

## Hepatitis B Virus Infection Among Household Contacts of Patients with Acute HBsAg-positive Hepatitis

**Summary:** Sixty-seven household contacts of 31 index cases with acute HBsAg-positive hepatitis were investigated for *Hepatitis B virus* (HBV) markers. Follow-up findings in 50 household contacts revealed that six spouses and/or sexual partners had developed acute clinical hepatitis B. Three of these six contacts were drug addicts. A further seven contacts showed serological changes compatible with exposure to HBV, but had no signs of acute clinical hepatitis. Six of these seven contacts were spouses and/or sexual partners of their index case. Possible prophylactic or post-exposure measures only seem to be necessary in the spouses and/or sexual partners of patients with acute hepatitis B.

**Zusammenfassung:** *Hepatitis-B-Virus-Infektion bei Personen mit Familienkontakt zu Patienten mit akuter HBsAg-positiver Hepatitis.* Siebenundsechzig Personen, die in häuslichem Milieu Kontakt zu 31 Fällen mit akuter HBsAg-positiver Hepatitis hatten, wurden auf Hepatitis-B-Virus (HBV) Marker untersucht. In Verlaufskontrollen bei 50 Personen mit Kontakt zu den Hepatitis-Kranken zeigte sich, daß sechs Ehegatten und/oder Geschlechtspartner eine klinisch akute Hepatitis B entwickelt hatten. Weitere sieben Kontaktpersonen wiesen serologische Veränderungen auf, die mit einer Exposition gegenüber HBV vereinbar waren; doch hatten diese Personen keine klinisch manifeste Hepatitis. Sechs dieser sieben Kontaktpersonen waren Ehegatten und/oder Geschlechtspartner des jeweiligen Hepatitis-falles. Prophylaktische oder therapeutische Maßnahmen nach Exposition scheinen nur bei Ehegatten und/oder Geschlechtspartnern von Patienten mit akuter B-Hepatitis erforderlich zu sein.

### Introduction

The risk of contracting *Hepatitis B virus* (HBV) infection is especially high among drug addicts, male homosexuals and some groups of hospital personnel (1, 2, 3). The vast majority of patients with acute hepatitis B are known to recover and the time in which household contacts are at risk of contracting HBV infection is therefore limited. Peters et al. (4) found that all household contacts of patients with acute hepatitis B were at risk of infection,

while Koff and co-workers (5) found this risk to be mainly associated with sexual contacts. Since hyperimmune serumglobulin (HBIG) is now available for the treatment of HBV and since a vaccination against HBV infection will soon be available (6), it is of practical importance to identify those contacts in whom prophylactic or post-exposure treatment may be necessary.

In this prospective study, the sexual and non-sexual household contacts of patients with acute hepatitis B were followed clinically and serologically in order to evaluate the risk of their contracting HBV infection.

### Patients and Methods

From May 1977 to December 1978, a consecutive group of 92 patients with acute hepatitis verified from biopsies and circulating hepatitis B surface antigen (HBsAg), were asked to participate in this study. Thirty-one patients (index cases) and 67 of their household contacts agreed to participate.

**Index cases:** Twenty-two were men (including five male homosexuals), and nine were drug addicts (eight of whom were men). The mean age was 30.2 years (range 16 to 69 years).

**Household contacts:** Thirty were the spouses and/or sexual partners of the index cases, five were parents, two were siblings, six were children and 24 were other household contacts. The first sera from household contacts were collected within two days after their index case had been admitted. We had intended to conduct a serological follow-up for six months, but this was only possible as described in results.

**HBsAg and antibody (anti-HBs)** were determined by solid phase radioimmunoassays (Ausria-II and Ausab, Abbott, North Chicago, USA).

**Antibody to hepatitis B core antigen (anti-HBc)** was determined by a solid phase radioimmunoassay (Corab, Abbott, North Chicago, USA).

**HBeAg and antibody (anti-HBe)** were determined by solid phase radioimmunoassays as previously described (7).

Received: 26 February 1981

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## Results

**Index cases:** HBsAg was cleared in 25 cases while six men became HBsAg and hepatitis B e-antigen (HBeAg) carriers (defined as positive for more than six months).

**Household contacts:** The 25 index cases who cleared the HBsAg had a total of 55 household contacts (Figure 1, left), five of whom were anti-HBs-positive in the first serum sample and were therefore considered immune. There was no follow-up for nine contacts, and of the remaining 41 contacts, three were followed for a period of between one and three months, 24 for three to six months and 14 for more than six months. Of the 12 household contacts of the six index cases who became HBsAg carriers (Figure 1, left), there was no follow-up for three, two were followed for one to three months, two were followed for three to six months and five were followed for more than six months.

Of the 12 household contacts from whom no follow-up serum samples were taken, nine showed no signs of previous exposure to HBV, two were anti-HBc-positive and one had both anti-HBc and anti-HBe. In the first serum sample from the remaining 50 household contacts, 43 showed no serological signs of previous exposure to HBV, six were anti-HBc-positive and one was both anti-HBc and anti-HBe-positive.

Of the 43 household contacts who had no serological signs of previous exposure to HBV, five developed acute clinical hepatitis with circulating HBsAg and HBeAg and three developed anti-HBc during the follow-up. Of the six household contacts with anti-HBc in the first serum sample, one contracted acute clinical hepatitis and later developed anti-HBs and anti-HBe but no HBsAg or HBeAg was detected. Two contacts developed anti-HBs and anti-HBe with no signs of acute clinical hepatitis, two cleared the anti-HBc during the follow-up and one had anti-HBc which remained unchanged during the follow-up. The one patient with anti-HBc and anti-HBe in the first serum sample presented both throughout the follow-up.

The household contacts who developed acute clinical hepatitis B are shown in Figure 1, right. Time is given as the interval in weeks between the onset of symptoms in the index case and in the household contact. Table 1 shows the clinical and serological changes observed with respect to the type of contact in the 50 household contacts from whom follow-up serum samples were available. None of the six contacts who developed acute hepatitis B were homosexuals; three, however, were drug addicts and two of these had used the same syringe as their index case. In the group of contacts who only showed serological changes, two were drug addicts and one was a male homosexual. Of the 37 household contacts presenting neither serological changes nor signs of acute hepatitis B, five were drug addicts and six were male homosexuals.

Table 1: The follow-up findings in 50 household contacts of 31 patients with acute HBsAg-positive hepatitis.

Outcome of index case	Household contacts			
	Type of contact	Acute clinical hepatitis B	Serological changes but no signs of hepatitis	Neither serological changes nor signs of acute hepatitis
Cleared the HBsAg (n = 25)	sex (n = 20)	4*	5	11
	non-sex (n = 21)	0	1	20
Became HBsAg carrier (n = 6)	sex (n = 4)	2**	1	1
	non-sex (n = 5)	0	0	5

\* One household contact had shared a syringe with the index case. This contact developed acute hepatitis B but no HBsAg was detected.

\*\* One household contact had shared a syringe with the index case.

Outcome of index case	Cleared the HBsAg (n=25)	Became HBsAg carrier (n=6)
Total number of household contacts	55	12
Anti-HBs positive in first sample	5	
Escaped follow-up	9	3
Household contacts with follow-up samples	41	9
Developed acute clinical hepatitis B	4	2
Serological changes only	6	1



Figure 1: Left - a flow-chart of 67 household contacts in relation to the outcome of the index cases. Right - the time which elapsed between the onset of symptoms in the index cases and the six household contacts who developed acute hepatitis B.

## Discussion

In 1971 *Hersh et al.* suggested that HBV may be transmitted by the venereal route (8), and later results suggest that HBV could be transmitted by HBsAg-positive semen and saliva (9). In our study, acute clinical hepatitis B was only observed in the sexual contacts of index cases. Only in one non-sexual contact did the appearance of anti-HBc indicate exposure to HBV. In six household contacts, the only sign of HBV infection in the first serum sample was anti-HBc. Of these six, five showed serological changes during the follow-up and one of these five developed acute hepatitis B, confirming that humans may develop acute clinical hepatitis B when only anti-HBc is present in the serum. Thus household contacts with only anti-HBc in their sera should be observed, as should those with no serological evidence of exposure to HBV at the first contact.

In accordance with our findings in which five of 24 spouses and/or sexual partners developed HBsAg-positive acute hepatitis, *Koff et al.* found that two of 13 spouses and/or sexual partners developed HBsAg-positive acute hepatitis (5). *Peters et al.* had similar results in two of ten spouses (4). Of the 24 sexual partners and/or spouses, seven were drug addicts, three of whom developed acute clinical hepatitis B. Two of these three addicts had used the same syringe as their index case. Of the 12 spouses and/or sexual partners who were neither drug addicts nor

homosexuals, three developed acute clinical hepatitis B, suggesting that these contacts should also be carefully observed. In such post-exposure situations, HBIG seems to prolong the incubation period of the HBV infection (10), and since immune globulin and/or vaccination in post-exposure situations has proven to be of some value in other viral infections such as measles, smallpox and rabies (11, 12), this combination could be a possibility for treating sexual contacts when the index case is admitted to the hospital (6, 13).

In the acute phase of the HBV infection, there seems to be no relationship between the risk of infection among household contacts and the outcome of their index case. However, as the contacts of HBsAg carriers are continually at risk of contracting HBV infection, our findings are not contradictory to the high infection rate usually found among household contacts of HBsAg carriers (14, 15).

In conclusion it seems that prophylactic or post-exposure procedures are only necessary in the spouses and/or sexual partners of patients with acute hepatitis B.

## Acknowledgements

This study was supported by the Danish Medical Research Council (No. 512-20553, 512-15529, 512-15478), the Ebba Celinder Foundation, the Købmand i Odense Johann og Hanne Weimann f. Seedorffs Foundation and the Krista og Viggo Petersens Foundation.

## Literature

1. **Hardt, F., Aldershvile, J., Dietrichson, O., Juhl, E., Nielsen, J. O., Schlichting, P., Skinhøj, P., Tage-Jensen, U.:** Hepatitis B virus infections among Danish surgeons. *J. Infect. Dis.* 140 (1979) 972-974.
2. **Janzen, J., Tripatzis, I., Wagner, U., Schlieter, M., Müller-Dethard, E., Walters, E.:** Epidemiology of hepatitis B surface antigen (HBsAg) and antibody to HBsAg in hospital personnel. *J. Infect. Dis.* 137 (1978) 261-265.
3. **Szmunn, W., Harley, E. J., Ikram, H., Stevens, C. E.:** Sociodemographic aspects of the epidemiology of hepatitis B: In: *Vyas, G. N., Cohen, S. N., Schmid, R. (eds.): Viral Hepatitis. The Franklin Institute Press, Philadelphia 1978, pp. 297-320.*
4. **Peters, C. J., Purcell, R. H., Lander, J. J., Johnson, K. M.:** Radioimmunoassay for antibody to hepatitis B surface antigen shows transmission of hepatitis B virus among household contacts. *J. Infect. Dis.* 134 (1976) 218-223.
5. **Koff, R. S., Slavin, M. M., Conelly, J. D., Rosen, D. R.:** Contagiousness of acute hepatitis B. *Gastroenterology* 72 (1977) 297-300.
6. **Szmunn, W., Stevens, C. E., Harley, E. J., Zang, E. A., Oleszko, W. R., Williams, D. C., Sadovsky, R., Morrison, J. M., Kellner, A.:** Hepatitis B vaccine. *N. Engl. J. Med.* 303 (1980) 833-841.
7. **Aldershvile, J., Frösner, G. G., Nielsen, J. O., Hardt, F., Deinhardt, F., Skinhøj, P., The Copenhagen Hepatitis Acuta Programme:** Hepatitis B e antigen and antibody measured by radioimmunoassay in acute HBsAg-positive hepatitis. *J. Infect. Dis.* 141 (1980) 293-298.
8. **Hersh, T., Melnick, J. L., Goyal, R. K., Hollinger, F. B.:** Non-parenteral transmission of viral hepatitis type B (Australia antigen-associated serum hepatitis). *N. Engl. J. Med.* 285 (1971) 1363-1364.
9. **Scott, R. M., Snitbhan, R., Bancroft, W. H., Alter, H. J., Tingpalapong, M.:** Experimental transmission of hepatitis B virus by semen and saliva. *J. Infect. Dis.* 142 (1980) 67-71.
10. **Grady, G. F., Lee, V. A. et al.:** Hepatitis B immune globulin - prevention of hepatitis from accidental exposure among medical personnel. *N. Engl. J. Med.* 293 (1975) 1067-1070.
11. **Christie, A. B. (ed.):** Infectious Diseases: Epidemiology and clinical practice, Churchill Livingstone, Edinburgh, London, New York 1974, pp. 247, 397-398.
12. **Jawetz, E., Melnick, J. L., Adelberg, E. A. (eds.):** Review of Medical Microbiology. Lange Medical Publications, Los Altos, California, 1972, pp. 383-384, 405-406, 420-422.
13. **Purcell, R. H., Gerin, J. L.:** Hepatitis B vaccines: A status report: In: *Vyas, G. N., Cohen, S. N., Schmid, R. (eds.): Viral Hepatitis, The Franklin Institute Press, Philadelphia 1978, pp. 491-505.*
14. **Hess, G., Born, M., Dormeyer, H., Zöller, B., Arnold, W., Knolle, J.:** Hepatitis B virus markers among family contacts of asymptomatic HBsAg carriers. *Scand. J. Gastroenterol.* 14 (1979) 373-378.
15. **Perrillo, R. P., Gelb, L., Campbell, C., Wellinghoff, W., Ellis, F. R., Overby, L., Aach, R. D.:** Hepatitis B e antigen, DNA polymerase activity, and infection of household contacts with hepatitis B virus. *Gastroenterology* 76 (1979) 1319-1325.