

## Lack of evidence for increased risk of hepatitis A infection in homosexual men

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### SUMMARY

In 1997, prevalence of and risk factors for hepatitis A virus (HAV) infection were evaluated in 146 homosexual and 286 heterosexual men attending a Sexually Transmitted Disease (STD) Clinic in Rome, Italy. Total HAV antibody (anti-HAV) was detected in 60·3% of homosexuals and 62·2% of heterosexuals. After adjustment for the confounding effects of age, years of schooling, number of sexual partners, use of condoms, and history of STD, homosexuals were not found to be at increased risk of previous HAV exposure than heterosexuals (OR 1·1; 95% CI 0·7–1·9). Independent predictors of the likelihood of anti-HAV seropositivity among homosexuals and heterosexuals were: age older than 35 years and positive syphilis serology which is likely a proxy of lifestyles that increase the risk of faecal–oral infections.

These findings do not support a higher risk in homosexual men but could suggest a role for the vaccination of susceptible patients attending STD clinics.

### INTRODUCTION

Hepatitis A virus (HAV) infection is considered to be a risk for homosexual men [1–3]. Several outbreaks of HAV have been reported among homosexuals [4–7]. Because the virus is transmitted by the oral–faecal route, it may be transmitted by oral–anal contact [1].

However, some studies have shown that the prevalence of antibodies to HAV (anti-HAV) among homosexual men is similar to that found in heterosexual men [8] and in the general population [9, 10].

Safe and effective vaccines for preventing HAV infection have recently been licensed for use in Italy, where currently no data are available to support routine immunization of homosexual men.

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We report here the results of a case-control study comparing anti-HAV prevalence in homosexual and heterosexual men attending a Sexually Transmitted Disease (STD) clinic in Rome, Italy. The determinants of HAV infection in both groups have also been evaluated.

### PATIENTS AND METHODS

The study population was composed of male patients seen at the STD outpatient clinic of the 'S. Maria e S. Gallicano' Hospital in Rome, Italy, from January to December 1997. All male patients attending the clinic were recruited on a random day each week. After informed consent, all patients provided a blood sample and were administered an anonymous questionnaire by a trained study clinician to collect information on age, education, sexual preference, number of sexual partners, use of condoms in the

Table 1. General characteristics of homosexual and heterosexual subjects attending a clinic for sexually transmitted diseases. Rome, Italy, 1997

	Homosexuals (n = 146)		Heterosexuals (n = 286)		$\chi^2$ P value
	n	%	n	%	
Age (years)					
≤ 35	89	61.4	159	55.6	NS
> 35	56	38.6	127	44.4	
Years of schooling					
> 8	42	29.0	160	55.9	< 0.01
≤ 8	103	71.0	126	44.1	
Number of sexual partners in the previous year					
0-4	95	66.0	246	86.0	< 0.01
> 4	49	34.0	40	14.0	
Use of condoms					
Yes	105	72.4	89	31.1	< 0.01
No	40	27.6	197	68.9	
Diagnosis					
Normal physical examination	91	63.6	117	44.0	< 0.01
Non-ulcerative STD*	29	20.3	61	22.9	
Genital herpes (current)	0	0.0	59	22.2	
Genital herpes (previous)	1	0.7	7	2.6	
Primary syphilis	2	1.4	0	0.0	
Secondary syphilis	0	0.0	2	0.8	
Positive syphilis serology	20	14.0	20	7.5	

\* Non-ulcerative STD included gonorrhoea, genital warts, non-gonococcal, urethritis (NGU) due to *Chlamydia trachomatis* or *Ureaplasma urealyticum*, vaginal or cervical infection due to *Trichomonas vaginalis*, *Candida albicans* or chlamydia, scabies, and *Phthirus pubis* infestation.

previous year, history of intravenous drug use, blood transfusions, and STDs. Intravenous drug users, blood transfused, and anti-HIV positive subjects were excluded from the study.

Antibodies against hepatitis A (anti-HAV) were determined using a commercially available assay (Abbott Laboratories, North Chicago, IL).

The  $\chi^2$  test was used to evaluate differences between proportions where appropriate. A *P* value < 0.05 was considered to be significant. The influence of potential confounding factors on HAV seroprevalence in the two groups of subjects was controlled by a multiple logistic regression analysis [11]. To identify independent predictors of anti-HAV seropositivity among homosexual and heterosexual men, two separate logistic regression models were run. In both models anti-HAV was the outcome variable; age, years of schooling, number of sexual partners, use of condoms, and history of STDs were the independent variables. For each variable the reference category was the most favourable level of exposure (youngest age, highest

number of education years, lowest number of sexual partners, use of condoms, negative history of STDs).

## RESULTS

A total of 432 subjects were enrolled in the study enclosing 286 heterosexuals and 146 homosexuals. The general characteristics of the study population by sexual orientation are shown in Table 1. The age distribution was similar in the two groups. A higher proportion of homosexuals reported 13 or less years of schooling (71 vs. 44.1%), four or more sexual partners in the year before the clinic visit (34.0 vs. 14.0%), use of condoms (72.4 vs. 31.1%) and a normal physical exam (63.6 vs. 44.0%), as compared to heterosexuals.

The crude anti-HAV prevalence was 60.3% (88/146) among homosexuals and 62.2% (178/286) among heterosexuals (OR 0.9, 95% CI 0.6-1.4). After adjustment for the confounding effect of age, years of schooling, number of sexual partners, use of condoms,

Table 2. *Anti-HAV prevalence among homosexuals and heterosexuals attending a clinic for sexually transmitted diseases. Rome, Italy, 1997*

	Number positive/ Number tested	%	Crude		Adjusted	
			OR	95% CI	OR*	95% CI
Heterosexuals	178/286	62.2	1		1	
Homosexuals	88/146	60.3	0.9	0.6–1.4	1.1	0.7–1.9

\* Adjusted for age, years of schooling, number of sexual partners, use of condoms, and history of STD.

Table 3. *Variables associated with anti-HAV positivity among homosexuals. Crude and adjusted odds ratio (OR) derived by multiple logistic regression analysis. Rome, Italy, 1997*

Variable	Number positive/ number tested	%	Crude OR	95% CI	Adjusted OR*	95% CI
Age (years)						
≤ 35	38/89	42.7	1		1	
> 35	49/56	87.5	9.4	3.6–25.6	8.2	3.0–22.2
Years of schooling						
> 13	24/42	57.1	1		1	
≤ 13	63/103	61.2	1.2	0.5–2.6	0.9	0.4–2.2
Number of sexual partners						
0–4	50/95	52.6	1		1	
> 4	36/49	73.5	2.5	1.1–5.7	2.4	1.0–5.9
Use of condoms						
Yes	63/105	60.0	1		1	
No	24/40	60.0	1.0	0.5–2.3	1.4	0.6–3.4
Diagnosis†						
Normal physical examination	46/91	50.5	1		1	
Non-ulcerative STD	19/29	65.5	1.9	0.8–4.4	1.5	0.5–4.0
Positive syphilis serology	19/22	86.4	6.2	1.7–22.7	2.0	0.5–8.4

\* Each variable is adjusted for all the other variables in the table.

† Genital herpes (current or previous) was not considered in this table, because there was only one subject in this category.

and history of sexually transmitted disease, homosexuals were not found to be more at increased risk of previous HAV exposure than heterosexuals (OR 1.1; 95% CI 0.7–1.9) (Table 2).

### Homosexual men

The relative odds of HAV infection were highest for age > 35 years (OR 9.4, 95% CI 3.6–25.6), and positive syphilis serology (OR 6.2, 95% CI 1.7–22.7) by univariate analysis. A positive association was also found between HAV-positivity and reporting four or more sexual partners in the previous year (Table 3). After adjusting for the confounding effect of the other variables by logistic regression analysis, independent predictors of anti-HAV seropositivity among homosexuals were: age older than 35 years (OR 9.1, 95% CI 3.3–25.2) and reporting four or more sexual

partners in the previous year (OR 2.5, 95% CI 1.0–6.0) (Table 3). Subjects reporting positive syphilis serology were at increased risk of HAV infection (OR 2.0, 95% CI 0.5–8.4), although the estimated OR were not statistically significant.

### Heterosexual men

By univariate analysis, anti-HAV positive heterosexual men were older than 35 years (OR 5.2, 95% CI 2.9–9.4), had a lower education level, reported more frequently the use of condoms and were more likely to have a diagnosis of genital herpes (OR 9.5, 95% CI 2.3–42.8) or a positive syphilis serology (OR 2.7, 95% CI 1.4–5.3) (Table 4). After controlling for the confounding effect of the other variables, a significant association remained between HAV infection and age older than 35 years (OR 4.5, 95% CI 2.4–8.2), 8 or less

Table 4. Variables associated with anti-HAV positivity among heterosexuals. Crude and adjusted odds ratio (OR) derived by multiple logistic regression analysis. Rome, Italy, 1997

Variable	Number positive/ number tested	%	Crude OR	95% CI	Adjusted OR*	95% CI
Age (years)						
≤ 35	74/159	46.5	1		1	
> 35	104/127	81.9	5.2	2.9–9.4	4.7	2.5–8.7
Years of schooling						
> 8	84/160	52.5	1		1	
≤ 8	94/126	74.6	2.6	1.6–4.6	2.0	1.1–3.7
Number of sexual partners						
0–4	158/246	64.2	1		1	
> 4	20/40	50.0	0.6	0.3–1.2	0.7	0.3–1.7
Use of condoms						
Yes	44/89	49.4	1		1	
No	134/197	68.0	2.2	1.3–3.8	1.7	0.9–3.3
Diagnosis						
Normal physical examination	60/117	51.3	1		1	
Non-ulcerative STD	37/61	60.7	1.5	0.8–2.8	1.2	0.6–2.4
Genital herpes current/previous	49/66	74.2	9.5	2.3–42.8	6.1	1.3–29.5
Positive syphilis serology	20/22	90.9	2.7	1.4–5.3	2.1	1.0–4.4

\* Each variable is adjusted for all the other variables in the table.

years of schooling (OR 2.2, 95% CI 1.2–4.0), current or previous genital herpes infection (OR 6.1, 95% CI 1.2–4.7), and a positive syphilis serology (OR 2.1, 95% CI 1.0–4.4) (Table 4).

## DISCUSSION

Prospective studies carried out a decade ago in countries of low endemicity of HAV infection have shown that homosexuals are at increased risk of HAV infection. In fact, the incidence rates per year of HAV infection among homosexual men were 30% and 14% in Seattle and Amsterdam, respectively [1, 2]. Further lines of evidence come from studies on outbreaks of hepatitis A among homosexuals [4, 5, 7]. Sexual oral–anal contact became increasingly more common because it was thought to be safer with respect to HIV transmission. This practice has been suggested as the most plausible explanation for the increased risk of HAV infection in these groups [1, 3, 5, 12].

The objective of our study was to investigate if the findings of the above-mentioned studies could be applied to homosexuals from other populations. For this purpose, we excluded subjects acknowledging use

of intravenous drugs, for which an increased risk of HAV infection is recognized.

Our data show that homosexual and heterosexual men attending a STD clinic in Rome, Italy, had similar anti-HAV prevalence rates, suggesting that, in areas where HAV is of intermediate endemicity, homosexuality is not a risk factor for anti-HAV infection. In our population, 46% of heterosexuals and 43% of homosexuals were already anti-HAV positive by age 35 (Tables 3, 4). A high proportion of immune subjects and different sexual behaviour of Italian male homosexuals may both account for the discrepancy between our results and those of other studies. Unfortunately, information on oral–anal sexual contacts was not available for the subjects included in this study.

However, our findings are in agreement with those previously reported in a Belgian [9] and a Spanish study [8]. In a recent US study, the HAV prevalence among homosexuals was similar to the age-adjusted prevalence estimated for the general United States population [12].

Interestingly, in our study, the highest prevalence rates of anti-HAV were found in heterosexual (91%) and homosexual men (86%) who had a positive

syphilis serology. This association remained also after adjusting for the confounding effect of age.

An association between hepatitis A and B and syphilis among homosexual men has been reported in a Danish study [13], and a relation also has been observed between syphilis and HBV, HCV, and HIV among heterosexual STD patients [14]. A positive syphilis serology is likely a proxy of lifestyles that increase the risk of both parenteral and oral-faecal infections.

In conclusion, more studies need to be performed on the risk of HAV infection for homosexuals as compared to that of the heterosexual population. The positive association of anti-HAV positivity with syphilis serology in STD patients, if confirmed by further studies, suggests consideration of vaccination against hepatitis A for susceptible STD patients.

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