

## ORIGINAL ARTICLE

# A national survey of genitourinary medicine clinic attenders provides little evidence of sexual transmission of hepatitis C virus infection

M A Balogun, M E Ramsay, J V Parry, L Donovan, N J Andrews, J A Newham, C McGarrigle, K A Harris, C G Teo

*Sex Transm Infect* 2003;**79**:301–306

See end of article for authors' affiliations

Correspondence to: Dr M Adekoyejo Balogun, PHLS CDSC, Immunisation Division, 61 Colindale Avenue, London NW9 5EQ, UK; kbalogun@phls.nhs.uk

Accepted for publication 13 February 2003

**Objective:** To determine the prevalence and genetic diversity of hepatitis C virus in genitourinary medicine clinic attenders and to assess the extent of sexual transmission of the virus.

**Methods:** A cross sectional, unlinked, anonymous survey in 14 genitourinary medicine clinics situated in England, Wales, and Northern Ireland. Serum specimens from genitourinary medicine clinic attenders, retained as part of the Unlinked Anonymous Prevalence Monitoring Programme (UAPMP) serum archive, were tested in small pools, for the presence of antibody to hepatitis C virus (anti-HCV). The main outcome measures were prevalence of antibodies to hepatitis C virus and identification of hepatitis C virus genotypes.

**Results:** Testing of 17 586 specimens from 1995 showed an adjusted prevalence of anti-HCV in genitourinary medicine clinic attenders of 1.03% (95% CI: 0.89 to 1.16) overall and 0.65% (95% CI: 0.51 to 0.78) among those who did not report injecting drug use. Prevalence in injecting drug users attending genitourinary medicine clinics was 36.9% in both 1995 and 1996. Heterosexual injecting drug users had a higher prevalence of anti-HCV than homosexual/bisexual injectors. The most common hepatitis C genotypes were types 3a and 1a. There was a high degree of concordance between genotype and serotype.

**Conclusions:** The low prevalence of anti-HCV in genitourinary medicine clinic attenders who deny injecting drugs suggests that the majority of hepatitis C infections have been acquired in adult life, mostly by injecting drug use, and that the hepatitis C virus is rarely transmitted sexually. The use of needle exchanges may explain the relatively low prevalence observed in the injecting drug users.

Hepatitis C virus (HCV) infection has a worldwide distribution and the main routes of transmission have been described.<sup>1</sup> Evidence exists that sexual transmission of hepatitis C virus can occur although the extent of ongoing sexual transmission is less clear.<sup>2,3</sup> Studies of the sexual partners of known hepatitis C positive individuals suggests that the rate of sexual transmission is low but such studies have predominantly been performed on long term monogamous heterosexual relationships.<sup>4,5</sup> Other studies have suggested that multiple sexual partners,<sup>6</sup> sexually transmitted disease clinic attendance,<sup>5</sup> and prostitution<sup>7,8</sup> are associated with an increased risk of HCV infection.

Of the known behavioural risks associated with HCV infection, injecting drug users (IDUs) are among those at highest risk from infection. A number of studies of IDUs in Europe and the United States have found prevalences of antibodies against HCV (anti-HCV) of between 60% and 90%.<sup>9,10</sup> In many of the cross sectional studies undertaken, HCV infection correlated more strongly with injecting practices than with sexual behaviour.<sup>11</sup>

Since 1990 a number of genitourinary medicine (GUM) clinics in England, Wales, and Northern Ireland have contributed to the Unlinked Anonymous Prevalence Monitoring Programme (UAPMP).<sup>12</sup> These surveys have been used to monitor the prevalence of human immunodeficiency virus type 1 (HIV-1) in GUM attenders by sexual orientation and injecting drug use. Anonymised unlinked serum specimens were therefore available to be tested for the presence of anti-HCV. Testing these specimens would determine the baseline prevalence in GUM clinic attenders, and thereby provide an indication of the importance of sexual transmission, and contribute to the

future surveillance and control of HCV infection. This paper describes the results of testing these specimens for HCV infection.

## METHODS

### Serum archive

Residues remaining from syphilis serology were unlinked and anonymised using established methods and tested for the presence of anti-HIV-1 as part of the UAPMP.<sup>13</sup> Archived sera selected by age group and centre from non-injecting drug users at GUM clinics in 1995 were tested for anti-HCV antibodies (table 1). All specimens from GUM attenders in 1995 and 1996 who had reported injecting drug use were also tested. Seven of the 14 participating centres were from the London area. Ethical clearance for the study had been obtained from the ethics committee in each locality where the UAPMP operated.

### Pooling

A pooling strategy for testing the serum specimens for anti-HCV, similar to one previously described for anti-HIV, was utilised.<sup>14</sup> This methodology had been used successfully to test for anti-HCV in over 40 000 antenatal specimens from the UAPMP 1996 archive.<sup>15</sup> The initial protocol was shown to have a sensitivity of approximately 99% when using pools of 12 specimens when compared with testing individual specimens for anti-HCV antibodies. Specimens from non-injecting GUM clinic attenders were therefore tested in pools of 12. As the prevalence of hepatitis C infection in IDUs has been shown to be high it was most efficient to test these specimens individually.

**Table 1** Total number of specimens tested from GUM serum archive (1995)

	Age group (years)					Total
	<20	20–24	25–34	35–44	45+	
London						
Number tested from archive	1229	2211	3342	2252	1148	10182
Serum archive	2163	7923	16125	5236	2231	33678
Outside London						
Number tested from archive	1040	1678	1942	1526	1218	7404
Serum archive	3111	7283	10246	3755	1755	26150
Total number tested from archive	2269	3889	5284	3778	2366	17586
Total serum archive	5274	15206	26371	8991	3986	59828

### Serological testing

The pools of 12 serum specimens were tested using the Ortho HCV 3.0 enzyme linked immunosorbent assay (ELISA) test system (enhanced SAve). Each specimen that had been incorporated in a reactive pool was subsequently tested individually by the standard (short) protocol for the Ortho HCV 3.0 ELISA test system (enhanced SAve). Each individual serum specimen that was reactive by the Ortho assay was tested also by the Monolisa anti-HCV Plus (Sanofi Diagnostics Pasteur). Specimens with discordant results or those that were weakly reactive in either or both assays were further tested with a recombinant immunoblot assay (Ortho HCV RIBA 3). Individually tested IDUs were tested according to the Ortho standard protocol and reactive specimens were investigated as described above for the non-injecting drug users.

### PCR and genotyping

Specimens from non-injectors and IDUs that were RIBA indeterminate were examined by reverse transcription-polymerase chain reaction (RT-PCR) for the presence of HCV RNA. Specimens that had discordant ELISA results but were RIBA negative were also examined by RT-PCR. Simple systematic randomisation was used to select a 12% and 50% sample by age of anti-HCV positive IDUs and non-injectors respectively for PCR analysis. RNA was extracted from PCR positive specimens using the Amplicor HCV Specimen Preparation Kit (Roche Diagnostic Systems, Welwyn Garden City, Herts, UK). The HCV 5' non-coding region (5'-NCR) was amplified by nested PCR.<sup>16</sup> The products of positive RT-PCRs were digested with restriction enzymes, the digests of which were analysed using the restriction fragment length polymorphism (RFLP) system to determine HCV genotype.<sup>15</sup>

### Serotyping

Specimens that were investigated by PCR (both non-injectors and injectors) were also examined by serotyping. The Murex HCV Serotyping 1–6 Assay, which utilises synthetic peptides representing the variable antigenic regions derived from the NS4 gene (non-structural) of HCV, was used for the detection of antibodies to serotypes 1, 2, 3, 4, 5, and 6.

### Statistical analysis

Data from all patients who attended in 1995 (regardless of their injecting history) were analysed to provide a complete profile of the clinic attenders from that year. Data from IDUs who attended in 1995 and 1996 were also analysed as a single group. For analytical purposes, all specimens that were either anti-HCV or PCR positive only were included in the overall estimates of prevalence of HCV. Initially the proportions of positive specimens were compared using a  $\chi^2$  test. Multivariable logistic regression was used to compare the prevalence of HCV by region, age, sex, country of birth, sexual orientation, injecting drug use, and HIV status. Interactions between all of the factors were also examined. Statistical significance was

taken at the 5% level. To adjust for the differential sampling by age, sex, sexual orientation, and injecting drug use, the observed prevalence was applied to the original number of specimens available, enabling an estimate of the overall prevalence in the clinic population (table 1).

## RESULTS

### Overall findings

A total of 17 586 specimens collected from GUM clinic attenders in 1995 were tested, and 349 were found to be HCV positive. This includes three RIBA indeterminate (one non-injector) and four RIBA negative specimens (all non-injectors) that were subsequently found to contain HCV RNA. Sixteen specimens were found to be RIBA indeterminate but PCR negative. All of these indeterminate specimens were from the London area: 10/16 (62.5%) were in the 25–34 age group and 11/16 (68.8%) were identified as IDUs. Of all survey clinic attenders, 16 965 did not report illicit injecting drug use, of whom 120 were HCV positive (table 2). Taking into account the specimens selected for testing by age, sex, sexual orientation, and injecting drug use from the original number of specimens available from the archive gives an adjusted prevalence of 1.03% (95% CI: 0.89 to 1.16) for all GUM clinic attenders in 1995, and 0.65% (95% CI 0.51 to 0.78) for the subset of non-injectors. Among the 621 specimens from IDUs, 229 (36.9%) were HCV positive, including the two RIBA indeterminate specimens that contained HCV RNA.

The adjusted prevalence in the London area (1.44%; 95% CI 1.23 to 1.65) was three times higher than in the combined geographical area outside of London (0.49%; 95% CI 0.34 to 0.66). The overall adjusted prevalence was higher in males (1.26%; 95% CI 1.05 to 1.47) than females (0.78%; 95% CI 0.60 to 0.95). Prevalence increased with age, the highest prevalence being in those aged between 25–34 and 35–44 years in both males and females. In males, the adjusted prevalences were 1.45% and 1.90% in those aged between 25–34 and 35–44 years respectively, compared to 0.89% and 1.99% in females of the same age groups. Multivariable logistic regression analysis (table 3) demonstrated a significant variation in prevalence by age ( $p < 0.0001$ ). Prevalence also varied by centre and the overall variation between centres was highly significant ( $p < 0.0001$ ) after controlling for all other factors. The prevalence of HCV did not differ significantly by sex ( $p = 0.71$ ) or by country of birth (UK/abroad) ( $p = 0.98$ ) after controlling for all factors.

The overall prevalence of anti-HIV-1 in this study was 2.08% (365/17 586) and the overall prevalence of HCV in the anti-HIV-1 positive specimens was 6.58% (24/365). HCV prevalence did not differ significantly by HIV status (OR = 1.74,  $p = 0.08$ ).

HCV prevalence was lower in the homosexual/bisexual group (OR=0.55,  $p = 0.0013$ ) compared to heterosexuals. Further analysis of interactions showed that this effect was

**Table 2** Prevalence of anti-HCV in GUM clinic attenders (1995) by injecting drug use and geographical area

	Age group (years)				
	<20	20–24	25–34	35–44	45+
<b>IDU</b>	positive/number tested (%)				
London	2/16 (12.5%)	21/78 (26.9%)	101/226 (44.7%)	55/94 (58.5%)	12/20 (60.0%)
Outside London	3/26 (11.5%)	4/59 (6.8%)	15/73 (20.5%)	14/24 (58.3%)	2/5 (40.0%)
<b>Non-IDU</b>	positive/number tested (%)				
London					
Female (heterosexual)	0/822 (0.0%)	2/904 (0.22%)	10/1329 (0.75%)	13/783 (1.66%)	5/341 (1.47%)
Male (heterosexual)	0/345 (0.0%)	6/891 (0.67%)	11/1111 (0.99%)	14/923 (1.52%)	10/566 (1.77%)
Male (homosexual/bisexual)	0/47 (0.0%)	1/337 (0.30%)	11/676 (1.63%)	3/452 (0.66%)	3/221 (1.36%)
Outside London					
Female (heterosexual)	0/406 (0.0%)	0/708 (0.0%)	1/747 (0.13%)	7/685 (1.02%)	4/470 (0.85%)
Male (heterosexual)	0/562 (0.0%)	1/702 (0.14%)	5/816 (0.61%)	5/639 (0.78%)	2/616 (0.32%)
Male (homosexual/bisexual)	0/46 (0.0%)	1/209 (0.48%)	4/306 (1.31%)	1/178 (0.56%)	0/127 (0.0%)

present in the IDUs but not in the non-injectors ( $p$  value for interaction = 0.0009). This can be seen in the crude prevalence estimates for the IDUs for whom the HCV prevalence was 39.9% (198/496) in the heterosexual group and 24.8% (31/125) in the homosexual/bisexual group.

### Injecting drug users

The prevalence of HCV in IDUs in each of the 2 years sampled was identical at 36.9% (1995, 95% CI: 33.1 to 40.8 (229/621); 1996, 95% CI: 33.3 to 40.5 (261/708)) Four of these specimens (two from 1995 aged 25–34 years and two from 1996 aged

35–44 years) were identified as indeterminate after RIBA testing, but were found to be HCV RNA PCR positive. These four specimens were categorised as HCV positive. Of the remaining 15 RIBA indeterminate specimens (11 from 1995, four from 1996) all were PCR negative. Fourteen (93%) of these indeterminate specimens were from the London area and 11 (73%) were from IDUs aged between 25–34 years.

There was a significantly higher prevalence of HCV in injectors in the London area compared to the geographical area outside of London both in 1995 (44.0%  $v$  20.3%;  $p < 0.0001$ ) and 1996 (44.3%  $v$  22.0%;  $p < 0.0001$ ). Multivariable logistic regression analysis demonstrated a significant variation in prevalence by centre ( $p = 0.041$ ), the centre variation being largely explained by the significantly higher prevalence seen in London. The majority of infections were in males in both 1995 (65.5%; 150/229) and 1996 (69.7%; 182/261); however, this difference was not significant after controlling for all other factors ( $p = 0.62$ ). In the combined years prevalence increased with age to peak in those aged between 35–44 years in both males and females. In those aged under 20 years prevalence was 10.5% (8/76), compared to 17.4% (48/276) in those aged 20–24 years, 38.2% (247/646) in those aged 25–34 years, 56.6% (155/274) in 35–44 year olds, and 56.1% (32/57) in those aged 45 years and over. There was a highly significant variation in prevalence by age ( $p < 0.0001$ ).

Variation by sexual orientation was highly significant ( $p = 0.0004$ ). In those injectors identifying themselves as heterosexual prevalence was 39.9% (198/496) in 1995 compared to 39.2% (227/579) in 1996. For the homosexual and bisexual injecting drug user group prevalence was 24.8% (31/125) and 26.0% (33/127) for 1995 and 1996, respectively. After controlling for all factors there was no significant difference in prevalence by country of birth ( $p = 0.52$ ). Anti-HIV-1 prevalence in IDUs from both years was 4.8% (64/1329). In 1995 the prevalence of anti-HIV in HCV positive specimens was 7.9% (18/229) compared to 6.5% (17/261) in 1996.

### HCV genotyping and serotyping

Specimens from IDUs from 1995 and 1996 were combined. A total of 78 specimens from both years, 59 from selected anti-HCV positive injecting drug users and 19 RIBA indeterminate injecting drug users were tested for HCV RNA by PCR. Thirty eight (64.4%) of the 59 positive specimens and four (21.1%) of the 19 indeterminate specimens were found to be PCR positive. Genotyping identified type 3a as the most prevalent genotype (42.8%) followed by genotype 1a (28.6%). The number of specimens genotyped was too small to demonstrate significant differences by age, area, or over time.

Of the overall 349 HCV positive specimens collected in 1995 (inclusive of the injectors), 175 (50.1%) were tested by PCR, of which 117 (66.9%) were found to contain HCV RNA. Genotyping of these specimens identified type 3a as the most

**Table 3** Multivariable analysis for all GUM clinic attenders in 1995

Factor	Level	Odds ratio (95% CI)	Change in deviance (d/f) p value
Centre*	E	1.00 (baseline)	<0.0001
	A	0.71 (0.35 to 1.42)	
	B	1.37 (0.78 to 2.40)	
	C	0.62 (0.32 to 1.18)	
	D	0.79 (0.26 to 2.43)	
	F	1.14 (0.64 to 2.03)	
	G	0.84 (0.41 to 1.66)	
	H	1.15 (0.42 to 3.13)	
	I	0.42 (0.17 to 1.00)	
	J	0.51 (0.24 to 1.08)	
	K	0.26 (0.09 to 0.77)	
	L	0.31 (0.13 to 0.69)	
	M	0.22 (0.08 to 0.58)	
N	0.45 (0.21 to 0.98)		
Age	<20	0.35 (0.13 to 0.94)	<0.0001
	20–24	1.00 (baseline)	
	25–34	2.71 (1.78 to 4.11)	
	35–44	4.66 (3.00 to 7.24)	
	45+	4.30 (2.52 to 7.32)	
Country	Abroad	1.00 (baseline)	0.98
	UK	0.97 (0.70 to 1.36)	
	Unknown	0.99 (0.52 to 1.87)	
IDU	No	1.00 (baseline)	<0.0001
	Yes	98.0 (72 to 134)	
Gender	Female	1.00 (baseline)	0.71
	Male	0.95 (0.71 to 1.26)	
Sexual orientation	Heterosexual	1.00 (baseline)	0.0013
	Homosexual	0.55 (0.37 to 0.80)	
HIV status	Negative	1.00 (baseline)	0.08
	Positive	1.74 (0.93 to 3.27)	

\*Centres A–G based in London.

**Table 4** Comparison of serotyping and genotyping results in all GUM attenders (1995–6)

Serotype	Genotype								PCR negative	Total
	1a	1a/1b	1b	2a	2b	3a	3b	4		
1	32	2	13	0	0	1	0	0	5	53
1 and 3	0	0	0	0	0	1	0	0	0	1
2	0	0	0	4	2	0	0	0	2	8
3	0	0	0	0	0	29	1	0	3	33
4	0	0	0	0	0	0	0	1	1	2
Untypeable	0	0	3	1	2	10	0	1	7	24
Total	32	2	16	5	4	41	1	2	18	121

common genotype (37.6%), followed by type 1a (27.4%) and then 1b (19.7%). There is no evidence of different genotypes in different age groups ( $p=0.26$ ). Grouping genotypes into types 1, 2, and 3 showed that there is no significant variation either by geographical area ( $p=0.19$ ) or by history of injecting drug use ( $p=0.19$ ).

Of the total of 610 HCV positive specimens from both years in non-injectors and injectors, 121 were serotyped of which 103 (85.1%) were from PCR positive specimens and 18 (14.9%) from PCR negative specimens. Twenty four specimens (17 PCR positive and seven PCR negative) were untypeable (table 4). By serotyping the majority were type 1 (46.6%), followed by type 3 (29.1%), type 2 (5.83%), type 4 (0.97%), and one reactive as both 1 and 3.

There was a high degree of concordance between serotype and genotype (table 4). All but one of the 48 type 1 serotypes had corresponding genotypes of 1a, 1a/1b, or 1b. The remaining type 1 serotype corresponded to a 3a genotype. All of the type 3 serotypes corresponded to either genotype 3a or 3b, serotype 2 to either 2a or 2b, and the single serotype 4 to genotype type 4. The specimen with the mixed 1 and 3 serotype genotyped as 3a only.

## DISCUSSION

The overall prevalence of HCV in GUM clinic attenders in 1995 (adjusted for differential sampling by age, sex, sexual orientation, and injecting drug use) was 1.03%. The prevalence of hepatitis C was strongly related to age and to geographical area, with higher hepatitis C positivity in the London area than the rest of England and Wales. The adjusted prevalence of infection in GUM clinic attenders who did not report injecting drug use was low (0.65%) and suggests that the risk of sexual transmission of hepatitis C virus infection in the United Kingdom is low. The pattern of age specific hepatitis C prevalence rates in clinic attenders who did not report injecting resembles that for injectors. Hepatitis C positivity is also higher in the London area. As the prevalence of injecting drug use is higher in the London area,<sup>17</sup> this may reflect limited sexual transmission from drug users or undisclosed drug use. The risk factors for hepatitis C in UK GUM clinics differ from those for HIV, where most infection occurs in homosexual and bisexual males in London. Because of this, the number of co-infections with hepatitis C and HIV is low.

Reports of confirmed hepatitis C infection from laboratories in England and Wales suggest that the virus is not commonly acquired sexually.<sup>18</sup> This is supported by the low prevalence of infection in clinic attenders who did not report injecting drug use in this survey. It has been suggested that among sexually transmitted disease clinic attenders, co-infection with HIV or other sexually transmitted infections may increase the rate of sexual transmission of HCV.<sup>6, 17</sup> This is not supported by this survey or by previous studies among females in a London GUM clinic,<sup>20</sup> and of female sex workers in London.<sup>21</sup> A study

of GUM clinic attenders in Scotland found overall a low prevalence of antibody to hepatitis C virus in non-injectors,<sup>22</sup> but a high prevalence in clinic attenders that had injected drugs. These authors concluded that the probability of the hepatitis C virus being acquired through sexual intercourse is extremely low. A study of sexually transmitted disease clinic attenders in the United States found an overall antibody prevalence to hepatitis C virus of 7.7%.<sup>23</sup> Hepatitis C infection, was however, mainly associated with injecting drug use and the authors concluded that sexual transmission occurred infrequently. The rate of antibody positivity to hepatitis C virus has been reported not to exceed 1% in the spouses of hepatitis C virus infected haemophiliacs.<sup>24</sup> A study of couples infected with the virus also suggests that overestimation of the risk of sexual transmission masks transmission by other parenteral routes.<sup>25</sup>

Furthermore, most evidence suggests that hepatitis C is not readily spread by sex between men. A cohort analysis of European homosexual men comparing the estimated incidence of hepatitis C, hepatitis B, and HIV suggested that sexual transmission of hepatitis C was a rare event.<sup>26</sup> Our study confirms the low prevalence of hepatitis C in homosexual men attending GUM clinics. The lack of overlap between the HIV and hepatitis C epidemics in the United Kingdom is also emphasised by the lower prevalence of hepatitis C in homosexual/bisexual injecting drug users than in heterosexual injectors. A higher hepatitis C prevalence was also found in heterosexual injectors in Australia compared with homosexual IDUs.<sup>27</sup> In the latter study, hepatitis C prevalence was also higher in opiate users than in stimulant users and the differences in UK prevalence may reflect the different pattern of drug use in homosexual men. The lower prevalence may also be due to homosexual men adopting safer injecting practices than heterosexuals because of heightened awareness of the risk of HIV.

In this study, hepatitis C prevalence was highest among clinic attenders who reported injecting drug use; 37% of attenders in both 1995 and 1996 were hepatitis C positive. The use of needle exchanges in England may explain the relatively low prevalence observed in our study, particularly in younger IDUs. Prevalence of hepatitis C in IDUs was strongly related to age, both inside and outside of the London area, as described in a previous Australian study.<sup>27</sup> It is likely that the increase with age reflects increased duration of drug use. A study from Spain found that duration of drug use was the only drug related variable strongly associated with anti-HCV prevalence.<sup>28</sup> The presence of hepatitis C was also associated with duration of injecting drug use and frequency of needle sharing in an Italian study.<sup>29</sup>

The most common hepatitis C genotypes in GUM clinic attenders are 1a and 3a; genotype 4 was rare. Mixed infections were rarely identified with only two specimens containing a mixture of genotypes 1a and 1b. No significant differences were shown in genotypes by age and the distribution is similar to that described previously in the United Kingdom. A

### Key messages

- There is little evidence of sexual transmission of HCV among groups at risk from sexually transmitted infections
- The overall prevalence of antibody to the hepatitis C virus is low in non-drug injecting GUM clinic attenders
- Most of the HCV infections in GUM clinic attenders have been acquired by injecting drug use

study from the north east of England found that most of the patients genotyped were type 1 (69%) followed by genotype 3 (21%).<sup>30</sup> A later UK study from a number of risk groups found that the majority of hepatitis C infections were types 1a (32%), 1b (15%), and 3a (37%),<sup>16</sup> and genotype distribution was similar in all groups except haemophiliacs. The findings of this survey are also similar to those from a number of European countries.<sup>31</sup> It has been suggested that genotypes 1a and 3a were introduced into Europe by needle sharing among IDUs.<sup>31</sup> The consistency of the hepatitis C genotype distribution in all the specimens typed suggests the predominance of a common transmission route, most probably injecting drug use.

This study has demonstrated a high degree of correlation between genotyping and serotyping methods. Serotyping may give inaccurate results because of cross reactivity between types and false negative results because of a lack of sensitivity.<sup>32-33</sup> Serotyping may also be unsuitable for specimens from immunosuppressed patients as they may have insufficient antibody for detection.<sup>32</sup> Concordance between serotyping and genotyping, at least for types 1 to 3, however, was high in our study. It is apparent that for epidemiological purposes hepatitis C types can be established by methods based on serological typing. Advantages of serotyping include its speed, ease of use, and its ability to type anti-HCV positive/RNA negative specimens. Serological assays are at present, however, unable to differentiate between subtypes.

It is apparent that, in the United Kingdom, injecting drug use is the main source of hepatitis C infections and that sexual transmission contributes little to the pool of infected individuals. The potential for increased transmission of hepatitis C through the sharing of injecting equipment still remains. Control of hepatitis C infection in England and Wales will therefore depend upon continuing to aim prevention programmes at IDUs.

### ACKNOWLEDGEMENTS

We would like to thank all the laboratory and clerical staff who contribute to the Unlinked Anonymous Prevalence Monitoring Programme (UAPMP) genitourinary medicine survey. The UAPMP is coordinated by the Public Health Laboratory Service Communicable Disease Surveillance Centre (PHLS CDSC) and the Public Health Laboratory Service Sexually Transmitted and Bloodborne Virus Laboratory, where the surveys serum specimens are stored. We thank Ms Tina Endericks who helped put the archive of specimens from genitourinary medicine clinic attenders together. We would also like to thank Professor Angus Nicoll and Dr Noel Gill for obtaining ethical clearance and Dr Philip Mortimer for assisting in the application for funding and reading the manuscript.

Funding: The Department of Health.

Conflict of interest: None.

### CONTRIBUTORS

MAB, MER, JVP, and CGT designed the study and applied for funding; CM and JAN supervised the archive construction; JVP developed the laboratory methods for hepatitis C antibody testing and, with JAN, supervised the antibody testing and serotyping carried out by LD; KAH carried out the PCR testing and genotyping supervised by CGT; JAN and MAB supervised the data collection; MAB did the epidemiological analysis and NJA did the statistical analysis; MAB and MER wrote the paper with contributions from all authors.

### Authors' affiliations

**M A Balogun, M E Ramsay**, Immunisation Division, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ, UK

**J V Parry, L Donovan, J A Newham, K A Harris, C G Teo**, Sexually Transmitted and Bloodborne Virus Laboratory, PHLS Central Public Health, Laboratory, 61 Colindale Avenue, London NW9 5HT, UK

**N J Andrews**, PHLS Statistics Unit, 61 Colindale Avenue, London NW9 5EQ, UK

**C McGarrigle**, HIV and STD Division, PHLS Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ, UK

### REFERENCES

- 1 **Macdonald M**, Crofts N, Kaldor J. Transmission of hepatitis C virus: rates, routes and co-factors. *Epidemiol Rev* 1996;**18**:137-48.
- 2 **Tedder RS**, Gilson J, Briggs M, *et al*. Hepatitis C virus: evidence for sexual transmission *BMJ* 1991;**302**:1299-302.
- 3 **Skidmore SJ**, Colliingham KE, Drake SM. Sexual transmission of hepatitis C. *J Med Virol* 1994;**42**:247-8.
- 4 **Hallam NF**, Fletcher ML, Read SJ, *et al*. Low risk of sexual transmission of hepatitis C virus *J Med Virol* 1993;**40**:251-3.
- 5 **Brettler DB**, Mannucci PM, Gringeri A, *et al*. The low risk of hepatitis C virus transmission among sexual partners of hepatitis C infected hemophiliac males: an international multicenter study. *Blood* 1992;**80**:540-3.
- 6 **Daikos GI**, Lai S, Fischl MA. Hepatitis C virus infection in a sexually active inner city population. The potential for heterosexual transmission. *Infection* 1994;**22**:72-6.
- 7 **Thomas DL**, Cannon RO, Shapiro C, *et al*. Hepatitis C, hepatitis B and human immunodeficiency virus infections among non-intravenous drug using patients attending clinics for sexually transmitted diseases. *J Infect Dis* 1994;**169**:990-5.
- 8 **Nakashima K**, Kashiwagi S, Hayashi J, *et al*. Sexual transmission of hepatitis C virus among female prostitutes and patients with sexually transmitted disease in Fukuoka, Kyushu, Japan. *Am J Epidemiol* 1992;**136**:1132-7.
- 9 **Van Ameijden**, Van den Hoek JA, Mientges GH, *et al*. A longitudinal study on the incidence and transmission patterns of HIV, HBV and HCV infection among drug users in Amsterdam. *Eur J Epidemiol* 1993;**9**:255-62.
- 10 **Donahue JG**, Nelson KE, Munoz A, *et al*. Antibody to hepatitis C virus among cardiac surgery patients, homosexual men, and intravenous drug users in Baltimore, Maryland. *Am J Epidemiol* 1991;**134**:1206-11.
- 11 **Villano SA**, Vlahov D, Nelson KE, *et al*. Incidence and risk factors for hepatitis C among injection drug users in Baltimore, Maryland. *J Clin Microbiol* 1997;**35**:3274-7.
- 12 **Nicoll A**, Gill ON, Peckham CS, *et al*. The public health applications of unlinked anonymous seroprevalence monitoring for HIV in the United Kingdom. *Int J Epidemiol* 2000;**29**:1-10.
- 13 **Annual Report of the Unlinked Anonymous Prevalence Monitoring Programme**. Prevalence of HIV in England and Wales in 1996.
- 14 **Parry JV**, Mahoney A, Mortimer PP. Are seroepidemiological surveys for human immunodeficiency virus infection based on tests on pools of serum specimens accurate and cost effective? *Clin Diagn Virol* 1993;**1**:167-78.
- 15 **Balogun MA**, Ramsay ME, Parry JV, *et al*. The prevalence and genetic diversity of hepatitis C infection in antenatal clinic attenders in two regions of England. *Epidemiol Infect* 2000;**125**:705-12.
- 16 **Harris KA**, Gilham C, Mortimer PP, *et al*. The most prevalent hepatitis C virus genotypes in England and Wales are 3a and 1a. *J Med Virol* 1999;**58**:131-7.
- 17 **Johnson AM**, Wadsworth J, Wellings K, *et al*. *Sexual attitudes and lifestyles*. Oxford: Blackwell Scientific Publications, 1994.
- 18 **Ramsay ME**, Balogun MA, Collins M, *et al*. Laboratory surveillance of hepatitis C virus infection in England and Wales: 1992 to 1996. *Comm Dis Public Health* 1998;**1**:89-94.
- 19 **Tor J**, Llibre JM, Carbonell M, *et al*. Sexual transmission of hepatitis C and its relation with hepatitis B virus and HIV. *BMJ* 1990;**311**:1130-3.
- 20 **Evans BA**, McCormack, Kell PD, *et al*. Trends in female sexual behaviour and sexually transmitted diseases in London, 1982-1992. *Genitourin Med* 1995;**71**:286-90.
- 21 **Ward H**, Day S, Weber J. Risky business: health and safety in the sex industry over a 9 year period. *Sex Transm Infect* 1999;**75**:340-3.
- 22 **Goldberg D**, Cameron S, Sharp G, *et al*. Hepatitis C virus among genitourinary clinic attenders in Scotland: unlinked anonymous testing. *Int J STD AIDS* 2001;**12**:17-21.
- 23 **Weinstock HS**, Bolan G, Reingold AL, *et al*. Hepatitis C virus infection among patients attending a clinic for sexually transmitted disease. *JAMA* 1993;**269**:392-4.
- 24 **Brackmann SA**, Gerritzen A, Oldenburg J, *et al*. Search for intrafamilial transmission of hepatitis C virus in hemophiliac patients. *Blood* 1993;**81**:1077-82.
- 25 **Zylberberg H**, Thiers V, Lagorce D, *et al*. Epidemiological and virological analysis of couples with hepatitis C virus. *Gut* 1999;**45**:112-16.
- 26 **Melbye M**, Biggar RJ, Wantzin P, *et al*. Sexual transmission of hepatitis C virus: cohort study (1981-9) among European homosexual men. *BMJ* 1990;**310**:210-12.
- 27 **Van Beek I**, Buckley R, Stewart M, *et al*. Risk factors for hepatitis C virus infection among injecting drug users in Sydney. *Genitourin Med* 1994;**70**:321-4.

- 28 **Bolumar F**, Hernandez-Aguado I, Ferrer L, *et al*. Prevalence of antibodies to hepatitis C in a population of intravenous drug users in Valencia, Spain, 1990–1992. *J Epidemiol* 1996;**25**:204–9.
- 29 **Girardi E**, Zaccarelli M, Tossini G, *et al*. Hepatitis C virus infection in intravenous drug users: prevalence and risk factors. *Scand J Infect Dis* 1990;**22**:751–2.
- 30 **Watson JP**, Brind AM, Chapman CE, *et al*. Hepatitis C virus: epidemiology and genotypes in the north east of England. *Gut* 1996;**38**:269–76.
- 31 **Silini E**, Bono F, Cividini A, *et al*. Molecular epidemiology of hepatitis C virus infection among intravenous drug users. *J Hepatology* 1995;**22**:691–5.
- 32 **Castelain S**, Zawadzki P, Khorsi H, *et al*. Comparison of hepatitis C virus serotyping and genotyping in French patients. *Clin Diag Virol* 1997;**7**:159–65.
- 33 **Halfon P**, Ouzan D, Hacene K, *et al*. Serotyping and genotyping of hepatitis C virus (HCV) strains in chronic HCV infection. *J Med Virol* 1997;**52**:391–5.

## ECHO

### Vaginal leucocytes predict bacterial infection in prepubertal girls



Please visit the Sexually Transmitted Infections website [www.stijournal.com] for link to this full article.

**D**octors managing vulvovaginitis before puberty recommend microscopic examination of vaginal fluid for leucocytes at the first visit, with microbiological investigation. Finding leucocytes raises the chances of finding bacterial pathogens, they say.

The authors carried out a retrospective review of girls aged 2–12 years with symptoms of vulvovaginitis. Sexual abuse was not suspected. Vaginal discharge was the commonest symptom, present in 92% of 80 girls. Vaginal secretions were collected aseptically for microscopic examination, Gram staining, and culturing to isolate candida and bacteria.

Bacterial infections occurred in 29 (36%) of all girls, 59% of them with group A  $\beta$  haemolytic streptococci, 24% with *H influenzae*, and 24% with *S aureus*—10% alone and 13% in mixed infections. Candida was not isolated. Twenty five girls with symptoms and bacterial infections received antibiotics and their infection resolved.

Leucocytes were seen in vaginal fluid from 24/29 girls with cultured pathogens and 21/51 without, a sensitivity of 83% and a specificity of 59% for bacterial infection.

Vulvovaginitis is the commonest gynaecological problem in this group. While many girls have no specific cause identified, vulvovaginitis can result from infection with specific bacterial pathogens. The authors point to drawbacks to their study, specifically not screening for sexually transmitted pathogens, on the assumption that the girls had not been abused, and the lack of a control group or repeat screening after antibiotic treatment.

▲ *Archives of Disease in Childhood* 2003;**88**:324–326.