We thank Dr Gordon Murray for his supervision of the statistical analysis.

Appendix

The APACHE II score is a simplified form of the original APACHE system, which attempts to measure reliably and objectively the severity of disease so that a patient's immediate prognosis may be estimated. The system is based on the principle that the outcome from an acute illness relates to the degree of disturbance in the physiology of the main organ systems, to the patient's age, and to the presence or absence of pre-existing severe chronic health problems.

The main part of this scoring system is an acute physiology score comprising 12 readily available physiological measurements. The value of each measure is given a weight varying from 0 to 12 depending on its deviation from a predetermined normal range and on its relative importance to patient outcome as determined by an expert multidisciplinary panel and by a review of past experience. The resulting acute physiology score varies from 0 to 45; a higher score representing a greater degree of physiological derangement and a higher risk of death. To estimate prognosis this score is combined with additional points for advanced age and pre-existing chronic health problems relating to the hepatic, cardiovascular, respiratory, renal, and immune systems to form the full APACHE II score. This score has a theoretical range of 0 to 71, but an observed range of 0 to 50 is more probable. The higher the score the greater the patient's acute risk of death.

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Sexual transmission of hepatitis C virus and its relation with hepatitis B virus and HIV

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Abstract

Objective—To determine the extent of transmission of hepatitis C virus in sexual partners of intravenous drug misusers and to examine the relation between the prevalences of HIV, hepatitis B virus, and hepatitis C virus infections in homosexual men and intravenous drug misusers and their sexual partners.

Design—Serum samples collected between 1984 and 1988 were tested for hepatitis B virus markers and antibodies against hepatitis C virus by enzyme linked immunosorbent assay (ELISA) and for HIV antibody by enzyme immune analysis and western blotting.

Setting—Large referral university hospital with an external AIDS clinic in the metropolitan area of Barcelona, Spain.

Subjects—243 Intravenous drug misusers, 143 of their regular heterosexual partners, and 105 homosexual men.

Main outcome measures—Prevalences of hepatitis C virus, hepatitis B virus, and HIV infections.

Results—In all, 178 of the 243 (73%) intravenous drug misusers, 16 out of 143 (11%) of their partners, and 17 of the 105 (16%) homosexual men had antibodies against hepatitis C virus. The presence of hepatitis C virus infection was unrelated to sex, age, the presence of HIV or hepatitis B virus infections, or the Centers for Disease Control stage of HIV. In sexual partners of intravenous drug misusers there were strong correlations between the presence of hepatitis C virus infection and that of HIV ($p=0.001$) and hepatitis B virus ($p=0.013$) infections.

Conclusions—Intravenous drug misusers have a high risk of acquiring hepatitis C virus, hepatitis B virus, and HIV infections, but the presence of

hepatitis C virus infection seems to be unrelated to the presence of the other two viruses. Homosexual men have a high prevalence of HIV and hepatitis B virus infections with a low prevalence of hepatitis C virus infection, the presence of which is not related to that of the other two infections. Conversely, heterosexual partners of intravenous drug misusers have low prevalences of the three virus infections, but the presence of hepatitis C virus infection correlates significantly with the presence of HIV and hepatitis B infections. The rate of sexual transmission of hepatitis C virus seems to be low, even in partners of people known to be seropositive for this virus.

Introduction

A complementary DNA clone derived from a blood-borne non-A non-B hepatitis virus genome that has been named hepatitis C virus has been isolated,¹ and a specific recombinant based immunoassay to capture circulating antibodies against hepatitis C virus is now available.² This virus has been shown to be the virus present in most (79-85%) patients with non-A non-B hepatitis after transfusion, and 60-78% of haemophiliacs, 48-70% of intravenous drug misusers, and 20% of patients undergoing haemodialysis have antibodies against it.³⁻⁶ These antibodies have, however, also been found in patients with chronic hepatitis, cirrhosis, or hepatocellular carcinoma who have not had a blood transfusion.^{7,8} This epidemiological evidence is worrying, and other overriding risk factors that are not bloodborne or transmission routes could be involved in patients who have not undergone transfusion. The transmission of hepatitis C virus through sexual contact is of concern and preliminary data are

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contradictory,^{3,9} but in about 10% of the patients with non-A non-B hepatitis the only identifiable source of infection is heterosexual activity with multiple partners or with a person with hepatitis.¹⁰

Intravenous drug misusers, homosexual men, and heterosexual partners of infected patients are at risk of acquiring hepatitis B virus and HIV. Neither the relation between the presence of these viruses and that of hepatitis C nor the presence of antibodies against hepatitis C virus in sexual partners of intravenous drug misusers, has, however, been clearly defined. To evaluate the effect of concurrent hepatitis C and B virus infections and HIV infection and the sexual transmission of hepatitis C virus we investigated the prevalence of serum markers of these three viruses in a wide cohort of homosexual men and intravenous drug misusers and their heterosexual partners in a metropolitan area with a high prevalence of HIV and hepatitis B virus infection.

Subjects and methods

SUBJECTS

We used serum samples collected between 1984 and 1988 from 491 subjects and kept frozen at -30°C . All of the patients had been admitted to our hospital. Homosexual men had been admitted because of HIV related infections or for screening for antibodies against HIV. Intravenous drug misusers had been admitted for programmed detoxification or because of medical complications (mainly drug related infections and AIDS). All regular heterosexual partners of intravenous drug misusers were enrolled in a prospective survey for the study of risk factors for heterosexual transmission of HIV and voluntarily screened for antibodies against HIV.

Intravenous drug misusers—Serum samples were obtained from 243 intravenous drug misusers (201 men, 42 women; mean age 25.4 years, range 16-41 years). The mean addiction time was 43.4 months (range 1-167 months). About 90% of them had shared needles sporadically or habitually.

Heterosexual partners of intravenous drug misusers—There were 143 heterosexual partners of intravenous drug misusers (22 men, 121 women; mean age 24.6 years, range 16-44 years) with no other risk factors for HIV transmission (such as parenteral drug misuse or having received a blood transfusion) apart from sexual exposure. The mean length of sexual relationship was 44.6 months (range 1-276 months, with a mean (SD) number of 12.5 (8.5) episodes of sexual intercourse monthly, as previously reported.¹³ Serum samples obtained at the same time as those of the intravenous drug misuser index patient were available in 48 cases.

Homosexual men—Serum samples were obtained from 105 homosexual men (mean age 34.0 years, range 18-59 years) and a mean of 8.8 couples each month (range 1-100 couples). All of them had engaged in active and passive anal intercourse and were recruited mainly from a large cohort of homosexual men attending our AIDS clinic as outpatients.

METHODS

Antibodies against hepatitis C virus were screened for with a second generation enzyme linked immunosorbent assay (ELISA) that used a recombinant hepatitis C virus antigen polypeptide (c100-3) (Ortho Diagnostics, Raritan, New Jersey, United States). Antibodies against HIV were screened for with a competitive enzyme immune analysis (Behring, Barcelona, Spain) and selected samples confirmed by western blotting (Dupont, Rockville, Massachusetts, United States).

Tests for serum hepatitis B surface antigen, hepatitis B core antibody, and hepatitis B surface antibody

were performed by enzyme immune analysis with commercial kits (Behring, Barcelona, Spain). Hepatitis B core antibody IgM was assayed with a commercial MicroELISA kit (Organon, Teknika Española, Barcelona, Spain) and was done only when the test for hepatitis B core antibody gave a positive result and that for hepatitis B surface antibody a negative result in the same patient.

Statistical analysis—The χ^2 or Fisher exact test and Student's *t* test methods were used for statistical comparisons. Results are given as percentages and as mean (SD) values. Analyses were performed with a commercial statistical package.

Results

INTRAVENOUS DRUG MISUSERS

In all, 183 of the 243 (75%) intravenous drug misusers tested positive for antibodies against HIV. HIV staging according to revised criteria from the Centers for Disease Control was possible in only 161 seropositive subjects.¹¹ Of these, 40 (25%) were staged as HIV-II, 51 (32%) as HIV-III, 34 (21%) as HIV-4C2, and 36 (22%) as HIV-IVC1 or HIV-IVD. There was no association between sex and a positive result for HIV antibody, but those negative for the antibody were slightly younger than those who were seropositive (24.3 (4.1) *v* 25.8 (4.2); $p=0.019$). We have reported elsewhere in the same collective a greater habit of sharing needles and a longer time of addiction in those intravenous drug misusers in Barcelona positive for HIV antibody than in those negative for the antibody ($p<0.001$).¹²

Overall, 29 out of 225 (13%) intravenous drug misusers were positive for hepatitis B surface antigen, 97 out of 222 (44%) were positive for hepatitis B surface antibody, and 197 out of 225 (88%) were positive for hepatitis B core antibody. Twenty two out of 113 patients (19%) were positive for antihepatitis B core antigen IgM. Antibodies against hepatitis C virus were detected in 178 out of 243 (73%) subjects. There were no significant associations between hepatitis C virus seropositivity and sex, age, or the presence of antibodies against HIV, hepatitis B core antigen, or hepatitis B surface antigen or hepatitis B core antigen IgM (table I). There was a clear association between hepatitis B virus (indicated by the presence of antibodies against hepatitis B core antigen) and HIV seropositivity (155 out of 225 had antibodies against hepatitis B core antigen and HIV, and 12 out of 225 were negative for antibodies against both hepatitis B virus and HIV; $p=0.012$). The presence of antibodies against hepatitis C virus was also unrelated to the Centers for Disease Control stage in those infected with HIV (30 out of 40 (75%) of those staged as HIV-II, 39 out of 51 (76%) of those staged as HIV-III, 27 out of 34 (79%) of those staged as HIV-IVC2, and 22 out of 36 (61%) of those staged as HIV-IVC1, $p=0.293$). Seven out of 12 patients negative for both HIV and hepatitis B virus antibodies had antibodies against hepatitis C virus.

HETEROSEXUAL PARTNERS OF INTRAVENOUS DRUG MISUSERS

Antibodies against HIV were found in 25 out of 143 (17%) subjects. Three out of 127 (2%) tested positive for hepatitis B surface antigen, 33 out of 126 (26%) were positive for hepatitis B surface antibody, and 44 out of 126 (40%) were positive for hepatitis B core antibody. Three out of 11 sexual partners were positive for antihepatitis B core antigen IgM. Overall, 16 out of 143 partners had antibodies against hepatitis C virus (table II). Although four out of 37 partners of subjects known to be positive for hepatitis C virus antibody had antibodies against hepatitis C virus, none of the

TABLE 1—Correlations between age, sex, and various markers for hepatitis B virus and seropositivity for hepatitis C virus in intravenous drug mis: DCD Figures in parentheses are percentages

	Seropositive subjects (n=178)	Seronegative subjects (n=65)	p Value
Mean (SD) age (years)	25.2 (3.9)	26.0 (4.9)	0.227
Sex (ratio of men to women)	5:3:1:0	3:6:1:0	0.289
Positive for hepatitis B surface antigen	21/169 (12)	8/56 (14)	0.718
Positive for hepatitis B surface antibody	72/167 (43)	25/55 (46)	0.761
Positive for hepatitis B core antibody	147/169 (87)	50/56 (89)	0.650
Positive for hepatitis B core antigen IgM	20/90 (22)	2/23 (9)	0.243
Positive for HIV antibody	135/178 (76)	48/65 (74)	0.749
CDC stage:			0.295
HIV-II	30 (75)	10 (25)	
HIV-III	39 (77)	12 (24)	
HIV-IVC2	27 (79)	7 (21)	
HIV-IVC1	22 (61)	14 (39)	

CDL=Centers for Disease Control.

partners of the 11 intravenous drug misusers negative for hepatitis C virus antibody was positive for the antibody; but these results were not significant ($p=0.339$). There was a strong correlation between seropositivity for hepatitis C virus and that for HIV ($p=0.001$) and between the presence of hepatitis C virus infection and that of hepatitis B virus (indicated by the presence of antibodies against hepatitis B surface and core antigens); $p=0.013$ and $p=0.031$ respectively). There was no correlation between the presence of antibodies against hepatitis C virus and a positive result for hepatitis B surface antigen, nor was there a correlation between sex and a positive result for hepatitis C virus, hepatitis B virus, or HIV antibody. There were 71 sexual partners who were negative for HIV and hepatitis B virus antibodies, and two of them were positive for hepatitis C virus antibody.

HOMOSEXUAL MEN

In all, 87 out of 104 (84%) homosexual men were positive for HIV antibody. Four out of 73 men (5%) were positive for hepatitis B surface antigen, 51 out of 73 (70%) for hepatitis B surface antibody, and 59 out of 73 (81%) for hepatitis B core antibody; hepatitis IgM was found in two of 19 subjects. Seventeen of the 105 homosexual men tested were positive for hepatitis C virus antibody. The presence of these antibodies was not related to seropositivity for HIV or hepatitis B virus (table II). A strong correlation was found between seropositivity for HIV and that for hepatitis B virus ($p=0.001$). None of the eight patients negative for HIV and hepatitis B virus antibodies had antibodies against hepatitis C virus.

Discussion

We found a high prevalence of antibodies against hepatitis C virus (73%) in intravenous drug misusers. The figures are consistent with previous reports,^{3,4,14} and no associations were found between the presence of antibodies against hepatitis C virus and serological evidence of HIV or hepatitis B virus infection. Neither age nor sex was related to seropositivity for hepatitis C

virus. In subjects positive for HIV antibody, seropositivity for hepatitis C virus was independent of the Centers for Disease Control stage of HIV at which the patient was classified. These data suggest a high rate of parenteral spread of hepatitis C virus among the intravenous drug misusers, with a close resemblance to that observed for hepatitis B and HIV infections in this population and without apparent relation to the development of overt AIDS. Hepatitis C virus infection is probably acquired by intravenous drug misusers early in the course of their addiction and, although not significant, a trend to loose hepatitis C virus antibodies when overt AIDS develops has been observed. Further studies are needed, however, on other infectious or environmental cofactors implicated in the transmission of hepatitis C virus in intravenous drug misusers because nearly two thirds of patients who are negative for HIV and hepatitis B virus antibodies acquire hepatitis C virus infection.

Surprisingly, the homosexual men seemed to be relatively spared from this infection, and only 16% of them had antibodies against hepatitis C virus. This is quite unexpected because other parenterally and sexually transmitted viruses like HIV and hepatitis B virus are prevalent in homosexual men, and our patients must be considered as heavily infected (83% and 81% for HIV and hepatitis B virus, respectively) due to bias in our selection of patients attending our AIDS clinic. These data point to a low rate of transmission of hepatitis C virus through sexual intercourse in homosexual men. In preliminary reports the prevalence of hepatitis C virus was significantly higher in homosexuals positive for HIV antibody,^{14,15} but this was not observed in our series, perhaps because of the increased prevalence of HIV infection. Interestingly, all patients negative for HIV and hepatitis B virus antibodies were also negative for hepatitis C virus antibody, so we conclude that HIV and hepatitis B virus are more readily transmitted by the sexual route than hepatitis C virus.

The absence of hepatitis C virus antibodies in heterosexual partners of intravenous drug misusers without the infection and the finding that all four partners positive for hepatitis C virus were partners of index patients is interesting. Nevertheless, despite this close relation, the degree of sexual transmission to regular partners of intravenous drug misusers seems to be very low in couples with one partner known to be infected with hepatitis C virus. In fact only 11% of sexual partners of unknown hepatitis C virus antibody state acquired the infection (although a 73% seropositivity for hepatitis C virus could be expected). This percentage is consistent with the low frequency (4.5%) of the infection among partners of haemophiliac patients known to be positive for hepatitis C virus antibody.⁹

In our study sexual transmission from men to women seemed to be as efficient as transmission from women to men. The presence of antibodies against HIV and hepatitis B virus in couples is associated with a greater risk of transmission of hepatitis C virus.

Further studies are required to determine specific risk factors for sexual transmission of hepatitis C virus in couples with a high risk of hepatitis C virus infection. The high risk practice will probably be found to be similar to the variables implicated in sexual transmission of HIV and hepatitis B virus. The findings in this study suggest that there are three different patterns related to transmission of hepatitis C virus, HIV, and hepatitis B virus. Firstly, intravenous drug users carry a high risk of acquiring all three infections, but the presence of hepatitis C virus infection is not related to the presence of the other two. Secondly, heterosexual partners have low prevalences of the three viruses and the acquisition of hepatitis C

TABLE II—Correlations between age, sex, and various markers for hepatitis B virus and seropositivity for hepatitis C virus in homosexual men and heterosexual partners of intravenous drug misusers. Figures in parentheses are percentages

	Seropositive subjects	Seronegative subjects	p Value
<i>Homosexual men</i>			
Mean (SD) age (years)	32.4 (6.1)	34.3 (9.6)	0.439
Positive for HIV antibody	15/17 (88)	72/87 (82)	0.841
Positive for hepatitis B surface antigen	1/13 (8)	3/60 (5)	0.999
Positive for hepatitis B surface antibody	8/13 (62)	43/60 (72)	0.697
Positive for hepatitis B core antibody	11/13 (85)	48/60 (80)	0.999
<i>Heterosexual partners</i>			
Mean (SD) age (years)	27.0 (6.7)	24.3 (5.4)	0.098
Sex (ratio of men to women)	0:1:1:0	0:2:1:0	0.999
Positive for HIV antibody	8/16 (50)	17/127 (13)	0.001
Positive for hepatitis B surface antigen	0/3	3/124 (2)	
Positive for hepatitis B surface antibody	8/14 (57)	25/112 (22)	0.013
Positive for hepatitis B core antibody	9/14 (64)	35/112 (31)	0.031
Partner of an index patient	4/4 (100)	33/44 (75)	0.339

virus is strikingly related to that of the other two. Finally, homosexual men have a high prevalence of HIV and hepatitis B virus infections with a low prevalence of antibodies against hepatitis C virus, the presence of which is not related to the presence of either HIV or hepatitis B virus.

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Women in prison and use of illicit drugs before arrest

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From 1979 to 1988 the number of sentenced women in prison rose by 32% yet the number of women sentenced for drug offences increased by over 400%.¹ We present the results of a retrospective survey of drug use before arrest among female prisoners.

Subjects, methods, and results

We interviewed a random sample of 272 women serving a prison sentence (a quarter of the prison population) about drug use in the six months before arrest. Data collected included the type of drug and the frequency and route of use. Dependence on a drug was defined as daily use plus withdrawal symptoms on abstinence and an acceptance by the woman that she was dependent. Drug users were asked about their previous contact with treatment agencies and their current attitude to treatment without drugs.

Cannabis was the illicit drug that had been used most commonly, with 82 women reporting use at least once a week. It was excluded from consideration of drug dependence as it is of minor clinical importance.

Sixty three women (23%; 95% confidence interval 18% to 28%) were identified as drug dependent (table). Most had used opiates, alone or in combination with other drugs, and most had injected during the six months before their arrest. Of these 63 women, 24 had been sentenced for drug offences and 32 for theft. Thirty seven stated that they would accept treatment if it was offered, including 17 who seemed to have a strong desire for treatment. The 26 women who expressed no desire for treatment usually stated that drugs were no longer a problem; only one or two were resigned to a return to dependency. Two drug users were positive for HIV (the number tested was unknown).

Comment

Nearly a quarter of sentenced female prisoners were dependent on drugs at the time of their offence. Despite recent diversification in facilities for treating drug users² one third of the women who were dependent on drugs reported having had no contact with services before entering prison. Our findings support the claim by the advisory council on the misuse

Type of drug used before arrest by female prisoners who were drug dependent, and number reporting previous treatment for dependency

Type of drug	Injected during six months before arrest	Reported previous treatment for drug dependency	Total
Opiates alone	22	22	34
Opiates and other drugs	14	14	16
Non-opiate drugs	6	4	13
Total	42	40	63

of drugs that prison or the courts can offer an important point of contact for drug users not seen elsewhere.³ Women's prisons have no equivalent of the therapeutic regimens available to men at Grendon and Wormwood Scrubs annexe. Many of the women expressed a desire for treatment. Motivation is difficult to assess in prison; the only real test is to make treatment available.

Past criticism of provision for drug users drew attention to the absence of effective liaison at the time of release.¹ A recent policy statement by the Home Office on developing services in prisons emphasises the need for coordination between prisons and outside agencies and encourages prison doctors to take a more active role in this process.⁵

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Notice of inadvertent duplicate publication

The *BMJ* regrets that the paper entitled "Quality of life of elderly people after surgery for benign oesophageal stricture" by Dr B N M Jayawardhana and others (16 December 1989, pp 1503-4) was substantially similar to a paper published in *Age and Ageing* entitled "Benign oesophageal stricture: the place of surgery in the management of elderly patients" (January 1990, pp 31-5). Although these papers included some of the same group of patients and addressed the same question, neither editor was informed of the existence of the other paper, in contravention to our instructions to authors and to internationally agreed guidelines.