Hepatitis C virus transmission among oral crack users: viral detection on crack paraphernalia
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Objective Epidemiological studies present oral crack use as a potential independent risk factor for hepatitis C virus (HCV) status, yet actual HCV transmission pathways via crack use have not been evidenced. To this end, this exploratory study sought to detect HCV on crack-use paraphernalia used by street crack users.

Methods Crack-use paraphernalia within 60 min of use was collected from 51 (N) street-crack users. HCV RNA detection was conducted through eluate sampling and manual RNA extraction. Participants provided a saliva sample to test for HCV antibody, and had a digital photograph taken of their oral cavities, to assess the presence of oral sores as a possible risk factor for oral HCV transmission.

Results About 43.1\% (n=22) of the study participants were HCV-antibody positive. One (2.0\%) of the 51 pipes tested positive. A minority of the participants presented oral sores. The pipe on which HCV was detected was made from a glass stem; its owner was HCV-antibody positive, and there was full rater agreement on the presence of oral sores in the pipe owner’s oral cavity.

Conclusions HCV transmission from an infected host onto paraphernalia as a precondition of HCV host-to-host transmission via shared crack paraphernalia use seems possible, with oral sores and paraphernalia condition constituting possible risk modifiers. Larger-scale studies with crack users are needed to corroborate our findings. Eur J Gastroenterol Hepatol 20:29–32 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Background Hepatitis C virus (HCV) infection is a public health problem associated with significant morbidity, mortality, and costs [1,2]. The HCV disease burden in Canada is primarily driven by illicit drug use, which causes the majority of new HCV infections [3,4]. Most research has focussed on injection drug use as the primary risk factor for HCV transmission [5,6]. Recent epidemiological studies have identified (oral) crack use (i.e. smoking) as a potential independent predictor of HCV seropositivity [7,8]. These findings are, however, based on statistical analyses with many assumptions (e.g. linearity of effects), and do not empirically specify HCV-transmission pathways by way of oral crack use in real world conditions. This type of HCV transmission through the sharing of crack-use paraphernalia might be suggested epidemiologically; however, alternatively, crack users might more commonly engage in other high-risk behaviours related to HCV transmission, such as unsafe drug injection or high-risk sexual practices, which might explain their elevated HCV status [3]. Currently, outreach interventions (e.g. Safer Crack Use Kit (SCUK) distribution programmes) aiming at street crack users are being implemented in several Canadian cities; these are based on the primary rationale of HCV prevention [9].

For HCV to be transmitted directly through oral drug-use activity, several conditions must be fulfilled. First, HCV must contaminate an oral drug-use implement through contact with HCV-contaminated blood or saliva. Second, HCV must remain viable on the implement until a new host is exposed to it. Next, the HCV present on the noninjection drug-use implement must be transferred from one user to another (e.g. by paraphernalia sharing). Lastly, once an individual is exposed to HCV, a failure of the local immune response in the oral mucosa must occur, so that HCV can establish chronic infection.

Studies have shown that crack smokers have a high incidence of oral burns or cuts, typically facilitated by the ‘makeshift’ materials (e.g. manipulated glass bottles, pop cans with sharp edges) used for smoking, metal wool filters, and the typical high-frequency use patterns of crack use [9–11]. The sharing of crack pipes is common within the subcultural dynamics of crack use [9,10]. Although the epidemiological and behavioural characteristics
associated with crack use and the virology of HCV seem to satisfy the criteria for potential HCV transmission in this population, it remains unknown whether HCV can contaminate oral crack-use implements, which is one important condition to satisfy the biologic plausibility of HCV transmission through this route. On this basis, our exploratory study evaluated the presence of HCV on crack-use paraphernalia, and its association with the risk characteristics of its respective user, under real-life conditions.

Methods
The objective of this study was to collect required evidence of the plausibility of HCV transmission by way of crack smoking, specifically (i) to examine whether HCV can be detected on the crack-use paraphernalia of crack users; (ii) to assess the presence of oral sores and the HCV status among the crack users from whom the pipes had been collected; and (iii) to explore possible associations between the results from (i) and (ii).

The fieldwork was conducted by two field researchers and two staff members from a community health agency, who were familiar with the sociobehavioural characteristics of crack users in a downtown Toronto neighbourhood where street crack use was common. Eligibility criteria included observed or reported oral crack use in the preceding 60 min and willingness to participate in the study protocol. The study protocol consisted of (i) collection and sampling of the participant’s crack paraphernalia for HCV RNA, (ii) digital photographs of the participant’s oral cavity, and (iii) saliva sample collection for HCV antibody. In return, participants were provided with a ‘health kit’ tailored to modify crack use-related risk behaviour, and a monetary reimbursement of $15 after completing the protocol. The study was approved by the Centre for Addiction and Mental Health Research Ethics Board and was conducted anonymously (i.e. no personal information was collected) over three afternoons in July 2006.

Field methods
Eligible study participants were street-recruited by the research staff and brought to the community health clinic for assessment, before which they were given a brief explanation of the study and their verbal consent was obtained.

After obtaining the participant’s crack paraphernalia, the proximal end of the pipe was wiped repeatedly with a cotton swab impregnated with 500 μl of 3% beef extract. The swabs were then placed in a sterile tube containing a further 250 μl of eluate, agitated for 1 min, and placed in a portable cooling unit at 4°C. Furthermore, each participant self-administered an oral salivary HCV-antibody test. Finally, digital photographs were taken of each partici-

pant’s oral cavity (spread open and gums displayed with the participant’s assistance).

Digital photos of the crack pipes collected were taken, which were qualitatively assessed for their condition after the field phase, using the categories ‘good’, ‘fair’, and ‘poor’. The photographs of the participants’ oral cavities were assessed by three physicians with clinical expertise in the treatment of street drug users, for the presence of oral sores, ulcers, or cuts. The three assessors independently assessed the 4 × 6-inch photo prints, and dichotomously recorded either the ‘presence’ or the ‘absence’ of the described oral injuries, on the basis of the photographic evidence.

Molecular methods
Salivary samples were tested for HCV antibodies through standard methodology: HCV 3.0 SAVe Elisa screen test (Ortho Diagnostics, Raritan, New Jersey, USA) and Bio-Rad Monolisa anti-HCV Plus version2 confirmation test (Bio-Rad Laboratories Inc., Montreal, Canada) [12]. Further validation indicated anti-HCV sensitivity of 96.4%, and specificity of 100% for the analysis methods used [13].

Crack pipe-eluate samples were tested with previously validated methodology [14]. In summary, RNA was manually extracted (Qiagen Inc., Mississauga, Canada) and tested for the presence of HCV RNA through reverse transcriptase-polymerase chain reaction (PCR) techniques (COBAS AMPLICOR v2.0: Roche Molecular Systems, Pleasanton, California, USA). Samples were tested on three independent runs, each with positive and negative controls by a technical expert in performing PCR.

Before the field phase, we independently validated our molecular methods in a laboratory setting. The above technique successfully detected the presence of HCV on all of four authentic crack-use pipes when 10μl of 5000 IU/ml HCV was manually placed on the pipe and allowed to air dry for 60 min. All pipes with higher concentrations of HCV tested positive by reverse transcriptase-PCR, and all pipes with 10μl of 2500 IU/ml HCV tested negative for the presence of HCV RNA. All pipes were tested at both 30 and 60 min.

Results
The study sample consisted of 51 self-reported street crack users. The sample was diverse in terms of sex, ethnicity (white and black), and age.

One (2.0%) of the 51 pipes tested positive for the presence of HCV RNA. The assessment of photographs of participants’ oral cavities for the presence of sores resulted in moderate interrater agreement (Fleiss Kappa
Our exploratory study examined the presence of HCV seropositivity of the sample was 43.1% (n = 22). The pipe on which HCV was detected was made from a glass stem with no cracks. Its owner had a large oral sore present on the lip; there was full agreement among the three medical experts regarding the presence of the sores, and the participant was found to be HCV seropositive. In 71% (5 out of 7) of the cases in which there was rater agreement on the presence of sores, the respective participant was found to be HCV seropositive; this proportion was only 39% (17 out of 44) for the remaining cases, translating to an odds ratio of 4.0 (95% CI: 0.7–22.8).

**Discussion**

Our exploratory study examined the presence of HCV RNA on crack-use paraphernalia collected from a small sample (n = 51) of street crack users, to explore the biological possibility of HCV transmission via crack use.

Our data present several key implications as well as the need for further inquiry. Our results suggest that HCV transmission by crack pipe-sharing might be possible, although given the small number of HCV-contaminated pipes identified, its likelihood in real-world conditions might be limited. This finding, nevertheless, calls for the systematic and methodologically rigorous examination of the possibility of HCV transmission through crack use, especially given the epidemiological evidence for crack use as a risk factor for HCV status, and the currently implemented interventions (e.g., SCUK) to prevent HCV transmission among crack smokers [7,9]. Future inquiries should ideally use large sample sizes, and should include a prospective study population of HCV-negative crack users, in whom potential seroconversion – and related causal factors – can be systematically evaluated.

Several potential modifiers can influence the likelihood at which HCV transmission, related to crack use, occurs. First, the presence of sores in the user’s oral cavity might crucially increase the chance of HCV-infected blood contaminating paraphernalia during smoking activities. A relationship between oral sores and HCV positivity seemed to be indicated in our sample, pointing to a potential transmission modifier suggested by the literature [10,11]. The small sample, however, did not allow for sufficient power to detect association effects. The causal inferences thus need to be more systematically explored in future research.

Second, HCV transmission might be influenced by the material or quality of the crack-use paraphernalia used: for example, the use of makeshift metal or glass pipes that facilitate oral cuts or the use of materials with differential heat transmission properties impacting the presence of oral burns or sores [9,10]. The majority of the pipes collected – including the one on which HCV was found – were made from glass components and were in relatively good condition; this fact is likely to be explained by the SCUK distribution programmes at the study site.

Our study presents several limitations highlighting the need for future systematic inquiries. First, our study sample was small, and therefore included an even smaller number of HCV seropositive participants. HCV transmission via crack use paraphernalia necessarily requires an HCV-infected source host, transferring HCV infected saliva or blood particles onto the paraphernalia. Consequently, the actual HCV contamination rate of pipes among the sub-sample of HCV seropositive participants (4.5%) might be a more meaningful estimate of HCV contamination. Second, the pipes collected may not have been used (only) by the participant from whom the pipe was retrieved, although this would not detract from our study focus on actual HCV detection on recently used crack pipes. Third, crack pipes may have been used last at a time greater than 60 min prior to sampling for HCV, potentially leading to lower detection rates. The HCV detection threshold on pipes was 5000 IU/ml if 10 ul of sample was present on the distal end of the pipe. Although this represents a sensitive molecular technique it is not certain that HCV below the detection limit was not present on additional pipes. The actual possibility for subsequent HCV transmission from pipe to host however with potentially lower concentrations of HCV would likely be minimal. Finally, although we have demonstrated the possibility of presence of HCV on crack smoking implements, this circumstance alone does not ensure transmission from one host to another. HCV material found on contaminated pipes may be nonviable, and the local innate immune response of the oral mucosa of the target host may effectively prevent HCV transmission even after exposure. Finally, while salivary tests are a reliable method to determine a person’s HCV antibody status, some 10–25% of persons indicating HCV antibodies spontaneously clear the virus and hence are not carriers of active HCV infection [16,17].

Besides further systematic study efforts needed to determine the possible pathway – and its determinants – of HCV transmission by way of oral crack use, our study presents tentative implications for current (controversial)
interventions geared at crack users, e.g. SCUK distribution programmes. Given the demonstrated possibility of HCV transmission via crack use, measures aimed at reducing these risks should be supported for the time being; SCUK programmes are a rare tangible measure aimed at crack users as a high-risk population characterized by high levels of marginalization and compromised health [7,18,19].

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Conflict of interest: none declared.

References
18 Inciardi JA. Crack, crack house sex, and HIV risk. *Arch Sex Behav* 1995; 24:249–269.