Infection with hepatitis B virus after open heart surgery

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Transmission of hepatitis B virus from hospital staff to patients has been described as rare in Britain,¹ although a more recent review found an average of one outbreak a year between 1975 and 1990.² Subclinical infections and the prolonged incubation period of hepatitis B virus may make it difficult to detect an outbreak and surveys that rely on only clinical cases underestimate the risks of transmission, the impact of continuing morbidity, and the likelihood of secondary spread of infection.¹ Chronic carriage with possible liver disease is more common after subclinical infection³ and may increase the chance of further spread of infection to sexual partners. In addition, a low overall risk of infection at surgery may obscure higher risks of infection with particular procedures. In Trent region two cases of acute hepatitis B presented in neighbouring health districts four weeks apart. Both were in patients who had undergone cardiothoracic surgery in the same unit during the preceding six months. Neither patient had risk factors for hepatitis B infection. This case cluster instigated an investigation into the source of the outbreak.

The outbreak

The first two patients to be identified as positive for hepatitis B surface antigen presented with jaundice in February and March 1988. The patient's general practitioners sent serum for testing to different virology laboratories. The laboratory responsible for pre-operative screening for hepatitis B surface antigen found the second case shortly after being notified of the first case of hepatitis B by the neighbouring district laboratory. Stored serum was analysed to confirm that both patients were negative for the antigen before the operation. On recognition of a case cluster an outbreak control team was set up by the infection control committee responsible for the cardiothoracic unit. The source of infection was sought by reviewing blood products received by both patients and, after counselling, by testing for hepatitis B surface antigen all staff in both operating teams, perfusion technicians, and intensive care staff not known to be immune to hepatitis B. Subtype analysis was done on all serum samples testing positive for hepatitis B surface antigen.

Initial findings

The Regional Blood Transfusion Centre confirmed that the donors of blood products used in the operations remained negative for hepatitis B surface antigen and hepatitis B core antibody or had redonated and remained negative for hepatitis B surface antigen with no history of jaundice. A surgical trainee, who was the only staff member positive for hepatitis B surface antigen, tested positive for hepatitis B e antigen and had the same surface antigen subtype (ad) as the patients. He first started operating in the cardiothoracic unit in August 1987 and stopped doing all invasive procedures voluntarily in April 1988 when his

hepatitis B surface antigen status was established, shortly before the third and fourth cases of hepatitis B presented.

The trainee was from continental Europe and had no history of jaundice or recent illness. Inquiries revealed that in 1986, while in his country of origin, he had received a needlestick injury from a patient believed to be infected with hepatitis B virus. He had been treated with a single dose of hepatitis B immune globulin and no serological investigation had been done. In Britain he had received two doses of hepatitis B vaccine, the first in October 1987 as part of the vaccination programme for cardiothoracic surgical staff. He had been screened for antibody to hepatitis B surface antigen before vaccination as this was then our policy (prevaccination immunity screening was later abandoned because it was not cost effective). The stored prevaccination serum was reanalysed and found to be positive for hepatitis B surface antigen and hepatitis B e antigen. IgM to hepatitis B core antigen was not detected. The hospital records were urgently reviewed to identify patients whose surgical procedures had involved the infected surgeon.

Patient survey

A total of 744 patients passed through the cardiothoracic unit between 17 August 1987 and 6 April 1988. As soon as the outbreak was recognised these patients and their general practitioners were informed by letter of a potential risk of hepatitis B infection and given the number of a telephone advice line staffed by public health physicians. We issued a press release giving similar information including the telephone advice line number. Routine testing of patients for hepatitis B surface antigen before bypass surgery and storage of serum allowed us to study asymptomatic infection. The operating theatre records were reviewed by a public health doctor with the help of the surgeon identified as the carrier. In all, 361 patients had undergone invasive surgical procedures at which the trainee assisted. Patients who had had procedures judged to carry minimal risk of transmission of blood-borne infection such as bronchoscopy were excluded.

The 361 patients were informed by letter that a risk of infection could not be excluded and they were asked to consent to a blood test at least six months after the operation (for many patients six months had already passed since their operation). General practitioners were informed of the nature of the possible risk to their patients and asked to take blood samples. Individual arrangements were made with 17 patients who wished to be tested and whose doctors felt unable to participate. The remaining patients and their general practitioners were reassured by letter that the earlier general warning could be withdrawn. The telephone inquiry line remained open while the survey was in progress and over 300 calls were received.

Counselling of patients positive for hepatitis B surface antigen resident in three health districts was

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coordinated from the department of virology. Telephone counselling of patients and their general practitioners was used when they could not attend the virology department. Sexual partners of patients found to be positive for hepatitis B surface antigen were offered screening and hepatitis B vaccine was given to non-immune partners.

LABORATORY INVESTIGATION

All serum samples were tested for hepatitis B surface antigen by radioimmunoassay and samples testing positive were analysed for hepatitis B e antigen and antibody by enzyme immunoassay. Subtyping of hepatitis B surface antigen positive samples and testing for IgM antibody to hepatitis B core antigen were done by radioimmunoassay at the Department of Virology, University College and Middlesex School of Medicine, London. Samples negative for hepatitis B surface antigen collected after the operation were tested for IgG to hepatitis B core antigen by radioimmunoassay and, if the result was positive, the preoperative and postoperative samples were retested in parallel for antibodies to hepatitis B core antigen and hepatitis B surface antigen by radioimmunoassay. Due to widespread concern among patients about any possible risk of HIV infection the surgeon was given counselling and consented to be tested for HIV antibodies; the result was negative.

CASE DEFINITIONS

A symptomatic case was defined as a patient who developed acute hepatitis B within six months of cardiothoracic surgery; all patients in this group were negative for hepatitis B surface antigen before the operation. Asymptomatic infection was defined as seroconversion for markers of hepatitis B virus infection without a history of hepatitis. Natural immunity was defined as the presence of a titre of over 100 mIU/ml antibody to hepatitis B surface antigen or to hepatitis B core antigen, or both, in preoperative serum. No patients were known to have received hepatitis B vaccine before operation.

Results of survey

In all, 280 of the 361 patients at risk were tested (table I). Of 28 patients in whom markers of hepatitis B infection were detected in postoperative serum, five patients had symptomatic hepatitis, 12 had asymptomatic infection, eight were naturally immune before the operation, and three had no preoperative serum available. The subtype of hepatitis B surface antigen could be determined in nine out of the 11 antigen positive patients, and all were the same subtype as the surgeon (ad). Among three categories of operation (valve replacement, coronary artery bypass grafting, and non-bypass procedures) the highest risk of infection was from valve replacement, with seven infections occurring in 52 operations in non-immune patients (13.5%). Numbers were insufficient to assign significance to any difference in risk of transmission of infection by operation type.

All 17 patients shown to have acquired hepatitis B

virus markers after the operation were in the group of 217 patients who had wire sternal closure (17/217 infected v 0/52 without wire sternal closure infected; p=0.05, Fisher's exact test). The 17 patients had all had a cardiopulmonary bypass. Of the 81 patients not tested, six died less than six months after the operation without clinical evidence of hepatitis, and the remainder did not present for serological screening after three reminder letters.

The female spouses of two patients became infected before vaccination. One spouse was symptomatic and positive for hepatitis B surface antigen and IgM to hepatitis B core antigen two months after her partner's icteric illness. The other spouse was asymptomatic and before vaccination, 10 months after her partner's operation, was positive for hepatitis B surface antigen with no IgM antibodies to hepatitis B core antigen. Both women were hepatitis B surface antigen subtype ad and had no other risk factors for hepatitis B. They did not become hepatitis B virus carriers. Of nine other known sexual partners of patients found to be positive for hepatitis B surface antigen, seven responded to hepatitis B vaccine without acquiring antibody to hepatitis B core antigen. One partner was not vaccinated because she had left the country, but on her return she had no serological markers of hepatitis B virus infection and her spouse was then negative for hepatitis B surface antigen. One sexual partner refused follow up after vaccination.

In three patients with antibodies to hepatitis B virus recent infection could not be proved because no preoperative serum was available. Two had other risk factors for infection with hepatitis B virus, and one was a child with congenital heart disease who was found to be positive for hepatitis B surface and e antigen (subtype ad) with no IgM antibodies to hepatitis B core antigen nine months after operation. The child had no record of previous testing for hepatitis B virus markers but had had other cardiac operations and received transfusions since birth. No markers of hepatitis B virus infection were found in the child's parents or siblings, who were given hepatitis B vaccine. Two adult patients who had had thoracic surgery without bypass had IgG to hepatitis B core antigen in single postoperative samples. One of these patients was from an endemic area and had a titre of over 500 mIU/ml for antibody to hepatitis B surface antigen; the other patient was negative for hepatitis B core IgM.

Four of the 11 adults found to be positive for hepatitis B surface antigen remained positive for hepatitis B e antigen for over six months. Only one had presented with symptomatic illness. All were given interferon; one patient was unable to tolerate more than two weeks of the three month course and two became negative for hepatitis B surface and e antigen within five months of finishing interferon treatment, less than three years after operation. One further adult remained positive for hepatitis B surface antigen for over six months and had antibody to hepatitis B e antigen when first screened. The surgeon started taking interferon in April 1988 and antibody to hepatitis B e antigen appeared two months into the course, associated with a temporary increase in serum alanine aminotransferase concentrations. He became negative for hepatitis B surface antigen by September 1988 and returned to theatre work when he had remained negative for three months. At follow up in May 1991 he remained negative for hepatitis B surface antigen and had antibody to hepatitis B surface antigen. He has not been tested for hepatitis B virus DNA.

Risk of infection

Hospital staff are known to have an occupational risk of infection with hepatitis B but the transmission of

TABLE I—Number of patients at risk and results of serological survey

	Valve replacement	Coronary artery bypass graft	Other bypass surgery	Non-bypass surgery	Total
Operation	72	185	43	61	361
Serological test	53	153	32	42	280
Susceptible to hepatitis B*	52	148	31	38	269
Symptomatic acute hepatitis B	1	4			5
Asymptomatic infection	6	5	1		12
Total infected (% of those susceptible)	7 (13)	9 (6)	1 (3)		17 (6)

Eight patients had markers of hepatitis B infection in preoperative serum and three patients had postoperative serological evidence of infection but no preoperative serum was available.

TABLE II—Reported outbreaks of hepatitis B after open heart surgery

Place	Year	Source	Staff hepatitis B status	No of patients infected			Carriers	Secondary spread
				Icteric	Anicteric	Total		
Kansas ^a	1974-5	Inhalation therapist/blood gas analyst	P	2	4	6		1
Norway ^b	1978	Surgeon	P	2	3	5	4	4
Netherlands ^c	1979	Surgeon	P	3	NS	3	NS	NS
	1979	Perfusion technician*	C	6	NS	6	NS	NS
	1981	Perfusion technician*	C	5	NS	5	NS	NS
United Kingdom ^d	1980-3†	Surgical registrar	P	5	NS	5	NS	NS
	1980-3	Perfusion technician	C	6	NS	6	NS	NS
Leicester	1987-8	Trainee surgeon	C	5	12	17	5	2
United Kingdom ^d	1990	Trainee surgeon	C	2	3	5		
All serological surveys				11	22	33	9	7

P=Transmission during prodrome of acute icteric hepatitis B.
C=Transmission by high infectivity carrier positive for hepatitis B e antigen.

NS=Not stated in reference.
*Same person in two outbreaks.
†Exact date not stated.

infection from staff to patients is generally thought to be much less common. This assumption may not apply to open heart surgery. For the period 1980-3 the estimated annual risk to patients of acquiring symptomatic acute hepatitis B from staff after surgery in England and Wales was one in a million compared with an annual occupational risk of developing symptomatic acute hepatitis B in surgeons of 25 per 100 000.¹ Interestingly, all 11 cases of hepatitis B in surgical patients considered for this estimate occurred after open heart surgery, although the risk was assumed to be spread over all surgical procedures. However, heart surgery accounted for only 30 000 of the 2·25 million operations performed annually in England and Wales at that time,⁴ making the risk for heart surgery patients nine per 100 000 surgical procedures.

Outbreaks of hepatitis B associated with surgery have also given rise to conflicting reports on the incidence of subclinical infection. In an outbreak in the United States traced to a gynaecological surgeon no appreciable subclinical transmission was found,⁵ but in a similar outbreak in Britain subclinical transmission was the commonest outcome.⁶ In two previous outbreaks associated with open heart surgery (table II)⁸ secondary spread to family contacts of patients positive for hepatitis B surface antigen occurred and subclinical infection was also the commonest outcome. If 70% of patients infected at open heart surgery are asymptomatic (table II) the importance of this route of transmission may be underestimated. Many cardiothoracic patients require postoperative monitoring of anticoagulant treatment and in some cases reoperation or further cardiac catheterisation is necessary potentially exposing hospital staff to infection from subclinically infected patients.

Screening after outbreaks

Screening enabled us to offer early interferon treatment to hepatitis B e antigen carriers, most of whom were asymptomatic. Since the numbers involved were small it is difficult to assess whether seroconversion to antibody to hepatitis B e antigen and clearance of hepatitis B surface antigen occurred more often and more rapidly than could have been expected spontaneously. The two seroconversions did not appear to follow the hepatitis-like illness often observed in successful interferon treatment¹⁰ and seen in the surgical trainee. In an outbreak after open heart surgery that occurred before recombinant interferon was available, four out of five infected patients remained positive for hepatitis B e antigen two and a half years after surgery.⁸ Our avoidance of such an adverse outcome may be attributable to interferon and we believe interferon should be offered to any patients or health care workers becoming hepatitis B e antigen carriers.

The distribution of potentially infected patients over several counties with a total population of 2·7 million

led us to a survey based on general practitioners sending serum to the virology laboratory where preoperative samples were stored. Successful management of a community based outbreak of hepatitis B in general practice has been described.¹¹ General practitioners welcomed full involvement initially at a time when there was public anxiety and press coverage of fatal fulminant hepatitis B in a public figure. Despite an early press conference some press reports confused hepatitis B virus and HIV infection, giving rise to needless worry. There was evidence of denial of illness in one patient who received letters from the outbreak control team but did not seek medical attention despite becoming jaundiced. His illness came to light only when his spouse also became jaundiced.

Preventing hepatitis outbreaks

The type of operation most often associated with infection, prosthetic valve replacement, is regarded by cardiothoracic surgeons as presenting a high risk of needlestick injury.¹² We consider that the wire sternal closure and cardiopulmonary bypass are also important in infection. Wire closure of the sternum has been shown to give rise to a high rate of glove perforation¹³ and is the part of the operation that a junior surgeon is most likely to perform. Cardiopulmonary bypass itself presents a potential route of transmission of hepatitis B¹⁴ and is also associated with a temporary reduction of serum immunoglobulin and complement¹⁴ and depression of cell mediated immunity,¹⁵ which may affect the outcome of exposure to hepatitis B virus. Modification of surgical technique could protect both patients and staff from hepatitis B and HIV infection.¹⁶⁻¹⁹ The use of wound closure techniques that regularly result in glove perforation should be reviewed.

This outbreak confirms the need for hepatitis B vaccination of medical students before embarking on a surgical career. Hepatitis B vaccine is 90% effective overall, and it is recommended that health care staff likely to experience parenteral exposure to blood should be vaccinated and that evidence of seroconversion should be checked after vaccination.²⁰ Despite this recommendation a recent survey of 206 vascular surgeons in Britain showed that 37% had never been immunised and 45% of those immunised had never had their immunity checked, suggesting that many surgeons remain unprotected a decade after the introduction of vaccine.²¹ This omission is of importance not only for surgeons' own health but for that of their families and their patients.

This outbreak also shows that vaccination of practising surgeons may well be too late; indeed transmission of hepatitis B by a vaccinated surgeon is well recognised.²² An interim report indicates that the United Kingdom has experienced another case of transmission of hepatitis B virus to patients at open

heart surgery since the one we have described.² There have now been four recorded outbreaks in this select group of surgical patients in Britain in less than 10 years. Current arrangements for controlling infection, including staff vaccination and preoperative screening of patients for hepatitis B surface antigen, are clearly not completely effective.

At present the only group of NHS staff recommended to be negative for hepatitis B surface antigen before employment are dialysis unit staff²³ because of the susceptibility of renal patients to infection and ease of spread of infection in such units. It has been suggested that all surgeons should be screened before employment and redirected to other work if found to be positive for surface antigen.¹⁶ Fear of enforced disruption of a career achieved after long and arduous training would lead most staff to oppose any such screening.

We believe that health care workers positive for hepatitis B surface antigen should not be automatically excluded from participating in open heart surgery for two reasons. Firstly, most people identified will have antibodies to hepatitis B e antigen, will lack detectable circulating hepatitis B virus DNA, and will be low infectivity carriers.^{24,25} Secondly, of nine reported nosocomial cardiothoracic outbreaks (table II), four were associated with staff with acute icteric hepatitis and five with hepatitis B e antigen carriers. There is no evidence that staff who are healthy hepatitis B surface antigen carriers with antibody to hepatitis B e antigen pose any risk to cardiothoracic surgical patients and there is therefore no justification for restricting their activities. However, it would seem sensible for hepatitis B carriers working in open heart surgery to be aware of their serostatus. In future, assays for hepatitis B virus DNA may replace current assays for hepatitis B e antigen and antibody as a measure of infectivity, but the excellent correlation between the possession of antibody to hepatitis B e antigen and the absence of hepatitis B virus DNA in health care workers²⁴ makes antibody to hepatitis B e antigen an acceptable practical indicator of infectivity.

Conclusions

We suggest that staff in contact with the blood of patients at open heart surgery should be screened for hepatitis B surface antigen if they are not known to have antibody to the antigen. Our evidence does not allow us to generalise beyond open heart surgery, which we believe poses a special risk for transmission of hepatitis B virus. Such screening should be regularly repeated in people who do not respond to hepatitis B vaccine, as has been advocated for all surgeons.²⁶ These people should be aware that they are at risk of acquiring and transmitting hepatitis B virus despite vaccination. The few hepatitis B surface antigen carriers found to be positive for hepatitis B e antigen

should be offered interferon, and if this fails to affect their infectivity a change in duties should be considered. Although immunisation of staff is an important component of infection control procedures for open heart surgery, a preventive strategy limited to staff immunisation alone will not prevent a repetition of our experience.

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ANY QUESTIONS

Why do epileptic fits stop?

Many people believe that an epileptic seizure occurs when a positive feedback loop or loops develop within an aggregate of neurons that release excitatory transmitters, predominantly aspartate and glutamate, that overwhelm local inhibitory mechanisms. The principal inhibitory neurotransmitter is γ aminobutyric acid. Endogenous opioids may also have an inhibitory role, and there is evidence for release of endogenous opioids in vivo after seizures with a consequent increase in the seizure threshold.¹ There is also evidence that this may occur in

humans who have serial absence seizures.² The role of endogenous opioids in terminating other seizure types in humans remains undetermined. Their involvement opens out the possibility of new strategies of antiepileptic drug treatment.—J S DUNCAN, senior lecturer in neurology, London

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