Nosocomial hepatitis A infection in a paediatric intensive care unit

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SUMMARY Seven members of staff in a paediatric intensive care unit and two of their relatives developed hepatitis A over a period of five days. A 13 year old boy who was incontinent of faeces prior to his death, was presumed to be the source of infection. Two hundred and sixty seven other members of staff underwent serological testing and were given prophylactic pooled gamma globulin. Twenty three per cent were immune before exposure. Of people born in the United States, those at highest risk of developing the disease are physicians, dentists, nurses and those under the age of 40. Of those born outside the United States, being white and under the age of 30 are the two main risk factors. Data from a questionnaire sent to 19 nurses at risk (six cases, 13 controls) suggested that sharing food with patients or their families, drinking coffee, sharing cigarettes and eating in the nurses' office in the intensive care unit were associated with an increased incidence of hepatitis. Nurses with three or four of these habits were at particular risk. The costs of screening and prophylaxis were US\$64.72 per employee, while prophylaxis alone would have cost US\$8.42 per employee. Assessing risk factors on the one hand and costs of prophylaxis on the other are important elements in the control of nosocomial infections.

Hepatitis A, usually spread through food, has recently been described as an important cause of nosocomial infection.^{1,2} Several papers report its transmission by blood^{3,5} or platelet⁶ transfusion. Although sometimes the mode of transmission is unknown,⁷ a major source of cross contamination in hospitals may be the patient with diarrhoea whose hepatitis has not yet been diagnosed.^{8–12} The patient discussed in this paper may have infected staff during the prodromal period while he was incontinent of faeces. This outbreak was studied to identify important risk factors among staff who acquired hepatitis A by comparing their demographic characteristics and the results of a questionnaire with similar data from exposed but uninfected staff at risk.

The outbreak

In 1981 the paediatric intensive care unit at The New York Hospital comprised eight beds in two rooms staffed by 21 nurses. In early September there was an outbreak of hepatitis A, with nine primary and one secondary case.

On 3 September the department of epidemiology was advised that five intensive care nurses and the husband of one of them had developed hepatitis (Figure); three nurses were ill enough to require admission to hospital. The next day two of the inpatient nurses were reported as having positive titres of anti-hepatitis A virus (HAV) IgM which confirmed the diagnosis of hepatitis A. Two additional cases, a junior doctor and the sister of another nurse, were discovered. All members of staff assigned to the intensive care unit and the adjacent general paediatric ward as well as patients in the unit, were considered to have been exposed. Following serological testing for serum glutamic pyruvic transaminase activity (SGPT) and titres of hepatitis B surface antigen (HB_sAg), and both anti-HAV and anti-HAV IgM for hepatitis A, each received inoculation with pooled gamma globulin as prophylaxis against hepatitis A. Pooled gamma globulin was also given to those closely associated both with patients and staff.

Sharing of food and drinks was forbidden. The paediatric intensive care unit was closed for four weeks following the last case and thoroughly

Figure Epidemic curve of outbreak in paediatric intensive care unit

cleaned. A temporary intensive care unit was set up immediately adjacent to it and patients were transferred there after their parents had given written informed consent, and they had received prophylactic pooled gamma globulin.

Abnormal SGPT activity was reported in an asymptomatic nursing administrator, but this was attributed to prophylaxis with isoniazid following a positive Mantoux test. After her anti-HAV IgM titre was reported positive she became symptomatic and was taken off duty; she was the last primary case.

The local health department knew of no other clusters of hepatitis A infection in the community. There were no other cases either in the adjacent paediatric unit or in the main hospital. As the cases occurred simultaneously and in the same place, investigation of this outbreak focused on a possible common source in the paediatric intensive care unit.

The incubation period for hepatitis A is 15 to 50 days (mean about 28 days)¹³ and the period of exposure was between 12 July to 16 August. As one infected nurse was on holiday from 21 July to 2 August and the infected couple (nurse and her husband) went on holiday on 16 August, the period of exposure was narrowed to the 13 days from 3 August to 15 August. Interviews with the six infected nurses outlined their timetables for this period, and identified a 13 year old boy with metastatic malignant glioma as the likely source of infection. He had been admitted to the hospital on 22 June and transferred to the paediatric intensive care unit on 10 July where he remained until his death on 7 August. Although he was never jaundiced, he was incontinent of faeces for several days before he died.

During the five days 3–7 August, the six infected nurses worked either day or evening shifts. On 4 August the junior doctor who became infected inserted a catheter into the patient. Because there was no necropsy, tissue and serum were unavailable for serological testing for hepatitis A. His parents and two sisters often visited him and brought food which they shared with the patient and staff. They were tested for hepatitis A (anti-HAV IgM and anti-HAV) on 15 October. At about the same time a questionnaire designed to assess risk of infection with hepatitis A was given to the 19 nurses and 10 doctors who worked in the paediatric intensive care unit during the presumed period of exposure. Staff from the adjacent paediatric unit were not included because there were no cases of hepatitis in their area.

The only secondary case, the cousin of an infected nurse, had stayed with her from 21–25 August. Although he received prophylactic gamma globulin on 7 September, signs and symptoms of clinical hepatitis, unconfirmed by antibody studies, appeared on 25 September.

Methods

Case definition. The diagnosis of hepatitis A was made when appropriate clinical findings, abnormal liver function tests, and a positive IgM test for antibody to hepatitis A were present.

Assays. HB_sAG titre was determined by the AusriaTM II-125 system. Antibody to hepatitis A virus was detected by the HAVABtm procedure and IgM antibody to hepatitis A virus was identified by using the HAVABtm-M method (Abbot Laboratories).

Questionnaire. A questionnaire designed to assess variables associated with hepatitis A infection was sent to the 19 nurses and 10 housemen who worked in the paediatric intensive care unit and were, therefore, the most likely to have been exposed. This group included seven people (six nurses, one doctor) who became infected. The questionnaire comprised 40 questions about eating, drinking and smoking habits at work.

To analyse the results of the questionnaire and identify habits that may have been associated with an increased risk of acquiring hepatitis A, a 2×2 contingency table was made for each question by cross tabulating the responses to the questions and the outcome (development of hepatitis). For each table a p value was calculated by Fisher's exact test to measure the strength of an association between the question and the development of hepatitis A having arisen by chance. In addition, for each table, the odds of developing hepatitis A were computed for those who answered yes as well as for those who said no. By dividing the number of cases by the number of controls, the odds can be calculated. Results were examined for nurses alone and for nurses and doctors combined. Probabilities of <0.05 were accepted as significant.

Results

Hepatitis screening. A total of 323 asymptomatic people who thought they had been exposed to hepatitis A underwent serological testing and received prophylactic pooled gamma globulin within 48 hours of the first case report before the extent of the outbreak was known. None of them had positive titres for HB_sAg, or had abnormal results of liver function tests. Demographic characteristics of the 267 employees in this group are shown in Table 1. Serological testing showed positive anti-HAV titres in 23.6% of the staff who were, therefore, immune prior to exposure.

Table 2 shows that place of birth, age, race and profession were associated with immunity. Using the method of recursive partitioning, it was found that among those people born in the United States doctors, dentists, nurses or those under the age of 40 were less likely to be immune to hepatitis A (8.8%) than native born staff who were over the age of 40 and in other professions (72.2% immune). For employees born elsewhere, being white or under the age of 30 was associated with increased risk (28.6% immune) compared with black, hispanic, and Asian members of staff who were over the age of 30 (77.1% immune).

The 56 other people who underwent serological testing and received prophylactic pooled gamma

globulin were patients, or 'significant other' of exposed patients or staff. None of the 323 people who received prophylaxis with pooled gamma globulin subsequently developed clinical hepatitis A.

Serological screening of members of the family of the boy suspected of starting the outbreak 10 weeks after his death, showed that both parents were positive for anti-HAV; thus they had longstanding

Table 1 Demographic characteristics of employees serologically tested for immunity to hepatitis

	Immune (n=63)	No tested (n=267)	% Immune
Age (years)			
15-29.9	15	145	10.3
30-39.9	20	78	25.6
40-64.9	28	44	63.6
Sex			
Male	25	98	25.5
Female	38	169	22.5
Race			
White	18	182	9.9
Black, Hispanic, Asian	42	82	51.2
Mixed race	3	3	100.0
Country of birth			
USA	30	212	14.2
Europe	2	6	33.3
Latin South America	21	38	55.3
Asia	10	10	100.0
New Zealand	0	1	0.0
Job			
Dentist	0	3	0.0
Social Worker	0	2	0.0
Physiotherapist	0	2	0.0
Doctor	4	47	8.5
Paramedic	1	9	11.1
Nurse	13	86	15.9
Occupational/speech therapist	1	5	20.0
Radiologist/radiographer	10	46	21.7
Dietitian	3	9	33.3
Respiratory therapist	5	14	35.7
Security officer	4	8	50.0
Laboratory technician	1	2	50.0
Aide	15	25	60.0
Patient transporter	5	5	100.0
Other	1	4	25.0

Table 2 Results of serological tests of employees

Group	Immune	Susceptible	% Immune
Born in USA			
Doctor or dentist	2	46	4.2
Nurse	7	69	9.2
Other under age 40	8	61	11.6
Other age 40 or older	13	5	72.2
Born outside USA			
White or under age 30	6	15	28.6
Black, hispanic, Asian and age 30 or older	27	8	77.1

immunity. Positive anti-HAV IgM titres in both sisters showed that their immunity was associated with recent infection.

Questionnaire. Results are summarised and presented for the 19 nurses alone, as this group had the greatest exposure. Because only one of 10 doctors contracted hepatitis, no conclusions about this group are possible. Examination of data from these doctors showed that the odds in favour of nurses and doctors contracting hepatitis were not significantly different.

In the group of nurses none of the *p* values was significant, although several of the trends were suggestive; due to the small sample size only an extreme outcome would have yielded a *p* value of <0.05 . Of the 40 questions asked, four yielded suggestive results. Table 3 shows the responses of the six patients and the 13 controls, and the odds of developing hepatitis A for both groups. Sharing food with patients or their families, drinking coffee, sharing cigarettes and eating in the nurses' office on the intensive care unit were all associated with an increased incidence of hepatitis. Furthermore, the greater the number of these four questions affirmatively answered, the more likely was the nurse to have been infected. This is particularly striking when the odds of acquiring hepatitis A in nurses who answered yes to two questions are compared with those of answering yes to four questions (Table 3). In the sample of 19 nurses no pattern in the responses to the four questions was seen. Answering yes to one question, therefore, was not related to answering yes to another question.

Possible explanations for the sister of one nurse and the husband of another becoming infected may be found in the answers to the individual questionnaires by these nurses, and further interviews. The

Table 4 Costs for screening and prophylaxis for employees

Item	Unit cost (US\$)	Cost for 267 units (US\$)
SGPT	7.50	2002.50
HB _s AG	11.00	2937.00
Anti-HAV	18.90	5046.30
Anti-HAV-IgM	18.90	5046.30
Pooled gamma globulin (2 ml)	8.42	2248.14
Total	64.72	17 279.64

nurse whose sister caught hepatitis lived in hospital accommodation and worked the evening shift; on one occasion during the five days when infection was most likely to have occurred she returned home and prepared dinner for herself and her sister. The nurse whose husband became infected said that she borrowed and shared cigarettes, as well as taking opened packets of cigarettes home. Her husband also smoked.

Table 4 summarises the individual costs for each screening test used and for the pooled gamma globulin. Cost per employee and the total for all 267 employees are also shown. These are the full costs to the hospital.

Discussion

When the first six cases of hepatitis were reported, neither the source nor the magnitude of the outbreak were known; consequently, all employees, patients and their 'significant others' with potential exposure to the environment of the paediatric intensive care unit and the adjacent paediatric unit were encouraged to undergo serological testing and to receive prophylaxis. Of the 323 people who received pooled gamma globulin, 204 were asymptomatic at risk staff with normal serum SGPT activity. None of them later developed clinical hepatitis A. Previous studies have shown that pooled gamma globulin given early in the incubation period can be protective in 80–90% of cases.^{14 15}

During interviews with the infected nurses, it became clear that the 13 year old boy with metastatic malignant glioma, who had been incontinent of faeces for several days before he died, was probably the source of the infection. He was never jaundiced, had not had liver function tests performed during the final weeks of his illness, and necropsy was not done. There were therefore no tissue specimens or sera that could be tested for the presence of hepatitis A antigen. Furthermore, by the time of his death he had been in hospital continuously for seven weeks. Thus if he had had hepatitis he must have been

Table 3 Preference questionnaire comparing a case of hepatitis with controls in exposed susceptible nurses

		<i>Hepatitis</i>		<i>Odds</i>	
			<i>Yes</i>	<i>No</i>	<i>Yes/No</i>
A	Do you share food with patients or their families?	Yes	4	4	1.00
		No	2	9	.22
B	*Do you drink coffee from the coffee pot in the ward?	Yes	5	6	.83
		No	1	6	.17
C	Do you share cigarettes?	Yes	3	5	.60
		No	3	8	.38
D	Do you eat in the nurses' office in the ward?	Yes	5	10	.50
		No	1	3	.33
Summary					
E	No of above questions (A-D) answered positively	1 or 2	2	11*	.18
		3 or 4	4	2	2.0

*One nurse did not respond to B but responded to A, C, and D.

infected in the hospital, and there were no other patients with hepatitis A in the hospital during this period. The staff recalled, however, that his family visited regularly and had often brought food which they shared with both staff and the boy. They also complained occasionally of not feeling well. Ten weeks after the patient's death serological testing of both his sisters showed anti-HAV IgM, although they denied signs and symptoms of hepatitis. As IgM antibodies appear early and in most cases are present only for the first few months following infection,^{16 17} this finding is usually regarded as specific and sensitive for recent hepatitis A.¹⁸ Kao *et al*¹⁹ reported that in five (13.5%) of 37 cases anti-HAV IgM persisted for longer than 200 days; towards the end of the positive period in these five patients, however, titres were very low. Without the radioimmunoassay it would have been impossible to have identified the patient as the source of infection retrospectively.

If this patient was the source, his faecal incontinence probably occurred during the prodromal phase. Viral particles have been detected in the stool of patients with hepatitis A from five to seven days before the onset of jaundice in addition to abnormal transaminase activity²⁰⁻²²; this is the time of maximum excretion of the virus for some patients. Because the diagnosis of hepatitis is not usually apparent at that stage, they may not have been appropriately isolated in the hospital. Thus the period has been reported as the most likely time for cross infection.⁸⁻¹² Some investigators have suggested that the amount of virus excreted diminishes so abruptly after the onset of jaundice and increase in transaminase activity that special isolation procedures are no longer necessary after symptoms of hepatitis.²³ Their faeces should be handled with the same precautions that would be used for all inpatients. There is, however, no universal agreement on this point. Some studies have shown that virus excretion does continue after the onset of jaundice.²⁴⁻²⁵ Consequently, isolation is appropriate to prevent transmission of the virus.

Careful handwashing is one of the most important ways of preventing the spread of hospital acquired infection.²⁶ One group of investigators, however, observed the frequency of handwashing in a medical intensive care unit and found that compliance with the rule that hands should be washed after each contact with a patient was only 41%.²⁷ Although it was not mentioned in our questionnaire, it is likely that inadequate handwashing in the paediatric intensive care unit was an important contributing factor in the spread of the hepatitis A virus from the presumed source to the six nurses and one junior doctor.

Analysis of the data from the questionnaire given to the 19 nurses, who all had the same exposure to hepatitis A because they all cared for the boy concerned, suggested that sharing food with patients or their families, drinking coffee, sharing cigarettes and eating in the nurses' office may also have contributed to the spread of infection. These habits were more common in the six cases of hepatitis than they were in the 13 exposed but uninfected nurses. Furthermore, nurses who did three or four of these were more likely to acquire hepatitis than those who did one or two. Because eating sweets and biscuits and drinking coffee in the wards is common among hospital staff, another important prophylactic measure would be to discourage any habit that entailed touching the mouth such as eating, drinking, and smoking while on duty.

The sister and husband were primary not secondary cases because they developed hepatitis at about the same time as the nurses to whom they were related. Both nurses specifically denied ever taking food home, and neither relative ever visited the intensive care unit. Although not completely satisfactory, the most reasonable explanation seems to be some other form of faecal contamination. The nurse whose sister was infected left the intensive care unit for a short time in the middle of her shift to prepare dinner, which she shared with her sister. Probably she had not washed her hands adequately before leaving work and so contaminated their food with hepatitis virus. The nurse whose husband became ill was certain that she took cigarettes home. Because she often shared them with friends, her cigarettes may have been contaminated by her colleagues who took them from the pack without washing their hands properly after contact with patients.

Immunity to hepatitis A increases with age, is inversely proportional to social class and economic status, and is found in a high proportion of the residents of underdeveloped countries where hygiene is poor.²⁸ Unlike hepatitis B, it is not considered to be an occupational risk for doctors. The prevalence of anti-HAV among them was similar to that among volunteers donating blood for the first time in the general population, matched for social class and economic status.²⁹ The rate of immunity in the 267 employees screened in this outbreak (Table 1) followed these general trends. It was highest in older people and in those who were born outside the United States of America (Table 2). Although it is independent of race,²⁷ the confounding variables in this sample are that non-white employees tended to be from lower socioeconomic groups who were more likely to have been born in developing countries. The 19 staff nurses

and 10 paediatric house officers considered to be at greatest risk for hepatitis infection during this exposure were in the groups with the least immunity (Table 2). Data on risk and susceptibility are important for establishing priorities for immunoprophylaxis of staff following exposure to infection.

If the source of hepatitis and magnitude of the outbreak had initially been more clearly defined, fewer screening tests would have been needed. In a large group of employees it may be reasonable to concentrate control measures on those at high risk of infection. The most cost effective plan, therefore, may be to give prophylaxis with pooled gamma globulin to all high risk employees and omit the screening tests.

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