

## CLINICAL RESEARCH

## Prevalence and incidence of hepatitis A among male homosexuals

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### Abstract

In a study of 689 male homosexuals 290 (42%) were found to have antibodies to hepatitis A virus. The 399 men who did not have antibodies were followed up for up to 690 days, and 35 cases of hepatitis A were detected. The attack rate at the end of the study was 14%. The incidence climbed steadily, indicating that the cases of hepatitis A did not occur in clusters. Statistical analysis showed that the prevalence of antibodies to hepatitis A virus was significantly correlated with the duration of homosexual activity ( $p < 0.006$ ), and this was independent of age. The incidence of hepatitis A was found to be correlated with the number of different sexual partners in the preceding six months.

It is concluded that hepatitis A is a sexually transmitted disease among homosexual men in countries with a low rate of exposure to hepatitis A during childhood.

### Introduction

Male homosexuals have a high risk of contracting various sexually transmitted diseases, including enteric infections. As the

incidence of hepatitis A in northern Europe is decreasing and most adults are now susceptible,<sup>1-3</sup> one can expect hepatitis A to be sexually transmitted among homosexual men. There have been some reports of outbreaks of hepatitis A among male homosexuals.<sup>3-6</sup> As studies of prevalence and incidence have been contradictory, however,<sup>6-7</sup> we decided to study the prevalence and incidence of hepatitis A among a large group of male homosexuals and to examine their relation to several risk factors.

### Subjects

#### STUDY POPULATION

The study population was selected from a group of male homosexuals who had participated in an efficacy trial with a heat inactivated hepatitis B vaccine from November 1980 to December 1982.<sup>8</sup> Men could enter this trial if they were between 16 and 50 years of age, were negative for hepatitis B virus markers, had a serum alanine transferase activity of  $< 50$  IU/l, had no serious illness, and had had at least two different male sexual partners in the preceding six months. For the present study we selected those men who lived in and around Amsterdam.

#### CONDUCT OF THE STUDY

At the beginning of the study (month 0) the participants were asked about their medical history and lifestyle. Age was noted in years at the time of the interview. The duration of homosexual activity was defined as the number of years from the time of the first homosexual contact until the time of the interview. Each person was asked to estimate the number of different sexual partners in the six months preceding the month of the interview.

Blood was collected every month for the first five months and every three months thereafter. The first blood sample (month 0) was tested for the presence of antibodies to hepatitis A virus. If this was negative the blood sample taken at the end of the trial was tested again for antibodies. If a seroconversion was found, all samples taken during the study were tested retrospectively for antibodies to hepatitis A virus. All blood samples had been tested for serum alanine transferase during the study as part of the vaccine trial. A hepatitis A virus infection was defined as follows: IgM specific antibodies to hepatitis A virus present

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in at least two sequential blood samples, or seroconversion for antibodies to hepatitis A virus confirmed in at least one subsequent blood sample.

LABORATORY METHODS

Total antibodies to hepatitis A virus and IgM specific antibodies to hepatitis A virus were measured by an enzyme linked immunosorbent assay (Organon, Oss, The Netherlands). Alanine transferase activity was measured by an automated kinetic method.

STATISTICAL METHODS

To study the association between potential risk factors and the prevalence of antibodies to hepatitis A virus a stepwise logistic regression was used.<sup>9</sup> This regression model assumes a linear relationship between the log odds—that is, the logarithm of the ratio of the probabilities of having antibodies (P(+)), and having no antibodies (P(-)),—and the risk factors  $x_1 \dots x_n$ :

$$\ln \frac{P(+)}{P(-)} = \beta_0 + \beta_1 x_1 + \dots + \beta_n x_n$$

The programme automatically selects the risk factors that are significantly associated with the prevalence of antibodies to hepatitis A virus and only those factors are included in the final model.

To investigate the incidence of hepatitis A during follow up, life table methods were used.<sup>10</sup> Overall attack rates were estimated with the product limit method, and the relation with risk factors was examined with Cox's proportional hazards regression model.<sup>11</sup> This regression model assumes the following relation between the risk factors and the ratio of the risk of seroconversion at time  $t$ —the relative risk—for different values of risk factors, ( $y_1, \dots, y_n$ ) and ( $x_1, \dots, x_n$ ) respectively:

$$\ln \frac{\lambda(t(y_1, \dots, y_n))}{\lambda(t(x_1, \dots, x_n))} = \beta_1(y_1 - x_1) + \beta_2(y_2 - x_2) + \dots + \beta_n(y_n - x_n)$$

Results

CHARACTERISTICS OF PARTICIPANTS

A total of 689 homosexual men participated in the study. Their mean age was 30.8 years (SD 7.0) and the mean duration of their homosexual activity 11.0 years (SD 7.0). Table I shows some other characteristics of the study group.

TABLE I—Characteristics of 689 homosexual men whose serum was examined for the presence of antibodies to hepatitis A virus

Characteristic	
No	689
Mean age in years (SD)	30.8 (7.0)
Mean duration of homosexuality in years (SD)	11.0 (7.0)
No (%) with > 10 different sexual partners in preceding six months	241 (35)
No (%) with history of syphilis	128 (19)
No (%) with history of jaundice	78 (11)
No (%) with anal sexual contact	511 (74)

PREVALENCE AND INCIDENCE OF HEPATITIS A

At the beginning of the study 290 of the 689 homosexual men (42%) had antibodies to hepatitis A virus. Among the 399 with no antibodies 35 cases of hepatitis A occurred during the follow up period. Most of the men (32) had a raised serum alanine transferase activity ( $\geq 50$  IU/l; normal value  $< 21$  IU/l) at least once, and 28 also had jaundice. Only three men had no symptoms at all, seroconversions being found only at the end of the study.

The attack rate of hepatitis A virus was calculated by the product limit method and was found to be 14% at the end of the study (690 days). As can be seen in fig 1 the curve of the attack rate climbed steadily, indicating that the infections were not occurring in clusters.

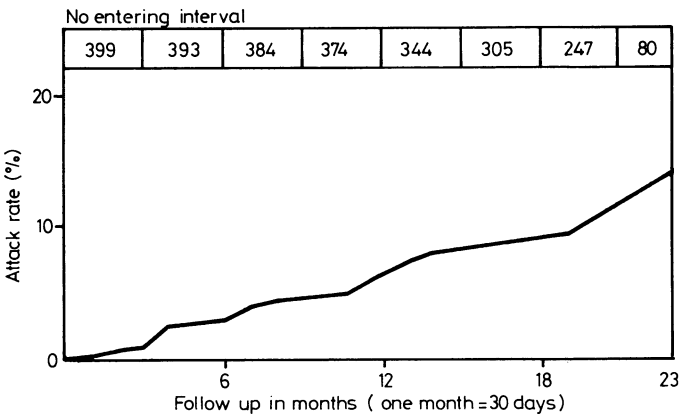


FIG 1—Life table attack rate of hepatitis A among susceptible male homosexuals.

ASSOCIATION BETWEEN THE PREVALENCE OF ANTIBODIES TO HEPATITIS A VIRUS AND POTENTIAL RISK FACTORS

Evaluation by stepwise logistic regression showed that three characteristics of the homosexual men were significantly correlated with seropositive antibodies to hepatitis A virus (table II). Age had the highest influence ( $p < 0.00001$ ), the probability of having antibodies increasing with rising age. The next important risk factor was a history of jaundice ( $p < 0.00001$ ), and the third characteristic with a significant influence ( $p < 0.006$ ) was the duration of homosexual activity, which was independent of age. With each year of homosexual activity the probability of having antibodies to hepatitis A virus increased with 1.15% (fig 2). Other characteristics were not found to be significantly correlated with the prevalence of antibodies to hepatitis A virus.

TABLE II—Characteristics correlated with seropositivity for hepatitis A virus in homosexual men: evaluation by stepwise logistic regression

Characteristic	Coefficient ( $\beta$ )	Standard error (SE)	$\frac{\beta}{SE}$	p value
Age	0.113	0.02	5.89	$< 0.00001$
History of jaundice	1.485	0.22	6.89	$< 0.00001$
Duration of homosexual activity	0.046	0.02	2.52	$< 0.02$
Constant	-3.212	0.54	-5.97	$< 0.00001$

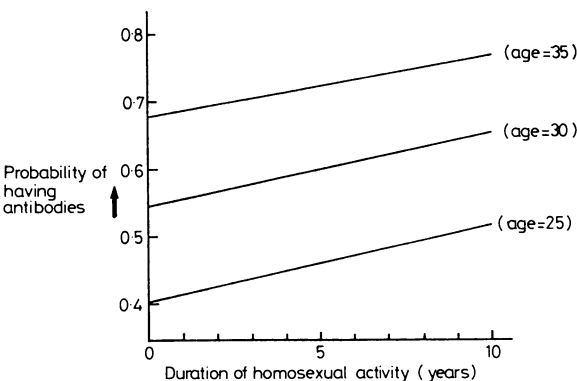


FIG 2—Correlation between probability of having antibodies to hepatitis A virus and duration of homosexual activity among 689 homosexual men: evaluation by stepwise logistic regression. Age was kept constant at 25, 30, and 35 years, and history of jaundice set to 0 (no history).

ASSOCIATION BETWEEN THE INCIDENCE OF HEPATITIS A AND POTENTIAL RISK FACTORS

Evaluation by regression with incomplete survival data showed that two characteristics of the susceptible homosexual men were significantly correlated with the acquisition of hepatitis A during the follow up period (table III). A positive history of syphilis at the beginning of the study increased the probability of contracting hepatitis A by a factor

of 2.25. For the number of different sexual partners in the preceding six months, the relative risk of contracting a hepatitis A virus infection multiplied by a factor of 1.25 for each category, as shown in fig 3. For those men with more than 100 different sexual partners the risk was 6.0 times higher than for those men with one steady partner.

TABLE III—Characteristics correlated with the risk of contracting hepatitis A among 399 susceptible homosexual men: evaluation by regression with incomplete survival data

Characteristic	Coefficient ( $\beta$ )	Standard error (SE)	$\beta$ SE	p value	$e^{\beta}$
No of different sexual partners in preceding six months	0.22	0.08	2.61	<0.01	1.25
History of syphilis	0.81	0.39	2.10	<0.04	2.25

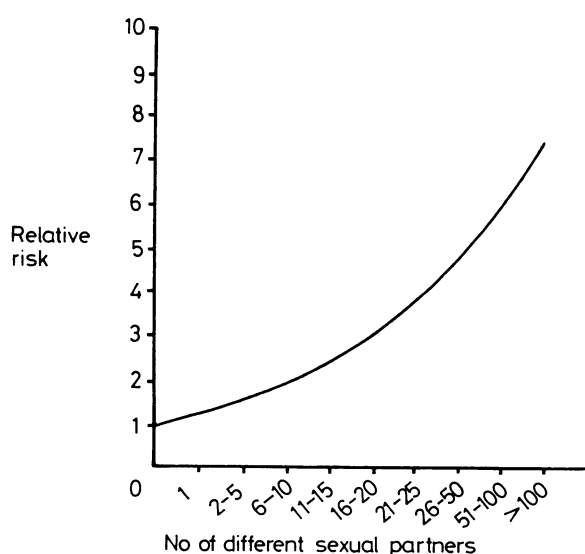


FIG 3—Association of number of different sexual partners in preceding six months and relative risk of contracting hepatitis A among 399 susceptible homosexual men.

## Discussion

Of the 689 homosexual men 42% were found to have antibodies to hepatitis A virus. It should be noted that we probably selected men with a relatively low prevalence of antibodies to hepatitis A virus as the participants were negative for hepatitis B markers. Hepatitis B is sexually transmitted among homosexual men and the prevalence of hepatitis B is related to the duration of homosexual activity and the number of different sexual partners.<sup>12, 13</sup> We therefore selected men with a relatively short duration of homosexuality, a relatively low number of different sexual partners, or both, which influenced the prevalence of antibodies to hepatitis A virus. Among the 399 susceptible homosexual men 35 cases of hepatitis A were detected, and the curve of the attack rate climbed steadily, which indicates that the cases were not clustered in time and occurred throughout the follow up.

For comparison we studied a group of 50 heterosexual men who had participated in an immunogenicity study with heat inactivated hepatitis B vaccine. In this group, who were all negative for hepatitis B markers and had a mean age of 29.8 years (SD 5.3), a significantly lower prevalence of antibodies to hepatitis A virus (16%) was found ( $\chi^2=14.3$ ,  $p<0.001$ ). The 42 susceptible heterosexual men were serologically followed up for a mean period of 6.0 months (SD 1.7), and no cases of hepatitis A were detected.

A strong relation was found between the duration of homosexual activity and the prevalence of antibodies to hepatitis A virus, and this relation was independent of age. The probability

of having antibodies to hepatitis A virus increased by 1.15% with each year of homosexual activity. The number of different sexual partners in the preceding six months was not correlated with seropositivity for antibodies to hepatitis A virus. This may indicate that individual sexual habits do change over time and that the number of lifetime sexual partners cannot be inferred from the number of different partners during a relatively short period. The strong relation found between age and presence of antibodies to hepatitis A virus is not surprising, as there is good evidence that men in the older age groups have had a much higher risk of exposure to hepatitis A virus during childhood than younger men.<sup>1, 2</sup> The correlation found in this study between the number of different sexual partners in the preceding six months and the incidence of hepatitis A also indicates that hepatitis A virus infections are sexually transmitted among susceptible homosexual men. The other characteristic related to the attack rate of hepatitis A virus was a history of syphilis. It seems likely that the number of different sexual partners is a common risk factor for both syphilis—a well known sexually transmitted disease among homosexual men<sup>14</sup>—and hepatitis A.

From the study of Corey and Holmes it appears that the transmission of hepatitis A among homosexual men occurs by direct oroanal contact.<sup>6</sup> We asked a subgroup of 82 of our participants—the subgroup can be considered representative for the whole group—how many of them had oroanal contact, and 62 (76%) admitted to this sexual practice.

It can be concluded from our findings that hepatitis A is a sexually transmitted disease among promiscuous homosexual men in those countries where most young men do not have antibodies to hepatitis A virus because of a low rate of exposure to hepatitis A virus during childhood.

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