Hepatitis C Virus Seroconversion among Young Injection Drug Users: Relationships and Risks

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The present study examined reasons for the high incidence of hepatitis C virus (HCV) infection among young injection drug users (IDUs). IDUs <30 years old who tested negative for HCV antibody were enrolled in a prospective cohort. Risk factors for seroconversion were examined using time-dependent regression analyses: 48 of 195 IDUs seroconverted to HCV, for an incidence rate of 25.1/100 person-years (95% confidence interval, 18.7–32.9/100 person-years). Independent risk factors included sharing needles with an HCV-infected sex partner (borderline statistical significance, P = .11) or a person who was not a sex partner, sharing nonsterile drug-preparation equipment, pooling money with another IDU to buy drugs, and exchanging sex for money. Ubiquitous behaviors among young IDUs, such as the forming of injecting or sexual partnerships and consequent sharing of needles and drug preparation equipment, are risk factors for HCV. Interventions to reduce HCV transmission must recognize the importance of relationships on injecting risk.

Hepatitis C virus (HCV) infection is highly prevalent (50%–95%) among injection drug users (IDUs) and is transmitted via contaminated needles and syringes. Although the frequency of injecting with a needle and syringe previously used by someone else (“needle borrowing” or “needle sharing”) has decreased during the past 15 years [1–6], HCV incidence rates continue to be high [7–14].

Although young IDUs use needle exchanges at high rates [15], recent estimates of the incidence of HCV infection among IDUs <30 years old have been in the range of 10–23/100 person-years [7, 8, 13–16], comparable to rates of 10–13/100 person-years among IDUs of all ages in pre-needle exchange studies [10, 11]. Young IDUs continue to report needle borrowing, perhaps as a result of strict paraphernalia laws that discourage IDUs from carrying their own sterile equipment [17, 18]. However, needle borrowing may also persist for social reasons, including, for example, the obligation of reciprocity and the need to demonstrate trust in relationships based on obtaining drugs [19–21] and in sexual partnerships [22, 23]. Ethnographic data suggest that both partnerships and larger social groups based on obtaining drugs provide companionship and safety and facilitate drug purchasing [20]. However, they may also provide the social context for injecting risk [18, 20, 21].

In addition to needle sharing, injecting partners may prepare, divide, and inject drugs together [18, 24–27], and sharing of both needles and drug-preparation equipment is likely to occur in these group-injecting settings. Sharing drug-preparation equipment is very common among IDUs in the United States [27, 28] and has been associated with HCV infection in 3 cross-sectional studies [16, 29, 30] and 2 prospective studies [7, 13, 14]. The process of backloading—that is, dividing dissolved drug by using one syringe to squirt drug solution into the back of other syringes—may also occur in group-injecting settings. Backloading is more common among younger IDUs than among older IDUs [31] and has been described as a risk factor for HCV infection in several studies [7, 16, 32, 33].

We conducted a prospective epidemiological study of young IDUs in San Francisco, to examine the reasons for the continuing high risk of HCV infection. We set out to explore the relationship between HCV seroconversion and sharing needles and, at the same time, to examine other behaviors that might expose young IDUs to contaminated blood, including sharing drug-preparation equipment, backloading, injecting others, and being injected by others. In addition, we examined the type of partner from whom needles were borrowed (sexual or otherwise) and considered the risk behavior of pooling money to
Materials and Methods

From 1 January 2000 through 30 September 2001, we tested persons <30 years old who had injected drugs during the previous month for HCV, to screen for a prospective cohort study of HCV seroconversion. Recruitment done was by outreach workers and by word of mouth. HCV-negative participants were invited to enroll in the cohort and were scheduled for retesting and reinterviewing every 3 months. All testing included pre- and posttest counseling. Intensive contact information was recorded to assist in tracking. Participants were reimbursed $10 for completing an interview and $20 for returning for serologic test results at screening and at follow-up.

Participants were interviewed, and blood was drawn and tested for HCV at screening and at cohort follow-up visits. The questionnaire included demographic information and drug-use behaviors in the previous 3 months. Drug-use behaviors included frequency of injecting, drugs injected, borrowing a needle/syringe, pooling money to buy drugs, and backloading. Drug-preparation equipment investigated included cookers, spoons, or baggies in which drugs are dissolved; cotton used to filter impurities from drug solutions; and water used to dissolve drugs or rinse needles and syringes. Participants were asked whether they had used drug-preparation equipment in which someone else's needle/syringe had already been or injected the residue from a cooker or cotton. Those who responded in the affirmative were further asked whether any of the needles that had previously been used with this equipment were dirty (sharing “nonsterile” drug-preparation equipment).

The study also included an ethnographic component. The ethnographer observed instances of drug purchasing, preparing, and injecting and spent many hours interacting with young IDUs in their usual environments, using participant-observation methods [34]. She focused on the behaviors related to pooling money to buy drugs and the patterns of young female IDUs in sexual relationships.

Anti-HCV was detected using a second generation EIA (EIA-2; Abbott Laboratories). Specimens found to be initially reactive by EIA-2 were repeated in duplicate. Repeat reactive samples were assumed to be seropositive. All specimens that were EIA-2 negative were retested using EIA-3 (Ortho Clinical Diagnostics), a test with enhanced sensitivity [35, 36] and specificity [37]. EIA-3 reactive samples were confirmed using the HCV RIBA-3.0 test system (Chiron). In addition, all EIA-2- and EIA-3-negative specimens were tested for presence of HCV RNA using the Procleix, HIV-1/HCV Assay (Gen-Probe). This highly sensitive assay is currently used in US blood banks to detect HCV infection before the development of detectable HCV antibody [38, 39]. HCV seroconverters were defined as persons who tested EIA-2- or EIA-3-positive after having previously tested negative on both tests. The date of putative HCV transmission used in the analyses was the midpoint between the last negative HCV antibody test and the first positive HCV antibody test. For 22 of 48 HCV seroconversions, HCV RNA was detected on the visit prior to antibody seroconversion using the Procleix Assay (TMA), and, for these cases, the date of transmission was 30 days prior to the first positive TMA test result. This date is used because the period in which HCV RNA is detectable but HCV antibody is not detectable is, on average, 60 days [40]. Specimens were also tested for antibody to human immunodeficiency virus (HIV) and markers of hepatitis B virus (HBV) infection, as described elsewhere [15].

For statistical analyses, we compared how cohort enrollees who had at least 1 follow-up visit by 31 December 2001 differed from those who had none and report P values from χ² tests of association or Kruskal-Wallis tests (for continuous variables). HCV seroconversion rates, overall and by the variables of interest, were calculated using person-time of observation, and confidence intervals (CIs) for the rates were calculated under the assumption of an exponential distribution. Behaviors reported at the time of the last HCV-negative blood sampling were used for nonseroconverters; behaviors reported at the time of the first HCV-positive blood sampling (TMA-positive or EIA-2-positive) were used for seroconverters. We calculated hazards ratios (HRs), to compare the rates between levels of time-dependent behaviors using Cox proportional-hazards regression-counting process methods. Several persons ceased injecting for at least one 3-month time period in the study, and these time intervals during which no injecting risk occurred were excluded from the analyses of risk factors for seroconversion. To further examine needle borrowing, we created a composite variable that reflected the partnership and HCV status of the person from whom needles were borrowed. We included that variable in a multivariate time-dependent Cox regression model in addition to the other variables for which at least 1 level was associated with HCV seroconversion in bivariate analysis, with P < .05.

Results

A total of 776 persons were screened for anti-HCV, and 472 (61%) tested negative by EIA-2. Of these, 389 (82%) returned to receive their serologic test results, and 291 (75%) of those enrolled in the cohort: 195 (67%) returned for at least 1 follow-up visit, and the total observation time (to seroconversion or remaining HCV negative) was 191 person-years. Forty-eight persons seroconverted to HCV, for a seroconversion rate of 25.1/100 person-years (95% CI, 18.7–32.9/100 person-years).

The median age of the participants was 22 years (interquartile range [IQR], 19–25 years), 64% were male, 80% were white, and median duration of stay in San Francisco before the study was 5 months (IQR, 1–24 months). Two percent of the participants were HIV positive, and 14% had evidence of exposure to HBV (HBV surface antibody, core antibody, or antigen positive). Sixty-seven percent had ever borrowed a needle/syringe, and 85% had ever shared drug-preparation equipment.

Ninety-six enrolled participants completed no follow-up because they moved away from San Francisco (n = 50), died (n = 1), withdrew from the study (n = 6), or were lost to follow-up (n = 39). Those 96 subjects were similar (P ≥ .05) to those who completed follow-up by sex, age, race, number of
years injecting, homelessness, drug injected most often during the prior 30 days, ever or recently (prior 3 months) borrowed a needle, ever or recently shared drug-preparation equipment, recently backloaded, recently pooled money to buy drugs, HCV status of main sex partner, and HIV serostatus. Those who did not complete follow-up had spent significantly less time in San Francisco prior to the interview (median, 1 month; IQR, 0.3–5 months) than those who did complete follow-up (median, 5 months; IQR, 0.7–24 months; \( P < .01 \)) and were more likely to have been traveling during the prior 3 months (79% vs. 55%; \( P < .01 \)). Those without follow-up had injected for fewer days during the prior month (median, 15 days [IQR, 7–29 days] vs. median, 22 days [IQR, 10–30 days]; \( P < .01 \)).

Risk factors for seroconversion. Twenty-three participants stopped injecting for a total of 42 3-month follow-up intervals, and there were no HCV seroconversions during these intervals (95% CI, 0.9–7/100 person-years). Analyses excluded the periods with no injecting risk, so that 195 baseline and 434 follow-up interviews were used in the current analyses.

HCV seroconversion was not significantly associated with age, race, years of injection drug use, or homelessness, although the incidence rate was somewhat elevated (with borderline statistical significance) for the oldest and longest-duration injectors (table 1). The incidence rate was higher for young women than for young men and for those who had spent time in jail or prison during the previous 3 months, but these differences did not reach statistical significance.

Borrowing a needle at least once during the most recent 3-month observation period was associated with increased risk, but the trend in risk with number of persons from whom needles were borrowed was not statistically significant (table 1). Having a main sex partner who was an IDU was associated with needle borrowing (\( P = .01 \)), and we created strata depending on whose needle was borrowed (table 1). HCV seroconversion was significantly increased among those who had borrowed from an infected main sex partner and among those who had borrowed from someone who was not a sex partner (with borderline statistical significance), compared with those who borrowed from an HCV-negative main sex partner or a main sex partner whose HCV status was unknown.

We examined sharing drug-preparation equipment (defined as sharing cookers, cottons, or rinse water or injecting the residue from a cooker or cotton), stratified by the reported sterility of the drug preparation equipment. Sharing drug-preparation equipment was reported by 61.5% of subjects at their last interview, and, of these, 46.7% had used only sterile equipment, whereas the remaining 53.3% had shared nonsterile drug-preparation equipment. The risk of HCV infection was not increased for sharing sterile drug-preparation equipment but was significantly increased for sharing nonsterile drug-preparation equipment (table 1). Sharing nonsterile drug-preparation equipment was associated with having a main sex partner who was an IDU (\( P < .01 \)). Backloading was associated with HCV seroconversion on bivariate analysis, with borderline statistical significance. This association did not differ by the sterility of the needle used to backload (data not shown).

Pooling money with one person to buy drugs was a risk factor for seroconversion. We further examined pooling money to buy drugs. At a follow-up interview, 93% of IDUs reported that, the last time they pooled money to buy drugs with another person, they also injected with that person. Pooling money to buy drugs was associated with other risk variables: the proportion who reported sharing nonsterile drug equipment or borrowing needles from main sex partners who were not known to be HCV-infected increased with the number of pooling partners (figure 1). The proportion who borrowed needles from persons who were not sex partners was increased for those who had pooled money to buy drugs with \( \geq 2 \) IDUs. In addition, the proportion who borrowed a needle from a main sex partner who was known to be HCV infected was highest among those who pooled with only 1 person (figure 1).

We examined variables that might represent sexual transmission of HCV. We found that exchanging sex for money was a risk factor for seroconversion, but having a main sex partner who was an IDU was not (table 1).

We constructed a multivariate model that included the variable representing from whom needles were borrowed and all the other variables that were associated (\( P < .05 \)) with HCV seroconversion on bivariate analysis. These variables were sharing nonsterile injecting equipment, pooling money to buy drugs, and selling sex. All variables remained statistically significant, except borrowing a needle/syringe from an infected sex partner, for which the number of observations was small (table 2). Pooling money to buy drugs was statistically significant in this model, despite known associations with needle borrowing and sharing drug-preparation equipment, which were thought to be on the causal pathway for HCV seroconversion. When sharing "nonsterile" drug-preparation equipment was removed from the model, the adjusted HR for borrowing from an infected sex partner increased to 3.4 (95% CI, 1.4–7.9) and became statistically significant.

Ethnographic results. In light of indications that pooling money to buy drugs was common, the ethnographer investigated reasons for and factors associated with pooling money to buy drugs. She found that pooling money allowed IDUs to (1) "buy and use more," that is, to purchase drugs in larger quantities, thereby getting a better price; (2) reduce the time needed to accumulate enough money to purchase the minimum amount that is available for sale on the street; and (3) establish and cement social relations of reciprocity and friendship, "like having a beer together" or "being sociable." On examining the sexual partnerships of young injectors, the ethnographer found that most young female IDUs were in sexual relationships, frequently with older men. These partnerships provided benefits, including sex, companionship, money, drugs, protection,
<table>
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<td>0.12</td>
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and stability, in addition to drawbacks, such as increased economic burden and loss of control over the injecting process.

"Paul is going to show me how to be in a real relationship... I hope he will help me look after myself better—stay indoors and do less drugs."

"Jessica has used alone mostly since Dan went to jail. I ask if it has been harder looking out for herself, and she says it has actually been easier. She only has to worry about getting half the money to buy drugs each day."

"Even after we came out to San Francisco he still always copped [bought] the drugs and did everything. He wouldn't let me hit myself or even cook up the drugs. I only learned how to do everything when he went to jail."

Discussion

We found a high rate of HCV seroconversion (25.1/100 person-years; 95% CI, 18.7–32.9/100 person-years) in a cohort of young IDUs in a city with an extensive needle-exchange program. Young IDUs who stopped injecting effectively ended their risk for HCV. Among those who continued to inject, we found that variables associated with the context of injecting were predictors of infection. Needle borrowing from an infected sex partner or from a person who was not a sex partner was associated with HCV risk. In addition, pooling money to buy drugs, an indicator variable for being in injecting partnerships, was an independent risk factor. Our study also added to the growing body of literature suggesting that HCV may be transmitted via shared nonsterile drug-preparation equipment. It is notable that those who reported sharing only sterile equipment were not at increased risk of HCV infection, compared with those who had shared nonsterile equipment. Injecting heroin was associated with seroconversion in bivariate analysis (with borderline statistical significance), and this association may be explained by group use of cookers necessary to dissolve black tar heroin.

These results indicate that behaviors that are ubiquitous in the culture of injecting drugs, such as the sharing of injecting or sexual partnerships with other IDUs, are risk factors for HCV. The majority of young female IDUs are in sexual relationships with older male IDUs [41], putting them at high risk for HCV. Our ethnographic observations suggested that young female IDUs often enter into sexual relationships with older male IDUs to protect themselves from violence and to provide drugs and money. Sexual relationships can result in high rates of needle and equipment sharing, because the dynamics of jealousy and intimacy lead to men tending to control the injection and preparation process. In our study, risk was not increased for those who borrowed needles from HCV-negative sex partners. Not surprisingly, risk was increased when borrowing from a less intimate partner whose HCV status may not be known.

Most young IDUs reported pooling money to buy drugs, an indication of the extremely social nature of injecting. Ethno-

![Figure 1](image)

**Figure 1.** Relationship between risks of sharing needles and drug-preparation equipment and pooling partnerships. HCV, hepatitis C virus; IDU, injection drug user; +, positive; -, negative.
Table 2. Results of Cox proportional time-dependent hazards models of hepatitis C virus (HCV) seroconversion, by behaviors during the previous 3 months (N = 195 persons, 597 time intervals).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted HR (95% CI)</th>
<th>P</th>
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<tbody>
<tr>
<td>Needle borrowing, by partnership†</td>
<td>1.0</td>
<td>—</td>
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<tr>
<td>Did not borrow</td>
<td>2.2 (0.8-5.7)</td>
<td>0.1</td>
</tr>
<tr>
<td>Borrowed needle from</td>
<td>0.7 (0.3-1.5)</td>
<td>0.4</td>
</tr>
<tr>
<td>HCV-positive/unknown main sex partner</td>
<td>2.6 (1.2-5.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Other, not sex partner</td>
<td>2.0 (1.0-3.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Shared nonsterile drug preparation equipment</td>
<td>3.2 (1.2-8.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>No. of persons with whom pooled money to buy drugs</td>
<td>1.9 (0.8-4.3)</td>
<td>0.15</td>
</tr>
<tr>
<td>Exchanged sex for money</td>
<td>2.2 (1.1-4.4)</td>
<td>0.03</td>
</tr>
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NOTE: CI confidence interval; HR, hazard ratio.  
† When shared contaminated drug preparation equipment is excluded from the model, the adjusted HR is 3.3 (95% CI 1.4-7.9), P = 0.01.

associated with HCV seroconversion. Lack of statistical power may have also limited the examination of variables with borderline associations on bivariate analysis, such as injecting for ≥8 years, backloading, injection heroin, injecting daily, and injecting other IDUs.

What can be done to prevent HCV infections among young IDUs? Interventions to assist IDUs in stopping injecting should be considered very seriously. However, although drug treatment for youth was a priority for San Francisco's "Treatment on Demand" program, begun in 1996 [42], drug treatment is still not easily accessible to young IDUs. Thus, reductions in sharing needles and drug-preparation equipment are necessary among those continuing to inject. However, we found that sharing needles and drug-preparation equipment were embedded in injecting and sexual relationships. These relationships provide the social context of injecting risk [43], are a normal part of the injecting landscape, and provide economic and social benefits to young IDUs. Interventions to reduce HCV transmission should reduce needle sharing with infected partners and sharing of nonsterile drug-preparation equipment, while recognizing the importance of injecting and sexual relationships among young IDUs. We believe that understanding these relationships and incorporating them into interventions is necessary for reducing the risks for HCV transmission among young IDUs.

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