

## Hospital transmission of hepatitis B virus in the absence of exposure prone procedures

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### SUMMARY

In February and in June 1998, two people developed acute hepatitis B following in-patient care in a district general hospital. Initial enquiries indicated their infections were not attributable to staff undertaking exposure-prone procedures (EPPs). We report the findings and implications of the subsequent investigation: a multi-disciplinary, multi-agency investigation, including molecular epidemiological analysis. Occupational Health records showed that staff involved in EPPs with the patients were HBsAg negative. No contact between the patients was identified nor were there failures in sterilization. The patients' HBV strains were identical, indicating a common source. A total of 231 out of 232 staff who might have treated either patient were tested for HBsAg; the remaining doctor, working abroad, was HBsAg- and HBeAg-positive and had the same HBV strain as the patients. On two occasions the doctor's hand had been cut while breaking glass vials, but there was no documentation linking these events to the two patients. The doctor had been vaccinated in 1993 and tested for anti-HBs prior to commencing work in 1997. The doctor was recalled to Occupational Health but did not attend and was not followed up. In total, 4948 patients potentially treated by the doctor received an explanatory letter and 3150 were tested for HBsAg. Only one was positive, and HBV sequencing showed no link to the doctor. Occasionally transmission of HBV from health-care workers can occur in a non-EPP setting and the implications of this require examination by those setting national policy. Occupational Health Services should investigate clinical health-care workers who do not respond to vaccination. They should ensure HBV carriers are identified and offer them appropriate advice to prevent transmission to patients.

### INTRODUCTION

Health-care workers (HCWs), particularly surgeons who perform exposure-prone procedures (EPPs) can

transmit HBV to their patients [1–4]. EPPs are those where the HCW cannot see the tips of his/her fingers while undertaking the procedure [5]. Accordingly, UK guidelines exclude all individuals who are

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HBeAg positive, and also those who are anti-HBe positive with HBV DNA levels greater than  $10^3$  genome equivalents/ml, from performing EPPs [5, 6]. In contrast, such transmission has only been documented once in non-EPP settings [7]. We report on an investigation into two persons with acute symptomatic HBV infection shortly after receiving in-patient care.

### Case histories

#### Case 1

In February 1998, a 65-year-old man was admitted with acute HBV infection. His only risk factors were surgery for a perforated duodenal ulcer in the same hospital in October 1997 and crown dental treatment in Canada 1 month earlier. The patient's surgical operators were not the source of the infection since they had been successfully immunized. The patient made a good recovery.

#### Case 2

In June 1998, a 30-year-old woman was admitted with acute HBV infection. Her risk factors were a series of bowel operations, in the same surgical unit as Case 1, during November 1997 to February 1998 and the receipt of three units of packed red cells. The blood donors were HBsAg negative. She made a complete recovery.

### The Incident Group

An Incident Group was established to investigate if there had been a common source within the hospital. This Group comprised consultants in public health medicine and representatives from the local occupational health department, an external consultant occupational physician, infection control nursing, infectious diseases medicine, general surgery, general practice, microbiology, molecular virology, the Scottish Centre for Infection and Environmental Health and public relations. The Group also sought advice from the Public Health Policy Unit of the Scottish Office (now Scottish Executive) Department of Health and from the UK's Advisory Group on Hepatitis and Advisory Panel for Health Care Workers infected with Bloodborne Viruses.

### METHODS AND FINDINGS

There were four sequential components to the investigation.

### Determining the likely hospital source

#### *Exclusion of the surgical team*

HCWs in the United Kingdom cannot work in posts that may involve EPPs without their anti-HBs levels (if negative, their HBsAg status), being known. The surgical teams of both cases had been immunized successfully against HBV except for one non-responder who was HBsAg negative and therefore non-infectious.

#### *Exclusion of direct contact between patients*

The two patients did not know each other, nor been in contact. They lived some distance apart and there was no overlap of primary-care practitioners.

#### *Exclusion of failures in infection control procedures within the hospital*

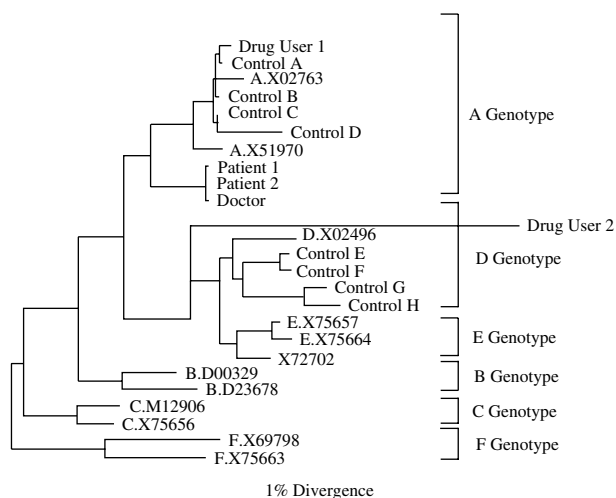
The two patients underwent surgery in the same operating theatre complex, but no failures in sterilization or infection control procedures were reported between 18 and 23 February 1998.

#### *Proving that the two patients were infected with the same virus*

Surface and core genes of HBV from the two infected patients, and from a convenience sample of nine acutely and three chronically infected controls from the West of Scotland, were analysed using standard PCR/sequencing phylogenetic methods (details available upon request). Sequences representative of genotypes A to F in international databases were included for comparison. There was 100% and 99.5% nucleotide homology in core and surface genes respectively (Fig.). The control samples from the same geographical area did not have the same sequence. These results strongly suggested that the two patients were infected from a single source.

### Identifying an HCW as the possible source of infection

A list of all HCWs who were, or might have been, in contact with either patient was collated. There was a wide range of personnel, totalling 232, including doctors ( $n=17$ ), theatre staff (26), reception/recovery staff (24), ward staff (135), phlebotomists (10), physiotherapists (16), and radiography staff (4) – who rarely, or never, would have performed EPPs. The list



**Fig.** Phylogenetic tree showing the relationship between the controls, as described in the text, reference sequences of each genotype from international databases, the two patients and the doctor who was responsible for the transmission. Note that the two patients and the doctor had identical sequences within genotype A which were different to controls taken within the same 10-year period from Scotland.

included nine EPP staff, one of whom was common to both. It was considered possible that an on-call doctor covering several wards might have attended to one of the patients but did not record the activity (e.g. replacement of cannulae, the administration of i.v. drugs) in the case-notes.

Of the 232 HCWs identified, 231 were tested and found to be negative for HBsAg. The 'missing' HCW was a former surgical house officer who was working abroad. Following consent, a specimen from this missing HCW (from July 1997) was tested: HBsAg and HBV DNA were positive. A subsequent sample (from 1998) was HBeAg positive. The infected HCW had not attended either of the patients' operations, but there was case-note evidence that the HCW had administered antibiotics intravenously to Case 2 on 19 December 1997 and had attended Case 1 on several occasions between 3 and 10 October 1997; the HCW could recall Case 2 who had been admitted several times, but not Case 1. When performing venepuncture or inserting intravenous lines, the HCW did not usually wear gloves. The HCW could recall two incidents during the 6-month period in the surgical unit when a hand was cut while breaking the top of a glass vial. There was frank bleeding on one occasion. These events could not be linked to the two patients. In fact neither patient could recall any

incident during their hospital stay which could have resulted in a breach of infection control. The virus from the HCW was identical in both HBV core and surface genes to Case 1 and 99.5% homologous to Case 2.

### Identifying why infection in HCW had not been prevented

A course of HBV vaccine had been received by the HCW while a second-year medical student, but there was no recall of post-vaccination serological testing. In mid-1997 the HCW's anti-HBs level was < 10 mIU/ml. The HCW was asked by letter to return to the Occupational Health department but did not make contact with, nor was re-contacted by its staff. It is likely that the non-response was due to concurrent hepatitis B. There was no history of jaundice.

### Identifying the extent of HBV transmission to other patients

(a) A data linkage exercise was performed involving the records of diagnosed cases of HBV infection held at the hospital's microbiology laboratory and the lists of in-patients potentially at risk of infection. No matches were revealed.

(b) A 'lookback' investigation was conducted. This included all in-patients of the hospital's surgical unit and a nearby hospital's medical unit during the 6-month period of the HCW's attachment to both. As the route of transmission was uncertain, and since patients' case-notes can be incomplete, patients were not stratified into risk categories.

Letters were sent to 4948 potentially at-risk patients, excluding those who had died or were considered by their GPs to be too physically or mentally disabled to receive one. The letter outlined the background to the incident, the low chances of someone having acquired HBV from the HCW, the telephone number of a helpline (1743 calls were made over a 14-day period) and the offer of an HBsAg test. The Incident Group decided that anti-HBc testing (followed by PCR testing to detect any HBV DNA and, if present, DNA sequencing analysis), although it might have identified infected individuals who were clearing their virus, should not be performed. It would have been of no benefit to patients and might have caused unnecessary anxiety as to the route of infection and clinical implications.

In total, 3150 (64%) underwent HBsAg testing and one, a 68-year-old woman, was HBsAg positive. Her virus was different from those of the HCW and the two patients. Second HBsAg tests were offered to 698 persons who could have been incubating HBV infection at the time of their first tests; none of the 292 tested was positive.

(c) As a medical student, the HCW had performed a small number of non-EPPs in various hospitals throughout the West of Scotland. A data linkage exercise was conducted to determine if any known HBV-infected cases had been patients in those hospital units. Laboratory reports of all persons diagnosed as HBsAg positive in Scotland are held centrally at the Scottish Centre for Infection and Environmental Health (now Health Protection Scotland). These were linked with the Information and Statistics Division's Scottish Morbidity Record dataset which holds details on all patient admissions to hospitals. None were linked. Consequently, no patient notification exercise was undertaken.

## DISCUSSION

Without DNA sequence analysis to link the viruses [8], the investigation might have terminated prematurely. It could be argued that insufficient information was available on Scottish sequences to make sure that a significant number of random sequences were not identical to the two patients. However, none of the control strains from the same geographical area were the same. Another issue relates to the interpretation of non-identical sequences. It is not well established whether either one, two or more nucleotide differences are sufficient to prove that the sequences are not derived from a common source.

The Health Board was willing from an early stage to pay for laboratory investigation, but it was only by chance that a suitable laboratory was sited in Scotland. We would recommend that a few centres are funded to deal with such outbreaks of infectious diseases, and not only those due to bloodborne viruses.

That the infections were not acquired in the operating theatre setting led to debate concerning the case for checking the HBV status of all, rather than just the health-care staff performing EPPs, who might have been in contact with either patient. We are only aware of one other published instance of transmission

in a non-EPP setting, and there were unusual circumstances [7]. It is not known if trauma to the HCW's hand whilst opening glass vials was the cause of our transmissions. Given that volumes as low as 0.1  $\mu$ l have been associated with transmission (viral titres are commonly  $10^9$  genomes/ml), it is plausible [9]. That so few non-EPP transmissions from HCW cases have been reported may also reflect the difficulties of recognizing a possible HCW-patient transmission incident and then performing the investigations to test such a hypothesis. It is estimated that only one-third of HBV-infected cases develop acute clinical HBV infection. Since the virus is easily transmitted through unprotected sexual intercourse and injecting drug use, symptomatic cases, particularly in the 15–50 years age group, generally do not arouse suspicion of other sources of infection. The variability of the incubation period for HBV infection (6 weeks to 6 months) also makes it difficult to relate the acquisition of HBV to a risk event.

It is questionable whether or not the transmissions could have been prevented. With knowledge of the HCW's HBeAg status, the employing hospital would have prohibited involvement as an assistant at operations; however, the HCW would still have been eligible to perform non-EPPs. Nevertheless, knowledge of the HCW's infection would have enabled targeting of the HCW for intensified training. This opportunity was missed as the Occupational Health department did not determine the reasons for the HCW's non-response to vaccination. Although the HCW did not return for further assessment, it was the department's duty to ensure follow-up and prohibit undertaking of EPPs. Strict guidelines to check the HBV status of, and vaccinate, prospective medical students prior to training were only introduced since this case.

The decision to offer patients identified from the lookback exercise hepatitis B testing was not unanimous. A consensus favouring this action was reached because (i) it would gauge the extent of the problem and may provide clues as to how infection was being transmitted, (ii) family contacts of persons found to be infected could be vaccinated against HBV infection, and (iii) persons found to be infected could undergo clinical assessment and follow-up. For most lookback exercises the target patient group is obvious as infection has been transmitted usually in an EPP setting. Here, the mode of transmission was uncertain but definitely occurred in a non-EPP setting. Accordingly,

the net was spread widely. Despite this, of 3150 individuals tested, only one unrelated carrier of HBsAg was identified.

## RECOMMENDATIONS

1. Due consideration should be given to the introduction of standardized, quality-assured molecular epidemiological techniques for outbreak investigation, probably on a national basis.
2. Occupational Health departments must observe official guidelines, especially in relation to establishing if a non-responder is a carrier of HBV; high standards can only be maintained if adequate resources and training opportunities are available, and audits are conducted routinely. The same principles apply to medical student occupational health services.
3. We do not believe it is necessary to exclude HBeAg positive non-EPP staff.
4. Consideration should be given to investigating the possibility of hospital-acquired or other health-care-acquired infection, in both EPP and non-EPP settings, in cases of acute HBV infection in persons without any other identifiable risk factors in order to gather more information in this area.

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## APPENDIX. Incident Group members

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## DECLARATION OF INTEREST

None.

## REFERENCES

1. Harpaz R, Von Seidlen L, Averhoff FM, et al. Transmission of hepatitis B virus to multiple patients from a surgeon without evidence of inadequate infection control. *N Engl J Med* 1996; **334**: 549–554.
2. The Incident Investigation Teams and others. Transmission of hepatitis B to patients from four infected surgeons without hepatitis Be antigen. *N Engl J Med* 1997; **336**: 176–184.
3. Polakoff S. Acute hepatitis B in patients in Britain related to previous operations and dental treatment. *BMJ* 1986; **293**: 33–36.
4. Heptonstall J. Outbreaks of hepatitis B virus infection associated with infected surgical staff. *Comm Dis Rep CDR Review* 1991; **1**: R81–R85.
5. UK Health Departments. Protecting health care workers and patients from hepatitis B: recommendations of the Advisory Group on Hepatitis. London: Her Majesty's Stationery Office, 1993.
6. Scottish Executive Health Department. Hepatitis B health care workers. *NHS HDL* (2000) 3.
7. Grob PJ, Bisschof B, Naeff F. Cluster of Hepatitis B transmitted by a physician. *Lancet* 1981; **11**: 1218–1220.
8. Kao JH, Heptonstall J, Chen DS. Molecular methods of measurement of hepatitis B virus, hepatitis C virus, and human immunodeficiency virus infection: implications for occupational health practice. *Occup Environ Med* 1999; **56**: 730–734.
9. Hollinger FB. Hepatitis B virus. In: Fields BN, Knipe DM, Howley PM, et al. eds. *Fields virology*, 3rd edn. Philadelphia: Lippincott–Raven, 1996: 2757.