

High prevalence of hepatitis C virus infection in Belgian intravenous drug users and potential role of the "Cotton-filter" in transmission : the GEMT* study

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Abstract

Aims : To estimate viral seroprevalences for HCV, HBV and HIV among belgian intravenous (IVDU) and non intravenous (non-IVDU) drug users ; to assess risk factors for HCV infection in IVDU ; to assess feasibility of chronic hepatitis C follow-up in this population.

Design : Cross-sectional study. Demographic and behavioural characteristics were obtained by a standardized questionnaire. Serum samples were tested for HCV, HBV and HIV.

Subjects and setting : 329 patients (244 IVDU and 85 non-IVDU) attending ten general practitioners in 1995.

Results : HCV seroprevalence was 78.3% ; it was 35.7% for HBV and 0.9% for HIV in IVDU, vs 2.4%, 8.3% and 0%, respectively, in non-IVDU. In logistic regression analysis, independent risk factors for HCV infection were : 1/ sharing of syringes and/or of "cottons" used as filters (adjusted prevalence odds ratio [POR] = 31.7 ; 95% confidence interval [CI] = 9.8 - 102.5), 2/ duration of injecting upper than one month (adjusted POR = 8.6 ; CI = 3.0-24.7) and 3/ age (adjusted POR = 1.2 by year of difference ; CI = 1.0-1.3). A biochemical follow-up was obtained in 70% of HCV seropositive users ; 79.5% of them had chronic hepatitis C (mean value of ALT = 3.5 times upper normal value, range 1.1-23.0). Among these, 24.7% went through liver biopsy during the three years follow-up period of the study.

Conclusions : HCV seroprevalence is very high among belgian IVDU. Prevention strategies have to focus on neophytes injectors. They must be urgently revisited for what concern needles/syringes exchange programs : "cottons" must be included. Follow-up and treatment of chronic hepatitis C seem to be poorly effective among drug users. (*Acta gastroenterol. belg.*, 2000, 63, 147-153).

Key words : intravenous drug users, general practice, hepatitis C virus, prevalence, risk factors.

Introduction

Hepatitis C virus (HCV) infection among intravenous drug users (IVDU) is a major problem of public health. In previous studies, prevalence of anti-HCV antibodies ranged from 55% to 100% worldwide (1-30). Incidence ranged from 5% to 30% (10,31-36) and far more in high-risk people as less than twenty years old users (36), prisoner users (20, 36, 37) and those injecting cocaine (15,35, 38). Two major risk factors related to injection have been emphasized : needle/syringe sharing or borrowing (6,7,10,16,22,23,27,30,31,39,40,41) and total duration of injecting (3,8,10,21,27). Sharing of other injecting equipment (spoons, filters, injection water) suspected by some authors (20,22,40,42) was never investigated.

This epidemiological cross-sectional study was con-

ducted by belgian general practitioners (GP) of GEMT (*Groupe d'Etude des Maladies liées à la Toxicomanie*) and was designed for a triple purpose : 1/ to assess seroprevalences for HCV, HBV and HIV among belgian IVDU in comparison to non-IVDU, 2/ to refine correlations between HCV infection and various risk behaviours related to injecting and 3/ to appraise feasibility of follow-up to detect potential candidates for therapy.

Patients and methods

Population study and data collection

During the year 1995 ten GP recruited illicit drug users attending them into the study. Nine of them had inner-city family practice (Charleroi, population 200,000) and cared this patients mostly by methadone maintenance therapy (MMT). The tenth was working in a short-term residential clinic for drug users ("*Transition*", Gilly) where classical detoxification treatments were performed. Inclusion criteria were past or actual use of heroin ; addiction to associated drugs such cocaine, benzodiazepines, amphetamines or alcohol was not exclusion criterion. By face to face interview, data were collected using a standardized questionnaire : date of birth, gender, starting age of heroin use, intravenous drug use (ever/never), total duration of injecting, frequency of injecting (daily, occasionally [from daily to monthly], exceptionally [monthly or less frequently]), alone or in group usually injecting, disinfection before injecting (always/not always), sharing (ever/never) of needles/syringes, of spoons in which the drug is diluted and of "cottons" used as filters. Patients sera were tested for viral markers of HCV, HBV and HIV and for alanine aminotransferase (ALT). All patients were prospectively followed until June 1998. ALT values and initially negative viral markers were screened twice a year. In addition, GP had to notice if liver biopsy or PCR test for HCV RNA determination were performed.

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Laboratory methods

Serological tests were carried out in various laboratories. Anti-HCV antibodies were measured by MEIA or ELISA methods (second or third generation) and confirmed by RIBA-2 test (positive if two or more positive among the four antibodies anti-C1, anti-C2, anti-NS3 and anti-NS4). Hepatitis B surface antigen (HBsAg) and core antibodies (HBcAb) were assayed by ELISA test, and surface antibodies (HBsAb) by radioimmunoassay (positive if > 10 UI/ml). Anti-HIV antibodies (IgM and IgG) were screened by ELISA test and confirmed by Western blotting. ALT values were expressed in multiple of upper limit of normal (ULN).

Statistical analysis

Two tailed chi-squared test (or Fisher's exact test when indicated) and Student's t-test were used to assess univariate associations between serological test results and demographic or behavioural variables, with p value $< .05$ for difference. Relative risk of prevalence with 95% confidence interval was used to compare strengths of various associations. To adjust for confounding factors and to assess independent risk factors for HCV, multivariate logistic regression models were used as follows: with anti-HCV positivity as dependent variable and risk behaviours associated at $p < .20$ level in univariate analyse, plus age and gender, as covariates, backward stepwise selections using the -2 log likelihood decrease were performed with a probability exclusion criterion of 0.10, giving for each factor this adjusted prevalence odds ratio and adjusted p . SPSS software (version 7.5) for a personal computer was used for all calculations.

Results

Demographic characteristics

329 heroin users were included, among them 244 IVDU (at least one injection) and 85 non-IVDU (never injected). 74% were men ($n = 244$) and 26% were women ($n = 85$). This 3:1 sex ratio did not significantly differ between IVDU and non-IVDU. Mean age at inclusion was 25.9 years (SD 4.7, range 16-45) and median was 25.2 years (interquartile range 23-29). IVDU were significantly older than non-IVDU: their mean ages were respectively 26.3 years (SD 4.6) and 24.8 years (SD 4.9) ($p = .008$). Men (26.7 years, SD 4.9) were significantly older than women (25.2 years, SD 3.6) ($p = .007$). Mean age of first injection was 21 years and ranged from 13 to 34 years, without significant difference with respect to gender.

Viral seroprevalences

Seroprevalences for HCV, HBV and HIV are shown in Table I. Risk of HCV and HBV infection appeared

closely related to injecting: prevalence rate of anti-HCV antibodies was 78.3% (CI 73.1-83.5) for IVDU and 2.4% (CI 0-5.6) for non-IVDU, and prevalence rate of all HBV viral markers was 35.7% (CI 29.6-41.8) for IVDU and 8.3% (CI 2.3-14.4) for non-IVDU (8.4% vs 0% for HBsAg, 27.7% vs 8.3% for anti-HBs and anti-HBc antibodies confounded). All these differences were statistically significant. We only observed 2 patients with anti-HIV antibodies, these 2 patients were IVDU (prevalence rate 0.9%).

Risk behaviours related to injecting

Data were missing for 3-29% of the 244 IVDU with regard to the different behaviours investigated. Most of IVDU had risk-taking behaviours: 65% of them (153/236) shared syringe, 57% (134/236) shared "cotton", 60% (125/207) shared spoon, 56% (125/223) never disinfected syringe before injecting, 73% (127/174) injected daily or more and 68% (153/225) injected in group. Total duration of injecting was known for 213 subjects. Mean duration was 33.5 months (SD 43.1, range 1-240), median was 12 months (interquartile range 5-48). 18% (39/213) of IVDU injected less than 1 month and 29% (62/213) injected 36 months or more (Fig. 1).

As shown in Table II, most of these risk behaviours were significantly associated with HCV infection, when individually considered in univariate analysis. Syringe sharing (RR = 1.7, CI 1.4-2.0) and "cotton" sharing (RR = 1.3, CI 1.1-1.5) were strongly correlated. In contrast, spoon sharing and undisinfecting before injecting did not appear as risk factors for HCV infection. Concerning the duration of injecting (Fig. 1), a striking prevalence rate of 46% was found for the duration of one month or less. After a 1 year period of injection, prevalence rate was significantly higher (77.6%, $p = .001$) but beyond this time seroprevalence rate increased without no more significant difference between the different durations. For this reason we pooled the duration periods upper one month. Duration of injecting upper one month appeared strongly associated with higher risk of HCV infection (RR = 1.8, CI 1.3-2.5). Moreover, difference between "occasionally" and "exceptionally" injecting users was not significant and these groups were pooled ("not daily"). Injecting daily (RR 1.5, CI 1.1-1.9) and injecting in group (RR 1.3, CI 1.1-1.5) were both significantly related to HCV infection too. No significant difference was found between men and women.

The prevalence rate for HCV infection observed among IVDU who never shared syringes or needles was 54%. A bivariate stratified analysis demonstrated the interaction between syringe and "cotton" (Fig. 2). Among users who shared syringes, no statistically significant difference appeared between those who shared cotton too (seroprevalence 86%) and those who did not (seroprevalence 95%) ($p = .068$) (data not shown). On the other hand, among users who did not shared

Table I. — Seroprevalences for HCV, HVB and HIV among 329 belgian Drug Users during 1995 : the GEMT Study, Charleroi

	IVDU (n = 244)				non-IVDU (n = 85)				
	N tested	%	(n)	95% CI	N tested	%	(n)	95% CI	p
Anti-HCV Ab +	244	78.3	(191)	73.1 - 83.5	85	2.4	(2)	0 - 5.6	<.001
All HBV markers +	238	35.7	(85)	29.6 - 41.8	84	8.3	(7)	2.3 - 14.4	<.001
HBs Ag +	238	8.4	(20)	4.9 - 12.0	84	-	-	-	.006
Anti-HBs (or HBc*) Ab +	238	27.7	(66)	22.0 - 33.5	84	8.3	(7)	2.3 - 14.4	<.001
Anti-HIV Ab +	228	0.9	(2)	0 - 2.1	85	-	-	-	N.S.

Note. IVDU = Intravenous drug users. Non-IVDU = Non intravenous drug users. NS = not significant.
* if HBsAg negative.

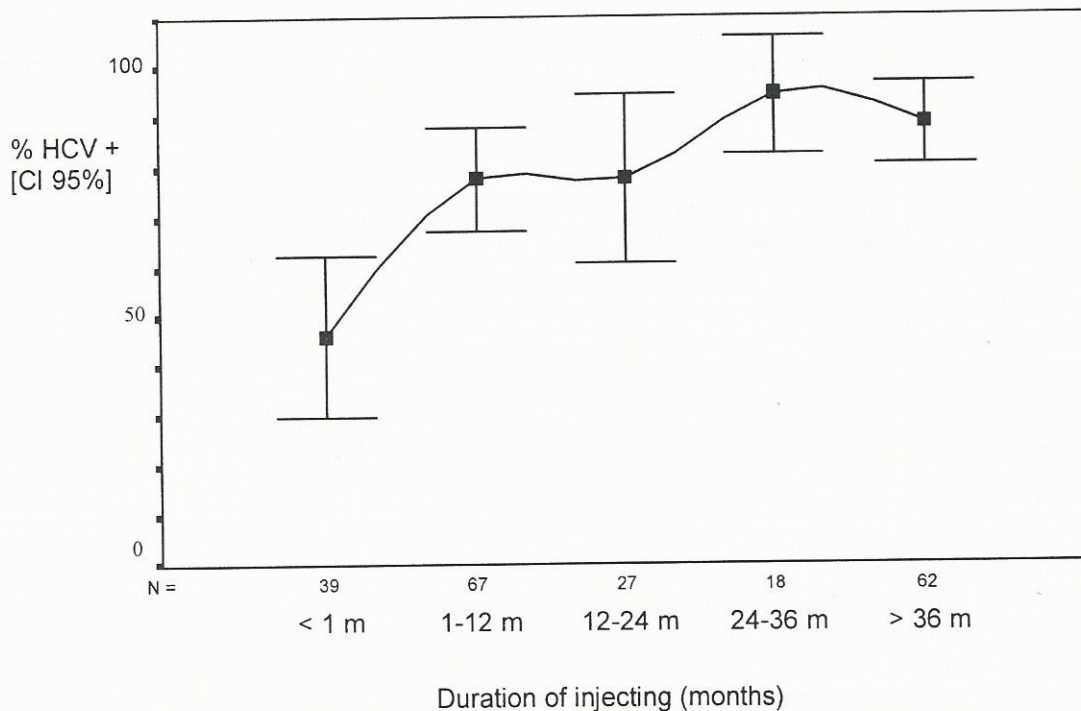


Fig. 1. — HCV Seroprevalence and Duration of Injecting

syringes, relevant difference was shown between those who only shared cotton (seroprevalence 84%) and those who did not do (seroprevalence 18%) ($p < .001$). According to this result, we identified major risk behaviour as syringe and/or «cotton» sharing (RR= 4.8, CI 2.5-9.4).

Syringe sharing (RR = 1.5, CI 1.0-2.3) was the only risk behaviour significantly associated with HBV infection.

Multivariate analysis

Many of these relationships could have been confounded by other variables. Syringe was more frequently shared 1/ in users injecting from more than 36 months than in those injecting from less than one month (82% vs 51%, $p = .001$), 2/ in users injecting in group than in those injecting alone (76% vs 37%, $p < .001$) and 3/ in

users sharing spoon than in those who did not (73% vs 57%, $p = .021$). To control confounding bias, multivariate analysis by logistic regression was performed, with better assessment of own risk of each risk factor by adjusting for all the others. Moreover, this procedure allowed to take users age into account and to see if this variable was independent risk factor or surrogate for duration of injecting. In a preliminary model we tested “syringe sharing” and “cotton sharing” ignoring their interaction. Results confirmed that these two risk factors were independent : adjusted OR was 5.9 (CI : 2.4-14.2) for syringe sharing and 4.2 (CI : 1.7-10.3) for cotton sharing. In a subsequent model we tested therefore the global risk factor “sharing syringe and/or cotton”. From this final model of logistic regression three independent risk factors were identified (Table III) : sharing syringe and/or cotton (OR = 31.7, CI 9.8-102.5), injecting during more than one month (OR = 8.6, CI 3.0-24.7) and

Table II. — Univariate analysis of associations between behavioural/demographic and serological characteristics among the 244 Intravenous Drug Users

Variable	HCV					HBV				
	Total	% HCV+	RR	95% CI	p	Total	% HBV+	RR	95% CI	p
Syringe sharing										
Never	83	54.2	1.0	—	—	81	27.2	1.0	—	—
Ever	153	90.2	1.7	1.4-2.0	<.001	149	41.6	1.5	1.0-2.3	.030
«Cotton» sharing										
Never	102	66.7	1.0	—	—	99	39.4	1.0	—	—
Ever	134	85.8	1.3	1.1-1.5	<.001	131	34.4	0.9	0.6-1.2	N.S.
Syringe and/or «Cotton» sharing										
Never	38	18.4	1.0	—	—	37	21.6	1.0	—	—
Ever	199	88.9	4.8	2.5-9.4	<.001	194	39.2	1.8	1.0-3.4	.042
Spoon sharing										
Never	82	81.7	1.0	—	—	79	45.6	1.0	—	—
Ever	125	80.8	1.0	0.9-1.1	N.S.	122	35.2	0.8	0.6-1.1	N.S.
Disinfecting										
Always	98	82.7	1.0	—	—	96	39.6	1.0	—	—
Not always	125	74.4	0.9	0.8-1.0	N.S.	125	33.6	0.8	0.6-1.2	N.S.
Gender										
Women	66	84.8	1.0	—	—	65	36.9	1.0	—	—
Men	178	75.8	0.9	0.8-1.0	N.S.	173	35.3	1.0	0.7-1.4	N.S.
Duration of injecting										
< 1 month	39	46.2	1.0	—	—	38	26.3	1.0	—	—
> 1 month	174	83.3	1.8	1.3-2.5	<.001	170	36.5	1.4	0.8-2.4	N.S.
Injecting in group										
Alone	72	65.3	1.0	—	—	71	32.4	1.0	—	—
Not alone	153	82.4	1.3	1.1-1.5	.005	149	38.9	1.2	0.8-1.8	N.S.
Frequency of injecting										
Not daily	47	55.3	1.0	—	—	45	26.7	1.0	—	—
Daily or more	127	81.9	1.5	1.1-1.9	<.001	125	40.0	1.5	0.9-2.6	N.S.

Note. HCV = anti-HCV antibodies. HBV = hepatitis B seropositivity (all markers).
 RR = Relative Risk of prevalence. CI = Confidence Interval. NS = not significant.

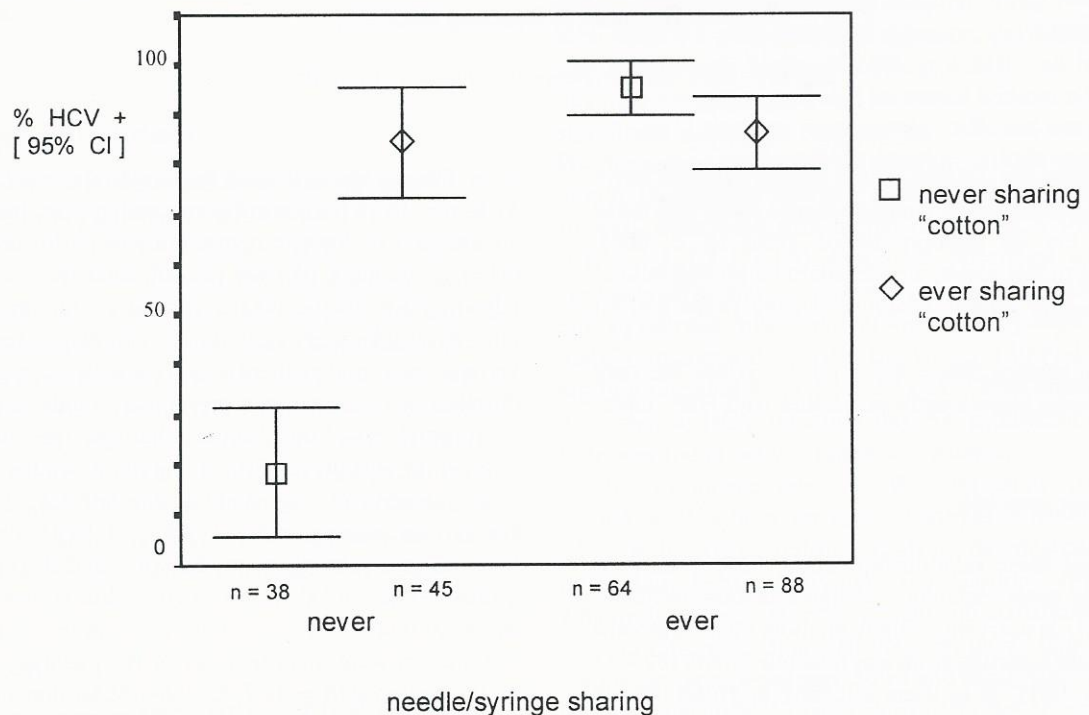


Fig. 2. — HCV Seroprevalence and sharing of injecting equipment

Table III. — Multiple Logistic Regression Analysis of Determinants of HCV Infection among Intravenous Drug Users

Risk Factors	N	unadjusted POR [CI 95%]	p	adjusted POR [CI 95%]	adjusted p
Syringe and/or «Cotton» sharing					
Never	38	1.0	—	1.0	—
Ever	199	35.6 [14.0 – 90.5]	<.001	31.7 [9.8 – 102.4]	<.001
Duration of injecting					
< 1 month	39	1.0	—	1.0	—
> 1 month	174	5.8 [2.8 – 12.3]	<.001	8.6 [3.0 – 24.7]	<.001
Age (years)	244	untested	—	1.2 [1.0 – 1.3] *	.009
Injection in group					
Alone	72	1.0	—	—	—
Not alone	153	2.5 [1.3 – 4.7]	.005	—	—
Frequency of injecting					
Not daily	47	1.0	—	—	—
Daily or more	127	3.7 [1.8 – 7.6]	<.001	—	—
Gender					
Women	66	1.0	—	—	—
Men	178	0.6 [0.3 – 1.2]	.130	—	—

Note. POR = prevalence odds ratio for anti-HCV positivity. CI = confidence interval.

* POR for one year older, to multiply by number years of difference.

age (OR = 1.2 by year of difference, CI 1.0-1.3). On the other hand, injecting in group and injecting daily were confounding variables and disappeared as risk factors.

Follow-up of HCV infected patients

Among the 191 IVDU anti-HCV positive, 24 (12.6%) were coinfecting with HBV (HBsAg positive) and have been excluded from this part of the analysis. Among the 167 remaining patients, 117 (70%) have been followed (minimum three determinations of ALT on one year). 24 of them (20.5%) had persistent normal ALT values. In 93 patients (79.5%), ALT values remained increased during more than six months (mean value of ALT = $3.5 \times \text{UNL}$, range 1.1-23.0). A liver biopsy and HCV RNA determination were performed in 23 (24.7%) of these 93 patients during the 3 years period of the study. Interferon (IFN) therapy was initiated in 10 patients (43% of the 23 patients in whom a liver biopsy was performed and 11% of the 93 followed patients with a chronic hepatitis C). Around 15% of patients dropped out this 3 years follow-up, mostly because of withdrawal from methadone treatment or imprisonment. Data concerning liver histology and results of IFN therapy were not collected in this study.

Discussion

Prevalence of hepatitis C infection

Our study assessed the high prevalence of HCV infection (78%) among belgian IVDU, according to the rates observed in other countries (1-30). In contrast, a very low seroprevalence for HIV (< 1%) was observed. Higher infectiousness of HCV and low preepidemic level of background prevalence of HIV likely explain some of the difference (43).

Prevalence of HCV infection among non-IVDU was

2% in our study. In contrast to previous studies (13,25, 44,45), our data suggest that the risk of HCV infection is not higher in non-IVDU than in the general belgian population (prevalence : 0.9% (46)).

Risk factors related to injecting

We found a high prevalence of HCV infection among IVDU who never shared needles or syringes. Our study highlights the risk of HCV transmission related to sharing "cotton". "Cottons" — in our country usually cigarette filter tips — are used by IVDU to filter impurities contained in street-heroin : they immerse it in the spoon where drug was first dissolved, and stick their needle into before sucking in syringe. This device is frequently shared or borrowed. Furthermore these "cottons", expected to contain some residual heroin, are sold at low price for penniless users. Other studies are needed to confirm our finding which could already lead to two practical messages : 1/ the information of drug users concerning the potential risk of the "cotton" and 2/ its inclusion in needles/syringes distribution and exchange programs. On the other hand, spoon sharing did not seem to be a risk factor in our study. Other equipment such water for injection has not been investigated.

As already reported (3,8,10,21,27) a strong relationship between HCV infection and duration of injecting was observed. However, prevalence rates did not significantly increase after one year of injecting, suggesting that most of IVDU are infected within the first year of injecting. Moreover, about 20% of IVDU included in our study were short-term injectors (Table II). This special feature emphasises the precocity of HCV infection among IVDU : within the first month of injecting, nearly one of two users was already infected. Since neophyte injectors attend seldom prevention and harm reduction programs, information of this people represents a very

difficult challenge. Most relevant option is likely peer education, training current users to teach their initiates how to avoid risky behaviours.

A biochemical follow-up of at least 1 year has been performed in 70% of HCV seropositive IVDU. However, 75% of the patients with chronic hepatitis C (CHC) did not go through liver biopsy and only 10% has been treated with IFN. This low result could be explained by the fact that most drug users are immersed in current various problems and are not able to take into account the potential risks of their disease. Moreover, most physicians are discouraged to propose a biochemical follow-up and a liver biopsy in patients with poor expected compliance or with persistent heroin injection. This pessimistic point of view stands in contrast with the fact that drug abusers are potentially good responders to IFN therapy ; their young age, the short course of their CHC and the non 1b genotype found in most of them (10,29,47-54) are good prognostic factors to the IFN response (55,56).

Limitations of study

Caution must always be taken using seroprevalence rates to determine infection risk factors because the actual date of infection is unknown. In addition, the high prevalence of HCV infection found in our clinical setting could be non representative of HCV prevalence among belgian IVDU : drug users attending GP's practice may differ from those who do not, because they potentially present higher frequency of drug related diseases.

Correlations between risk behaviours and HCV infection may have been underestimated by misclassification (i.e. underreporting of sharing) : data have been collected retrospectively and drug users are often considered as poor reliable people. However a recent study assessed good reliability, rounding 90%, of drug users self-reports (57). This bias is limited in our study. First, most of our patients were managed in long-term methadone treatment and repeated contacts have led to a more trustful relationship with caregiver. Second, our study population was younger than population generally observed in similar studies and patients had a shorter story of heroin use and a better ability to remember exposure at risk factors.

There was an evident investigation bias for estimation of feasibility of follow-up. HCV-seropositive IVDU : patients were recruited by GP particularly involved in this problem and our results are likely overestimated with respect to more general practice.

Conclusion

There is a challenge in these data for those who attempt to control the spread of HCV infection among IVDU. They stress two aspects which must be reconsidered in prevention programs. First, additional effort is

needed to reach and educate newer injectors, because of the high risk of first injections. Second, preventive measures must include other injecting equipment than needles and syringes, specially "cottons" used as filters.

APPENDIX

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