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Hepatitis in dialysis units in the United Kingdom: a Public Health Laboratory Service Survey

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SUMMARY

A prospective study of hepatitis that began in 1968 and continues to include more than half the dialysis units in the United Kingdom shows that type B infection has been completely controlled in such units since the last outbreak ended in 1973. Though occasionally a single patient has developed hepatitis B surface antigenaemia in the course of dialysis or after transplantation, the infection has not spread to other patients or staff in the survey units.

A detailed analysis of the results in 1974–75 shows clustering of patients with raised aminotransferase levels in about one-fifth of the units but, unlike past outbreaks of hepatitis B, these clusters are not accompanied by clinical hepatitis among staff. The possibility that some of the clusters are caused by hepatitis viruses other than type A or B is discussed. It is concluded that, when reliable tests for type non-A non-B infections become available, the continued existence of the survey will allow prompt assessment of any viral hepatitis problems that may still exist in UK units.

INTRODUCTION

A prospective survey of the incidence of hepatitis in haemodialysis units began in 1968. In January 1970 it was combined with a hepatitis B prevention programme based on regular tests for hepatitis B surface antigen (HBsAg) on sera from patients and staff before entry and at regular intervals afterwards, dialysis in isolation of infected patients and appropriate cross-infection precautions. The study results showed a tenfold decrease in the incidence of hepatitis B among patients and staff from 1970 to 1973. The continued control of hepatitis B is reported here together with provisional assessments, based on routine aminotransferase (AT) tests of patients and staff, of the possible extent of type non-A, non-B hepatitis in the units.

Detailed analyses of incidence are restricted to the years 1974–75 because, although collaborating unit directors and virologists continued to report any clinical hepatitis or HBsAg positive test results, there has been since 1976 a gradual decrease in the number of units supplying the records needed to determine the denominators on which incidence rates are based: this tendency began after an encouraging report of successful control of outbreaks was published in 1976 (PHLS 1976).

Table 1. *Incidence of hepatitis B* in patients and staff of haemodialysis units in the U.K. in* 1970–1975

Person category	Year	No. of units surveyed	No. of people in unit during year (for ⩾ 1 week)	No. of person years in unit	No. of hepatitis B infections	Incidence rate per 100 persons	Incidence rate per 100 person years
Patients	1970	28	770	376	38	4·9	10·1
	1971	29	886	481	31	3·5	6·4
	1972	29	978	497	14	1·4	2·8
	1973	33	1034	458	3	0·3	0·7
	1974	33	1116	480	4†	0·4	0·8
	1975	34	1296	558	3‡	0·2	0·5
Staff	1970	28	1421	835	19	1·3	2·3
	1971	29	1456	961	11	0·8	1·1
	1972	29	1372	979	6	0·4	0·6
	1973	33	1355	940	1	0·1	0·1
	1974	33	1510	1045	0	0·0	0·0
	1975	34	1717	1227	0	0·0	0·0

* Clinical hepatitis B and symptomless HBs antigenaemia.
† One in each of four units.
‡ One in each of three units.

METHODS

These have been described elsewhere (Polakoff, Cossart & Tillett, 1972; PHLS 1974).

Definitions

HBsAg associated infections. Clinical hepatitis B or HBs antigenaemia arising in (*a*) a patient being dialysed in a unit or within six months of leaving a unit; (*b*) a member of staff working in a unit or within six months of leaving a unit.

Raised serum aminotransferase levels. Any aminotransferase level reported to be above the upper limit of normal according to the method and the limits of normal used at individual laboratories. Sub-groups of patients with aminotransferase levels more than two and a half times the upper limit of normal are described separately.

RESULTS

Incidence of HBsAg associated infections in survey units

The number of collaborating units was 33 in 1974 and 34 in 1975. The incidence of HBsAg among patients was 0·4% in 1974 and 0·2% in 1975. There were no clinical attacks of hepatitis among patients being dialysed or staff working in the units during the two years (Table 1). In 1974, HBsAg was detected in four patients, each in the care of a different unit. Two were HBsAg negative during dialysis treatment in the units: one developed acute hepatitis B five months after a transplant and the other – a patient from the Middle East – was found HBsAg positive two weeks after receiving a transplant from his sister, who had not been tested for HBsAg. It is unlikely that these patients acquired their infections in the dialysis units where no other hepatitis B virus (HBV) infections were found before

or afterwards. Another patient was a visitor from the USA, reported HBsAg negative but found HBsAg positive after a week of dialysis in the unit. The fourth patient was found HBsAg positive after one month of dialysis in the unit: his entry specimen, which was HBsAg negative by routine methods was found positive by electron microscopy restrospectively. The two patients who were HBsAg positive during the course of treatment in the units were isolated for further dialyses and there were no other HBsAg infections in the patients or staff.

In 1975, one patient in each of three units became HBsAg positive within two to four months of receiving transplants. There were no known sources in the units in which these patients had been treated and no other HBsAg infections were found there afterwards.

In 1976 and 1977 none of the patients and staff of the survey units became HBsAg positive.

In 1978, one unit had two patients who developed HBs antigenaemia but these infections were unrelated. The first patient was found HBsAg positive two months after she received a transplant; this patient had left the unit some months before the second patient began dialysis in the unit. HBsAg was detected in the serum of the second patient seven months after entry to the unit. She was transferred to hospital isolation, then to home dialysis and none of the other patients or staff was found HBsAg positive afterwards.

In 1979 and 1980 in eight units HBs antigenaemia developed in one patient being dialysed in the unit or within six months of leaving. The appropriate procedures were instituted in each unit and the infection did not spread to other patients or staff. Of the eight patients, five became HBsAg positive within a few weeks or months of beginning dialysis in the units. Four appeared to be new infections in the incubation period at the time of entry to the units. However one patient was a low titre HBsAg carrier on entry. The entry specimen was found to be positive retrospectively by electron microscopy though negative by routine haemaglutination tests and the patient was also HBe antibody positive. One patient became HBsAg positive three months after receiving a transplant; antibody to HB core antigen (anti-HBc) was present in his serum before operation which suggests reactivation rather than recent infection. The other two patients developed HBsAg long after entry to the units; they had had blood transfusions during the relevant time but investigation of the donors to one was reported to have excluded blood transfusion as the source of the infection.

Prevalence of HBsAg carriage in patients under care of the units

In 1975, 2757 patients were being maintained under the care of the 34 units, 1296 by dialysis in the units, 839 by dialysis at home (including two patients in hospital isolation) and the remaining 622 with transplanted kidneys (Table 2). Of the 2757 patients 21 were HBsAg carriers in 1975 and a further ten – not tested in 1975 – had been persistent carriers previously; if these ten are assumed to have continued carriage the prevalence rate of HBsAg among all the survey patients in 1975 was 1·1%. The differences in the HBsAg carrier rates between the three groups of patients resulted from the policies adopted to control and prevent hepatitis B outbreaks; also some carrier patients transferred to home dialysis became HBsAg negative eventually, whereas those who received transplants remained HBsAg positive.

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Table 2. *Prevalence in* 1975 *of HBsAg carriage among patients with chronic renal failure under care of survey units*

		Dialysis			
		In unit	At home*	Transplanted	Total
Number of patients		1296	839	622	2757
HBsAg carrier patients	No.	0	10 (12)	11 (19)	21 (31)
	%	0·0	1·2 (1·4)	1·8 (3·1)	0·8 (1·1)

Figures in brackets ( ) include two patients on home dialysis and eight with transplants who were previously HBsAg carriers but were not tested in 1975.

* Two patients in hospital isolation included.

Table 3. *Prevalence of aminotransferase (AT) levels above upper limits of normal in patients in survey units, years* 1973–1975

	No. units in survey with abnormal AT levels in > 2 patients			Patients in all units with abnormal AT levels			Patients in units with abnormal AT levels in > 2 patients with abnormal AT levels		
Year	Total	No.	%	Total	No.	%	Total	No.	%
1973	33	4	12·1	1034	45	4·4	169	36 (13)	21·3 (7·7)
1974	33	7	21·2	1116	57	5·1	362	48 (13)	13·3 (3·6)
1975	34	7	20·6	1296	55	4·2	390	52 (14)	13·3 (3·6)

In brackets ( ) number and percentage of patients with aminotransferase (AT) ⩾ 2½ upper limit of normal.

Other types of hepatitis

Though clusters of patients with AT levels above the upper limit of normal were previously reported from some of the units, it was not until 1973 that monthly routine AT test results of patients were reported regularly.

In 1973, four units had three or more patients with raised AT levels; in 1974 and 1975 there were seven units in this category (Table 3). One of these was a unit with an outbreak of hepatitis which began before 1968 (Eastwood *et al.* 1968) and which laboratory tests proved was not due to type A or type B infections (Galbraith *et al.* 1975). The four units reported in 1973 continued to have patients with abnormal results of AT tests in 1974, but among the seven units reported in 1974 two had no patients with raised AT levels in 1975. Over the three years, less than one-third of the abnormal AT levels reported were more than two and a half times the upper limits of normal.

Only a portion of the units reported results of regular three monthly AT tests of staff (Table 4). However the units in which there were patients with raised AT levels were well represented among those reporting. These were as follows, two of four in 1973, six of seven in 1974 and five of seven in 1975. Of the 11 units reporting in 1973 there was only one member of staff with clinically apparent non-B hepatitis. This individual did not work in a unit in which there were patients with abnormal AT levels. Of the 15 units reporting in 1974 there were eight staff with

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Table 4. *Units from which regular reports of aminotransferase (AT) tests of staff received: incidence of raised levels among staff*

Year	No. units	Staff category	Staff in all units: Total	Staff in all units: No. affected*	Staff in all units: %	Staff in units with abnormal AT* levels in > 2 patients: Total	Staff in units with abnormal AT* levels in > 2 patients: No. affected*	Staff in units with abnormal AT* levels in > 2 patients: %
1973	11	Doctors/Nurses	344	1	0·3	63	0	0·0
		Unit Technical & other Ancillary	188	0	0·0	47	0	0·0
1974	15	Doctors/Nurses	463	2	0·4	162	2	1·2
		Unit Technical & other Ancillary	278	6	2·2	105	6	5·7
1975	14	Doctors/Nurses	530	0	0·0	168	0	0·0
		Unit Technical & other Ancillary	284	0	0·0	81	0	0·0

* Defined as an aminotransferase (AT) level above upper limit of normal for the first time.

abnormal AT levels; all eight were in two of the units in which there were affected patients. None of the staff had more than slightly raised AT levels; all three in one unit had transient AT abnormalities in 1974, but among the five in the other unit slightly abnormal levels persisted in 1975. Of the eight with AT abnormalities only two were among medical and nursing staff. None of the staff in any of the 14 units reporting regular AT tests of staff in 1975 had newly raised AT levels.

DISCUSSION

The continued absence of hepatitis B infection from dialysis units in the UK since 1973 is rewarding for staff in the collaborating units and laboratories who have implemented the prevention programme energetically over the years. Evidence of success in a few other countries in which similar strategies have been adopted and the continued hepatitis B prevalence in many other units throughout the world (Wing *et al.* 1978) leave little doubt that the satisfactory outcome in the UK was due to the prevention programme.

A small outbreak that arose in a UK unit not included in the survey provides a salutary reminder that failure to observe a screening programme fully may quickly reverse the success achieved. In this unit a patient who had recently been dialysed in the Middle East was admitted for dialysis without the usual pre-entry screening. Other patients in the unit were screened regularly for HBsAg every fortnight, but it was six weeks before this patient was tested. He was then found to have high titre HBsAg and was HBe antigen positive; he was isolated immediately, but five out of the six non-immune patients dialysed at the same time and in the same room had already been infected and two of them became long-term HBsAg carriers. Prompt institution of the standard control measures prevented further spread. None of the staff was infected (PHLS CDR unpublished).

Though the screening programme combined with adequate cross-infection

precautions prevents outbreaks in the units, from time to time HBs antigenaemia must be expected to develop in a single patient because, even in a low incidence area such as the UK, HBV infection circulates in the general community in which patients live. HBV infection may well seem more common among unit patients than in the general population, as the patient with chronic renal failure tends to respond by developing persistent HBsAg, which is revealed by the next routine test, whereas the most common response in the general population is an inapparent infection, with transient HBs antigenaemia, which passes unnoticed. Another possible cause of HBs antigenaemia in a single patient is a previous blood transfusion from a donor, in the early incubation period of infection, in whose serum HBsAg is not yet detectable by the most sensitive tests. Such donors are believed to have caused some of the small number of post-transfusion hepatitis type B infections which were not prevented by routine HBsAg screening of blood donations (personal communication D. S. Dane). Among transplanted patients there are relatively more HBsAg carriers who almost invariably remain positive and highly infective if they are positive either at the time of transplant or afterwards. Some apparent acquisitions of HBsAg after transplantation are, probably, re-activations of infections in patients who have anti-HBc (Nagington, Cossart & Cohen, 1977). If this is so, it is reassuring that none of these anti-HBc positive patients transmitted the infection to other patients or staff during their dialysis treatment in the units before receiving their transplants. However, it should be kept in mind that HBsAg positive patients present a particular risk to staff during phlebotomy procedures, transplant operations and during rejection episodes. Acute hepatitis B has been reported in a member of a transplant team and in a nurse in an intensive care unit who tended an HBsAg positive patient during a rejection crisis (PHLS CDR unpublished). Neither of these two staff reported inoculation or contamination accidents for which specific immunoglobulin can be supplied promptly from Public Health Laboratories.

The production of vaccines in the USA found to be safe and effective among healthy adults (Szmuness *et al.* 1980) and reports of trials in units in France (Crosnier *et al.* 1981*a*; Crosnier *et al.* 1981*b*) suggests that vaccines should afford effective protection for patients and staff. Nevertheless, the study results show that even among healthy adults a small percentage failed to respond to vaccination and remained susceptible to HBV infections. Dialysis unit patients tended to fail to respond to the vaccines more often, particularly male patients and those of more than 50 years (Stevens *et al.* 1980; Crosnier *et al.* 1981*a*). In many countries with endemic HBV infection in dialysis units the use of HB vaccines should reduce the hazard to both patients and staff. In the UK, HB vaccines should be used as an additional precaution but, because of the tendency among dialysis unit patients to fail to respond to vaccination, the UK prevention programme which is at present completely effective should be maintained.

The extent, or indeed the existence, of a hepatitis non-A, non-B problem in dialysis units cannot be satisfactorily assessed until specific laboratory tests become available. Agents other than hepatitis viruses may cause clusters of patients to develop hepatic dysfunction e.g. drugs used in therapy (Simon *et al.* 1979), toxic components of equipment (Neergaard *et al.* 1971), viruses such as cytomegalovirus, EB virus. However, directors of the units or the virological

laboratories did not report identification of any causal agent among patients with raised AT levels. Whatever the cause or causes, there is an interesting difference between the epidemiological patterns of HBV outbreaks in the past and these clusters: clinical attacks were common among staff in units with HBV outbreaks but none of the staff in units with AT clusters had symptons of hepatitis and few had any AT abnormality. Furthermore, of the eight staff members with any evidence of hepatic dysfunction, six were ancillaries whereas during HBV outbreaks most of the the infections were among those most directly in contact with patients and their blood i.e. doctors and nurses. It is of course true that some transient AT abnormalities may have been missed because there were three-monthly intervals between tests of staff but there is no reason to believe that more should have been missed among one staff group than the other. If some of the clusters of affected patients are in fact caused by hepatitis viruses circulating in the units as HBV once did it is difficult to understand their failure to spread widely among staff. It is of course possible that personal precautions used by staff, such as gowns, gloves and masks, in addition to the general cross-infection precautions observed in the units, served to protect staff.

It is proposed to continue this collaborative survey which will provide the necessary framework for appropriate investigations as soon as tests become available to find out whether or not there is a hepatitis non-A, non-B problem in UK units and, if there is, to determine its nature and extent so that appropriate preventive action can be designed.

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