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Screening for transmission of hepatitis within a liver unit

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SUMMARY

Detailed screening of the patients and staff in a unit specializing in liver disease was carried out over a year to ascertain whether transmission of the serum hepatitis virus was occurring and whether the situation was comparable in any way to that found in a Renal Haemodialysis Unit. Of the 154 patients with liver disease tested on admission, 6% were found to have Australia antigen in the serum and throughout the year there were rarely less than two patients in the ward at any one time with positive serum. No instances of clinical hepatitis were detected in the other patients following their stay in the ward or in their attendant medical, nursing and lay staff. Six staff members were found to have Australia antigen in their serum. In four of these, all nurses, it was present in the first sample tested and so the infection may have been acquired earlier. Temporary elevations in both plasma bilirubin and serum aspartate aminotransferase levels were found in another five staff members whose serum was negative for Australia antigen and who clinically were well. In a further eight and apparently healthy staff members, an isolated but persistent elevation of the plasma bilirubin was noted. In both groups these changes could represent the spread of subclinical infectious hepatitis and it is recommended that in units dealing with 'liver patients' not only should considerable care be taken during diagnostic and therapeutic procedures but the medical and nursing staff should be screened at regular intervals.

INTRODUCTION

The outbreaks of hepatitis in renal haemodialysis units which have affected both staff and patients are currently the cause of considerable concern. In the majority of instances the cause has been serum hepatitis as shown by the finding of Australia antigen (Knight *et al.* 1970; Hawe, Goldsmith & Jones, 1971). Although the mode of entry into the unit has not always been clear, likely routes include blood transfusion and the admission of a patient who has had hepatitis previously and remained a carrier of virus. Spread within the unit subsequently is not surprising in view of the exposure to blood during haemodialysis procedures and shunt care. Furthermore, it has been shown that the serum hepatitis virus can be transmitted not only by the parenteral route but also orally (Giles, McCollum, Berndtson & Krugman, 1969) and possibly by droplet infection. The identification

of Australia antigen in faeces and in urine has also been reported (Apostolov *et al.* 1971). Much of the above, it seemed to us, would also apply to units in which patients with liver disease were cared for. A significant number of patients would be expected to have Australia antigen in their serum and the various procedures used in their treatment, for instance blood transfusion and the Sengstaken tube for bleeding varices, or exchange transfusion and extracorporeal pig liver perfusion in fulminant hepatic failure, all involve considerable exposure of both medical and nursing staff to the patients' blood. In order to ascertain the extent of the risk, for we could find no information in the literature, we decided for a 1-year period to screen all patients on admission as well as their attendant staff at regular intervals using both liver function tests and examination of serum for Australia antigen.

DETAILS OF SURVEY AND METHODS

The Liver Unit comprises a 22-bed ward of the old 'Nightingale' type partly partitioned to form cubicles containing three to six beds, one of them being immediately adjacent to the nursing station and used for patients requiring intensive care. The research laboratories and office accommodation are immediately adjacent to the patient area.

About two-thirds of the patients in the ward at any one time have liver disease, the remainder having general medical conditions. The aim was to test all patients both on admission and again on discharge, those staying in the ward for longer than a month also being tested at monthly intervals. All members of the staff including nurses, doctors, research fellows, students and the domestic and secretarial staff, all of whom had some contact with the patients, were screened at monthly intervals. Those visiting the ward only occasionally, such as radiographers and physiotherapists, were not included.

All blood samples were tested for Australia antigen and the associated antibody by the immunodiffusion technique. The sera from patients with fulminant hepatic failure were also examined for Australia antigen by complement fixation, immunoelectrophoresis and electron microscopy (Zuckerman, 1970). In the case of the staff, the liver function tests were also estimated in the same sample using the S.M.A. 12/60 Autoanalyser.

Precautions taken routinely when a patient with suspected or proven hepatitis was admitted to the ward and also for those patients found to be Australia antigen positive, included the use of disposable crockery and cutlery. When blood was taken or other clinical procedures carried out, gloves were always worn. The same precautions were taken for the patients with fulminant hepatic failure who in addition were barrier nursed in the intensive care area. Gamma globulin was not given to either staff or patients.

RESULTS

During the year, a total of 154 patients with liver disease and 108 patients with general medical conditions were tested on admission to the ward. These together represented nearly 80 % of the total admissions over this period and accounted for

278 and 135 blood samples respectively. Particularly in the general medical patients further samples were often not obtained owing to a variety of reasons. A considerable number were emergency admissions and died shortly afterwards or were transferred to the care of other physicians and surgeons. There was also an appreciable early mortality in the liver disease group.

Neither Australia antigen nor the antibody was found in the serum of any of the general medical patients either in the initial or subsequent samples. An outpatient follow-up study carried out 3 months after their discharge from hospital also failed to reveal a single instance of clinical hepatitis that could have been contracted whilst in the ward.

Nine (6%) of the 154 patients with liver disease had Australia antigen in the serum on admission (Table 1). These included two patients with a primary hepatoma which had developed from an underlying cirrhosis. The antigen was found consistently in their serum throughout their stay in the ward. Of the remainder four patients had presumed serum hepatitis with a history of parenteral inoculation, three of them being drug addicts. The fourth patient with serum hepatitis and Australia antigen was a nurse who had been working in the Renal Haemodialysis Unit at Guy's Hospital during the outbreak of hepatitis there. The admission of these nine patients with positive sera had been fairly evenly spread through the year. The average duration of stay was 20 days, though one patient with positive serum was in the ward for over 2 months. Two other patients with presumed serum hepatitis, one of whom had been tattooed recently, were negative for Australia antigen, as were all those with the clinical diagnosis of infectious hepatitis.

Fulminant hepatic failure

The nine patients admitted during the year were treated by a variety of procedures involving direct contact of the medical and nursing staff with the patients' blood. Intravenous catheters were used for nutrition and measurement of central venous pressure, extracorporeal pig-liver perfusion and cross-circulation were

Table 1. *Results of testing for Australia antigen in the* 154 *patients with liver disease*

Diagnosis	Number of patients tested	Number of patients with positive sera
Serum hepatitis	6	4
Infectious hepatitis	9	0
Fulminant hepatic failure	9	2
Active chronic hepatitis	16	1
Primary biliary cirrhosis	15	0
Haemochromatosis	16	0
Alcoholic cirrhosis	11	0
Cryptogenic cirrhosis	12	0
Primary hepatoma with underlying cirrhosis	16	2
Hepatic secondary deposits	12	0
Other liver conditions	32	0
Total	154	9 (6%)

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carried out once each, haemodialysis twice, exchange blood transfusion three times and in two cases a tracheostomy was performed. The cause of hepatic necrosis was paracetamol overdose in one patient and two cases had occurred shortly after a halothane anaesthesia. Of the remaining six patients one was known to associate with drug addicts. Australia antigen was found in her serum and in one other patient in whom no contact history could be elicited. In none of the cases could antibody to Australia antigen be detected.

Samples from the seven patients which were negative on immunodiffusion were also negative for Australia antigen when examined by complement fixation, immuno-electro-osmophoresis and electron microscopy. The sera were also examined for the Milan antigen by immunodiffusion using the specific anti-serum (Del Prete *et al.* 1970) but in no case was a positive reaction obtained.

Screening of staff

The 'turnover rate' amongst the nurses and medical students was high; few had more than two or three samples tested whereas most of the clinicians and research workers had at least six samples tested during the year (Table 2). No instance of a clinical illness compatible with acute hepatitis was encountered, but in five staff members serum was found to be positive for Australia antigen and in one other the antibody was detected. Four of these were nurses. One nurse was positive on the first occasion tested, subsequent samples being negative. The other three were Agency Nurses on temporary duty in the ward and each had only one sample examined. The fifth staff member with Australia antigen was a clinician, who was positive at the first testing and had two other positive samples over the subsequent 6 months. He was the only one with a history of infectious hepatitis in the past. This was 8 years previously and we could find no evidence of persisting hepatitis at the time he was on the ward. The one staff member with antibody to Australia antigen in the serum was also a clinician. He had positive serum on three occasions during the year, some of the intervening samples tested being negative. In none of these six people was the presence of Australia antigen or the antibody associated with any evidence of clinical illness and in each instance tests of liver function carried out at the same time gave normal results.

Table 2. *Results of serial screening in* 152 *members of staff*

	Clinicians	Medical students	Nurses	Lay staff
No. of subjects	33	32	66	21
No. of samples examined	225	79	140	86
No. of subjects with Australia antigen	1	0	4	0
No. of subjects with antibody	1	0	0	0
No. with raised plasma bilirubin and aspartate aminotransferase	1	3	0	0
No. with raised plasma bilirubin only	1	7	0	0

Abnormal liver function tests were, however, found in three students, one clinician and one secretary during the course of the year. In each instance the changes were slight with serum bilirubin levels of up to 1·4 mg./100 ml. and a serum aspartate aminotransferase (SGOT) of up to 125 mU/ml. The abnormalities were also temporary, the tests carried out on the sample taken a month later showing a return to normal values. A persistent elevation of the serum bilirubin was found in eight other staff members with levels of 1·8 to 3·2 mg./100 ml., the other liver function tests being within the normal range.

DISCUSSION

The frequency with which Australia antigen was found in the different varieties of liver disease admitted to the ward during the year is very similar to that reported in other series from this country, positive sera being found most frequently in cases of serum hepatitis and occasionally in active chronic hepatitis and primary hepatoma (Dudley, Fox & Sherlock, 1971). Both of the patients with primary hepatoma and an underlying cirrhosis could have contracted the infection abroad, for one was an immigrant from the West Indies whilst the other was known to have had serum hepatitis following a course of bismuth injections whilst in the Far East in 1943. We were surprised not to find more positive sera in the patients with fulminant hepatic failure due to a presumed viral hepatitis. Whether the severity of the hepatitis in such patients is a reflexion of a greater susceptibility of the patient or of greater virulence or dose of the infecting agent is not known, but Almeida & Waterson (1969) have suggested that Australia antigen may be present in the serum of these patients in the form of immune complexes. If so we should have been able to detect these on electron microscopy which was carried out in all of these patients.

Nevertheless, there was a substantial reservoir of patients with Australia antigen in the ward more or less consistently throughout the year. Though the extent to which the nursing and medical staff were directly exposed to the blood of patients is less in a Liver Unit than in a Renal Haemodialysis Unit there were certainly plenty of opportunities for transmission of infection to have occurred. In fact, there was no evidence of spread of Australia antigen from the liver patients to other patients in the ward. The four nurses found to have Australia antigen in their serum were all positive on their first testing and it is possible, therefore, that they had contracted the infection before coming to the ward. However, the one doctor with Australia antigen in the serum had been working on the ward for some time prior to the survey as had the other doctor whose serum was positive for the antibody. His first sample was negative so that it seems likely that both of these doctors had acquired the infection whilst working on the ward.

The temporary but simultaneous elevations of serum aspartate aminotransferase and serum bilirubin found in a number of the staff, but whose sera were negative for Australia antigen, are difficult to interpret. Such abnormalities in liver function could result from subclinical episodes of infectious hepatitis. More detailed investigation, such as by liver biopsy, which might have provided con-

clusive information, was not considered justifiable as the staff concerned were both free of symptoms and signs. The persistently raised serum bilirubin found in others of the staff could again be evidence of infection by hepatitis virus. An alternative explanation is that these subjects had Gilbert's Syndrome (mild congenital unconjugated hyperbilirubinaemia) but if so this would represent an unusually high incidence of that condition (Powell, Hemingway, Billing & Sherlock, 1967).

It must be stressed that although Australia antigen is identifiable with, or is at the very least a close marker of serum hepatitis, we have at the moment no specific test for infectious hepatitis and spread of the latter agent within the ward has not been excluded. The most recent studies on the Milan antigen, which was originally identified in three outbreaks of infectious hepatitis, have shown its presence in other liver diseases and its aetiological significance has been questioned by Taylor and her associates (1972). At the moment, therefore, it would seem only reasonable that in any ward where there is a significant number of 'liver patients' there should be a strict code of practice for dealing with blood samples and other aspects of their investigations and treatment. Patients should certainly be screened for Australia antigen on admission and the adoption of a policy for screening the staff at regular intervals has much to commend it.

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