Sexual transmission of hepatitis C virus: cohort study (1981-9) among European homosexual men

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Abstract

Objectives—To determine the prevalence, incidence, and persistence of positivity for antibodies to hepatitis C virus (anti-HCV) and the potential for sexual transmission of the virus.

Design—A cohort analysis covering 1981-9 comparing estimated cumulative incidences of and seroconversion rates for anti-HCV with those of hepatitis B core antibody (anti-HBc) and antibodies to the human immunodeficiency virus (anti-HIV).

Setting—Copenhagen and Aarhus, Denmark.

Subjects—259 Male members of a Danish homosexual organisation.

Main outcome measures—Correlations of prevalence and incidence with a wide range of sexual lifestyle variables.

Results—Only four (1.6%) subjects were positive for anti-HCV in 1981. The estimated cumulative incidence of positivity for anti-HCV was 4.1% in 1984 (seroconversion rate during 1981-4 (2.5%) and remained at 4.1% in 1989 (seroconversion rate nil during 1984-9). In contrast, positivity for anti-HBC rose from 44.0% in 1981 to 52.7% in 1984 (seroconversion rate 15.5%) and 58.8% in 1989 (seroconversion rate 12.9%), and that for anti-HIV rose from 8.8% to 24.0% (seroconversion rate 16.7%) and 30.1% (seroconversion rate 8.0%) respectively. Three anti-HCV positive patients seroreverted three to five years later. None of the anti-HCV positive subjects had had a transfusion and only one gave a past history of intravenous drug use. Variables in sexual lifestyle correlated with the presence of anti-HBc but not with that of anti-HCV.

Conclusions—In contrast with hepatitis B virus and HIV, sexual transmission of hepatitis C virus seems to be a rare event. Furthermore, antibodies to the virus may become undetectable after several years.

Introduction

Although the classification and early descriptions of clinical non-A non-B hepatitis were derived primarily from cases associated with transfusion, this mode of transmission has recently been estimated to account for only 5-10% of patients with the disease in the developed world. 1 In a substantial proportion of cases no obvious route or source of transmission is found. In this respect, therefore, the importance of sexual transmission has been an open question. A possibility for better understanding has emerged with the molecular cloning of an agent designated hepatitis C virus, which seems responsible for most cases of parenteral non-A non-B hepatitis. 13 To date frequent transmission of hepatitis C virus by exposure to blood has been described in drug addicts and patients with haemophilia 14 whereas little has been reported on the frequency of sexual transmission of the virus. We have studied the prevalence and persistence of antibodies to hepatitis C virus among homosexual men and analysed their possible association with a range of lifestyle factors to see if there is evidence for a range of epidemiological profile that can be used to identify those at risk.

Subjects and methods

We studied a cohort of Danish homosexual men who had been followed up since 1981. 18 Briefly, 259 subjects were initially enrolled from volunteers belonging to a national organisation of homosexual men. At enrolment their average age was 32.0 years, their average duration of homosexual activity 12.2 years, and their average number of partners 24.9 a year. Cross sectional analyses were performed on all subjects comparing antibody state with lifestyle and demographic variables. In addition, longitudinal studies were done on subjects who subsequently to the 1981 visit were also seen in 1984 or 1989, or in both years. Compared with the original 1981 cohort members of this subset were slightly more experienced sexually (1984, 13.3 years of homosexual activity; 1989, 14.0 years) but otherwise were similar.

A log linear model was used to compute the non-parametric maximum likelihood estimate of the survival curves (1—estimated cumulative antibody incidence) from interval censored data, as detailed elsewhere. 12 We also calculated the seroconversion rates between years of testing using the same methodology. Associations between serological markers and variables in lifestyle were analysed by Spearman rank order correlations and linear regressions.

Serum samples were kept frozen at −70°C until assay and had not previously been thawed. All serum samples were tested for antibodies to hepatitis C virus (anti-HCV) by an enzyme linked immunosorbent assay (ELISA; Ortho Diagnostic Systems). Samples that were non-reactive to hepatitis C virus in the initial run were considered to be anti-HCV negative. Samples that were reactive to hepatitis C virus were retested and considered to be positive if reactive in both tests. Exposure to hepatitis C was determined by an assay for antibodies to hepatitis B core antigen (anti-HBc; CORZYME, Abbott Laboratories). This marker does not recognise patients immunised by vaccination.
Testing for HIV antibody (anti-HIV) was performed by an indirect second generation ELISA with western blot for confirmation.

Results

HEPATITIS C VIRUS

Of the 259 subjects in the original cohort, 250 (96·5%) had serum remaining for hepatitis tests. In 1981 four (1·6%) of these men were positive for anti-HCV. Three others seroconverted between 1981 and 1984 and one between 1981 and 1989 (table I). Using a log linear model we found the cumulative (since 1981) incidence of positivity for anti-HCV to be 4·1% in 1984 and also 4·1% in 1989 (table II). This analysis included anti-HCV positive subjects who later seroconverted.

Two of the three men who seroconverted to hepatitis C virus between 1981 and 1984 also seroconverted to HIV during that period. By 1989 these two subjects were profoundly immunosuppressed (CD4 to CD8 ratios 0·20 and 0·04) and one had lost antibody to hepatitis C virus. The third seroconverter was anti-HIV negative throughout, yet had also lost reactivity to hepatitis C virus by 1989.

None of the subjects on whom information was available had ever received a transfusion, and only one had ever used drugs intravenously (table I). Neither age, duration of homosexual activity, type of sexual activity, treatment for venereal disease, nor HIV state was significantly correlated with being anti-HCV positive (figure). The few anti-HCV positive subjects, however, tended to have more partners than seronegative subjects.

HEPATITIS B VIRUS AND HIV

Table II summarises the data on hepatitis and HIV. Anti-HBc was found in an estimated 44·0% of the men in 1981, 52·7% in 1984, and 58·8% in 1989. In 1981 being positive for anti-HBc was correlated with numbers of sexual partners a year (p<0·0001), older age (p<0·0001), years of homosexual activity (p<0·0001), number of previous treatments for gonorrhoea and syphilis (p<0·0001), and also being seropositive to HIV (p<0·02) or seroconverting later (p<0·03) (figure). In logistic regression analyses the strongest single variable was number of partners (in all models p<0·0001). In a model with the number of partners, age, and previous treatments for sexually transmitted disease, the cumulative incidence of anti-HBc positivity was 5·5% (95% confidence interval 2·6% to 8·4%) by 1984; in a model including age and previous treatments, it was 4·9% (2·1% to 7·7%) (p=0·004). There was no significant difference between those who had lost anti-HIV (n=24) and those who did not (n=31) in terms of anti-HBc positivity (p=0·5).

Table II also shows the cumulative incidence of positivity for anti-HCV. Anti-HCV positivity was strongly correlated with number of sexual partners (p<0·0001) and with homosexual activity (p<0·0001). No association with age or duration of homosexual activity was significant. The cumulative incidence of positivity for anti-HCV was 0·8% (95% CI 0·3% to 1·3%) by 1984; in a model including number of sexual partners and years of homosexual activity, it was 0·7% (0·2% to 1·2%) (p=0·04). There was no significant difference between those who had lost anti-HIV (n=22) and those who did not (n=31) in terms of anti-HCV positivity (p=0·6). The seroconversion rate for anti-HCV was 0·03 per year (95% CI 0·003 to 0·06) for men who seroconverted to HIV, and 0·02 per year (95% CI 0·01 to 0·04) for men who did not.

Table III shows the cumulative incidence of positivity for anti-HBc and anti-HCV by year of sexual activity and for HIV by number of sexual relations. The cumulative incidence of positivity for anti-HBc was 2·4% (95% CI 1·8% to 3·0%) by 1983 in the group of men who had never had a sexual partner, and 5·7% in the group who had had 5 or more sexual partners a year (p<0·0001). The cumulative incidence of positivity for anti-HCV was 0·8% (95% CI 0·3% to 1·3%) by 1984 in the group who had never had a sexual partner, and 4·7% in the group who had had 5 or more sexual partners a year (p<0·0001). The cumulative incidence of positivity for HIV was 0·4% (95% CI 0·2% to 0·6%) by 1983 in the group who had never had a sexual partner, and 2·9% in the group who had had 5 or more sexual partners a year (p<0·0001).

Table IV shows the cumulative incidence of positivity for anti-HBc and anti-HCV by year of sexual activity and for HIV by number of sexual relations. The cumulative incidence of positivity for anti-HBc was 2·4% (95% CI 1·8% to 3·0%) by 1983 in the group of men who had never had a sexual partner, and 5·7% in the group who had had 5 or more sexual partners a year (p<0·0001). The cumulative incidence of positivity for anti-HCV was 0·8% (95% CI 0·3% to 1·3%) by 1984 in the group who had never had a sexual partner, and 4·7% in the group who had had 5 or more sexual partners a year (p<0·0001). The cumulative incidence of positivity for HIV was 0·4% (95% CI 0·2% to 0·6%) by 1983 in the group who had never had a sexual partner, and 2·9% in the group who had had 5 or more sexual partners a year (p<0·0001).

Table V shows the cumulative incidence of positivity for anti-HBc and anti-HCV by year of sexual activity and for HIV by number of sexual relations. The cumulative incidence of positivity for anti-HBc was 2·4% (95% CI 1·8% to 3·0%) by 1983 in the group of men who had never had a sexual partner, and 5·7% in the group who had had 5 or more sexual partners a year (p<0·0001). The cumulative incidence of positivity for anti-HCV was 0·8% (95% CI 0·3% to 1·3%) by 1984 in the group who had never had a sexual partner, and 4·7% in the group who had had 5 or more sexual partners a year (p<0·0001). The cumulative incidence of positivity for HIV was 0·4% (95% CI 0·2% to 0·6%) by 1983 in the group who had never had a sexual partner, and 2·9% in the group who had had 5 or more sexual partners a year (p<0·0001).
Diarrhoea due to cryptosporidium infection in thalassaemia major

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Cryptosporidium has been increasingly recognised as a cause of diarrhoea in both immunocompetent and immunocompromised patients with the advent of adequate staining techniques. It is a coccidian parasite, which seems to be a single species able to infect a range of animal hosts. In immunocompetent adults it ranks third in the non-viral causes of gastrointestinal symptoms after salmonella and campylobacter, and in patients with AIDS it is the commonest cause of diarrhoea.

The severity of infection with cryptosporidium varies, and immunocompetent patients may be asymptomatic. Usually there is an attack of watery, non-bloody diarrhoea with abdominal pain, vomiting, and fever. Temperatures of up to 38°C have been reported. The illness is self-limiting, and symptoms may be short lived or persist for many weeks. In immunocompromised subjects the illness is prolonged and debilitating and may be fatal.

Case report

A 22 year old woman with β thalassaemia major had been dependent on transfusions since birth and recently desferoxamine for iron overload. She had had a splenectomy at the age of 7, and a test for HIV in March 1989 had yielded negative results. In June she presented to casualty with a 24 hour history of watery diarrhoea, colicky abdominal pain, vomiting, dizzi-