

## **TITLE PAGE**

### **TITLE:**

Intranasal transmission of hepatitis C virus: virological and clinical evidence

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**ABSTRACT:**

Background: Hepatitis C virus (HCV) is a major cause of liver-related morbidity and mortality worldwide. Although several primary routes of HCV transmission are known, about 1 in 5 cases are of unknown etiology. One potential source of infection that might account for the unexplained cases involves intranasal transmission of HCV through contaminated drug-sniffing implements, such as straws or spoons, shared by intranasal drug users. In this study, we assessed the virological and clinical preconditions necessary for intranasal HCV transmission.

Methods: 38 patients with chronic active HCV infection and a history of intranasal drug use were recruited from a community health clinic in New York City. Nasal swabs and drug sniffing implements were collected and tested for the presence of occult blood and HCV RNA. Each subject completed an epidemiological survey and was administered a clinical nasal examination.

Findings: Nasal pathology in this sample of chronic drug sniffers was moderate to high, and included epistaxis, rhinitis, rhinorrhea and blockage, mucosal lesions, nasal septal perforations, and saddlenose deformation. Occult blood was detected in 74% of nasal swab samples and 8% of sniffing implements. HCV RNA was detected in 13% of nasal swab samples and 5% of sniffing implements.

Interpretation: These findings confirm the essential virological and clinical preconditions necessary for HCV intranasal transmission and add support to previous epidemiological evidence indicating that intranasal drug use poses a risk for HCV infection. Additionally, these findings advance the debate regarding potential transmission of HCV in the context of ENT and related clinical practices.

**KEYWORDS:**

Hepatitis C virus; HCV transmission; HCV detection; intranasal drug use; nasal pathology

## INTRODUCTION

Hepatitis C virus (HCV) is a major cause of liver-related morbidity and mortality and a leading indication for liver transplantation worldwide.<sup>1,2</sup> It is estimated that over 180 million people globally are chronic carriers of HCV.<sup>3</sup> In the United States, an estimated 5 million people are chronically infected,<sup>4</sup> making HCV the most common blood-borne pathogen in the nation.

Transmission of HCV is known to occur parenterally through contact with contaminated blood, most notably in the context of injection drug use, transfusion of blood products prior to 1992, chronic hemodialysis, hospital-related and occupational exposure to blood, and perinatal transmission.<sup>5</sup> In addition, several studies have reported low levels of suspected sexual and household transmission of HCV.<sup>6</sup>

Although most of the primary routes of HCV transmission are known, up to 20% of infected individuals report no identifiable source of exposure.<sup>7</sup> Unexplained HCV cases—known as “sporadic” or “community-acquired” cases—are particularly common among drug-users who report no history of injection risk and no other identifiable source of transmission.<sup>8,9</sup> One hypothesis advanced to account for the high prevalence of unexplained HCV cases among noninjection drug users was proposed by researchers at the U.S. National Institutes of Health (NIH), who identified intranasal cocaine use as a significant risk factor for HCV among volunteer blood donors.<sup>10</sup> The investigators reasoned that viral hepatitis C might be transmitted through contaminated implements, such as straws or spoons, commonly used to nasally inhale powdered drugs, including heroin, cocaine, and methamphetamines. Chronic nasal inhalation of these substances (including the adulterants they contain) can cause tissue deterioration and bleeding of nasal membranes. Implements inserted into an eroded nasal cavity may come into contact with HCV-infected mucus or blood, which might then be transmitted to a susceptible individual sharing the same implement. The debate regarding this potential mode of transmission intensified when the National Heart, Lung and Blood Institute (NHLBI) Retrovirus

Epidemiology Donor Study (REDS) was unable to replicate the NIH findings, and could not confirm intranasal drug inhalation as an independent risk factor for HCV.<sup>11</sup> These conflicting reports prompted the American Association of Blood Banks (AABB) to add, and then shortly thereafter remove, intranasal cocaine use from their list of criteria used to screen potential blood donors.<sup>12</sup>

Two recent reviews of the literature have revealed further inconsistent findings among studies in which intranasal drug use was examined as a potential risk factor for HCV infection.<sup>13</sup> <sup>14</sup> Because intranasal drug use is often highly correlated with other known or suspected risk factors for HCV transmission, such as tattooing and high risk sexual behavior, it has proven difficult to isolate intranasal transmission of HCV from these other potential sources in studies examining relative risk. This has led to much misinformation among both health care providers and patients regarding potential intranasal transmission of viral hepatitis C.

In the present study, we take an alternative approach to testing the intranasal HCV transmission hypothesis. Applying Popper's concept of falsifiability, we attempt to refute the hypothesis by invalidating one or more of the necessary preconditions for drug-related intranasal transmission of hepatitis C. These preconditions include: (1) the presence of HCV RNA in the nasal cavities of chronically-infected intranasal drug users, (2) transference of HCV RNA molecules from the nasal cavity onto sniffing implements used by drug sniffers, (3) sustained viability of HCV RNA molecules on sniffing implements, (4) the occurrence of implement-sharing behavior among drug sniffers, and (5) intranasal HCV infection of susceptible individuals through contact with a contaminated sniffing implement. The present report focused on the virological and clinical evidence related to the first two preconditions. Specifically, we address two primary research questions: Does HCV RNA exist in the nasal secretions of serum-positive drug sniffers? And, if so, can HCV RNA be transferred onto the sniffing implements used by intranasal drug users. A secondary aim of the study was to examine clinical indications that might facilitate intranasal transmission of HCV—such as

frequency of epistaxis (nose bleeds) and other nasal pathologies—in a sample of HCV-positive chronic drug sniffers.

## **METHODS**

### *Cohort*

Our target population consisted of low-income urban intranasal drug-users with chronic active HCV infection. Eligibility criteria included (a) 18 years of age or older, (b) self-reported history of intranasal drug-use, and (c) positive anti-HCV or quantitative HCV PCR test. Study participants were recruited from a neighborhood health clinic in East Harlem, New York City. Previous research has shown that HCV prevalence is high (up to 29%) among noninjecting drug users in East Harlem and surrounding communities.<sup>9</sup> Overall, 60 eligible patients enrolled in the study. At enrollment, each participant read and voluntarily provided signed informed consent in accordance with NIH, HIPAA, and New York State policies. Of the 60 enrolled patients, 38 subsequently tested HCV RNA positive on serum PCR; the other 22 were enrolled on the basis of an anti-HCV positive test result, but were later confirmed HCV RNA negative. Since this study focused on potential transmission of HCV, analyses were limited to the 38 chronic active HCV infected subjects. Study protocols were approved by three institutional review boards.

### *Data Collection Procedures and Measures*

Patient Medical Records. In accordance with HIPAA regulations, voluntary consent was obtained from each patient to release the following medical information: quantitative HCV RNA test result and viral load; hepatitis B antibody test results, liver enzyme (ALT) levels, and liver biopsy history.

Epidemiological Survey. All subjects completed a brief 30 minute survey using a touch-screen PC interface and audio computer-assisted self-interview (ACASI) software (QDS, Nova Research). Topics covered in the survey included demographics, risk behaviors and co-factors

for HCV infection, past and current injection and noninjection drug use, health status, and nasal pathology symptoms. The survey was available in both Spanish and English.

Biological Samples. Blood samples were collected from each subject using standard clinical procedures for quantitative HCV RNA testing. Additionally, two nasal secretion samples (one from each nostril), and two experimental sniffing implements were collected from each subject. Nasal secretion samples were collected with Dacron swabs using a nasal swab technique. One of the nasal swabs was placed into a sterile tube containing 1 mL of TRIzol reagent (Gibco BRL) and stored at -70°C for later HCV RNA PCR. The other nasal swab was placed into a tube containing 1 mL of OBTI solution and stored at 4°C for later detection of occult blood. Sniffing implements consisted of new (packaged) plastic soda straws commonly used by intranasal drug users. Due to the potential harmful effects of intranasally administered powdered substances, subjects were instructed to "snort air," rather than sniff an inert powder, and asked to mimic their normal drug-sniffing behavior. The sniffing straws were then collected in a manner similar to the swabs.

Detection of HCV RNA. HCV RNA was isolated from 200 µl of serum samples by QIAamp MinElute column (Qiagen) based on manufacturer's protocol; HCV RNA from nasal secretions and sniffing implements was isolated by TRIzol (Gibco BRL) based on established protocols.<sup>15</sup> The first strand cDNA was synthesized by ImProm-IITM Reverse Transcription System (Promega) using gene-specific downstream primers targeting the HCV p22 core region with minor modification of the upstream primer (410R-5'-ATGTACCCCATGAGGTCGGC-3'). HCV cDNA was amplified by PCR through 40 cycles of denaturation (94°C-30s); annealing (58°C-30s) and elongation (72°C-45s) with primers 406F-5'-TAGACCGTGCACCATGAGC-3' and 410R as above. Subsequently, PCR products were resolved through 3% agarose gel electrophoresis, hybridized to <sup>32</sup>P-labeled internal probe (5'-AGGAAGACTTCCGAGCGGTCCG CAA-3') overnight in hybridization buffer ULTRAhyb (Ambion) at 42°C, and then exposed to Kodak film.

Cloning of HCV cDNA. HCV cDNA was amplified from randomly selected HCV-positive blood sample by the high fidelity pfu polymerase (Perkin Elmer) using the same pair of primers as described above. Subsequently the HCV cDNA was cloned into TA cloning vector (Invitrogen). The pTA\_HCV was used to prepare standard curves ranging from  $1 \times 10^6$  to 10 copies of HCV mRNA and run in parallel to each set of samples. The density of each sample DNA band was then measured by Kodak Image Analysis System; and the HCV copy number for the test sample was calculated based on the numeric value derived from the HCV titration curve. HCV copies in blood samples were calculated as number of copies/ml; HCV copies in nasal secretions and implements were calculated as number of copies/sample.

Detection of Blood in Nasal Secretions and Sniffing Implements. Traces of blood in nasal secretions and sniffing implements were detected by Hexagon OBTI Kit (BLUESTAR Forensic). To determine the concentration of blood in tested samples we prepared titration curves using two-fold dilutions (ranging from  $10 \mu\text{g/ml}$  to  $0.1 \mu\text{g/ml}$ ) of human hemoglobin (Sigma). The concentration of blood in each sample was established based on the comparison of the intensity of OBTI readings between the sample and hemoglobin titration curve.

Clinical Nasal Examination. A clinical assessment of nasal cavity pathology was conducted for each patient by a physician (D. Milano), aided by anterior nasal examination. The clinical examination rendered diagnoses on 8 nasal pathologies. Most nasal pathologies were clearly visible under rhinoscopic examination. Rhinitis was diagnosed on the basis of classic symptoms of mucosal appearance (i.e. swollen, granular, edemic, erythemic, hyperemic) and quantity and quality of nasal secretions.<sup>16</sup> Clinical examination alone did not permit differential diagnosis of allergic versus nonallergic rhinitis. Rhinosinusitis was defined by the symptomatic inflammation of the paranasal sinuses and nasal cavity. Along with mucosal inflammation, diagnostic symptoms include purulent nasal drainage, chronic nasal congestion, and facial pain, pressure, or fullness.<sup>17</sup>

### *Statistical Analysis*

Consistent with our research aims, analyses were performed to determine the sample prevalence of HCV RNA in nasal secretions and sniffing implements. The prevalence of occult blood in nasal secretions and implements was also determined. Ninety-five percent confidence intervals (95% CIs) were calculated around point estimates using the adjusted Wald method. Although it was informative to quantify uncertainty due to sampling error in the point estimates (in the form of confidence intervals), no attempt was made to quantify other sources of error, such as that introduced by simulating drug sniffing behavior.<sup>18</sup> Descriptive statistics such as proportions, means and standard deviations were calculated for sample descriptors and measures of nasal pathology. The small sample size precluded tests of significance (for example, to examine statistical associations between virological and clinical variables).

## **RESULTS**

Demographics and selected sample characteristics are presented in Table 1. More than one-half of the subjects were female. Median age was 44.8, with a range of 27 to 56 years. Nearly 60% of the sample was Latino (primarily Puerto Rican), about 32% was Black/African American, and about 10% was White/other. Only 60% completed high school and most reported less than \$500 in income in the last month. The mean number of years drug sniffing was 21. About 87% of participants also reported a past history of injection drug use. Recent antibody screening revealed that 34% were anti-HIV positive, and 45% were anti-HBV positive. All 38 patients included in the study had chronic active hepatitis C. HCV serum viral load ranged from 250 to 5,000,000 copies per ml, with a median of 5,000 copies per ml. Recent liver biopsies were performed on 6 of the 38 patients; all indicated CLD ranging from Stage 1 to 4. Recent ALT level results were available for 17 patients, and gave a mean of 46.7 (range: 16 to 118; S.D.: 26.7).

Laboratory results for the detection of occult blood and HCV RNA in nasal secretion samples and on sniffing implements are presented in Table 2. Nearly 74% (28/38) of nasal secretion samples collected from viremic drug sniffers contained trace amounts of blood. The quantity of blood detected in the nasal secretion samples ranged from 0.1 µg/ml to 10 µg/ml, with 80% of the specimens measuring less than 3 µg/ml. Blood was also detected on 8% (3/38) of the sniffing straws used to simulate intranasal drug use. Lower quantities of occult blood—ranging from 0.1 µg/ml and 2 µg/ml—were detected on the 3 straws on which blood was transferred during simulated drug sniffing. HCV RNA was detected in 13% (5/38) of nasal secretion samples. The quantity of HCV in the 5 PCR-positive nasal secretion samples ranged from 10 to 100 copies per sample. Combined with results from our 2004 study,<sup>19</sup> which detected HCV RNA in the nasal secretions of 1 in 5 HCV serum-positive patients, the prevalence of HCV RNA in nasal secretions of the pooled sample is 13.9% (6/43). Hepatitis C virus RNA was also detected in 5.3% (2/38) of the sniffing implements tested—one of which contained 50 and the other 100,000 copies RNA per sample. Prevalence estimates alone suggest that there is a wide discrepancy between the presence of blood (74%) and the presence of HCV RNA (13%) in the nasal secretion samples. As show in Table 2, of the 5 patients whose nasal secretions tested positive for HCV RNA, only 3 had traces of occult blood. Moreover, of the 28 patients who tested positive for occult blood 24 were negative for HCV RNA in their nasal secretions.

Moderate to high levels of nasal pathology were recorded in this cohort of chronic intranasal drug sniffers (see Table 3). The prevalence of rhinosinusitis (11%) is consistent with that of the general population in the U.S.<sup>20</sup> In contrast, the prevalence of rhinitis was particularly high at 71%. Over 40% of subjects reported experiencing rhinorrhea or nasal congestion at least once a week; and about 8% reported nose bleeds at least once a week. About half of the patients attributed these symptoms, at least in part, to intranasal drug use. The observed prevalence of mucosal lesions and crusting was moderate at 8% and 16%, respectively; although lifetime self-reports of these symptoms were considerably higher. Four patients (11%)

were observed to have nasal septal perforations; one patient had a naso-palatal perforation; and six patients (16%) displayed symptoms of saddlenose deformation, a collapse of the bridge of the nose. These extreme pathologies have been associated with advanced nasal cavity deterioration associated with long-term intranasal drug use.<sup>21 22</sup>

## **DISCUSSION**

Numerous bodily fluids have been tested for the presence of HCV RNA, including saliva, semen, vaginal fluid, urine, sweat, tears, breast milk, gingival crevicular fluid, and cerumen.<sup>23</sup> However, with the exception of a small pilot study conducted by our team in 2004, no virological studies have been conducted to determine whether HCV is present in the nasal secretions of chronically-infected patients. In our 2004 study, we detected HCV RNA in the nasal secretions of a single patient from a sample of five serum-positive subjects.<sup>19</sup> The present study expanded upon this preliminary work and included testing for blood and HCV RNA on the sniffing implements used by intranasal drug users.

Our findings reveal a high prevalence of trace quantities of blood (74%) in the nasal secretions of HCV-positive chronic drug sniffers. In addition, we confirmed that HCV RNA is present in the nasal secretions of a substantial proportion of HCV serum-positive patients. Most significantly, this study demonstrates that both blood and HCV particles can be transferred onto sniffing implements (i.e., straws) during simulated intranasal drug use. The point prevalence of HCV in the nasal swabs (13%) and on the sniffing straws (5%) observed in this study are likely conservative estimates. Samples were collected under controlled clinical conditions from isolated subjects who were not engaged in drug sniffing behavior. It is reasonable to assume that HCV will occur in the nasal secretions with greater frequency during episodes of active drug sniffing, which may exacerbate the discharge of nasal fluids and blood.

Data presented in Table 2 contradict the assumption that in HCV serum-positive patients, detection of blood implies the occurrence of HCV molecules. This discrepancy can be

explained by two factors. First, the two assays (PCR and OBTI) were not performed on the same samples. Second, the OBTI assay for blood relies on detection of immune complexes between human hemoglobin and monoclonal anti-hHb antibodies. This reaction occurs even in the absence of viable cells. In contrast, PCR can only detect HCV RNA from intact particles. Thus, in this sample of HCV RNA serum-positive patients, the discrepancy between the high prevalence of occult blood and relatively low detection of HCV RNA in the nasal secretions might be due to a rapid deterioration of viral RNA in this environment or destruction of viral particles by mucosal immunity.

Moderate to high levels of nasal pathology were documented through clinical examination or self-report in this sample, including rhinitis, rhinorrhea and congestion, nose bleeds, lesions and crusting of the nasal mucosa, naso-palatal and naso-septal perforations, and saddlenose deformity. These nasal symptoms might aggravate conditions that facilitate intranasal HCV transmission.

This study has several limitations. The method of recruiting a sample of clinic patients with specific conditions can result in a kind of bias known as Berkson's fallacy, in which not all members of a population are equally likely to be sampled, resulting in lack of generalizability. For instance, it is likely that compared to HCV-infected drug-sniffers from the target population our sample of health clinic attendees will include a higher proportion of individuals with advanced-stage liver disease; but the sample will also likely include more individuals receiving treatment for hepatitis C. It is unknown how these factors might have biased the sample with regard to prevalence and quantity of HCV RNA in nasal secretions. The collection of separate samples for blood and HCV RNA detection in each patient made it impossible to determine the source of viral hepatitis C in the nasal cavity.

The results of this study establish the validity of two primary virological preconditions necessary for intranasal HCV transmission: (1) the presence of blood and HCV in the nasal secretions of intranasal drug users, and (2) the transference of blood and HCV from the nasal

cavity onto sniffing implements, often shared by intranasal drug users. Consequently, these findings lend important virological and clinical support to the intranasal HCV transmission hypothesis, which might help to clarify existing epidemiological evidence. Additionally, detection of HCV in nasal secretions advances the debate regarding potential iatrogenic and nosocomial transmission of HCV in the context of ENT and related clinical practices. More research is needed to confirm intranasal transmission as a mode of viral infection and determine its impact on the wider HCV epidemic.

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The study sponsor (National Institutes of Health) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the article; or in the decision to submit the paper for publication.

## **Authors Contributions and Conflicts of Interest**

Sagiv Aaron: I declare that I participated in, and contributed substantially toward the design of the study, development of novel virological assays for data collection, the major portion of virological data acquisition, analysis and interpretation of data, and drafting and revising of the article for important intellectual content. I have seen and approved the final version. I have no conflicts of interest.

James McMahon: I declare that I participated in, and contributed substantially toward the conception and design of the study, development of study protocols, coordination of the interdisciplinary research team, analysis and interpretation of data, and drafting and revising of the article for important intellectual content. I have seen and approved the final version. I have no conflicts of interest.

Danielle Milano: I declare that I participated in, and contributed substantially toward the design of the study, development of clinical protocols, the major portion of clinical data acquisition, descriptive analysis and interpretation of data, and drafting and revising the article for important intellectual content. I have seen and approved the final version. I have no conflicts of interest.

Leilani Torres: I declare that I participated in, and contributed substantially toward the design of the study, development of study protocols, the major portion of epidemiological survey data acquisition, descriptive analysis and interpretation of data, and drafting and revising the article for important intellectual content. I have seen and approved the final version. I have no conflicts of interest.

Michael Clatts: I declare that I participated in, and contributed substantially toward the conception and design of the study and study protocols, interpretation of data, and drafting and revising the article for important intellectual content. I have seen and approved the final version. I have no conflicts of interest.

Stephanie Tortu: I declare that I participated in, and contributed substantially toward the conception and design of the study and study protocols, interpretation of data, and drafting and revising the article for important intellectual content. I have seen and approved the final version. I have no conflicts of interest.

Donna Mildvan: I declare that I participated in, and contributed substantially toward the design of the study, interpretation of data, and drafting and revising the article for important intellectual content. I have seen and approved the final version. I have no conflicts of interest.

Malgorzata Simm: I declare that I participated in, and contributed substantially toward the conception and design of the study, development of novel virological assays, supervision of laboratory activities for data acquisition, analysis and interpretation of data, and drafting and revising of the article for important intellectual content. I have seen and approved the final version. I have no conflicts of interest.

**Table 1.** Sample characteristics

<b>Demographics:</b>	<b>% (N)</b>
Female	55.3% (21/38)
Age; mean (Std. Dev.)	44.8 (6.5)
Race / Ethnicity:	
Hispanic / Latino	57.9 (22/38)
Black/African American	31.6 (12/38)
White	5.3 (2/38)
Other	5.3 (2/38)
Completed high school	60.5 (23/38)
Unemployed / Public Assistance	57.9 (22/38)
Income in last month:	
Less than \$500	55.3 (21/38)
\$501 to \$1,000	34.2 (13/38)
More than \$1,000	11.6 (4/38)
<b>Drug Use:</b>	
Ever injected illegal drugs	86.8 (33/38)
Ever sniffed illegal drugs	100.0 (38/38)
Type of drug ever sniffed:	
Heroin	84.2 (32/38)
Cocaine	84.2 (32/38)
Cocaine and heroin mixed	57.9 (22/38)
Years sniffed illegal drugs; mean (Std. Dev.)	20.5 (11.7)

**Medical/Health Information:**

Anti-HIV-positive	34.2 (13/38)
Anti-HBV-positive	44.7 (17/38)
Anti-HCV-positive	100.0 (38/38)
ALT levels; mean (Std. Dev.) †	46.7 (26.7)

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† n=17

**Table 2.** Detection of HCV RNA and blood in biological specimens from serum-positive patients (N=38)

Assay	Prevalence [95% Confidence Interval]		
Specimen			
<b>Blood Detection (OBTI)</b>			
Nasal secretions	73.7 (28/38) [57.8, 85.2]		
Sniffing straws	7.9 (3/38) [2.0, 21.5]		
<b>HCV RNA PCR</b>			
Nasal secretions	13.2 (5/38) [5.3, 27.8]		
Sniffing straws	5.3 (2/38) [0.5, 18.2]		
<b>Occult Blood in Nasal Secretions</b>			
	Pos.	Neg.	
<b>HCV RNA in Nasal Secretions</b>	Pos.	1	5
	Neg.	9	33
	28	10	38

**Table 3.** Frequency of nasal pathology symptoms

<b>Symptoms</b>	<b>%</b>
<b>Anterior nasal clinical examination:</b>	
Loss of nasal hairs	10.5 (4/38)
Rhinitis	71.1 (27/38)
Rhinosinusitis	10.5 (4/38)
Presence of nasal crusting / scabbing	15.8 (6/38)
Sores or erosion of nasal mucosa	7.9 (3/38)
Saddlenose deformation	15.8 (6/38)
Naso-palatal perforation	2.6 (1/38)
Nasal septum perforation	10.5 (4/38)
<b>Nasal pathology self-report:</b>	
Frequency of nose bleeds in the last year	
Never or rarely	68.4 (26/38)
Once or a few times a month	23.7 (9/38)
Once or a few times a week	5.3 (2/38)
Once or more a day	2.6 (1/38)
Experienced a runny or stuffy nose in the last year	
Never or rarely	42.1 (16/38)
Once or a few times a month	15.8 (6/38)
Once or a few times a week	34.2 (13/38)
Once or more a day	7.9 (3/38)
Reason for nasal symptoms	
Allergies	50.0 (19/38)
Cold or Flu	26.3 (10/38)

Drug sniffing	55.3 (21/38)
Have you ever noticed any of the following problems with your nose due to drug sniffing?	
Scabs in your nose	36.8 (14/38)
Sores in your nose	21.1 (8/38)
Poor sense of smell	34.2 (13/38)
Sinus pain	34.2 (13/38)
Headaches located in your forehead	42.1 (16/38)
Double vision	13.2 (5/38)
Has a doctor or other health care professional ever told you that the inside of your nose is damaged in any way from sniffing drugs?	18.4 (7/38)

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## References

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- <sup>1</sup> Thomas DL, Astemborski J, Rai RM, Anania FA, Schaeffer M, Galai N, et al. The natural history of hepatitis C virus infection. Host, viral, and environmental factors. *J Am Med Assoc.* 2000; 284:450-456.
- <sup>2</sup> Hollinger FB. Factors contributing to the evolution and outcome of cirrhosis in hepatitis C. *Clin Liver Dis.* 1999; 3(4):741-755.
- <sup>3</sup> Wasley A, Alter MJ. Epidemiology of hepatitis C: geographic differences and temporal trends. *Semin Liver Dis.* 2000; 20:1-16.
- <sup>4</sup> Edlin BR. Five million Americans infected with the hepatitis C virus: a corrected estimate. 56th Annual Meeting of the American Association for the Study of Liver Diseases (Boston). [abstract] *Hepatology.* 2005; 42(4 Suppl 1):213A.
- <sup>5</sup> Memon MI, Memon MA. Hepatitis C: an epidemiological review. *J Viral Hepat.* 2002; 9(2):84-100.
- <sup>6</sup> Ackerman Z, Ackerman E, Paltiel O. Intrafamilial transmission of hepatitis C virus: a systematic review. *J Viral Hepat.* 2000; 7:93-103
- <sup>7</sup> Wang CC, Krantz E, Klarquist J, Krows M, McBride L, Scott EP, et al. Acute hepatitis C in a contemporary US cohort: modes of acquisition and factors influencing viral clearance. *J Infect Dis.* 2007; 196(10):1474-1482.
- <sup>8</sup> Flamm SL, Parker RA, Chopra S. Risk factors associated with chronic hepatitis C virus infection: limited frequency of an unidentified source of transmission. *Am J Gastroenterol.* 1998; 93: 597-600.
- <sup>9</sup> Tortu S, Neaigus A, McMahon JM, Hagen D. Hepatitis C among noninjecting drug users: a report. *Subst Use Misuse.* 2001; 36(4):523-534.
- <sup>10</sup> Conry-Cantilena C, van Raden M, Gible J, Melpolder J, Shakil AO, Viladomiu L, et al. Routes of infection, viremia, and liver disease in blood donors found to have hepatitis C virus infection. *N Engl J Med.* 1996; 334:1691-1696.
- <sup>11</sup> Murphy EL, Bryzman SM, Glynn SA, Ameti DI, Thomson RA, Williams AE, et al. Risk factors for hepatitis C virus infection in United States blood donors. *Hepatology.* 2000; 31:756-762
- <sup>12</sup> Peters FT, Maurer HH, Hellstern P. Prevalence of illicit drug use in plasmapheresis donors. *Vox Sang.* 2003; 84:91-95.
- <sup>13</sup> McMahon JM, Tortu S. A potential hidden source of hepatitis C infection among noninjecting drug users. *J Psychoactive Drugs.* 2003; 35(4):455-460.
- <sup>14</sup> Scheinmann R, Hagan H, Lelutiu-Weinberger C, Stern R, Jarlais DC, Flom PL et al. Non-injection drug use and Hepatitis C Virus: A systematic review. *Drug Alcohol Depend,* 2007. 89(1):1-12.
- <sup>15</sup> Chomczynski P, Sacchi N. Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. *Anal Biochem.* 1987; 162(1):156-159.
- <sup>16</sup> Dykewicz M. Clinical approach to diagnosis and treatment of nonallergic rhinitis. *Clin Allergy Immunol.* 2007; 19:335-350.

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- <sup>17</sup> Rosenfeld RM, Andes D, Bhattacharyya N, Cheung D, Eisenberg S, Ganiats TG, et al. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg.* 2007; 137(3 Suppl): S1-31.
- <sup>18</sup> Phillips CV, LaPole LM. Quantifying errors without random sampling. *BMC Med Res Methodol.* 2003; 3:9.
- <sup>19</sup> McMahon JM, Simm M, Milano D, Clatts M. Detection of hepatitis C virus in the nasal secretions of an intranasal drug-user. *Ann Clin Microbiol Antimicrob.* 2004; 3(6):1-4.
- <sup>20</sup> Lethbridge-Cejku M, Rose D, Vickerie J. Summary health statistics for U.S. adults: National Health Interview Survey, 2004. National Center for Health Statistics. *Vital Health Stat.* 2006; 10(228):19 –22.
- <sup>21</sup> Villa PD. Midfacial complications of prolonged cocaine snorting. *J Can Dent Assoc.* 1999; 65(4):218-223.
- <sup>22</sup> Goodger NM, Wang J, Pogrel MA. Palatal and nasal necrosis resulting from cocaine misuse. *Br Dent J.* 2005; 198(6):333-334.
- <sup>23</sup> Ackerman Z, Paltiel O, Glikberg F, Ackerman E: Hepatitis C virus in various human body fluids: a systematic review. *Hepatol Res.* 1998; 11: 26-40.