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Incidence and risk factors of HCV and HIV infections in a cohort of intravenous drug users in the North and East of France

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SUMMARY

In order to evaluate the incidence and risk factors of infection by hepatitis C virus (HCV) among injecting drug users (IDUs), we conducted a prospective cohort study of HCV- and human immunodeficiency virus (HIV)-negative IDUs in the North and East of France. A total of 231 HCV and HIV IDUs who had injected drugs at least once in their lifetime were followed up every 3 months over a 12-month period. Serum anti-HCV and anti-HIV were tested at inclusion in the study and at the end of the follow-up. Data on injecting practices were collected at inclusion and at each visit. Of the 231 participants included, 165 (71·4%) underwent a final HCV and HIV serum test. The incidence was nil for HIV infection and 9/100 person-years (95% CI 4·6–13·4) for HCV infection. In a multivariable analysis, we found that syringe and cotton sharing were the only independent predictive factors of HCV seroconversion.

INTRODUCTION

With 500000–650000 persons affected, hepatitis C virus (HCV) is the leading cause of chronic viral hepatitis in France [1]. The long-term consequences of chronic HCV infection include cirrhosis, liver cancer, and end-stage liver disease that may require transplantation [2]. Since transmission through blood transfusion and organ transplantation was brought under control in the early 1990s, intravenous drug use has become the principal route of HCV transmission [3]. In order to prevent human immunodeficiency virus (HIV) and HCV transmission among injecting drug users (IDUs), in 1993 the French health authorities

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implemented a national risk-reduction programme based on easy access to syringes, opiate substitution, screening for HIV and HCV and counselling.

As reported in other countries [4, 5], the risk-reduction programme was associated with a decreasing prevalence of HIV infection, but not of HCV infection. In 1998, for instance, a national survey found that the prevalence of serum antibody positivity for HCV was 63% among French IDUs benefiting from specialized live-in care centres [6] and 58% among participants in syringe-exchange programmes [7]. According to this survey, 40% of IDUs had used the intravenous route in the last 2 years and 20% reported still sharing syringes and/or needles [7].

In order to understand the differential effectiveness of the risk-reduction programme on HIV and HCV transmission and to assess the specific modes of residual transmission of HCV among IDUs, we conducted a 12-month prospective cohort study of anti-HCV and anti-HIV antibodies among IDUs negative for both viruses recruited in the North and East of France.

METHODS

Study population

The persons eligible for the study were drug-user attendees of six care centres in Northern and Eastern France, who had injected drugs at least once in their lifetime and whose HCV serology was presumed to be negative. They were recruited between 1 March 1999 and 31 July 2000. Each eligible individual was first approached by the staff of the care centre, who gave him an appointment with a trained interviewer who was not a staff member. Those willing to participate did not receive any payment. If they signed a consent form and a 1-year commitment to the study, a saliva test for anti-HCV was performed and a standard questionnaire on their drug habits and injecting practices was administered in the course of a personal meeting with the interviewer. A blood sample for anti-HCV and anti-HIV testing was taken, either on the spot if conditions allowed, or in a medical laboratory freely chosen by the participant. Follow-up visits were planned every 3 months by the medical team over the total follow-up period of 12 months. When a participant missed an appointment, reminders were made by telephone or sent by mail, according to the information available, by the health-care team and by the interviewer. At each visit, subjects included were questioned on their drug habits and injecting practices in the same way as at inclusion and a saliva sample was taken for an HCV test. If the saliva sample was positive for anti-HCV, a blood sample for an anti-HCV test was taken in the same way as at inclusion. A blood sample for HCV and HIV antibody tests was taken from all the participants at the end of the follow-up. At inclusion and at each follow-up visit, the staff members of the care centres counselled participants about the risks and prevention of HIV, HCV and hepatitis B infection associated with intravenous drug use. The study was approved by the Ethics Committee of the Lille University Hospital and the National Commission on Data Protection.

Laboratory methods

Saliva was collected with a Salivette system (Sarstedt, Germany), consisting of a piece of cotton that the patient must chew for about a minute in order to soak it with saliva. The saliva was then extracted from the cotton by centrifugation and stored frozen at $-80\ ^{\circ}C$. Two third-generation enzyme-linked immunosorbant assay (EIA) tests for anti-HCV (EIA-3; Abbott Laboratories, Rungis, France [8], and EIA-3 Monolisa Bio-Rad Laboratories, Marnes la Coquette, France [9, 10]) were carried out on the saliva. If either or both were positive, a serum test was performed, using the EIA-3 technique. If this proved positive, a second test was carried out. All sera were considered positive for anti-HCV if both tests were positive. HIV antibody positivity was evaluated using an EIA-3 test.

Data collection

At inclusion, we collected information on age, sex, family situation, level of education, housing, social security coverage, history of past incarceration, history of drug use (age at onset of drug use, duration of periods during which the participant injected drugs), substances used, drug injection practices and behaviour during the last 3 months (sharing of syringes or equipment including cups, cotton and water, reuse of own syringes or equipment, syringe and equipment cleaning methods, etc.), prior screening history for HIV and HCV and results, other potential risk factors for HCV or HIV infection (tattooing, piercing, sexual orientation, number of sexual partners, use of condoms). At follow-up visits, information was collected on injection practices and behaviour since the last visit and interview.

Analysis

The final cohort was composed of those IDUs who tested negative for HCV and HIV antibodies at inclusion and who benefited from final HIV and HCV serum tests. HCV infection was defined as a repeated positive anti-HCV serum test in a participant who had been antibody negative at inclusion. Person time was computed for each member of the cohort as the time elapsing until that individual seroconverted or tested negative at the end of the study. Participants were classified according to the time elapsing between the last injection and inclusion, i.e. as regular injectors (at least one injection daily for 7 days, or at least one injection during the week prior to inclusion), occasional injectors (at least one injection during the year prior to inclusion) and former injectors (no injection during the year prior to inclusion).

In order to assess the representativeness of the final cohort, those who completed the 1-year follow-up were compared, with regard the inclusion variables, to those who dropped out. We defined the date of infection as the mid-point between the last negative saliva test and the first positive serum test. The incidence density rates for HIV and HCV infection depending on variables at the time of inclusion, as well as their Poisson 95% confidence intervals (CI), were calculated for 100 person-years (PY) of follow-up [11].

In order to assess risk factors for HCV infection, we used the Cox proportional risk regression model [12]. Since information on injecting practices, behaviour and other covariates was collected during the entire follow-up period, time-dependent covariates were included in the model. The assessment of their effects on the probability of occurrence of HCV seroconversion was handled by assuming that these time-dependent covariates have a fixed effect over time. For each follow-up visit, covariates were updated and a specific data format indicating the successive time-interval, the event status (HCV infection) and the covariate values was chosen with the view of using the time-dependent option in the Cox model. The time-interval between two intermediate questionnaires, or, for the first questionnaire, the 3-month period immediately preceding inclusion, were taken into account in the analysis with regard to variables, such as injecting practices, liable to evolve over time. Data were analysed using the proportional hazard regression procedure in SAS, version 8.2 (SAS Institute Inc., Cary, NC, USA).

The multivariable analysis included variables found to be associated with HCV infection, with $P<0{\cdot}20$. Since the size of the cohort did not allow the inclusion of all injecting-practice variables in the same model, four models were successively considered: model 1 estimates both the risk of sharing any or all drug preparation equipment (cotton, cup or water) and syringe sharing, adjusted by gender, geographical region, substitution, use of condoms, daily injection of cocaine and duration of injecting ($<2/>2$ years); models 2, 3 and 4 estimate the respective relative risk (RR) for the sharing of cotton, cup and water, adjusted for the same variables as in model 1 respectively. On account of the size of the cohort, sharing practices had to be grouped together as one in the same variable [no injecting = reference class, injecting without sharing, syringe sharing (possibly with equipment sharing), equipment sharing only (no syringe sharing)].

RESULTS

A total of 326 persons presumed to be negative for anti-HCV agreed to take part in the study and completed the inclusion questionnaire. Sixty-three persons positive for anti-HCV and 32 whose serological status was unknown were excluded from follow-up. Of the 231 HCV antibody-negative IDUs enrolled in the study, three (2%) died and 63 (27%) did not undergo a final serum test and were excluded from the analysis. There were 165 participants (71·4%) who underwent a final HCV serum test and attended at least one of the follow-up interviews. Forty (24%), 43 (26%), 49 (30%) and 33 (20%) of these 165 participants respectively completed 4, 3, 2 and 1 single follow-up questionnaire. The IDUs who completed the follow-up differed statistically from those who were lost to follow-up with regard to social security coverage, age at initiation of drug injection (i.e. before or after the age of 20 years) and substitutive treatment (Table 1). Forty-six of the individuals followed (28%) had a salary as their main source of income; 51 (31%) had already been imprisoned at least once. Of the 131 (79·4%) participants under substitutive treatment during the 3 months prior to inclusion, 49 (37%) were regular and 39 (30%) were occasional injectors. Seventy-five (57%) injected at least once during follow-up. Of the 34 participants not under substitutive treatment during the 3 months prior to inclusion, 25 (74%) injected at least once in the course of follow-up.

Among the 165 enrollees of the cohort who contributed a total of 178·4 PY of risk for HCV and HIV

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Table 1. *Comparison according to socio-demographic profile and drug-use practices between participants included (having undergone final blood sampling) and drop-outs*

	Included ($n=165$)		Drop-outs ($n=66$)			Total ($n=231$)	
	n	%	*n*	%	*P*	*n*	%
Age mean (years)	26·5		27·6		0·12	26·9	
Sex							
Male	136	82·4	59	89·4	0·19	195	84·4
Female	29	17·6	7	10·6		36	15·6
Geographical region							
East	55	33·3	25	37·9	0·51	80	34·6
North	110	66·7	41	62·1		151	65·4
Education							
Primary	22	13·3	9	13·3	0·65	31	13·4
High school (not completed)	99	60	42	63·6		141	61
High school diploma	16	9·7	8	12·1		24	10·4
Higher education	28	17	7	10·6		35	15·2
Work	47	28·5	27	40·9	0·07	74	32
Social security coverage	163	99·4	61	93·9	0·02	224	97
Housing							
Stable	149	90·8	54	84·4	0·16	203	89·2
Not stable	15	9·2	10	15·6		25	10·8
Imprisonment	51	30·9	26	39·4	0·21	77	33·3
Time of first injection							
$\leqslant 2$ years	41	24·9	18	27·3	0·7	59	25·5
>2 years	124	75·2	48	72·7		172	74·5
Age at the time of first injection							
<20 years	99	60·0	52	78·8	0·01	151	65·4
$\geqslant 20$ years	66	40·0	14	21·2		80	34·6
Substitutive treatment	131	79·4	43	65·2	0·02	174	75·3
Type of injector							
Long term	47	28·5	12	18·2	0·12	59	25·5
Occasional	49	29·7	28	42·4		77	33·3
Frequent	69	41·8	26	39·4		95	41·1
Syringe sharing	22	23·9	13	29·6	0·53	35	25·7
Equipment sharing	32	37·2	11	27·5	0·32	43	34·1

infection, 16 seroconverted for HCV during follow-up. No HIV seroconversion was detected. Among the 16 participants who seroconverted, three misssed at least one intermediate questionnaire. Four seroconversions were detected at the time of the first follow-up questionnaire, four at the time of the second, three at the time of the third and five at the time of the final questionnaire. The crude incidence density rate for HCV infection is therefore 9·0 PY (95% CI 4·57–13·4) in the total cohort and 11/100 PY (95% CI 4·7–17·1) among IDUs who had injected at least once during the 6 months prior to inclusion. Incidence rates according to exposure at the time of inclusion are shown in Table 2. Of the 16 participants who seroconverted, six injected regularly, nine occasionally and one did not admit to any injecting during the course of the study. Ten of these 15 injectors were under substitutive treatment. Eight of these 10 participants under substitution were cocaine injectors.

Risk factors for HCV infection

In univariable analysis, the RR of seroconversion associated with the sharing of any or all drug-preparation equipment was 3·6 (95% CI 0·43–29·2). The risk of HCV infection was 18·2 times greater

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Table 2. *Number of hepatitis C virus seroconverters and crude incidence rate according to exposure, as assessed at the time of inclusion* ($n=165$)

Characteristics	Sero-conversion	Incidence/100 PY (95% CI)
Sex		
Female ($n=29$)	5	16·67 (2–31)
Male ($n=136$)	11	7·41 (3–12)
Age		
>25 years ($n=76$)	5	6·09 (7–11)
⩽25 years ($n=89$)	11	11·43 (6–18)
Region		
East ($n=55$)	8	14·36 (4–24)
North ($n=110$)	8	6·52 (2–11)
Housing		
Stable ($n=149$)	13	8·09 (4–12)
Not stable ($n=15$)	3	17·84 (0–38)
Imprisonment		
No ($n=114$)	9	7·10 (0–12)
Yes ($n=51$)	7	13·57 (4–24)
Injecting for		
>2 years ($n=124$)	8	6·03 (2–10)
⩽2 years ($n=41$)	8	17·52 (5–29)
Age at the time of the first injection		
<20 years ($n=99$)	8	7·22 (2–12)
>20 years ($n=66$)	8	11·83 (4–20)
Substitutive treatment		
No ($n=34$)	5	14·09 (0·02–0·26)
Yes ($n=131$)	11	7·70 (0·03–0·12)
Type of injector		
Former ($n=47$)	2	3·86 (0–9)
Occasional ($n=49$)	5	9·23 (1–17)
Regular ($n=69$)	7	12·43 (4–20)
Injection during the past 6 months		
No ($n=62$)	4	5·87 (0–12)
Yes ($n=103$)	12	10·89 (5–17)
Daily injection of cocaine[a]		
No ($n=77$)	6	7·04 (1–26)
Yes ($n=19$)	6	36·54 (7–66)
Daily injection of heroin[a]		
No ($n=69$)	8	10·88 (3–18)
Yes ($n=27$)	4	14·22 (0–28)

[a] Among individuals having injected at least once during the 3 months prior to inclusion.

(95% CI 2·2–148·7) for cotton sharing, 3·6 times greater (95% CI 0·4–29·2) for cup sharing and 4·7 times greater for water sharing (95% CI 0·5–40·3). In each of these univariable analyses, the RR of seroconversion associated with syringe sharing was between 8·4 and 8·6 and was statistically significant (Table 3).

In multivariable analysis, the sharing of any kind of drug-preparation equipment was associated with a 2·5-fold increase in risk, which was not statistically significant. However, the RR associated with the sharing of cotton was 16·4 (95% CI 1·4–190·6). The RRs associated with cup sharing and with the sharing of water were respectively 2·5 and 4·9, but remained statistically non-significant. Syringe sharing increased the risk of HCV infection in all of the models, with a RR between 6·2 and 6·8 (Table 4). Substitutive treatment decreased the risk of HCV infection by approximately 60% in all the models, but not significantly so. The duration of injecting (more or less than 2 years) was no longer significantly associated with seroconversion in any of the multivariable models.

DISCUSSION

In this prospective cohort study of IDUs we have shown that the incidence of HIV infection was nil, compared to approximately 10% for HCV infection. Among all the risk factors studied, we showed that the sharing of syringes and that of injection equipment were the strongest determinants of HCV transmission. Among the latter, the sharing of the cotton used to prepare the drug carried the greatest excess risk of HCV infection.

This study does, however, have several limitations. First, the study population was a convenient sample of IDUs, and although we used multiple recruiting sites, the sample was not randomly selected. The extent to which our findings can be generalized to other IDUs is, therefore, unknown. Second, although we were able to follow-up 71·4% of the IDUs initially included, we were unable to obtain full longitudinal information on all of the participants, and differential loss to follow-up may have affected the study findings. When comparing the 165 participants studied and the 66 who dropped out, we observed no differences with respect to injection-related practices, duration or frequency of injection, age, place of residence, or homelessness. However, in comparison to those who dropped out the participants forming the final cohort had better social security coverage, began injecting later (i.e. after age 20 years) and were more frequently under substitutive treatment.

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Table 3. *Non-adjusted RRs estimated using the Cox models with time-dependent variables: analysis of data collected during follow-up (n = 165)*

Variables of interest	RR[a]	95% CI[a] of RR	*P*
Sex[b]			
Female	1	—	0·13
Male	0·42	0·15–1·22	
Age[b]			
⩾25 years	1	—	0·24
⩽25 years	1·85	0·64–5·33	
Region[b]			
East	1	—	0·16
North	0·49	0·18–1·31	
Housing			
Stable	1	0·23–4·67	0·95
Not stable	1·05		
Means			
Salary	1	—	0·35
Other	1·64	0·57–4·76	
Living alone (no partner or marital life)	0·81	0·28–2·34	0·70
Injecting for[b]			
>2 years	1	—	0·04
⩽2 years	2·84	1·05–7·65	
Age at the time of the first injection[b]			
<20 years	1	—	0·29
⩾20 years	1·71	0·63–4·65	
Substitutive treatment	0·34	0·11–0·99	0·07
Straw, tattooing or piercing	0·74	0·16–3·31	0·68
Condom use	0·33	0·09–1·17	0·06
Type of injector			
Occasional	1	—	0·64
Frequent	1·28	0·45–3·62	
Daily injection of cocaine	3·13	0·70–13·91	0·20
Daily injection of heroin	1·47	0·33–6·48	0·63
Sharing of preparation equipment[c]: overall	3·55	0·43–29·20	0·06
Syringe sharing	8·46	2·23–32·20	
Injection without sharing	1·28	0·28–4·29	
No injection	1	—	
Sharing of preparation equipment[c]: cotton	18·21	2·23–148·71	0·02
Syringe sharing	8·56	2·25–32·59	
Injection without sharing	1·17	0·35–3·96	
No injection	1	—	
Sharing of preparation equipment[c]: cup	3·55	0·43–29·20	0·06
Syringe sharing	8·46	2·23–32·20	
Injection without sharing	1·28	0·38–4·29	
No injection	1	—	
Sharing of preparation equipment[c]: water	4·72	0·55–40·28	0·05
Syringe sharing	8·44	2·22–32·10	
Injection without sharing	1·25	0·37–4·20	
No injection	1	—	

[a] RR, Univariable RR; 95% CI, confidence interval at 95% of RR.
[b] Non-time-dependent variables.
[c] Exclusively, i.e. with no syringe sharing. Conversely, syringe sharing may include individuals also sharing drug-preparation equipment.

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Table 4. *Adjusted RRs estimated using the Cox models with time-dependent variables: analysis of data collected during follow-up* ($n = 165$)

	Model 1		Model 2		Model 3		Model 4	
	Adj. RR[a]	95% CI	Adj. RR	95% CI	Adj. RR	95% CI	Adj. RR	95% CI
Sharing of drug preparation equipment[b]								
Global	2·50	0·29–21·62	—	—	—	—	—	—
Cotton	—[c]	—	16·41**	1·41–190·6	—	—	—	—
Cup	—	—	—	—	2·50	0·29–21·62	—	—
Water	—	—	—	—	—	—	4·88	0·52–45·89
Syringe sharing	6·82**	1·25–37·26	6·31**	1·13–35·35	6·82**	1·25–37·26	6·22**	1·12–34·60
Injection with no sharing	1·34	0·37–4·92	1·13	0·30–4·21	1·34	0·37–4·92	1·23	0·33–4·54
No injection	1	—	1	—	1	—	1	—
Sex (male/female)[d]	0·50	0·15–1·60	0·62	0·18–2·19	0·50	0·15–1·60	0·50	0·16–1·58
Geographical region (North/East)[c]	0·91	0·29–2·85	0·78	0·24–2·52	0·91	0·30–2·85	0·87	0·28–2·75
Substitutive treatment	0·41	0·12–1·40	0·37	0·11–1·27	0·41	0·12–1·40	0·38	0·11–1·32
Condom use	0·40	0·11–1·45	0·41	0·11–1·50	0·40	0·11–1·45	0·41	0·11–1·51
Daily injection of cocaine	1·14	0·17–7·91	1·16	0·16–8·53	1·14	0·17–7·91	1·25	0·17–8·97
Injecting for less than 2 years	1·49	0·47–4·75	1·63	0·50–5·30	1·49	0·47–4·75	1·60	0·50–5·20

[a] RR, multivariable RR; 95% CI, 95% confidence interval of RR.
[b] Exclusively, i.e. with no syringe sharing. On the other hand, syringe sharing may include persons who also share drug preparation equipment.
[c] Variable absent from model.
[d] Non-time-dependent variable.
** $P < 0·05$.

Third, exposure and covariate behaviour in this study were based on self-reported data. Biased results are possible if some behaviours are consistently under- or overreported. The quarterly frequency at which the questionnaires were administered probably contributed to reducing any potential recall bias. Fourth, collecting data in face-to-face interviews may have fostered 'socially desirable' answers [13]. These two potential biases would result in a dilution of the RRs.

The fifth and final limitation of our study is its lack of statistical power due to the limited number of participants included. The processing of all the data collected over time by means of a Cox model with time-dependent exposure did, however, reduce the negative impact of this drawback. The follow-up percentages were high enough to allow an analysis, taking into account the evolution of sharing practices over time to provide an interesting contribution compared to an analysis using final status (i.e. seroconverted or not) and measurement of risk practices at the time of inclusion.

Our cohort study also showed that despite an incidence rate of approximately 10/100 PY in the case of HCV, no HIV transmission occurred. Since HIV is about 10 times less infectious than HCV [14] and since the prevalence of HIV infection among IDUs is much lower than that of HCV infection, the risk of HCV infection is much greater for each single sharing of injection equipment with another IDU. Indeed, the prevalence of HIV infection in the drug-user population is low in Northern and Eastern France (<3%), whereas that of HCV infection is approximately 70% [15, 16]. The persistence of such a high incidence of HCV infection despite a risk-reduction policy that has proved effective for HIV is related to the fact that the residual rate of sharing remains too high to reduce further HCV transmission.

Almost 80% of the individuals included in our cohort had been under opiate substitutive treatment during the 3 months prior to inclusion. However, almost 40% of these patients were still regular injectors which indicates the limitations of opiate substitutive treatments. One of the explanations of this observation may be related to the emergence of cocaine consumption. In our study, cocaine injection was positively associated with seroconversion in

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univariable analysis and was close to being statistically significant in multivariable analysis ($P=0{\cdot}06$, results not shown). Cocaine injection was also found to be a risk factor for HCV seroconversion in a study using data collected at inclusion [17] and in another study carried out in Canada, in which the information collected covered the 6-month period prior to seroconversion [18].

Due to the eligibility criteria chosen (any drug user over age 18 years who had used a syringe for drug administration at least once in his/her lifetime), our cohort includes individuals with different profiles regarding injection frequency. For this reason, we distinguished three groups of IDUs on the basis of their current level of exposure: former injectors, occasional injectors and regular injectors. In our study, participants with a high-exposure profile had an HCV infection rate of the order of 13%; this is in agreement with the data provided by other prospective studies of IDUs, which indicate an HCV infection incidence rate between 4·2 and 25/100 PY [5, 17–25]. In the United States, a prospective study carried out between 1997 and 1999 estimated the HCV infection incidence rate at 10/100 PY among IDUs who had injected during the past 6 months [21]. In another study carried out between 1994 and 1997 in the same country, the incidence rate was 16·7/100 PY in a population of drug users who had injected in the course of the year [20]. In Canada, between 1994 and 1999, the incidence rate in a cohort of drug users who injected during the month preceding inclusion in the cohort was also estimated at around 16/100 PY [18]. This incidence rate was as high as 29/100 PY in the subgroup of individuals under 25 years of age [26]. However, any comparisons between the results of different studies must be made with caution, because the prospective or retrospective nature of the study [27, 28], the criteria for inclusion, the methods used for data collection and follow-up and the statistical methodology vary considerably from one study to the next.

Although the level of exposure was much greater among regular injectors, nearly 45% (7/16) of seroconversions occurred among occasional or former injectors at baseline. This point highlights the remaining high risk of HCV infection in the event of an occasional or unplanned injection. Unplanned or occasional drug injection may be associated with the use of injection equipment used by other IDUs or with reliance on a third party for the procurement of the substance, for its preparation and perhaps for its injection.

The frequency of syringe borrowing is about 20% in France, according to a survey conducted within the framework of syringe exchange programmes [7]. Twenty-four per cent of the individuals who were injectors during the 3 months prior to inclusion in our study had shared syringes. Therefore, the prevention of HCV infection is not just a matter of teaching aseptic injection techniques. Ready access to sterile equipment and the low cost of such equipment, or even its provision free of charge, is required in order to further reduce the transmission of HCV among IDUs. Besides the problem of the availability of sterile equipment, syringe sharing may be explained by the collective purchase and use of the substance due to economic constraints, resulting in the use of a common syringe [7], but also by social pressures, which favour injecting in a group [29]. In England, an intensified risk-reduction policy centring on the supply of sterile equipment has led to an HCV prevalence rate below 40% and to an incidence rate below 6% during the year following the first injection [30]. In 1997, the number of syringes distributed to IDUs in France [31] was half that distributed in England [30], for a somewhat similar number of injectors. Any factors favouring non-parenteral drug use are, therefore, bound to reduce the risk of HCV infection.

The second aim of the present study was to assess the role of drug-preparation equipment (except for syringe sharing) in HCV transmission. We therefore offered a prospective follow-up on a 3-monthly [24] rather than on a 6-monthly [21] or annual basis [20] in order to establish precise correlations between risk-related behaviour and possible seroconversion.

A statistical analysis carried out on the follow-up data by means of a Cox model using time-dependent variables made it possible to correlate occurrences of seroconversion with risk-related behaviour during the previous months. The use of a time-dependent Cox model seems to be more adapted than the baseline Cox analysis, which ignores the time-related information available and also assumes fixed covariate effects over the follow-up period. The data provided by the detailed questionnaire administered every 3 months allowed an evaluation of variations in behaviour over time with regard to sharing practices and of their possible associations with seroconversion – something that cannot be done with a model using data 'fixed' at any given time. The analysis of all the data from this cohort, from inclusion to end-date, in contrast to analysis of the sole data collected upon inclusion (data not shown), was able to detect

statistically significant associations between sharing practices and HCV seroconversion. Thus, cotton sharing appears to be an important and significant risk factor (RR 16·4, 95% CI 1·4–190·6). Cup sharing, as well as the sharing of water, increases the risk, but not significantly. Syringe sharing was also an important risk factor, with a RR of approximately 6·5 (95% CI 1·1–35·3). Inasmuch as the CIs of the RRs for the sharing of syringes and cotton are broad and overlapping, it would be imprudent to state that syringe sharing is a more important risk factor for seroconversion than cotton sharing.

Why is the filter-related RR of HCV infection so high? The filter used by IDUs has an absorbent effect and therefore concentrates the substance. For this reason, it is often saved in order to be used during an anticipated episode of withdrawal, in contrast to syringes or cups, which are intended for immediate use. Filter sharing may also be related to this perceived absorbent effect. Since used filters are very likely to have been contaminated during prior use, they probably play a key role in the spread of HCV infection, even more so than used cups. The frequency of equipment sharing between injectors is of the order of 55% according to a previous study [7]. In our study, 37% shared injection equipment. The role of cotton sharing as a source of contamination has already been demonstrated by other studies [20, 21, 24]. One of these studies, carried out on a cohort of 317 injectors who were antibody negative at the time of inclusion, showed that 54% of those who had HCV infection during the year subsequent to the study, and who had not shared syringes, had shared cups and filters [20].

We conclude that the incidence of HCV infection in a cohort of individuals of whom a majority were under substitutive treatment remains high. This estimation has encouraged the French public health authorities to reconsider the place of substance use in their anti-HCV programme, as reflected by special emphasis on information, as well as on access to screening and care for this difficult to reach population.

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