Opportunities for Prevention: Hepatitis C Prevalence and Incidence in a Cohort of Young Injection Drug Users

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The objective of this study was to compare sociodemographic, drug, and sexual risk characteristics between hepatitis C virus (HCV) baseline positive and negative young (13-24 years) injection drug users (IDUs) and to determine prospective risk factors for HCV seroconversion among the youth. Data were collected through the Vancouver Injection Drug Users Study (VIDUS). To date, more than 1,400 Vancouver-area IDUs have been enrolled and followed up; 234 were aged 24 years and younger. Semiannually, participants have completed an interviewer-administered questionnaire and have undergone serologic testing for human immunodeficiency virus (HIV) and HCV. Univariate and multivariate logistic regression analyses were undertaken to investigate predictors of baseline HCV positivity. In the multivariate analyses, Cox regression models with time-dependent covariates were used to identify predictors of HCV seroconversion. Of the 232 young injectors, 107 (46%) were HCV positive at baseline and a further 37 HCV seroconverted during the study period for an incidence rate of 37.3 per 100 person-years. Baseline positivity was associated with Aboriginal ancestry, older age, greater number of years injecting drugs, recent incarceration, sex trade work, more than 100 lifetime sexual partners, a previous sexually transmitted disease, living in the IDU epicenter, and injection more than once per day of heroin, cocaine, and speedball. Factors independently associated with HCV seroconversion were having a partner who uses injection drugs, requiring help to inject, and injection of cocaine more than once daily. In conclusion, unlike older IDUs, more than one half of young injectors were HCV negative at recruitment. Thus, there is a window of opportunity for prevention. However, the incidence rate of HCV among these young IDUs is alarming, suggesting that the opportunity to intervene is exceedingly small. (HEPATOLOGY **2002;36:737-742.**)

In North America, the leading cause of hepatitis C infection (HCV) is the sharing of contaminated equipment between injection drug users (IDUs).[1] The incidence of HCV infection among populations of IDUs ranges from 4.2 to 22.0[2-6] per 100 person-years, and the estimates of prevalence are between 30% and 90%.[2-4,7,8] Due to the rapid acquisition of HCV infection following initiation into use of intravenous drugs, young IDUs or recent injection initiates represent an important group for prevention of HCV. This may be particularly important in urban areas experiencing a high prevalence of blood-borne infections among IDU populations. Studies have shown that younger IDUs engage in high-risk behaviors to a greater extent than established users, which increases their vulnerability to blood-borne infections.[9,10]

The principal route for HCV infection among IDUs is using someone else's contaminated needle and/or other drug use equipment.[1,11] Young IDUs may have a lower antibody to HCV (anti-HCV) seroprevalence than older IDUs due to more recent initiation into injection drug use.[11] However, younger IDUs may share needles and other injection equipment more so than older IDUs.[12,13] Furthermore, younger IDUs may be more likely to have casual sexual partners, engage in sex trade work, and use

Abbreviations: HCV, hepatitis C virus; IDU, injection drug user; anti-HCV, antibody to hepatitis C virus; HIV, human immunodeficiency virus; VIDUS, Vancouver Injection Drug Users Study; RR, relative risk; CI, confidence interval; IQR, interquartile range.

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condoms inconsistently.[13-15] Thus, in addition to parenteral risk, young IDUs may engage in sexual behaviors that have been presumed to be risk factors for infection.[16]

Vancouver, Canada, has experienced an explosive epidemic of human immunodeficiency virus (HIV) and extensive spread of HCV among IDUs. Little is known about recent initiates and young IDUs. Identifying risk factors for HCV infection among young IDUs may provide important prevention clues for cities coping with outbreaks of blood-borne infections among IDU populations. We undertook this study to estimate the prevalence and incidence of HCV infection among IDUs aged 24 years and younger and to characterize sociodemographic characteristics and risk factors for HCV among the young IDU.

Patients and Methods

Data were collected within a prospective open cohort study of IDUs, the Vancouver Injection Drug Users Study (VIDUS). A description of this study has been previously published.[17] VIDUS has recruited more than 1,400 Vancouver-area IDUs since May 1996. The study office is located in a storefront in the downtown eastside of Vancouver. The downtown eastside is Vancouver's poorest neighborhood, where an estimated 5,000 IDUs reside in an area of approximately 10 city blocks; inexpensive housing in the form of hotels and single room occupancies abound.

Eligibility criteria included residing in the city of Vancouver and surrounding municipalities, having injected in the previous month, and aged 13 years and older. Participants were administered a questionnaire by trained nurse-interviewers and were eligible to return for follow-up every 6 months. At each visit, eligible participants were tested for HIV and HCV antibodies through a venous blood sample. This study was approved by the St. Paul's Hospital Committee on Human Experimentation.

Instrument. The VIDUS questionnaire is administered by trained nurses and interviewers and elicits information regarding sociodemographic, sexual, and drug risk characteristics. Continuous variables were elicited in reference to the 6 months before the interview. This includes the variables of sex trade work, frequency of injection, incarceration, housing situation, sexual behaviors, needle and equipment sharing, and help injecting. Sex trade work was defined as trading sex for money, drugs, or shelter. Needing help injecting was defined as ever requiring someone's help to inject drugs in the previous 6 months. The variable of other equipment includes cookers, cottons, spoons, and all other injection equipment aside from needles. Unstable housing was defined as living on the street or in a shelter, jail, hostel, or hotel.

Statistical Analysis. For the purposes of this study, young injectors were defined as those aged 24 years or younger at the time of recruitment. The rationale for the age cutoff is based on the age criterion for youth and/or adolescence used in reports on HIV/acquired immunodeficiency syndrome generated by the United Nations and the Centers for Disease Control in the United States and Canada.[18-20] Young injectors identified at baseline as anti-HCV positive were compared with baseline anti-HCV–negative youth using contingency table analysis. χ^2 and Fisher exact test were used to compare categorical variables, and the Wilcoxon rank sum test was used to compare continuous variables. Logistic regression models were used to identify independent predictors of baseline HCV positivity. Variables significant at $P < .05$ in univariate analyses were included in an unconditional logistic regression model. All reported P values were 2-sided.

Youth who became anti-HCV positive during the study period were compared with youth who remained HCV negative and had at least one follow-up visit. The date of seroconversion was estimated using the midpoint between the last negative and the first positive antibody test result. Cumulative incidence rates of HCV infection were calculated using Kaplan-Meier methods. In these analyses, time 0 was defined as the date of enrollment. Participants who consistently remained seronegative were considered to be right censored at the time of their most recent test result. Annual rates of HCV seroconversion were calculated with actuarial methods. Relative risks (RR) and 95% confidence intervals (CI) were obtained for risk factors of interest. Adjusted and unadjusted time-dependent Cox regression models were used to identify risk associations with HCV seroconversion among the young participants. All P values reported were 2-sided.

Results

Of the 1,437 participants enrolled in VIDUS, 232 were aged 13 to 24 years (median, 21 years) at baseline. Almost half of the young participants (107 [46%]) were HCV positive at baseline, their median age was 22 years (interquartile range [IQR], 20-23 years), and they had been injecting for a median of 4 years (IQR, 2-7 years). The median age of HCV-negative youth was 20 years (IQR, 18-22 years), and they had been injecting for a median of 1.3 years (IQR, 0.3-3 years).

Table 1 compares baseline sociodemographic, drug, and sexual risk variables between anti-HCV–positive and anti-HCV–negative youth. Baseline-positive youth were older, and their risk of being HCV positive more than doubled per 2-year increase in the number of years the youth had been injecting. As would be expected, HCV-positive youth were more likely to be infected with HIV

Table 1. A Comparison of Sociodemographic and Risk Variables Between Baseline HCV-Positive and -Negative Young IDUs

	HCV Positive (107, 46%)	HCV Negative (127, 54%)	Odds Ratios (95% CI)	*P*
Age (yr)				
≥19	15 (14)	46 (36)	1	.001
20-24	92 (86)	81 (64)	3.5 (1.8, 6.6)	
Years injecting				
0-1	21 (20)	65 (51)	1	.001
2-3	20 (19)	31 (24)	2.0 (0.9, 4.2)	
4-5	26 (24)	19 (15)	4.2 (2.0, 9.0)	
≥6	40 (37)	12 (9)	10.3 (4.8, 22.1)	
Female	55 (51)	63 (50)	1.1 (0.6, 1.8)	.784
Aboriginal ancestry	40 (37)	17 (13)	3.9 (2.1, 7.2)	.001
HIV positive	21 (9)	4 (2)	7.5 (2.8, 19.9)	.001
Incarceration	43 (40)	30 (24)	2.2 (1.2, 3.8)	.006
≥1 per day heroin	56 (52)	45 (35)	2.0 (1.2, 3.4)	.009
≥1 per day cocaine	43 (40)	22 (17)	3.2 (1.8, 5.8)	.001
≥1 per day speedball	20 (19)	8 (6)	3.4 (1.5, 7.8)	.004
≥1 per day crack	12 (11)	14 (11)	1.0 (0.4, 2.3)	.963
Needle borrowing	45 (42)	52 (41)	1.0 (0.6, 1.8)	.864
Sharing equipment	85 (79)	100 (79)	1.0 (0.6, 2.0)	.896
Help injecting	50 (47)	75 (59)	0.6 (0.4, 1.0)	.060
Sex trade	57 (53)	40 (32)	2.5 (1.5, 4.2)	.001
>100 lifetime partners	43 (40)	33 (26)	1.9 (1.1, 3.3)	.021
Condom with regular sex partners	15 (14)	26 (20)	0.6 (0.3, 1.3)	.196
Condom with casual sex partners	25 (23)	36 (28)	0.8 (0.4, 1.4)	.387
Condom with client sex partners	40 (37)	38 (30)	1.4 (0.8, 2.4)	.228
Previous sexually transmitted disease	46 (43)	35 (28)	2.0 (1.6, 3.4)	.013
Residing in downtown eastside	57 (53)	42 (33)	2.3 (1.4, 3.9)	.002

NOTE. IDUs were aged 24 years or younger. n = 234. All continuous variables are elicited in reference to the previous 6 months at the time of interview. All reported *P* values are 2-sided. Mantel-Haenszel method.

than HCV-negative youth. HCV-positive youth were more likely to be of Aboriginal ethnicity (37% vs. 13%; $P = .001$), have been incarcerated in the previous 6 months (40% vs. 24%; $P = .006$), engaged in sex trade work (53% vs. 32%; $P = .001$), have more than 100 lifetime sexual partners (40% vs. 26%; $P = .021$), have had previous sexually transmitted disease(s) (43% vs. 28%; $P = .013$), reside in the IDU epicenter (53% vs. 33%; $P = .002$), and inject heroin (52% vs. 35%; $P = .009$), cocaine (40% vs. 17%; $P = .001$), and speedballs daily (19% vs. 65%; $P = .004$). There was no difference between anti-HCV–positive and anti-HCV–negative youth with respect to always using condoms with regular (14% vs. 20%; $P = .196$), casual (23% vs. 28%; $P = .387$), and client sexual partners (37% vs. 30%; $P = .228$); using crack cocaine daily (11% vs. 11%; $P = .963$); being female (51% vs. 50%; $P = .784$); borrowing needles (42% vs. 41%; $P = .864$); or sharing other drug equipment (79% vs. 79%; $P = .896$).

Table 2 presents the results of our logistic regression modeling. Baseline anti-HCV positivity among the youth was independently associated with older age (OR, 1.29; CI, 1.11, 1.49), a greater number of years injecting (OR, 1.27; CI, 1.12, 1.42), daily injection of cocaine (OR, 2.58; CI, 1.30, 5.15), and sex trade work (OR, 2.30; CI, 1.21, 4.37).

There were 76 youth who had follow-up data and 51 who were lost to follow-up. There was no difference between the youth who returned for follow-up and those who did not with respect to female sex, those engaged in sex trade work, age, years injecting, incarceration in the previous 6 months, or types of drugs used. Aboriginal youth were significantly more likely than non-Aboriginal youth to return for follow-up visits.

Of the 76 HCV-negative youth that had follow-up data, 37 (49%) became anti-HCV positive over the study period for an incidence rate of 37.3 (CI, 26.2, 51.4) per 100 person-years. There was no difference between those who became HCV seropositive and those who remained negative with respect to female sex (62% vs. 51%; $P = .339$), Aboriginal ethnicity (19% vs. 18%; $P = .913$), and

Table 2. Logistic Regression Determining Associations of Anti-HCV Seroprevalence Among the Young IDUs in the VIDUS Cohort

Variable	Adjusted Odds Ratios (95% CI)
Age per year	1.29 (1.11, 1.49)
Years injecting per year	1.27 (1.12, 1.42)
Frequent cocaine injection ≥1 per day	2.58 (1.30, 5.15)
Sex trade yes vs. no	2.30 (1.21, 4.37)

NOTE. "Young" defined as aged 24 years or younger.

Table 3. Risk Associations for the Young IDU Who Tested Anti-HCV Positive During the Study Period

Characteristic	Risk Ratio (95% CI)	Adjusted Risk Ratio (95% CI)
Unstable housing	1.88 (0.93, 3.81)	1.86 (0.85, 4.03)
≥1 daily Heroin	2.07 (1.03, 4.15)	1.39 (0.63, 3.04)
≥1 daily cocaine	4.52 (2.23, 9.18)	3.04 (1.20, 7.70)
≥1 daily speedball	2.76 (1.05, 7.31)	1.01 (0.29, 3.37)
IDU partner	2.71 (1.35, 5.57)	2.48 (1.08, 5.66)
Previous sexually transmitted disease	1.91 (0.95, 3.85)	1.42 (0.60, 3.38)
Need help injecting	2.24 (1.09, 4.60)	2.48 (1.08, 5.66)
Borrowing needles	2.57 (1.27, 5.21)	1.13 (0.47, 2.73)

NOTE. All continuous variables are elicited in reference to the previous 6 months at the interview before seroconversion. Only the variables that reached marginal significance or significance are reported in the table. "Young" defined as aged 24 years or younger.

median age (20 years [IQR, 19-22 years] vs. 20 years [IQR, 18-22 years]). However, number of years injecting was higher among the seroconverters (2 years [IQR, 0.5-4 years] vs. 1 year [IQR, 0.5-3 years]) for those who remained negative.

Table 3 shows the results of our Cox regression model identifying risk associations with HCV seroconversion among the youth. Only variables that reached marginal significance or significance are shown in Table 3. Unadjusted risk associations for HCV seroconversion among the youth were daily heroin (RR, 2.07; CI, 1.03, 4.15), cocaine (RR, 4.52; CI, 2.23, 9.18), and speedball injection (RR, 2.76; CI, 1.05, 7.31); having a partner who uses injection drugs (RR, 2.71; CI, 1.35, 5.57); requiring help when injecting (RR, 2.24; CI, 1.09, 4.60); and borrowing needles (RR, 2.57; CI, 1.27, 5.21). In the adjusted model, the variables that remained significant were cocaine use (RR, 3.04; CI, 1.20, 7.70), having a partner who uses injection drugs (RR, 2.48; CI, 1.08, 5.66), and requiring help when injecting (RR, 2.48; CI, 1.08, 5.66).

Discussion

The HCV incidence rate of 37.3 per person-years among these young IDUs is alarming. One half of those who became HCV positive did so within the first 2 years of their injection career. This finding underscores the need for targeted interventions among new initiates in the early stage of injection drug use. Recent findings indicating the potential reversibility of HCV infection after exposure using interferon therapy are encouraging.[21] Treatment opportunities for HCV infection will be particularly important for young users given the rapid rates of HCV seroconversion that occur among IDU populations.[3,11]

In recent studies of young IDUs, Hahn et al. identified an HCV incidence rate of 11 per 100 person-years in San Francisco, whereas incidence rates of 16 and 23 per 100 person-years were found in Baltimore.[9,11] In all of these studies, "young" was defined as aged 30 years and younger. We found an anti-HCV prevalence of 46% at baseline in VIDUS, similar to the San Francisco cohort when restricted to 24 years and younger; however, our incidence rate was much higher. For every 2 years the youth continue to inject, their risk of being HCV positive doubles; thus, those who have been injecting for 6 or more years are 10 times more likely to be HCV positive. In the San Francisco, Baltimore, and Vancouver studies, greater number of years injecting was associated with HCV positivity.

We found a significant association between HCV positivity and HIV infection. Among HIV-positive youth, the prevalence of HCV at baseline was 88%, suggesting that coinfection will be an almost-universal problem among these young HIV-infected IDUs. It may be the case that interventions such as safe injection rooms, which have shown success in reducing risk behaviors, may help reduce the incidence of HIV and HCV among young IDUs in endemic cities.[22]

Females accounted for one half of the baseline HCV prevalent cases and 63% of the incident cases. In unadjusted and adjusted analyses, associations with seroconversion included requiring help to inject in the previous 6 months and having an IDU sex partner. Furthermore, although condom use did not reach statistical significance in our analyses, use of condoms in all sexual partnerships is well below 40% in this young cohort and sexual transmission should not be ruled out. Although other studies have suggested that intimate partnerships may be protective against blood-borne infections,[11] our findings suggest that young female IDUs may be at increased risk for HCV infection both through sexual and parenteral risk from their intimate partners. This may be particularly important for young IDUs because sexual partnerships may be less stable. Education and intervention programs among high-risk youth that address both sexual and drug risks may contribute to reducing blood-borne infections among youth who use injection drugs.

Frequency of injection, or injecting at least daily, was associated with HCV infection in Vancouver, Baltimore, and San Francisco among young IDUs.[9,11] Cocaine use has been a persistent risk factor for blood-borne infection among the VIDUS cohort, likely due to the increased frequency of injection that is characteristic of injection cocaine use.[17,23,24] However, many of the youth were also using heroin and speedballs along with cocaine on a daily basis. The amount of daily polydrug use occurring among these young injectors is concerning and warrants further investigation.

In previous studies of these young IDUs, we found high rates of sexual abuse and participation in sex trade work.[25] Sex trade work was again associated with baseline HCV prevalence. The links between childhood victimization, violence in the sex trade, and high-risk drug-using behaviors such as frequent polydrug use should not be ignored in considering intervention and treatment programs for young IDUs.

High and increasing rates of HCV have been found in Canadian prison populations.[26] We found an association between HCV prevalence and incarceration in the previous 6 months. Incarceration did not come out as a predictor of HCV seroconversion; therefore, we were unable to directly associate incarceration and HCV seropositivity. However, these data raise serious concerns about the potential for blood-borne infection transmission among young IDUs within the prison system.

In our study, almost 80% of the youth reported sharing ancillary drug equipment. This risk factor did not reach statistical significance, most likely because this behavior was saturated among these young IDUs; however, transmission through shared ancillary equipment should not be ruled out. The study by Hagan et al. showed a strong association between HCV seroconversion and sharing ancillary drug equipment.[6] For IDUs recently initiating injection use, the message that blood-borne infections, particularly HCV, can be transmitted through ancillary equipment may not have been heard, possibly because young IDUs are less likely to access services and therefore receive education and prevention information. Another reason for high proportions of sharing drug equipment among young IDUs could be the nature of their social network systems, which may be characterized by trust and sharing. Given the high-risk nature of sharing drug preparation equipment and the high proportion of youth reporting this behavior, youth-specific services such as peer group intervention programs may help reduce sharing equipment among this vulnerable population.

HCV prevalence was associated with living in the downtown eastside of Vancouver, the IDU epicenter. It has been argued that public policies concentrating IDUs into one small area within an urban setting have contributed to the rapid spread of blood-borne infections among IDU populations.[23] It is concerning that many of the youth reported residing within the IDU epicenter. It is likely that the lack of affordable housing options for high-risk youth outside of the IDU epicenter has contributed to this high incidence rate of HCV infection.

Needle borrowing in the 6 months before interview was reported among 40% of the youth, a finding similar to that of young IDUs in other cities with well-supported needle exchange programs.[9,13] Although it may be encouraging that more than one half of the young IDUs reported not sharing needles, other interventions are clearly required for those who continue to share. Borrowing needles was associated with HCV seroconversion univariately; however, it did not remain in the final model. Borrowing needles is likely the most efficient means for contracting HCV among IDUs; however, socially desirable responses may explain why it was not a direct measure of risk in this cohort. HCV seroconversion may also be explained by the high number of youth who reported sharing ancillary drug equipment. Interventions such as safe injection rooms may be particularly important for young IDUs to provide education on safe injection practices and clean equipment.

This study has several limitations that should be noted. We have included cross-sectional data of the baseline HCV prevalent youth to characterize young IDUs who may be most at risk and the types of behaviors in which they may be engaged; however, causal inference based on cross-sectional data need to be interpreted with care. Furthermore, the study instrument did not address the practices of tattooing and body piercing, which have been shown to be associated with HCV infection.[27] Another important limitation concerns generalizability. As with other observational studies with voluntary recruitment, our study may have limited potential for generalization. Although our results are not applicable to general populations, they likely reflect urban centers with a high prevalence of IDUs and HCV infections among these populations. We know of no difference in sampling for the VIDUS project that may have selected for any specific youth characteristics that may differ from other young IDUs. Nevertheless, because this is not a probability sample, bias in recruitment is always possible. As in most studies of IDUs, our study was based on self-reported behaviors and caution should be exercised in the interpretation of such data. Other studies of IDUs have found that socially desirable responses had only a negligible effect on the responses concerning risk behaviors for infection.[28]

For young IDUs living in endemic cities, the window of opportunity for HCV prevention is narrow. The links between high-risk polydrug use, unstable housing, sex trade work, and sexual partnership vulnerability should not be ignored. The complexities of these risk associations require a complex response. Although access to sterile syringes has reduced the transmission of blood-borne infections, we need to complement this service with others that address housing, vulnerability among peer group networks, condom use in intimate and casual partnerships, and the dynamic drug-using relationships of those who require help when injecting.

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