe Sharing	
	Proportion	%	Proportion	%
I _e I _u AR%	37/126 13/130	29 10 66	8/50 3/72	16 4 74
P _e (all seroconverters) PAR% (all injection drug users)	37/48	77 51	8/48	17 13
P _e (those who do not share syringes) PAR% (those who do not share syringes)			8/11	73 54

Note. I_a = incidence in the exposed (i.e., HCV incidence in injection drug users who practiced the risk behavior); I_u=incidence in the unexposed (i.e., HCV incidence in the referent population of injection drug users who did not practice the risk behavior); AR% = $(I_e^- - I_u)/I_e$; P_e = prevalence of the exposure in those with the disease (i.e., prevalence of risk behavior in the HCV seroconverters; PAR%– P_e^* AR%.

loss to follow-up could not have influenced our results to any important degree.²¹ We considered whether underreporting of syringe sharing might have led to the associations between cooker or cotton sharing and HCV infection. The finding of a small increase in risk associated with sharing rinse water may have been due to wording in the questionnaire, which did not specify whether potentially contaminated rinse

water was used to clean the syringe after injection. Similarly, we did not ask whether a sterile "draw syringe" was used during backloading, and this may have decreased our ability to detect any risk associated with this practice. In contrast, questions about sharing a cooker and cotton asked about using these materials after another injection drug user, and these practices were associated with higher risk of HCV seroconversion. There was no indication that the use of bleach to disinfect the syringe had any effect on the risk associated with syringe sharing; this is consistent with studies showing that the use of bleach has no effect on HIV transmission. 22,23

This pattern of results, coupled with the large magnitude of the risk ratios, makes it unlikely that bias could have caused us to identify safe injection behaviors as risk factors for HCV infection. Moreover, if underreporting of risk behavior were a serious source of bias in this study, we would have observed more infections among individuals who did not report any risk behavior. Our study's power to evaluate the risk of HCV associated with sharing a cooker, cotton, or rinse water or with backloading was reduced by the limited number of seroconverters (11) who did not share syringes. Practical difficulties in identifying a large cohort of HCV-negative injection drug users in combination with a high proportion who shared syringes reduced the number of subjects in our multivariate analysis.

In this study, the substantial risk of HCV associated with sharing syringes, cotton, and cookers, combined with the high proportion of injection drug users in the Seattle area who practice these behaviors, indicates that a sizable fraction of HCV infections among injection drug users in this population may result from using another injector's equipment. The impact of eliminating the sharing of syringes on the incidence of HCV appears particularly important, but eliminating the sharing of cookers and cotton among those who do not share syringes could also prevent a large fraction of infections. Protecting oneself and other drug injectors from HCV infection and its long-term consequences may require consistent adherence to a rather strict injection hygiene regimen. Effective risk reduction education messages should be developed and evaluated that stress not sharing cookers and filtration cotton as well as not reusing another person's syringe. \Box

Contributors

H. Hagan directed the study and analyzed the data. All authors contributed to the study design, data interpretation, and writing of the paper.

Acknowledgments

This study was funded by the National Institute on Drug Abuse (1R01DA08023 and 1F31DA05680), the Centers for Disease Control and Prevention (U62/ CCU006260), and the Association of Schools of Public Health (S425-16/16).

We would like to acknowledge the contribution of the staff of the RAVEN Study, particularly for their work to achieve excellence in data collection and data management and for their service to the study population.

This paper is dedicated to the late Dr Noreen V. Harris, who was the original principal investigator for the RAVEN Study.

References

- van den Hoek JAR, van Haastrecht HJA, Goudsmit J, de Wolf F, Coutinho RA. Prevalence, incidence and risk factors of hepatitis C virus infection among drug users in Amsterdam. *J Infect Dis.* 1990;162:823–826.
- 2. Chamot E, de Saussure P, Hirschel B, Deglon JJ, Perrin LH. Incidence of hepatitis C, hepatitis B and HIV infections among drug users in a methadone-maintenance programme. *AIDS*. 1992;6:430–431.
- van Ameijden EJC, van den Hoek JAR, Mientjes GHC, 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
- Crofts N, Hopper J, Bowden DS, Breschkin AM, Milner R, Locarnini S. Hepatitis C virus infection among a cohort of Victorian injecting drug users. *Med J Aust*. 1993;159:237–241.
- Levine OS, Vlahov D, Nelson KE. Epidemiology of hepatitis B virus infections among injecting drug users: seroprevalence, risk factors and viral interactions. *Epidemiol Rev.* 1994;16: 418–436
- Esteban JL, Lopez-Talavera JC, Genesca J, et al. High rate of infectivity and liver disease in blood donors with antibodies to hepatitis C virus. *Ann Intern Med.* 1991;115:443–449.
- 7. 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.
- van Beek I, Dwyer R, Dore GJ, Luo K, Kaldor JM. Infection with HIV and hepatitis C virus among injecting drug users in a prevention setting: retrospective cohort study. *BMJ*. 1998;317: 433–437.
- Garfein RS, Doherty MC, Monterroso ER, Thomas EL, 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.
- Hagan H, Des Jarlais DC, Friedman SR, Purchase D, Alter MJ. Reduced risk of hepatitis B and hepatitis C among participants in the Tacoma syringe exchange. *Am J Public Health*. 1995;85:1531–1537.
- Rezza G, Sagliocca L, Zaccarelli M, Nespoli M, Siconolfi M, Baldassarre C. Incidence rate and risk factors for HCV seroconversion among injecting drug users in an area with low HIV seroprevalence. Scand J Infect Dis. 1996;28:27–29.
- Des Jarlais DC. The first and second decades of AIDS among injecting drug users. *Br J Addict*. 1992:87:347–353.
- Grund JP, Friedman SR, Stern LS, et al. Syringemediated drug sharing among injecting drug users: patterns, social context and implications for transmission of blood-borne pathogens. Soc Sci Med. 1996;42:691–703.
- Rothman KJ. Modern Epidemiology. Boston, Mass: Little, Brown and Co; 1986.
- Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiologic Research: Principles and Meth-

- ods. New York, NY: Van Nostrand Reinhold Co; 1982:244.
- Cole P, MacMahon B. Attributable risk percent in case-control studies. Br J Prev Soc Med. 1971; 25:242–244.
- 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.
- Koester SK, Hoffer L. "Indirect sharing": additional HIV risks associated with drug injection. *AIDS Public Policy J.* 1994;9:100–105.
- Jose B, Friedman SR, Neaigus A, et al. Syringemediated drug-sharing (backloading): a new risk factor for HIV among injecting drug users. *AIDS*. 1993;7:1653–1660.
- Stark K, Muller R, Bienzle U, Guggenmoos-Holzmann I. Frontloading: a risk factor for HIV and hepatitis C virus infection among injecting drug users in Berlin. AIDS. 1996;10: 311–317.
- Greenland S. Response and follow-up bias in cohort studies. Am J Epidemiol. 1977;106: 184–187.
- Vlahov D, Astemborski J, Solomon L, Nelson KE. Field effectiveness of needle disinfection among injecting drug users. *J Acquir Immune Defic Syndr*. 1994;7:760–766.
- Titus S, Marmor M, Des Jarlais DC, Kim M, Wolfe H, Beatrice S. Bleach use and HIV seroconversion among New York City injection drug users. J Acquir Immune Defic Syndr. 1994;7: 700–704.

American Journal of Public Health January 2001, Vol. 91, No. 1