Title: Injection of drug residue as a potential risk factor for HCV acquisition among Montreal young injection drug users.

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Corresponding Author: Dr. Elise Roy, MD, MSc
Corresponding Author's Institution: Université de Sherbrooke
First Author: Elise Roy, MD, MSc
Order of Authors: Elise Roy, MD, MSc; Nelson Arruda, MSc; Pascale Leclerc, MSc; Nancy Haley, BSc, MD, FRSQ(C), FAAP; Julie Bruneau, MD, MSc; Jean-François Boivin, MD, FRCP(C), DSc

Abstract: Background: Preparing drugs or medications for injection may leave residues in containers and filters used by injection drug users (IDUs). Little is known about the specific practice of injecting someone else's drug residue as a possible route of HCV transmission. Methods: A prospective cohort study of street youth aged 14-23 years old was carried out between July 2001 and December 2005. For this analysis, youth who injected in the six months prior to interview were selected if they were HCV-negative and had completed at least one follow-up visit. Semi-annual visits involved completing an interviewer-administered questionnaire and providing a blood sample for HCV antibody testing. "Sharing behaviours" (any injection preparation behaviour that could entail IDUs using injection equipment used by others) including injecting someone else's drug residue were assessed at each interview. Predictors of HCV seroconversion were identified using Cox proportional hazards regression analyses. Two multivariate models were built, one considering sharing behaviours only, and one with cocaine injection forced into it. Results: Of the 175 participants, 60% were male and their mean age was 20.7 years old. In both models, residue injection was a predictor of HCV incidence, although with marginal statistical significance. The adjusted hazard ratio estimates were (2.15; 95% CI 0.99-4.67) and (2.11; CI 0.97-4.62) respectively. Conclusion: This epidemiological study underscores the role injection of drug residue may play in HCV transmission among IDUs. In the current context of the worldwide HCV epidemics, this question deserves further investigation.
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Injection of drug residue as a potential risk factor for HCV acquisition among
Montréal young injection drug users.

Élise Roy¹,², Nelson Arruda³, Pascale Leclerc², Nancy Haley²,⁴, Julie Bruneau⁵,⁶, Jean-François Boivin⁷

1. Université de Sherbrooke, Programme d’études et de recherche en toxicomanie, Faculté de médecine et des sciences de la santé, Université de Sherbrooke, Longueuil, Québec, Canada, J4K 0A8.

2. Direction de santé publique, Agence de la santé et des services sociaux de Montréal, Montréal, Québec, Canada, H2L 1M3.

3. Independent investigator and consultant.

4. Université de Montréal, Faculty of Medicine, Montréal, Québec, Canada.

5. Centre hospitalier de l’Université de Montréal (CRCHUM), Research Center, Montréal, Québec, Canada, H2X 1P1.

6. Université de Montréal, Faculty of Medicine, Department of Family Medicine, Montréal, Québec, Canada, H3T 1J4.

7. McGill University, Faculty of Medicine, Joint Departments of Epidemiology, Biostatistics, and Occupational Health, Montréal, Québec, Canada, H3A 1A2.

Corresponding author: Élise Roy, MD, MSc, Programme d’études et de recherche en toxicomanie, Faculté de médecine et des sciences de la santé, Université de Sherbrooke, 150, Place Charles-Le Moyne, Bureau 200, Longueuil, Québec, Canada, J4K 0A8. Tel. 450-463-1835 ext. 61823; Fax: 450-463-6578; Email: Elise.Roy@usherbrooke.ca.
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1. Introduction

It is estimated that the infection due to the hepatitis C virus (HCV) is the most frequent bloodborne infection among injection drug users (IDUs) in most countries of the world (Nelson et al., 2011). Prevalence rates would be of at least 60% in nearly 40 countries and North America appears to be one of the most affected regions of the world. For instance, in Canada, of the acute HCV cases with known risk factor information, injection drug use is associated with 63% of infections (PHAC, 2009). New or young injection drug users (IDUs) are the most at risk of HCV infection (Crofts et al., 1995; Garfein et al., 1998; van Beek et al., 1998; Hagan et al., 1999, 2001; Thorpe et al., 2000, 2002; Hahn et al., 2002; Miller et al., 2002; Des Jarlais et al., 2003; Judd et al., 2005; Maher et al., 2006, 2007; van den Berg et al., 2007; Roy et al., 2009). In the Vancouver (Canada) IDUs cohort study, HCV incidence rate was 37.3 per 100 person-years among participants aged between 13 and 24 years old at study entry (Miller et al., 2002). In Montréal, data from the Montréal street youth cohort study showed that 55% of young IDUs became HCV-antibody positive within the first four years of injection (Roy et al., 2009).

High-risk injection behaviours are the leading cause of HCV infections among IDUs. When IDUs share injection equipment, contact with contaminated blood constitutes the main mechanism for effective transmission of the virus. Risks of infection associated with various sharing behaviours, including sharing syringes, cookers, filters and water, have been examined in HCV incidence studies (Hagan et al., 2001, 2010; Thorpe et al., 2002; Hahn et al., 2002; Maher et al., 2006; Lucidarme et al., 2004). However, the risk associated with the practice of injecting someone else’s drug residue,
which involves sharing filters and/or cookers altogether, has been overlooked. Although
this behaviour has been previously described by ethnographers in the United States, in
Europe (Power et al., 1996; Bourgois 1998; Cólon et al., 2001; Koester et al., 2005;
Bourgois and Schonberg, 2009) and, very recently, in Canada (Roy et al., 2011), it has
rarely been measured and discussed explicitly in epidemiologic studies. In the few HCV
incidence studies where residue injection has been mentioned, it was combined with
other drug preparation equipment sharing practices into a single variable (Hahn et al.,
2002; Lucidarme et al., 2004). Nevertheless, two American studies have reported
significant prevalence figures on this specific practice, showing that around a third of
IDUs injected other people’s drug residue (Koester, 2005; Evans, 2009). No such data are
available for Canada.

Drug residues are used by IDUs to counter withdrawal symptoms or when
monetary resources are at their lowest, which gives them a currency value in the street
milieu. While injecting someone else’s drug residue can be technically considered as
ancillary injection paraphernalia sharing, not all IDUs perceived it to be risky (Roy et al.,
2011). Injection of someone else’s drug residue could entail risks for blood borne
pathogen acquisition or transmission. The aim of this paper was to examine whether this
practice is an independent predictor of HCV incidence taking into account the effect of
other sharing behaviours known to increase HCV risk among IDUs.

2. Methodology

2.1. Study design and participants
Using the Montréal street youth cohort study database (2001-2005), secondary analyses were carried out to examine the association between injecting someone else’s drug residue and HCV incidence among young IDUs. The methodology was described in detail elsewhere (Haley et al., 2004). Briefly, study interviewers enrolled participants through regular visits to all major street youth agencies in Montréal. Youth were eligible if 1) they had either been without a place to sleep more than once or had regularly used the services of street youth agencies (drop-in centres, shelters or outreach vans), in the previous year; 2) they were 14 to 23 years of age; and 3) they spoke French or English. Semi-annual visits were scheduled at the study office, located in the downtown area where most street youth spend time. Each visit involved signing a consent form, collecting contact information for follow-up, completing an interviewer-administered questionnaire, and collecting blood samples for HCV antibody testing. Participants received financial compensation (CDN $30) for each visit. Ethical approval was provided by the Institutional Review Board of the Faculty of Medicine, McGill University.

2.2. Data collection

Socio-demographic characteristics and high-risk drug use behaviours were assessed at each interview. “Sharing behaviours” (any injection preparation behaviour that could entail IDUs using injection equipment used by others) included using injection equipment already used by someone else (syringe, filter, container water), drug sharing behaviours (frontloading, backloading, dividing a drug in a syringe then pouring it into a container, dividing a drug directly in a container) and injecting someone else’s drug residue. The type of drugs most often used was also documented. The question about drug residue
injection referred to both illegal drugs and medication. It was worded as follows: “In the last 6 months, did you inject drug residue from cotton or filter? (If yes) had this cotton or filter been used by someone else before you?” All behavioural questions referred to the six months prior to interview.

2.3. Laboratory tests

Venous blood specimens were stored at 4°C and sent to the seroimmunology laboratory every day, where they were screened using Cobas Core third-generation HCV enzyme immune assay (EIA) by Roche. Reactive samples underwent further testing with another third-generation EIA (Axsym by Abbott). Samples that tested positive to both EIA were confirmed positive. Discordant samples were screened for viral RNA PCR (Cobas Amplicor HCV by Roche). Positive samples were confirmed positive, and negative samples were sent to the Laboratoire de santé publique du Québec for double ELISA confirmation. Subjects were considered as incident HCV cases (seroconverters) when they first tested HCV positive following one or more interviews where they were HCV negative.

2.4. Statistical analyses

Street youth who were HCV negative and currently injecting drugs at any visit were included in these analyses. Follow-up for the subjects who had ever injected drugs before entry into the cohort began at the visit during which they first reported having injected in the prior six months. Follow-up for youth whose initiation to injection occurred during the study period started at their first injection. For all subjects, follow-up
ended at their seroconversion (mid-point between last negative and first positive tests) or at their last visit, whichever came first. HCV incidence was estimated using the person-time method and confidence interval was calculated using the Poisson distribution. For predictor analyses, a model that took “sharing behaviours” into consideration was built using univariate and multivariate Cox regression analyses with time-varying covariates. Since time interval between two questionnaires could be longer than the six months planned, analyses included only intervals that were one year or shorter to lower risks of misclassification. Variables with p-value $\leq 0.20$ in univariate analyses were entered into initial multivariate Cox models. Following the purposeful selection procedure (Hosmer and Lemeshow, 1999), significant variables at the 5% level as well as those that showed a confounding effect on significant covariables (those that changed a significant variable’s coefficient by more than 20%) were retained in the final multivariate models. Cocaine injection is a known independent risk factor for blood-borne infections (Tyndall et al., 2003, Patrick et al., 2001; Roy et al., 2007). It is generally considered a surrogate marker of chaotic injection behaviours involving high injection frequency and significant risk of blood exposure that often goes unnoticed by IDUs. The variable “injecting mainly cocaine” can then be seen as a potential important confounder and was therefore forced into the model (presented as a second model).

3. Results

A total of 858 participants were recruited in the street youth cohort study, 235 (27.4%) of whom were HCV seronegative and injecting drugs at time of interview during the study period. Of the 235 individuals, 175 (74.5%) had at least one follow-up visit and
were included in the analysis. The majority were male (60%) and Canadian born (97.1%) and their mean age at first visit was 20.7 years old. Almost a fifth (18.3%) had injected “medication to get high” in the six months preceding the first visit included in the analyses (Table 1). Except for frontloading, which is an uncommon practice among Montréal’s IDUs, each sharing practice was reported by at least 10% of participants and residue injection was reported by 7% of them. Of the 175 participants cumulating 216.4 person-years of f-up, 57 seroconverted. The incidence rate was 26.3 per 100 person-years [95% CI: 19.2-34.1].

Univariate analyses showed that there was a statistically significant association (at a significance level of 0.05) between HCV incidence and needle and drug container sharing, dividing drug in a container, as well as drug residue injection (Table 2). In the first final multivariate model, only needle sharing and residue injection were independent predictors of HCV incidence (Table 3). Cocaine injection remained in the second final model as another independent predictor albeit not a confounder. The adjusted hazard ratio estimates were of the order of two, with lower values of 0.99 and 0.97 for the first and the second models, respectively.

4. Discussion

This is the first prospective cohort study that shows that injecting someone else’s drug residue, as an independent variable, could play a significant role in HCV transmission among IDUs. Although the association was marginally significant, these results are biologically plausible given recent laboratory studies showing that HCV can survive on both inanimate surfaces and syringes (Doerrbecker et al., 2011; Painstill et al.,
These findings are of great interest in view of the Canadian and worldwide magnitude of the HCV epidemic, with reported prevalence rates among IDUs as high as 60%-80% (Nelson et al., 2011). The high incidence level observed in this study cohort confirms the critical nature of the epidemic in the country.

The percentage of young IDUs having injected someone else’s drug residue (7% at baseline) was lower in our study than that reported by Koester (2005) and Evans (2009). This difference might be explained by the fact that these studies were held in Western United States where black tar heroin (a difficultly dissolvable form of heroin) predominates (Koester et al., 2005; Ciccarone and Bourgeois, 2003). During the cohort study (2001-2005), Montréal IDUs were mainly injecting either powder cocaine or heroin, and young street-involved IDUs were no exception (INSPQ, 2011; Steensma et al., 2005). Moreover, injecting someone else’s drug residue was not a frequent practice among study participants compared to other sharing practices such as cotton or container sharing. This is not surprising because injection of residue is often a last resort behaviour that one will engage in when in withdrawal or with no economic resources (Bourgois, 1998; Bourgois and Schonberg, 2009).

This study’s results do not show an association between other sharing practices (except for needle sharing) and HCV infection. Previous studies reported divergent results regarding the magnitude of the risks associated with these practices (De et al., 2008). It is important to underscore that contrary to the injection of residue, these practices may easily go unnoticed by users themselves, which may in turn lead to under-declaration during inquiries and a bias toward the null value (Rothman et al., 2008).
In Montréal, where this study took place, heroin had been the second most often injected drug before prescription opioid use started gaining ground between 2003 and 2004. Indeed, in the last decade, very high proportions of intravenous PO use among IDUs have been documented in Canada (Fischer et al., 2006; Leclerc et al., 2011; PHAC, 2006; Roy et al., 2012). According to the Canadian HIV and HCV Surveillance Network, among IDUs, 45.9% of participants had injected non-prescribed morphine, 32.9% hydromorphone, and 17.1% oxycodone in the six months preceding the interview (PHAC, 2006). In some regions, PO use among street-based users is even higher than that of heroin (Fischer et al., 2006).

Recent ethnographic work carried out in Montréal suggests that PO injection is more problematic than injection of cocaine or heroin powder because of its preparation process, which leaves larger quantities of residue (Roy et al., 2011). Moreover, when preparing a dose, IDUs may not be able to draw all the solution in one syringe since certain formats of POs (such as capsules) require large amounts of water to dissolve them. This means they might inject many times, using the filter/container repeatedly, (going back and forth between the vein and the filter) to inject a single dose. Then, the filter not only gets saturated with the substance but also gets contaminated with blood when the same syringe is reused to perform the multiple injections. Our study results suggest that these filters/containers may become paths of HCV transmission. It is very worrisome that drug residue injection (locally called “doing a wash”) appears to be common among PO injectors (Roy et al., 2011). Indeed, at the time of the ethnographic work, most IDUs, even health-conscious users who claimed never sharing drug preparation equipment, did not realize that “doing a wash” with someone else’s
filter/container was actually a sharing practice. “Washes” were regarded as an independent drug capable of producing a high or countering withdrawal symptoms rather than as a drug preparation equipment (Roy et al., 2011).

It should be underlined that, at the time of this cohort study, prescription drug misuse was not documented exhaustively. The present analysis did not permit to identify from which drug or medication the injected residue came from. Therefore, our results apply to the injection of any substance. Despite these reservations, we believe that these results augur badly in light of the North American increase of medication misuse, in particular that of prescriptions opioids (INCB, 2011; Johnston et al., 2010; SAMHSA, 2009, 2010).

Among the strengths of the study, its prospective design and its high retention rate should be underlined. As for the limitations, the results may not be generalized to all young IDUs given that the study was based on a convenience sample. Secondly, data collection method was based on self-reports, which may have introduced the possibility of both recall and social desirability biases. However, the impact of such biases was possibly limited by the short time spans between interviews and the open and non-judgmental attitude of the interviewers. Finally, to properly estimate the risk of bias related to losses to follow-up, the risk behaviours of the 175 participants included in the analyses were compared to those of the 60 participants not included in the analyses and no significant differences were observed.

5. Conclusion
In conclusion, many experts underscore the need to reinforce HCV prevention efforts, using a wide variety of strategies, ranging from drug initiation prevention to treatment of infected users (Vlahov et al., 2004; Grebely and Dore, 2011). Adopting safe injection behaviours is among the targeted strategies. Public health authorities must maintain surveillance of high risk behaviours in the IDU population, particularly in the context of drug market changes where forms of available drugs have a determinant impact on modes of consumption and on users’ injection behaviours. In response to these changes, supplied sterile drug injection equipment and prevention messages must be continuously revised in order to be adapted to the changing needs of IDUs.

Because this study is the first one to examine the risks of HCV transmission associated to residue injection, more research is needed to confirm these results. Given the ongoing epidemic of nonmedical use of prescription opioids among IDUs, the role of PO injection in HCV transmission should be further examined.
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Table 1. Drug use behaviours at first visit considered in the analyses

<table>
<thead>
<tr>
<th>Drug Use Behaviour</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection in the last 6 months of ...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>... cocaine</td>
<td>109</td>
<td>62.3%</td>
</tr>
<tr>
<td>... heroin</td>
<td>122</td>
<td>69.7%</td>
</tr>
<tr>
<td>speedball&lt;sup&gt;1&lt;/sup&gt;</td>
<td>31</td>
<td>17.7%</td>
</tr>
<tr>
<td>... medication to get high</td>
<td>32</td>
<td>18.3%</td>
</tr>
<tr>
<td>... other drugs&lt;sup&gt;a&lt;/sup&gt;</td>
<td>21</td>
<td>12.0%</td>
</tr>
<tr>
<td>Principal drug injected in the last 6 months&lt;sup&gt;b&lt;/sup&gt;:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cocaine</td>
<td>62</td>
<td>38.0%</td>
</tr>
<tr>
<td>Heroin</td>
<td>93</td>
<td>57.1%</td>
</tr>
<tr>
<td>Cocaine and heroin separately but with equal frequency</td>
<td>1</td>
<td>0.6%</td>
</tr>
<tr>
<td>Medication to get high</td>
<td>4</td>
<td>2.5%</td>
</tr>
<tr>
<td>Other drugs&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
<td>1.8%</td>
</tr>
<tr>
<td>Sharing the following injection equipment (last 6 months):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syringe&lt;sup&gt;c&lt;/sup&gt;</td>
<td>52</td>
<td>29.9%</td>
</tr>
<tr>
<td>Cotton or filter&lt;sup&gt;d&lt;/sup&gt;</td>
<td>25</td>
<td>14.5%</td>
</tr>
<tr>
<td>Container&lt;sup&gt;d&lt;/sup&gt;</td>
<td>54</td>
<td>31.2%</td>
</tr>
<tr>
<td>Dilution water&lt;sup&gt;e&lt;/sup&gt;</td>
<td>43</td>
<td>25.1%</td>
</tr>
<tr>
<td>Cleaning water&lt;sup&gt;d&lt;/sup&gt;</td>
<td>23</td>
<td>13.3%</td>
</tr>
<tr>
<td>Drug sharing behaviours (last 6 months):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontloading&lt;sup&gt;d,1&lt;/sup&gt;</td>
<td>1</td>
<td>0.6%</td>
</tr>
<tr>
<td>Backloading&lt;sup&gt;c,2&lt;/sup&gt;</td>
<td>22</td>
<td>12.6%</td>
</tr>
<tr>
<td>Method</td>
<td>Count</td>
<td>Percentage</td>
</tr>
<tr>
<td>-----------------------------------------------------------------------</td>
<td>-------</td>
<td>------------</td>
</tr>
<tr>
<td>Injecting residue</td>
<td>12</td>
<td>7.2%</td>
</tr>
<tr>
<td>Dividing drug in a syringe then poured in a container</td>
<td>18</td>
<td>10.5%</td>
</tr>
<tr>
<td>Dividing drug in a container</td>
<td>20</td>
<td>11.6%</td>
</tr>
</tbody>
</table>

\(^a\) Including hallucinogens (8.6%), amphetamines or ecstasy (5.1%) and other drugs (0.6%)

\(^b\) 12 missing values; \(^c\) 1 missing value; \(^d\) 2 missing values; \(^e\) 4 missing values; \(^f\) 9 missing values; \(^g\) 3 missing values.

1 **Frontloading**: Drug sharing technique used with syringes with detachable needles, which consists of removing the needle from the “receptive” syringe and inserting the needle of the “donor” syringe through the hub of the receptive syringe and squirting in a part of the solution.

2 **Backloading**: Drug sharing technique, which consists of squirting in a part of the solution from the “donor” syringe through the back of a “receptive” syringe whose plunger has been taken out.
<table>
<thead>
<tr>
<th>Predictors</th>
<th>Hazard</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male vs female)</td>
<td>1.27</td>
<td>0.39</td>
</tr>
<tr>
<td>Age</td>
<td>0.89</td>
<td>0.09</td>
</tr>
<tr>
<td>Sharing the following injection equipment:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syringe</td>
<td>2.87</td>
<td>0.0002</td>
</tr>
<tr>
<td>Cotton or filter</td>
<td>1.80</td>
<td>0.12</td>
</tr>
<tr>
<td>Container</td>
<td>1.98</td>
<td>0.02</td>
</tr>
<tr>
<td>Dilution water</td>
<td>1.35</td>
<td>0.32</td>
</tr>
<tr>
<td>Cleaning water</td>
<td>1.40</td>
<td>0.35</td>
</tr>
<tr>
<td>Drug sharing behaviours:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontloading</td>
<td>1.27</td>
<td>0.82</td>
</tr>
<tr>
<td>Backloading</td>
<td>1.45</td>
<td>0.26</td>
</tr>
<tr>
<td>Injecting residue</td>
<td>3.35</td>
<td>0.004</td>
</tr>
<tr>
<td>Dividing drug in a syringe then poured in a container</td>
<td>1.75</td>
<td>0.12</td>
</tr>
<tr>
<td>Dividing drug in a container</td>
<td>2.40</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Table 3. Multivariate Cox proportional hazard models of risk factors for HCV

<table>
<thead>
<tr>
<th>Model without Principal drug injected</th>
<th>Adjusted hazard</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.89</td>
<td>0.77</td>
</tr>
<tr>
<td>Gender (male vs female)</td>
<td>1.69</td>
<td>0.95</td>
</tr>
<tr>
<td>Sharing a syringe</td>
<td>2.54</td>
<td>1.44</td>
</tr>
<tr>
<td>Injecting residue</td>
<td>2.15</td>
<td>0.99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model with Principal drug injected</th>
<th>Adjusted hazard</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.92</td>
<td>0.81</td>
</tr>
<tr>
<td>Gender (male vs female)</td>
<td>1.49</td>
<td>0.84</td>
</tr>
<tr>
<td>Sharing a syringe</td>
<td>2.45</td>
<td>1.39</td>
</tr>
<tr>
<td>Principal drug injected - cocaine vs others</td>
<td>2.22</td>
<td>1.26</td>
</tr>
<tr>
<td>Injecting residue</td>
<td>2.11</td>
<td>0.97</td>
</tr>
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