

On the Role of Sexual Behavior in the Spread of Hepatitis B Infection

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There is a significant excess of serologic evidence of hepatitis type B infection in two high-promiscuity populations: patients with venereal diseases and their unrelated sexual contacts (15% to 18%) and male, but not female, homosexuals (37% to 51%). Spouses of asymptomatic chronic carriers of antigen had a higher prevalence (26% to 28%) than spouses of noncarriers (10% to 11%); however, the prevalence in the former is relatively low when compared with rates seen in other relatives of carriers. Persons who had a higher-than-average probability of exposure to potentially infective partners or whose patterns of sexual behavior made such exposure more likely (large numbers of sexual partners, long duration of homosexuality, involvement in predominantly anal intercourse) were found to have serologic evidence of hepatitis B more frequently than those with other patterns of sexual behavior. This study showed a strong association between serologic evidence of type B hepatitis and patterns of sexual behavior. However, whether or not transmission of hepatitis type B virus occurs through vaginal intercourse could not be ascertained.

TYPE B HEPATITIS VIRUS, it is now generally acknowledged, can be transmitted by nonpercutaneous routes (1-5). However, the exact mechanisms of virus transmission from person to person by means other than infected blood remain obscure.

Recent studies report that the hepatitis B virus can be transmitted by sexual contact. The hepatitis B surface antigen (HB_sAg) was reported to be present in menstrual blood (6), in semen (7, 8), and in vaginal secretions (9) of chronic antigen carriers. Numerous cases of type B hepatitis among sexual partners of symptomatic or asymptomatic carriers of HB_sAg have been described (10, 11) and an apparent excess prevalence of antigen or antibody to hepatitis B surface antigen (anti-HB_s) in heterosexual or homosexual patients with venereal diseases has been reported (12-14).

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On the other hand, two studies (15, 16) carried among prostitutes did not show any significant excess: HB_sAg, while in only one of these studies prostitutes were anti-HB_s positive more frequently than control women. Similarly, our own pilot study among 119 spouses of blood donors who were chronic carriers of HB_sAg provided little evidence of the significance of sexual transmission between married couples: spouses were found to have a high prevalence of anti-HB_s, while the presence of HB_sAg was documented much less frequently among spouses than among other members of the family (17).

Due to these inconclusive data, a retrospective study was carried out to ascertain the role of sexual behavior in testing the validity of the sexual-transmission hypothesis. Several large samples of people with varying patterns of sexual behavior were surveyed for serologic evidence of past or present hepatitis type B infection: spouses of antigen-carriers and noncarriers, patients with gonorrhea or syphilis and their sexual contacts, and homosexuals. Unfortunately, it was not possible to select a meaningful sample of prostitutes.

Our basic assumption was that if sexual transmission does in fact occur, then [1] the prevalence of serologic evidence of hepatitis B infection should vary significantly between these groups of people known or supposed to have various patterns of sexual behavior; [2] within each group the prevalence of hepatitis B events should be correlated with certain features relevant to the intensity and diversity of sexual behavior; and [3] spouses of carriers should be at higher risk than spouses of noncarriers or other comparable population groups.

We further speculated that because sexual behavior, particularly sexual outlets and number of sexual partners, depends on marital status (18), then it is reasonable to expect an excess of singles among antigen carriers as compared with noncarriers. Therefore, the marital status of a large number of blood donors, both antigen carriers and noncarriers, was analyzed.

Methods

POPULATIONS STUDIES

Sample Number 1: This study consisted of 238 spouses of white and black volunteer blood donors from New York City during routine screening, were found to be HB_sAg negative



Table 1. Comparison of the Four Study Samples and Controls According to Certain Sociodemographic and Epidemiologic Characteristics

Characteristics	Spouses of Noncarriers (n = 238)	Spouses of Carriers (n = 280)	Patients of Venereal Disease Clinics (n = 597)	Homosexuals (n = 674)	Controls (n = 700)
Men	17.5	13.2	72.4	92.9	64.2
Non-whites	10.5	20.0	59.6	13.9	8.6
≥40 years old	47.4	38.5	9.9	17.7	31.1
Foreign born	18.0	12.6	NA*	9.1	13.8
≥9 years of education	95.6	94.7	96.1	97.6	98.5
Residence in New York City	44.3	50.6	NA	98.1	45.4
≥10 sex partners in last 6 months	NA	NA	11.8	50.3	NA
History					
Viral hepatitis or jaundice	1.0	2.4	8.0	23.1	2.6
Venereal disease	4.2	2.8	45.6	59.5	3.7
Blood transfusion	3.1	2.9	2.8	2.9	3.3
Drug addiction	0	2.0	10.4	5.1	0.8
Heavy drinking	NA	NA	4.0	5.0	3.0

* NA = data not available.

of the index-donors were anti-HB_s positive). Because of an unusually high prevalence of HB_sAg and anti-HB_s seen among donors of oriental origin (19), they were excluded from this and other study samples. A comparison of the families who consented to participate with those who refused did not show significant differences with respect to a number of sociodemographic characteristics. Due to the fact that the majority of blood donors are white men, most of the spouses tested were white women.

Sample Number 2: This study consisted of 280 spouses (87% were wives) of white and black donors who were persistent carriers of HB_sAg (repeated detection of antigen in at least two specimens drawn 6 months apart). Due to the relatively high frequency of HB_sAg detection among blacks of this area (19), the proportion of blacks in this sample was larger than in Sample Number 1 (20% versus 10.5%).

The methods of selection and survey of Samples Number 1 and 2 have been described in more detail elsewhere (17).

Sample Number 3: This study consisted of 597 heterosexual patients attending two venereal disease clinics in New York City; 272 of them were either under treatment for syphilis or gonorrhea or had had treatment in the past, while the remaining 325, mostly unrelated sexual contacts of venereal disease patients, attended the clinics for screening and did not have a history of known venereal infection. The sexual identity and sexual behavior patterns of these 597 subjects were established during a personal, confidential interview; all were exclusively or predominantly heterosexual.

Sample Number 4: This study consisted of 674 homosexuals solicited to participate in this survey through two recognized homosexual organizations and two health clinics. Only persons who declared themselves as exclusively or predominantly homosexual were included in this sample. Ninety-three percent of the entire sample were men. No essential differences with respect to age, ethnicity, duration of homosexuality, and history of venereal disease between the surveyed homosexuals from different organizations and institutions were seen.

The frequencies of hepatitis B infections in these four study samples were compared with the results of screening by the same laboratory assays of a random, control sample of 10 000 healthy adults from the same area (volunteer blood donors).

Table 1 shows that, in addition to sex and ethnicity, the four samples surveyed differed from each other and from the control population in certain other characteristics known or supposed to be independently associated with the likelihood of exposure to hepatitis B infection. Hepatitis B frequency rates in the study samples were, therefore, standardized in reference to the controls taken as a normal standard (20).

Marital status was recorded among 590 male donors found to be HB_sAg positive during routine screening carried out in 1971-1973 and in a randomly selected sample of 663 male donors who donated during the same time period and who were

found to be antigen negative. Both groups of donors have been surveyed by means of a comprehensive self-administered questionnaire and were found to be comparable with each other in most of the analyzed variables, except ethnicity.

QUESTIONNAIRE SURVEY

All participating persons from the four study samples, as well as a 7% systematic subsample of the 10 000 controls, were surveyed for pertinent sociodemographic and epidemiologic information by means of a self-administered questionnaire. The questionnaire used in the survey of Samples Number 3 and 4 contained, in addition, a large number of questions dealing with sexual behavior. The rationale and objectives of the survey were explained to all participants, and assurances of strict confidentiality of information obtained were given.

The response-rate to the questionnaire survey among donors and their spouses was 72% and among the high promiscuity groups up to 85%.

LABORATORY METHODS

Screening for HB_sAg was done by radioimmune assay (21) and reverse passive hemagglutination (22); positive specimens were confirmed by neutralization methods. Screening for anti-HB_s was done by passive hemagglutination (23). Antigenic determinants *a*, *d*, and *y* were assayed by hemagglutination inhibition method (24). Screening for antibody against the core antigen (anti-HB_c) in a selected group of 302 specimens negative for surface antigen and antibody was done by complement fixation (25). Serologic tests were done under code and all positive results were confirmed by retesting. Serum glutamic pyruvic transaminase (SGPT) determinations were done by the spectrophotometric method. The chi-square and Mantel-Haenszel tests (20) were used to determine statistical significance between frequency rates.

Results

SEROLOGIC EVIDENCE OF HEPATITIS TYPE B IN THE STUDY SAMPLES

The overall rates of HB_sAg, anti-HB_s, and anti-HB_c detection in the four samples and controls are presented in Table 2. As can be seen, the frequency of hepatitis B detection in the group of spouses of noncarriers (Sample Number 1) was very close to that observed in the controls; prevalence rates in the donors, therefore, were used to compute relative risks (ratios of prevalence in a given sample to the prevalence found in controls).

Among the spouses of HB_sAg carriers, only two (0.7%) were found to be antigen positive; both were wives, one

Table 2. Risk

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Table 2. Results of Serologic Testing for Hepatitis Type B Infection in the Surveyed Populations

Characteristics	Spouses of Noncarriers	Spouses of Carriers	Patients of Venereal Disease Clinics	Homosexuals	Controls
Controls (n = 700)					
64.2					
8.6					
31.1					
13.8					
98.5					
45.4					
NA					
2.6					
3.7					
3.3					
0.8					
3.0					
Prevalence					
HB _s Ag	0.4	0.7	1.3	4.3	0.3
Anti-HB _s (≥1:8)	10.5	26.4	16.6	43.8	7.0
HB _s Ag or anti-HB _s					
Crude	10.9	27.1	17.9	48.1	7.3
Standardized for sex*	11.3	28.2	17.6	37.3	...
Standardized for age*	10.8	28.3	18.1	51.1	...
Standardized for ethnicity*	11.2	26.7	14.9	47.4	...
Anti-HB _s (≥1:8)†	ND‡	5.1	6.0	12.4	0
Relative risks§					
HB _s Ag	1.3	2.3	4.1	13.0	1.0
Anti-HB _s	1.5	3.7	2.4	6.3	1.0
HB _s Ag or anti-HB _s	1.5	3.7	2.4	6.6	1.0

* By direct method in relation to controls.
 † In negatives for surface antigen and antibody.
 ‡ For definition see text.
 § ND = not done.

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white and the other black. However, anti-HB_s was detectable in 26.4% of all tested spouses of carriers (25.4% of white and 33.9% of blacks), or 2 to 3 times as frequently as among spouses of noncarriers or controls. An excess prevalence of HB_sAg (1.3%) was seen in the sample of heterosexuals attending venereal disease clinics; however, the rate of all hepatitis B events (HB_sAg or anti-HB_s) in this sample was lower than in the spouses of HB_sAg carriers (17.9% versus 27.1%). Twenty-four percent of patients with venereal disease diagnoses were antigen or antibody positive, as compared with 16.6% of their unrelated sexual contacts. An unusually high prevalence, for this area, was seen in the sample of homosexuals: 4.3% were antigen positive (13 times more frequently than controls), and 43.8% were antibody positive (4 to 5 times more frequently than controls). The difference in cumulative prevalence rates between the four samples were essentially unchanged by adjustment for age, sex, or ethnicity. The only exception occurred for the group of homosexuals, where standardization for sex brought the adjusted rate slightly closer to rates for the other three groups. The frequency of antibody to core antigen in the spouses of carriers and the high promiscuity groups was also significantly higher than that observed in the controls. In the great majority of persons with detectable antigen, surface or core antibody-apparent parenteral exposure (blood transfusions or shared needles) could be excluded. The relative distribution of *ad* and *ay* subspecificities of the HB_sAg were similar to that seen in the general population of this area (19).

The homosexuals were found to have significantly higher titers of hemagglutinating anti-HB_s (log₁₀ geometric mean $\pm$ SD of titer = 2.56 ± 0.87) when compared with antibody-positives among the three other samples (1.91 ± 0.85). Antibody levels in the homosexuals were also much higher than those ordinarily seen in other, nontropical populations (26).

PREVALENCE ACCORDING TO SEX, AGE, AND ETHNICITY

As can be seen from data presented in Table 3, differences in prevalence of antigen or antibody by sex, age, and

ethnicity are small or statistically insignificant in the samples of spouses or heterosexuals from venereal disease clinics. In contrast, in the homosexual population there seems to exist a strong correlation with all three characteristics. Although no antigen and very little antibody was detected among female homosexuals, as many as 4.6% of all tested male homosexuals were antigen positive and 46.5% were antibody positive. Both antigen and antibody were also detected significantly more frequently in homosexuals 40 or more years old than in those under 40 years of age; this age-dependence seems to be related not to the age-factor as such but to duration of homosexuality. Certain differences in relation to ethnic background also seem to exist.

OTHER RISK FACTORS IN THE HOMOSEXUAL POPULATION

Due to the small number of female homosexuals surveyed and the negligible prevalence of hepatitis B events among them, further analysis will be confined to men. From more than 20 variables analyzed, Table 4 presents only those that seem to be associated with the prevalence of antigen, antibody, or both.

As many as 23% of the surveyed homosexuals gave a past history of viral hepatitis; the great majority of these events were recognized by a physician. Among those with such a history, serologic evidence of hepatitis B was detected in 65%; the latter frequency is significantly higher than that in homosexuals without a history of viral hepatitis ($P < 0.001$).

Relatively few of the homosexuals admitted to shared needle injections of narcotics (5.1% as opposed to 10.4% among patients attending venereal disease clinics). In those homosexuals with a history of drug-addiction, antigen was detected with nearly the same frequency as in those without such a history; however, the cumulative prevalence of both antigen and antibody was higher in the former than in the latter.

A well-known feature of homosexual behavior, primarily in men, is an extraordinarily high degree of sexual promiscuity (18). In the sample studied, nearly 54% reported 10 or more (up to 60) sexual partners during a

Table 3. Frequencies of Hepatitis Type B Detection in the Study Samples in Relation to Sex, Age, and Ethnic Background

Variable	HB _s Ag			HB _s Ag or Anti-HB _s			
	Spouses of Carriers	Heterosexuals	Homosexuals	Spouses of Noncarriers	Spouses of Carriers	Heterosexuals	Homosexuals
				%			
Men	0	1.4	4.6	10.0	28.9	20.4	51.1*
Women	0.8	1.2	0	10.0	26.8	11.5	6.3
<40 years old	1.2	1.1	4.4	10.0	26.2	16.8	47.7
≥40 years old	0	3.4	5.7	10.0	28.7	28.8	65.1*
White, non-Jews	0.5	0.7	4.6	9.3	25.8	13.6	46.4
Jews	0	0	3.0	11.4	20.0	14.1	63.0*
Blacks	1.8	2.0	8.3	0	33.9	19.0	53.3
Hispanic	†	1.4	5.8	33.3	†	25.0	63.5*

* Statistically significantly higher than in other comparable group(s); ($P < 0.01$).

† Included into the three other ethnic groups.

6-month period before this survey. When this group was compared with homosexuals reporting less than 10 partners during the same period, no differences with respect to antigenemia were seen; however, antibody was detected with a high excess (60.5% versus 30.9%).

When surveyed for the most frequently or exclusively used type of sexual method, 42% reported oral-genital, 26% anal-genital, and the remaining 32% equal use of both of the above. Among those reporting oral-genital methods, 2.3% were antigen positive and 39% were antibody positive; in the mixed-method group, 4.7% and 56%, respectively; and in the group reporting predominantly or exclusively rectal intercourse, 7.5% and 51%, respectively. These differences are statistically highly significant.

The cumulative prevalence of antigen and antibody (but not that of antigen only) also seems to depend on the duration of homosexuality. In homosexuals 30 or less years old, 33% of those with a duration of homosexuality of less than 6 years were hepatitis B positive, in contrast to a positivity rate of 50% to 58% among those with a longer duration; in the age group of 30 to 49 years old, these rates were 29% and 58% to 66%, respectively. The aforementioned dependence of prevalence on age at screening was found to be secondary to the duration of homosexuality. Similarly, persons who reported that they had been involved in homosexual practices beginning in childhood (11 years or younger) were found to be hepa-

titis B positive more frequently than those with a beginning of homosexuality at an older age; this association was also secondary to duration of homosexual life.

As many as 63% of all surveyed homosexuals gave a past or present history of gonorrhea, syphilis, or both. Similarly high frequencies of venereal infections in this population were reported by other workers (27, 28). Cumulative prevalences of antigen and antibody were 31.7% among persons without a history of venereal disease, 55.9% among those with a history of gonorrhea, 66.2% among those with syphilis, and as much as 80.3% among those with both syphilis and gonorrhea (chi-square = 68.621; $P < 0.001$). These differences, however, do not seem to be related to venereal disease as such, but to various characteristics that distinguish those persons with venereal disease from those without it. Persons who gave a history of venereal disease also reported a greater number of sexual partners within the preceding 6 months than those without such a history. They had practiced homosexuality for a longer period of time, they reported genital sores, abrasions, and similar lesions more frequently, and they had been involved more frequently in rectal intercourse. It would thus seem that the same factors that increased the risk of venereal disease also enhanced the likelihood of acquiring hepatitis B. In other words, association between hepatitis B and venereal disease does not seem to be a causal one.

An unusually high proportion of antigen-positive homosexuals was found to have abnormally elevated serum glutamic pyruvic transaminase (SGPT) levels; 62% of all carriers had levels higher than 40 Karmen units, and 48% had values higher than 60 Karmen units. In antigen positives from the other three samples, the frequency of SGPT abnormalities was similar to that ordinarily seen in asymptomatic carriers, that is, 20% to 25% (29).

UNMARRIED VERSUS MARRIED

Table 5 presents the proportions of unmarried men (single, divorced, separated, and widowed) of different ages among donors who were carriers of HB_sAg in comparison with donors who were noncarriers.

An excess of unmarried men among HB_sAg carriers is seen in all age groups. The observed difference in proportions of unmarried men between carriers and non-

Table 4. Relation Between Serologic Evidence of Hepatitis Type B and Certain Risk Factors in 626 Male Homosexuals

Risk Factor	Persons with Factor in Sample	HB _s Ag Positive	HB _s Ag or Anti-HB _s Positive
	no. (%)		%
Past viral hepatitis	144 (23.1)	7.0	65.0*
Drug addiction	32 (5.1)	6.3	68.8
≥10 sex partners last 6 months	338 (53.6)	4.8	60.5*
Predominantly anal intercourse†	159 (26.5)	7.5*	58.5*
≥10 years of homosexuality	233 (46.0)	3.9	64.0*
Present or past venereal disease	396 (63.3)	6.1*	62.1*

* Difference in prevalence between those with the factor and those without; statistically significant, ($P < 0.01$).

† Versus predominantly oral.

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Discussion

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carriers is statistically significant for both whites and non-whites. No such predominance of singles was found among female carriers.

Discussion

To prove conclusively by means of a cross-sectional, retrospective study that an infection such as asymptomatic type B hepatitis can be transmitted venereally, in addition to many other potential modes of transmission, is a difficult task indeed. Firstly, discussion of sexual behavior is a long-standing taboo and, therefore, collection of pertinent information presents great difficulties; if provided, there is no easy way to test its reliability. Secondly, populations that seem to be the most suitable for the study of venereal transmission, spouses and high-promiscuity groups, differ from each other with respect to many other characteristics that are independently associated with risk of type B hepatitis (Table 1); no statistical treatment can overcome these disparities in sample composition. Finally, and most importantly, because hepatitis B virus can most probably be transmitted through virus-containing saliva, urine, and other vehicles (5), it is practically impossible to differentiate between the role of sexual intercourse and that of some inapparent parenteral route or close personal contact that occurs between sexual partners, for example, kissing, touching, and so forth. Hence, even a strong association between promiscuity and hepatitis B prevalence does not yet prove that the virus is transmitted by sexual contact, particularly by vaginal intercourse.

On the other hand, the markers of hepatitis B infection used in this study (antigen, surface and core antibody, and transaminase elevation) are known to persist only in a proportion of persons exposed; hence, failure to detect these markers in a person's serum does not exclude past exposure to a potential route of transmission.

In reviewing the results obtained in the present study, two separate aspects of the role of sexual behavior in the spread of the hepatitis B virus should be distinguished: [1] the possibility that this virus can be transmitted by vaginal intercourse per se and, therefore, that hepatitis B may be regarded as a venereal disease, at least under certain circumstances; and [2] the indirect impact of certain sexual behavior patterns on the spread of hepatitis B virus in different population groups. An infectious agent may not be directly transmitted venereally, yet certain patterns of sexual behavior may sustain or inhibit its circulation and dissemination by means of other potential routes.

As to the possibility of sexual transmission, particularly by vaginal intercourse, observations made during this study are ambiguous; they neither exclude such a possibility nor do they provide convincing evidence in support of this hypothesis. Although observations made in high promiscuity samples (Numbers 3 and 4) are compatible with the sexual transmission hypothesis, the results of screening in the sample of spouses did not provide convincing evidence supporting this hypothesis.

In our pilot study we found that 4 out of 119 (3.4%) carriers' spouses tested were HB_sAg positive and as many

Table 3. Proportions of Unmarried Among Donors—Carriers of HB_sAg and Noncarriers (Men Only)

Age	Surveyed		Unmarried	
	Carriers	Non-carriers	Carriers	Non-carriers
	no.		%	
Less than 30 years old	252	233	56.3	48.5
30-39	168	152	29.8	14.5
40-49	111	158	19.8	10.7
50 or more years old	59	120	13.6	9.2
Total	590	663	37.6*	24.6*

* $P < 0.01$ (Mantel-Haenszel test).

as 36.4% were anti-HB_s positive, exceeding several times the rate among the general population. However, due to the fact that among other relatives of the index-carriers the prevalence of antibody was found to be equally high and antigen was detectable much more frequently, we speculated that sexual transmission does not seem to be of great importance in the intrafamilial spread of type B hepatitis (17). As the number of spouses tested in this study was substantially increased and ethnic-specific prevalence rates were computed, the rate of antigen detection among spouses became smaller and differences in prevalence between spouses and other relatives became greater. Three out of five spouse-carriers detected during the entire survey were observed in a small group of Orientals tested, Chinese and Filipino, groups known to have unusually high antigen prevalence (19), while prevalence in other ethnic groups was essentially the same as in the general population: 0.4% in whites and 1.8% in blacks. In comparison, the same survey showed that prevalence of antigen among siblings of both races was 15% to 30%; among parents, 12% to 25%; and among children, 1.5% to 6% (30). These relatively low antigen rates in spouses of carriers would be difficult to explain if sexual intercourse were of great importance as a route of transmission. Antigen carriers were not detected among spouses recently screened in Canada as well (31). It is also of interest that during extensive surveys carried out in high-prevalence areas, neither Blumberg and colleagues (32) nor Ceppellini and colleagues (33) were able to find both matings antigen positive. On the other hand, the excess prevalences of antibody to the surface and core antigens among spouses would seem to be compatible with the sexual transmission hypothesis.

More reliable evidence in support of sexual transmission has been presented with respect to patients with overt, serologically confirmed type B hepatitis. Secondary cases of hepatitis B among sexual partners of patients have been reported in this country (10), in England (11-14), in Spain (34), and in other areas. Mosley (35) recently reported that up to 18% of the spouses of patients with acute hepatitis B contracted the infection, while none of their other family members did. Our own observations made in families of chronic dialysis patients with acute, mostly anicteric hepatitis B, also showed a high attack rate among spouses (26). Likewise, surveillance of over 5000 family units with an index-patient with acute hepatitis, mostly type B (which was conducted in Poland

in the 1960s), showed high attack rates of secondary cases among spouses (3). These obvious differences between asymptomatic carriers and patients with acute illness in terms of potentials for sexual transmission may be related to varying levels of infectivity. Variations in infectivity associated with clinical manifestation are a well-known feature of many communicable diseases.

Observations made in the sample of homosexuals, contrary to those in spouses, are consistent with the sexual transmission hypothesis. Homosexuals, well known to change sexual partners much more frequently than any other population group (a modal male homosexual may have 1000 or more sexual partners throughout his life time*), were found to have prevalences of HB_sAg, anti-HB_s, and anti-HB_c rarely observed in industrialized countries. In addition, a close correlation between prevalence and various sexual behavior factors was observed; the prevalence of type B hepatitis events was found to be affected by the number of sexual partners, duration of homosexuality, and the methods of sexual intercourse used. Although the size of the lesbian sample was too small to warrant conclusions, the different patterns of prevalences among male and female homosexuals are of interest. In the latter group no antigen carriers were detected, while antibody was detected with the same frequency as among heterosexual women. This low prevalence may be related to the small number of sexual partners that most lesbians have; in the homosexual sample surveyed, the mean number of partners during the preceding 6 months was 1.8 for women, as opposed to 20 for men. Such a "dose-response" effect would indicate a strong association between type B hepatitis and sexual behavior.

Another point of interest in this population is the close parallelism in the distribution of venereal diseases and hepatitis B events. Both these infections behaved in a similar way and tended to be widespread in a group of persons with a specific pattern of sexual behavior. Thus, in this population hepatitis has a number of features in common with venereal diseases.

A relation between hepatitis B and sexual behavior does seem to exist in the sample of heterosexuals from venereal disease clinics as well, although due to the small numbers in the numerators these relations did not always yield statistical significance. Promiscuity, increased exposure, and higher risk of contracting hepatitis B would also explain the excess of unmarried people among antigen carriers detected in 1971-1973 (Table 5).

It should be noted that the high prevalence of antigen and antibody in homosexuals is in part associated with a high incidence of acute and chronic hepatitis B in this population. A considerable proportion of homosexuals tested (23%) gave a past history of acute viral hepatitis; the majority of antigen carriers (up to 62%) had biochemical evidence of liver damage, while the levels of antibody in those anti-HB_s positive were unusually high. A high proportion of persons with a recent episode of acute disease or with chronic active hepatitis would also

be suggested by the excess prevalence of antibody to core antigen (10% versus 0% in normal controls and 5% to 6% in the other samples).

An unexpected finding in this study was the high prevalence of hepatitis B in homosexuals whose sexual activity included rectal intercourse, and a relatively low prevalence among those whose activity involved predominantly oral-genital intercourse; the latter had a hepatitis B prevalence comparable with heterosexuals. Because oral intercourse generally involves swallowing of semen and close contact with saliva, both found to contain antigen, one would not expect such a difference. The high prevalence in homosexuals predominantly involved in rectal intercourse may be explained by two factors: [1] damage of the mucous membrane of the rectum that frequently occurs during rectal intercourse (the surveyed persons reported proctitis as one of the most common complications); and [2] the mucosa of the rectum may be a better portal of entry for virus than the digestive tract.

In summary, this study showed a strong association between patterns of sexual behavior and the prevalence of type B hepatitis infection. This study seems to confirm that in certain populations promiscuity, intimate contact with large numbers of sexual partners, and extragenital intercourse may be responsible for a large part of clinically apparent or inapparent infections. However, whether or not type B hepatitis is really transmitted by vaginal intercourse could not be ascertained in the present survey.

Our data would suggest that avoidance of rectal intercourse by homosexuals might substantially reduce the transmission of hepatitis B among them, and, due to the high risk of gonorrhea, syphilis, and hepatitis B for homosexuals, it would seem that they should be advised to refrain from blood donations. Although no exact incidence rates of homosexuality are available, studies carried out by Kinsey, Pomeroy, and Martin (18) in the 1940s indicated that a substantial proportion of men in the United States, particularly unmarried (up to 37%), are involved in homosexual activity.

Large-scale prospective studies dealing with sexually associated type B hepatitis, both overt and asymptomatic, seem to be indicated.

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References

1. KRUGMAN S, GILES JP, HAMMOND J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
2. PRINCE AM, HARGROVE RL, SZMUNESS W, et al: Immunologic distinction between infectious and serum hepatitis. *N Engl J Med* 282:987-991, 1970

* BELL AP: Personal communication.

1. SZMUNESS W: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
2. PRINCE AM, HARGROVE RL, SZMUNESS W, et al: Immunologic distinction between infectious and serum hepatitis. *N Engl J Med* 282:987-991, 1970
3. LONDON W: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
4. VILLARE J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
5. MAZZURCO L: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
6. LINNEMANN J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
7. HEATHCOTE J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
8. DARANI J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
9. HERSHMAN J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
10. LONDON W: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
11. HEATHCOTE J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
12. HEATHCOTE J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
13. JEFFREY J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
14. FULFORD J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
15. ADAMS J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
16. PAPAY J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
17. SZMUNESS W: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
18. KINSEY J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
19. SZMUNESS W: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967
20. SNEED J: Infectious hepatitis: evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 200:365-373, 1967

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3. SZMUNESS W, PRINCE AM: Epidemiologic patterns of viral hepatitis in Eastern Europe in the light of recent findings concerning the serum hepatitis antigen. *J Infect Dis* 123:200-212, 1971
4. LONDON WT, SUTNICK AI, BLUMBERG BS: Australia antigen and acute viral hepatitis. *Ann Intern Med* 70:55-59, 1969
5. VILLARJOS VM, VISONA KA, GUTIERREZ A, et al: Role of saliva, urine and feces in the transmission of type B hepatitis. *N Engl J Med* 291:1375-1378, 1974
6. MAZZUR S: Menstrual blood as a vehicle of Australia-antigen transmission. *Lancet* 1:749, 1973
7. LINNEMANN CC, GOLDBERG S: Hepatitis-B antigen in saliva and semen (letter). *Lancet* 1:320, 1974
8. HEATHCOTE J, CAMERON CH, DANE DS: Hepatitis-B antigen in saliva and semen. *Lancet* 1:71-73, 1974
9. DALANI M, GERBER M: Hepatitis-B antigen in vaginal secretions (letter). *Lancet* 2:1008, 1974
10. HERSH T, MELNICK JL, GOYAL RK, et al: Nonparenteral transmission of viral hepatitis type B (Australia antigen-associated serum hepatitis). *N Engl J Med* 285:1363-1364, 1971
11. HEATHCOTE J, SHERLOCK S: Spread of acute type-B hepatitis in London. *Lancet* 1:1468-1470, 1973
12. HEATHCOTE J, GATBAU P, SHERLOCK S: Role of hepatitis-B antigen carriers in non-parenteral transmission of hepatitis-B virus. *Lancet* 2:370-371, 1974
13. JEFFRIES DJ, JAMES WH, JEFFERISS FJG, et al: Australia (hepatitis-associated) antigen in patients attending a venereal disease clinic. *Br Med J* 2:455-456, 1973
14. FULFORD KWM, DANE DS, CATTERALL RD, et al: Australia antigen and antibody among patients attending a clinic for sexually transmitted diseases. *Lancet* 1:1470-1473, 1973
15. ADAM E, HOLLINGER FB, MELNICK JL, et al: Type B hepatitis antigen and antibody among prostitutes and bums: a study of possible venereal transmission. *J Infect Dis* 129:317-321, 1974
16. PAPAEVANGELOU G, TICHOPoulos D, KERMASTINOU T, et al: Prevalence of hepatitis B antigen and antibody in prostitutes. *Br Med J* 2:256-258, 1974
17. SZMUNESS W, PRINCE AM, HIRSCH RL, et al: Familial clustering of hepatitis B infection. *N Engl J Med* 289:1162-1166, 1973
18. KINSEY AC, POMEROY W, MARTIN CE: *Sexual Behavior in the Human Male*. Philadelphia, W. B. Saunders Co., 1948
19. SZMUNESS W, HIRSCH RL, PRINCE AM, et al: Hepatitis B surface antigen in blood donors: further observations. *J Infect Dis* 131:111-118, 1975
20. SNEDECOR GW: *Statistical Methods*, 6th ed. Ames, Iowa, Iowa State Univ Press, 1969
21. LING CM, OVERBY LR: Prevalence of hepatitis B virus antigen revealed by direct radioimmune assay with 125 I-antibody. *J Immunol* 109:834-841, 1972
22. HOLLINGER FB, FOXMAN V, DREESMAN GR: Assay of Australia antigen and antibody employing double antibody and solid-phase radioimmunoassay techniques and comparison with the passive hemagglutination methods. *J Immunol* 197:1099-1111, 1971
23. VYAS GN, SHULMAN NR: Hemagglutination assay for antigen and antibody associated with viral hepatitis. *Science* 170:332-333, 1970
24. PRINCE AM, BROTMAN B, IKRAM H: Hemagglutination assay: sub-typing by hemagglutination inhibition, an ultra-sensitive identity test for HB antigen, in *Hepatitis and Blood Transfusion*, edited by VYAS GN, PERKINS HA, SCHMID R. New York, Grune and Stratton, 1972, pp. 147-154
25. HOOPNACLE JH, GIFFERT RJ, BARKER LF: Antibody to hepatitis-B-virus core in man. *Lancet* 2:869-873, 1973
26. SZMUNESS W, PRINCE AM, GRADY GF, et al: Hepatitis B infection: a point-prevalence study in 15 U.S. hemodialysis centers. *JAMA* 227:901-906, 1974
27. BRITISH COOPERATIVE CLINICAL GROUP: Homosexuality and venereal disease in the United Kingdom. *Br J Vener Dis* 49:329-334, 1973
28. DRUSTIN LM, MAGANA J, YANO Y, et al: An epidemiological study of sexually transmitted diseases on a university campus. *Am J Epidemiol* 100:8-19, 1974
29. SZMUNESS W, PRINCE AM, BROTMAN B, et al: Hepatitis B antigen and antibody in blood donors: an epidemiological study. *J Infect Dis* 127:17-25, 1973
30. SZMUNESS W, HARLEY EJ, PRINCE AM, et al: Intrafamilial spread of hepatitis type B. *Am J Med Sci*, in press
31. BERRIS B, WAREL DM, SINCLAIR JC, et al: Hepatitis B antigen in families of blood donors. *Ann Intern Med* 79:690-693, 1973
32. BLUMBERG BS, FRIEDLANDER JS, WOODSIDE A, et al: Hepatitis and Australia antigen: autosomal recessive inheritance of susceptibility to infections in humans. *Proc Natl Acad Sci USA* 62:1108-1115, 1969
33. CEPELLINI R, BEDARIDA G, CARONARA AO, et al: High frequency and family clustering of Au antigen in some Italian populations, in *Atti Conv Farmital. Arzene Australia et Epatite Virale*. Torino, Minerva Med, 1970
34. BOSCH J, BRUQUERA M, RODES J: Familial spread of type-B hepatitis (letter). *Lancet* 2:457, 1973
35. MOSLEY JW: The epidemiology of viral hepatitis: an overview. *Am J Med Sci*, in press