

Viral Hepatitis in a Canadian Street-involved Population

S. Moses, MD, MPH^{1,2}

K. Mestery¹

K.D.E. Kaita³

G.Y. Minuk, MD, FRCPC³

ABSTRACT

Background: Data on the prevalence and compliance with management of viral hepatitis in the street-involved population are limited.

Method: Hepatitis A (HAV), B (HBV) and C (HCV) serology and compliance with HBV vaccination were documented in 533 street-involved individuals.

Results: The mean age of the study population was 25.7 years (range: 11-65) and 53% were female. Serologic evidence of HAV infection was present in 53%; HBV, 12% (3% ongoing infection); and HCV, 17%. HAV infections were associated with Aboriginal/Metis ethnicity and age over 25 years; HBV with injection drug use (IDU); and HCV with IDU, sex trade work and age over 25 years. Compliance with three-step HBV vaccination was 98%, 77% and 63%.

Conclusions: HAV, HBV and HCV are common infections in urban street-involved persons. Successful HBV (and presumably HAV) vaccination can be achieved in the majority of this population, but concerns exist regarding compliance with more long-term, parenterally-based antiviral therapies.

Advances in standards of living, antiviral therapies and immunoprophylaxis have resulted in significant changes in the prevalence of viral hepatitis throughout the world.¹⁻⁹ Despite these advances, street-involved people are one segment of the population that remains at relatively high risk of acquiring and transmitting hepatotropic viruses. These are largely young adults who are active in high-risk activities such as injection drug use, sex trade work, unprotected sex, tattoos and body piercing, etc. Unfortunately, data documenting the prevalence of viral hepatitis in this population are limited. Moreover, those studies that have been reported are largely confined to studies describing the prevalence of only one type of viral hepatitis, or various types of viral hepatitis but within only one subgroup (often injection drug users) of the street-connected population.¹⁰⁻¹⁴ Even more limited are data describing compliance rates with therapeutic and/or preventive measures in this population.¹⁵ Because such data are critical in designing effective public health measures to control and manage viral hepatitis within urban communities, we documented the prevalence of hepatitis A (HAV), B (HBV) and C (HCV) infections in a large, urban, street-involved population. We also documented the compliance rate of this population with HBV vaccination as a potential predictor of the success (or failure) of future vaccination and antiviral efforts.

METHODS

Study subjects were recruited between August 1, 1995 and April 1, 1996 in the inner city of Winnipeg, Manitoba, a centre with a population of approximately 650,000 individuals. Data on HBV vaccination was collected up to September 1998. The city's population is generally considered working and middle class with a relatively large representation of Native Canadians, often referred to as Aboriginals (10%), and fewer Southeast Asians (2%).

Street-involved people were identified as attendees of 11 inner city, sentinel sites who were actively participating in one or more of the following activities: 1) sharing needles, syringes and/or any other equipment used to inject drugs; 2) injection drug use; 3) sex trade work; 4) unprotected sex with two or more partners in the last year; 5) sniffing of solvents; 6) unprotected anal sex; 7) sub-

The translation of the Abstract appears at the end of the article.

1. Public Health Branch, Manitoba Health, Winnipeg, MB

2. Departments of Medical Microbiology, Medicine and Community Health Sciences, University of Manitoba, Winnipeg, MB

3. Liver Diseases Unit, University of Manitoba

Correspondence: Dr. G.Y. Minuk, Liver Diseases Unit, John Buhler Research Centre, 803F-715 McDermot Avenue, Winnipeg, MB R3E 3P4, Tel: 204-789-3204, Fax: 204-789-3971, E-mail: gminuk@cc.umanitoba.ca

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stance abuse or misuse, i.e. the use of alcohol, over-the-counter, prescription or illicit drugs to the point of interference with responsibilities and activities of daily living; 8) street involvement (i.e., homeless, gang-involved, 'hanging out' on the street) or 9) a history (self-reported) of two or more sexually transmitted diseases in the last year.

Subjects attending the sentinel sites who met the above criteria for being 'high risk' were recruited by a nurse or a physician to participate in the study. In a subsequent interview, a nurse or physician completed a data collection sheet with the subject, assuring them of the confidentiality of the information. After an educational session about hepatitis infections and prevention, subjects were invited to sign a consent form authorizing administration of the Hepatitis B vaccine. Blood was then drawn for hepatitis serology, immediately after which the first dose of the vaccine was given. Subjects were provided with literature on hepatitis and other relevant infections, and counselled about risk behaviours and lifestyle choices. They were then asked to return for the second and third doses of the vaccine at one and six months after the initial dose, as per the manufacturer's instructions. Individuals subsequently found to be susceptible to HBV infection (hepatitis surface antigen [HBsAg] and antibody to HBsAg [anti-HBs] negative) were offered the second and third doses of the HBV vaccine while those who were immune (anti-HBs positive) were counselled and those with active infection (HBsAg positive) were referred for further investigations and management.

Serology was obtained for the following tests: immunoglobulin G antibody to hepatitis A virus (IgG anti-HAV), HBsAg, anti-HBs and antibody to hepatitis C virus (anti-HCV). Positive screening tests for anti-HCV (by second generation enzyme-linked immunoassay) were followed by hepatitis C virus - RNA (HCV-RNA) testing using reverse transcriptase, polymerase chain reaction (RT-PCR). Only those positive by both assays (>90% of those tested) were considered HCV positive. All tests were performed by the Cadham Provincial Laboratory in Winnipeg, Manitoba, using commercially available assays or in the case of HCV-RNA testing, an in-house PCR assay with a sensitivity of 1,000 copies/ml and specificity of 98%.

Incidence rates of new HBV cases (IgM anti-HBc positive) within the city were available for a 1.5-year period prior to the onset of

TABLE I

Prevalence of High-risk Activities in Urban, Street-involved People by Aboriginal/Non-Aboriginal Status*

Risk Factor	Aboriginal (%) (First Nations or Metis) (N=317)	Non-Aboriginal (%) (N=183)	Overall (%) (N=500)
Multiple sex partners	263 (83%)	146 (80%)	409 (82%)
Injection drug use	105 (33%)	41 (22%)	146 (29%)
History of STD	112 (35%)	31 (17%)	143 (29%)
Solvent use	93 (29%)	11 (6%)	104 (21%)
Sex trade work	48 (15%)	26 (14%)	74 (15%)
Unprotected anal sex	29 (9%)	24 (13%)	53 (11%)

* Of the 533 participants, Aboriginal/Non-Aboriginal status was available for 500.

TABLE II

Hepatitis A, B and C Virus Infections in Urban, Street-involved People

	HAV (IgG Anti-HAV)	HBV (HBsAg or Anti-HBs)	HCV (Anti-HCV)
Individuals tested	408	432	432
Positive	215 (53%)	52 (12.0%) • 12 HBsAg (2.8%) • 40 Anti-HBs (9.2%)	74 (17.1%)

TABLE III

Hepatitis A, B and C Virus Infections by Aboriginal and Non-Aboriginal Status

	Metis	First Nations	Non-Aboriginal	Odds Ratio (95% CI)	P-Value
Anti-HAV	41.5% (22/53)	71.7% (152/212)	27.7% (33/119)	5.0 (3.1-8.0)	<0.001
HBsAg	1.9% (1/53)	2.3% (5/217)	4.5% (6/134)		NS
Anti-HBs	11.5% (6/52)	9.8% (21/214)	9.0% (12/133)		NS
Anti-HCV	22.3% (12/53)	19.4% (42/216)	14.4% (19/132)	1.5 (0.84-2.6)	0.17

the study, throughout the 9-month course of the study and for 2.5 years thereafter. These data were available from the provincial public health department surveillance system.

The study was submitted to Manitoba Health for ethical review and written informed consent was obtained from all participants prior to enrolment.

Statistical analysis

A Chi-square test was used to compare proportions and to evaluate univariate odds ratios for risk factors for HAV, HBV and HCV. The Student t-test was used to compare means. Stepwise logistic regression was used to calculate multivariate odds ratios. All data were analyzed using SPSS for Windows, version 9.0.

RESULTS

Demographics

A total of 533 individuals agreed to participate in the study (2 declined). The majority (53%) were female. The mean age of the study population was 25.7 years (range 11-65). The mean age of

males (27.1, range 13-65 yrs) was higher than that of females (24.4, range 11-60 yrs, $p < 0.05$). Three hundred and sixty-four of the participants (68%) listed the city centre as their primary residence while 90 (17%) resided in the suburbs. The remaining 81 (15%) individuals considered reservations or rural communities as their primary place of residence. Of the 533 participants, data on ethnic background were available for 500. Aboriginals constituted the largest proportion of the study group (63%) of whom 317 (52%) were First Nations (North American Indian) and 56 (11%) Metis (mixture of Aboriginal and French Canadian). In addition, there were 167 (33%) Caucasians and 16 (3.2%) other groups represented.

Risk factors

Overall, 29% of the population reported injection drug use. Other risk factors included: a history of multiple (two or more in the previous year) sex partners (82%), a history of sexually transmitted diseases (29%), sex trade work (15%) and

TABLE IV

Factors Associated with Hepatitis A Virus Infection (Uni- and Multivariate Analyses)*

	N	%	Univariate Analysis			Multivariate Analysis		
			OR	95% CI	P-Value	OR	95% CI	P-Value
Overall anti-HAV positive	215/408	52.7						
Age ≥ 25	117/180	65.0	2.5	1.6-3.7	<0.001	4.0	2.4-6.6	<0.001
Female	113/217	52.1			NS			NS
Aboriginal or Metis ethnicity	174/265	65.7	5.0	3.1-8.0	<0.001	6.6	3.8-11.5	<0.001
STD history	76/111	68.5	2.5	1.6-3.9	<0.001	2.0	1.2-3.3	0.01
Injection drug use	85/128	66.4	2.3	1.5-3.5	<0.001	1.6	0.99-2.7	0.06
Solvent use	71/96	74.0	3.3	2.0-5.5	<0.001			NS

* NS= Not significant

TABLE V

Factors Associated with Hepatitis B Virus Infection (Uni- and Multivariate Analyses)*

	N	%	Univariate Analysis			Multivariate Analysis		
			OR	95% CI	P-Value	OR	95% CI	P-Value
Overall HBV positive	52/432	12.0						
Age ≥ 25	28/194	14.4	1.5	0.8-2.7	NS			NS
Female	31/231	13.4			NS			NS
Sex trade work	15/67	22.4	2.6	1.3-5.1	0.004			NS
STD history	20/117	17.1	1.8	1.0-3.3	0.05			NS
Injection drug use	37/131	28.2	7.5	3.9-14.3	<0.001	6.6	3.3-13.1	<0.001
Solvent use	17/97	17.5	1.8	0.97-3.4	0.06			NS

* NS=not significant

TABLE VI

Factors Associated with Hepatitis C Virus Infection (Uni- and Multivariate Analyses)*

	N	%	Univariate Analysis			Multivariate Analysis		
			OR	95% CI	P-Value	OR	95% CI	P-Value
Overall anti-HCV positive	74/432	17.4						
Age ≥ 25	45/191	23.6	2.2	1.3-3.7	<0.005	2.8	1.4-5.8	<0.01
Sex trade work	26/67	38.8	4.2	2.3-7.5	<0.001	3.6	1.5-8.5	<0.005
STD history	30/113	26.5	2.2	1.3-3.7	<0.003			NS
Injection drug use	63/132	47.7	23.5	11.8-46.9	<0.001	23.7	11.1-50.8	<0.001
Female	46/229	20.1	1.5	0.9-2.5	NS			
Solvent use	30/67	30.9	2.9	1.7-5.0	<0.001			NS

* NS= Not significant

unprotected anal sex (11%). In many instances, multiple risk factors were identified. The distribution of these and other risk factors within the two largest groups (Aboriginals and Non-Aboriginals) are provided in Table I. With the exception of sex trade work where females were more often represented than males (24% versus 4%, $p < 0.001$), there were no significant gender differences within the various risk activities.

Serologic results

As shown in Table II, of the 408 serum samples available in adequate amounts for HAV testing, 215 (52.9%) were positive for IgG anti-HAV. A larger volume and number of samples (432) were available for HBV and HCV testing. Here, 52 (12%) tested positive for either HBsAg or anti-HBs (HBV seropositive) and 74 (17%) were confirmed anti-HCV positive. Of the 52 HBV seropositive individuals, 12 (2.8%) were HBsAg positive and 40 (9.2%) were anti-HBs positive.

Overall, 252 (58%) of the samples were positive for serologic evidence of either HAV, HBV or HCV exposure. A total of 19 (4.4%) individuals tested were positive for HBV markers (HBsAg or anti-HBs) without anti-HCV and 41 (9.5%) for anti-HCV without HBV markers. Serologic evidence of exposure to both HBV and HCV was present in 33 (8%) individuals while 4 (1%) had ongoing infections with both viruses.

Differences in viral prevalence rates between Aboriginal or Metis and non-Aboriginals were only significant for HAV infection (Table III).

Association of risk factors and serologic results

The results of univariate analysis for risk factors associated with HAV infections are provided in Table IV. Age greater than 25 years, Aboriginal or Metis ethnicity, a history of STD, injection drug use and sol-

vent use were all significantly associated with anti-HAV positivity, but only age and ethnicity remained significant following multivariate analysis (odds ratios of 4.0 and 6.6 respectively) ($p < 0.001$).

Following univariate analyses, the following risk factors for HBV exposure were identified (Table V): injection drug use, sex trade work and a history of sexually transmitted diseases. However, multivariate analysis revealed that only injection drug use was significantly associated with HBV infections ($p < 0.001$).

As shown in Table VI, univariate analyses for risk factors associated with HCV infection revealed that injection drug use, sex trade work, solvent use, a history of sexually transmitted diseases, and age over 25 years were associated with odds ratios greater than 2. Following multivariate analysis, injection drug use, sex trade work, and age over 25 years remained significant associations. Of note, sex trade work was

TABLE VII

Factors Associated with Completing a Three-dose Series of Hepatitis B Vaccine (Uni- and Multivariate Analyses)*

	N	%	Univariate Analysis			Multivariate Analysis		
			OR	95% CI	P-Value	OR	95% CI	P-Value
Overall compliant	293/468	62.6						
Age \geq 25	137/191	71.7	2.0	1.3-3.0	<0.001	1.9	1.2-3.0	<0.01
Non-Aboriginal	110/161	68.3	1.4	0.96-2.2	NS			NS
Anal sex	42/51	82.4	3.3	1.5-6.5	<0.005	2.8	1.5-6.7	<0.05
Solvent use	66/85	77.6	2.4	1.4-4.1	<0.005	2.8	1.5-5.3	<0.005

Not significant: gender, multiple sex partners, sex trade work, STD history, injection drug use

* NS= not significant

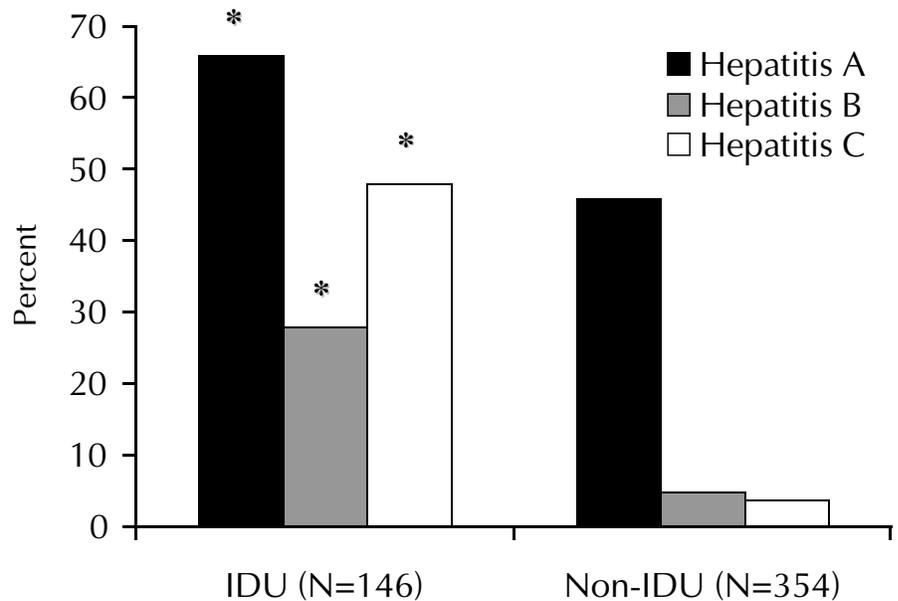
associated with a higher prevalence of HCV infection in both injection drug users and those who denied injection drug use. Specifically, the prevalence of HCV infection was 60% (CI: 42-76%) in sex trade workers with a history of injection drug use versus 44% (CI: 33-54%) in non sex trade workers with a history of injection drug use. In individuals who denied injection drug use, the prevalence of HCV infection was 16% (CI: 5.3-33%) in sex trade workers versus 2.3% (CI: 0.8-4.9%) in non sex trade workers.

With all viruses, infection rates were significantly higher in injection drug users than in individuals who denied injection drug use (Figure 1).

HBV vaccination

Of the 533 study participants, 523 (98%) received the initial dose of HBV vaccine. Shortly thereafter, the results of the original (pre-vaccination) HBsAg and anti-HBs testing became available and 52 individuals were discovered to be either HBsAg or anti-HBs positive and thus not eligible for vaccination. Of the remaining 471, 361 (77%) returned for the second vaccination step. The final dose of the vaccine was received in 293 of 468 (63%) individuals (2 individuals died of non-hepatic causes prior to the third dose and a third had to be rescheduled). Of note, none of 19 individuals who had reported a history of HBV immunization in the past were positive for anti-HBs, suggesting that in at least some cases, HBV vaccination had in fact not occurred.

The median time interval between the first two vaccine doses (target 30 days) was 35 days (range 10-651); between the second and third doses (target 150 days), 155 days (range 37-904); and between the first and third dose (target 180 days), 203 days (range 87-936). The success rate of HBV vaccination within the 11 study sites ranged from 12.5%-100% with 8 of the 11 sites having success rates exceeding 50%.



* $p < 0.001$ versus non IDU

Figure 1. Hepatitis A, B and C prevalence among injection and non-injection drug users. Prevalence ratios for hepatitis A: 1.4, 95% CI: 1.2-1.7; hepatitis B: 5.7, 95% CI: 3.2-10.0; hepatitis C: 12.8, 95% CI: 6.9-23.3 in 146 injection drug users (IDU) versus 354 non-IDU.

Univariate analyses for factors predicting completion of HBV vaccination (Table VII) identified age over 25 years, unprotected anal sex and solvent use, as positive predictor variables. The same predictor variables were maintained following multivariate analysis.

Reported new cases of hepatitis B

The reported incidence of new cases of hepatitis B (IgM anti-HBc positive) within the city over the period prior to, during and following the study are provided in Figure 2. A progressive decline in incidence was observed between the second and third quarters of 1996, representing the periods immediately following HBV vaccinations in this group. This decline was maintained thereafter.

DISCUSSION

The results of this study indicate that serologic evidence of HAV, HBV and HCV infections are higher in street-involved persons than has been reported in the general population of the country. The results also indicate that active HBV and HCV infections are more common in these individuals. Increased rates of HAV infection were associated with Aboriginal ethnicity and age over 25 years, HBV exposure with a history of injection drug use, and HCV infection with injection drug use, sex trade work and age over 25 years. Finally, a declining majority of these individuals will complete a three-dose series of HBV vaccination.

Although not studied concurrently, the anti-HAV seroprevalence in Canadians

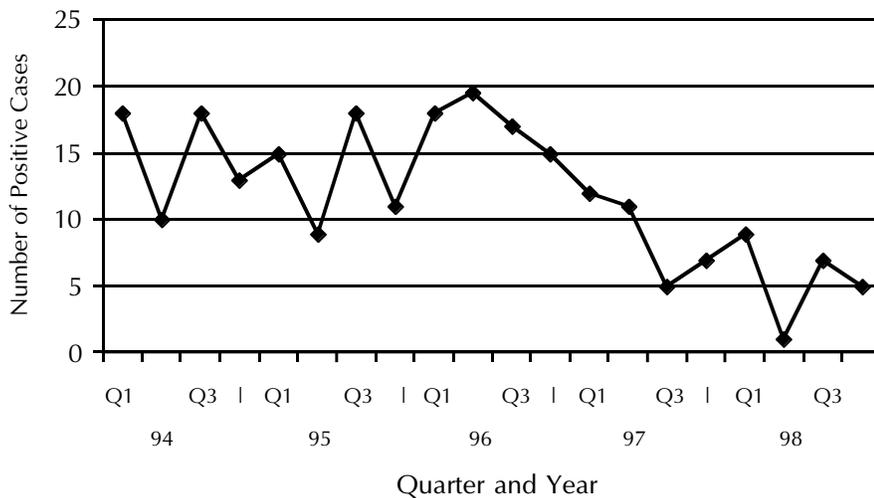


Figure 2. New HBsAg cases (IgM anti-HBc positive) in Winnipeg, by quarter.

between the ages of 20 and 30 (the mean age of this study population) is approximately 15-30%.¹⁶ Thus, anti-HAV positivity rates were higher in street-involved people than would have been predicted based on data from the general population. The reason for the higher rates is likely multifactorial. Because HAV is predominantly spread by the fecal-oral route, oral-anal intercourse is an efficient means of transmitting this virus.¹⁷ Although not specifically addressed in the study questionnaire, this practice is thought to be more common in street-involved people, particularly among those with a history of unprotected anal sex and sex trade work.¹⁸⁻²⁰ That HAV can be transmitted by parenteral routes (albeit infrequently) provides yet another possible route for HAV infection in these individuals.²¹ Finally, it is also possible that the high rates of HAV infection are unrelated to the activities described in street-involved people, but rather reflect the low socio-economic conditions present in their home life.^{22,23}

The prevalence of HBV exposure (12%) was also higher than that reported in the general population (5%) but lower than rates reported by others in similar high-risk populations.^{24,25} The reason for the latter discrepancy may relate to the "background" prevalence of HBV in the general populations of the previous studies.²⁶ The higher HBV rates in street-involved people in this study compared to the general population was not a surprising finding as HBV is known to be transmitted by certain parenteral and non-parenteral routes,

many of which are more common in street-involved people. Thus, serologic evidence of exposure was highest among injection drug users and individuals with frequent sexual exposures. Nonetheless, while injection drug use, sex trade work and a history of sexually transmitted diseases were all identified as being associated with HBV infections following univariate analyses, only injection drug use remained significant on multivariate analysis. Indeed, in absolute terms, injection drug users were 5 times more likely to have serologic evidence of HBV exposure than non-injection drug users.

Assuming that 5% of HBV-exposed adults subsequently develop chronic HBV infections, based on the 12% exposure figure in street-involved people, a 0.6% HBsAg positive prevalence would have been expected.²⁷ The explanation(s) for the higher than predicted HBsAg positive carrier figure (2.8% versus 0.6%) remain(s) to be determined. As age of exposure to HBV inversely correlates with the risk of progression to chronic infection, it is possible that these individuals were infected at a young age.^{28,29} Another factor that influences progression to chronicity is gender, with males being more likely to develop chronic infections than females.³⁰ However, the gender distribution in this study (48% males) was not in keeping with a male predominance. Because HIV serology was not performed, we cannot rule out the possibility that many of these subjects had an underlying immune-compromised state which would predispose to chronicity.

ty.³¹ In support of this possibility are results of a concurrent study in a 'high-risk' population of injection drug users in Winnipeg, wherein 12.6% of subjects were documented to be seropositive for HIV infection (unpublished data). Finally, it should be noted that the number of HBsAg positive cases was small, and therefore a type I error must also be considered.

The seroprevalence of anti-HCV in the general population of Canada is between 0.5 and 2%.³²⁻³⁴ Unlike HBV, HCV is largely transmitted by parenteral routes.³⁵ In this study, 17% of street-involved people had serologic evidence of HCV infection, presumably reflecting the large number of individuals attesting to injection drug use. Perhaps more surprising was the finding on multivariate analysis that sex trade work was associated with HCV infection (OR; 3.6, $p < 0.005$). Whether this finding reflects the relatively uncommon transmission of HCV through sexual/intimate contact or whether these individuals were reluctant to disclose a history of injection drug use is unclear.³⁶ An additional possibility is that sex trade workers inject more often and perhaps with higher-risk injection partners than non sex trade workers.

Safe and effective prophylaxis now exists for both HAV and HBV infections. Thus, it is encouraging that the majority of participants in this study complied with all three steps of the HBV vaccination series. Indeed, the subsequent decline in new HBV cases reported in this urban centre may well reflect the success of the HBV vaccination program in this high-risk group. Although it is not possible to rule out other factors which may have contributed to that decline, new public health programs were not put in place for HBV prevention, and there was no evidence of significant behavioural changes in this population during the study period. However, while encouraging for future HAV and HBV prevention, the declining compliance rates with second (77%) and third (63%) doses of the vaccine raise concerns regarding this population's commitment to long-term, parenterally-based antiviral therapies.

Aboriginals constitute approximately 10% of the city's urban population, yet 52% of the street-involved people in this study were First Nations and a further 11% were Metis (Aboriginal plus French

Canadian). Presumably, this reflects the low socio-economic status and high unemployment rates of this particular segment of the community. When analyzed separately, the Aboriginal group tended to be younger, more commonly solvent users and more often anti-HAV positive. The latter finding highlights the need for HAV vaccination in this group.

It should be noted that due to the non-random selection of participants in this survey, generalization of the results to other populations must be undertaken with caution. The self-selection and willingness of the participants to enroll in the project may have resulted in a bias toward a group at lower risk of infection and higher rates of compliance. The variation in interviewing skill, subject comfort, time spent with clients, as well as the highly sensitive subject matter, could also have influenced participants' responses towards socially acceptable answers.

In summary, the results of this study indicate that viral hepatitis is common in street-involved people. Both high rates of exposure and infection exist in this group. Injection drug use is the risk factor most often implicated as the source of infection. Successful vaccination can be predicted for the majority of those individuals susceptible to HAV and HBV infections, but concerns exist regarding this population's willingness to comply with long-term, parenterally-based antiviral therapies.

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RÉSUMÉ

Contexte : On manque de données sur la prévalence de l'hépatite virale et l'observance des traitements chez les personnes de la rue.

Méthode : Nous avons documenté le dépistage des virus de l'hépatite A, B et C (VHA, VHB et VHC) et l'observance du vaccin anti-VHB chez 533 personnes de la rue.

Résultats : La population étudiée avait en moyenne 25,7 ans (intervalle : 11-65), et 53 % étaient des femmes. Des signes sérologiques d'infection étaient présents chez 53 % des sujets pour le VHA, 12 % pour le VHB (dont 3 % d'infections actives) et 17 % pour le VHC. Les infections à VHA étaient associées à l'origine ethnique autochtone ou métisse et aux plus de 25 ans; les infections à VHB, aux utilisateurs de drogues injectables (UDI); et les infections à VHC, aux UDI, aux travailleurs du sexe et aux plus de 25 ans. Les taux d'observance du programme de vaccination anti-VHB en trois étapes étaient de 98 %, 77 % et 63 %, respectivement.

Interprétation : Les infections à VHA, VHB ou VHC sont communes chez les personnes de la rue. Il serait possible d'immuniser la majorité d'entre elles contre le VHB (et sans doute contre le VHA), mais l'observance des traitements antiviraux à long terme administrés par voie parentérale est loin d'être assurée.