

MEDICAL PRACTICE

Hospital Topics

Decrease in the Incidence of Hepatitis in Dialysis Units associated with Prevention Programme**Public Health Laboratory Service Survey***British Medical Journal*, 1974, 4, 751-754**Summary**

A prospective survey of hepatitis in more than two-thirds of the dialysis units in the United Kingdom since January 1968 shows that after a prevention and control programme was started in 1970 the rising incidence of hepatitis B was halted. The programme has continued, with a sustained decline in the incidence among patients from 4.9% in 1970 to 1.4% in 1972 and among staff from 1.3% in 1970 to 0.4% in 1972.

Introduction

A prospective study of the incidence of hepatitis among patients and staff of most of the dialysis units in the United Kingdom has been in progress since January 1968. The results for the years 1968-70,¹ showed a threefold increase in the incidence of hepatitis from 1968 to 1969. Although the rates were still low—6.4% among patients and 1.6% among staff in 21 units—it seemed likely that the upward trend would continue unless some means of intervention could be found. In 1969 laboratory tests for hepatitis B antigen (HBsAg)—formerly known as Australia antigen—became available and a pilot study showed that most hepatitis in the units was hepatitis B. After the pilot survey attempts were made to control the existing outbreaks by testing sera from

patients and staff for HBsAg regularly, dialysing infected patients outside the unit, and improving cross-infection precautions.

Nevertheless, it was soon realized that available resources might be used more effectively and economically. So in January 1970, in 24 units without evidence of hepatitis B, a preventive programme was instituted: initially this included HBsAg tests of sera from all patients and staff continuing or beginning treatment or duty in the unit and afterwards at regular intervals, and the transfer of any infected patient to isolation for dialysis. HBsAg tests of blood for transfusion were by then available for all units.

In 1970 the rising incidence of hepatitis was halted and infection did not spread after five of seven occasions on which HBsAg was found in the serum of a patient in a unit in which there was no previous evidence of hepatitis B.

Method

The following changes were made in 1971-2: almost all blood for transfusion was being tested by the regional transfusion services; immune osmoelectrophoresis replaced gel diffusion tests as the routine screening method for HBsAg in most laboratories; and after the publication of the Advisory Group Report² in July 1972 the interval between regular screening tests for patients in most units was reduced from three months to one. We added an extra category—HBsAg-associated infection—and redefined "other" hepatitis:

HBsAg-associated infection: HBsAg detected in one or more samples of serum from any person, with or without other evidence of hepatitis, or clinical hepatitis in any person believed to have been infected in the course of an outbreak of hepatitis B.

"Other" hepatitis: Clinical hepatitis, if evidence of hepatitis B infection is not detected by laboratory tests, and possible hepatitis

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The collaborators in the study are listed in the appendix.

TABLE I—Number of Haemodialysis Units in Survey with some Evidence of Hepatitis During the Years 1971-2

Year	Number of Haemodialysis Units									
	In Survey	Hepatitis Outbreak				Sporadic Hepatitis		Total		
		HBaG Associated Began	Continued	Began	Other* Continued	HBaG Associated	Other	HBaG Associated	Other	All
1971	29	3	2	0	1	3	2	8	3	10†
1972	29	0	1	0	1	4	1	5	2	7

*For definition see text.

†A sporadic HBAG associated infection was reported from a unit with an outbreak of "other" hepatitis (Unit 5).

TABLE II—Incidence of Hepatitis in Patients and Staff of Haemodialysis Units during Years 1971-2 compared with 1970

Category	No. of Survey Units	Year	No. of Persons in Unit during Year	No. of Person Years in Unit	No. of Hepatitis Infections			Incidence Rate				
					HBAG Associated	Other	All	HBAG Associated		Other	All	
								Per 100 Persons	Per 100 Person Years		Per 100 Persons	Per 100 Person Years
Patients	28	1970	770	376	38	20	58	4.9	10.1	2.6	7.5	15.4
	29	1971	886	481	31	20	51	3.5	6.4	2.3	5.8	10.6
	29	1972	978	497	14	9	23	1.4	2.8	0.9	2.4	4.6
Staff	28	1970	1,421	835	19	2	21	1.3	2.3	0.1	1.5	2.5
	29	1971	1,456	961	11	1	12	0.8	1.1	0.1	0.8	1.2
	29	1972	1,372	979	6	1	7	0.4	0.6	0.1	0.5	0.7

—that is, abnormal results of liver function tests with or without symptoms such as anorexia, malaise, abdominal pain—affecting any person in a dialysis unit without an outbreak of hepatitis B.

Results

There were 43 dialysis units in the United Kingdom at the beginning of 1972,³ and 29 were included in the survey in both years. The outbreaks in the units in 1971 and 1972 are shown in table I. Blood and blood product transfusions, which had been reduced from an average of 7.6 units in 1968 and 1969 to 6.5 units per patient year in 1970, were further reduced to 3.1 and 2.7 units per patient year in 1971 and 1972 respectively.

Table II shows the incidence of hepatitis in patients and staff in 1971-2 compared with 1970. The 17 HBAG associated infections of staff during 1971-2 involved doctors and nurses; technical and other staff were completely unaffected. All but one of the 17 infections were acquired during outbreaks. As in 1970 the patients with "other" hepatitis were, with only one exception, reported from unit 5 in which patients had abnormal results of serum transaminase tests but little other evidence of hepatitis; some had consistently raised serum transaminases for long periods or repeated episodes.

In each year only one member of staff developed "other" hepatitis. Both were nurses with clinical hepatitis but no evidence of HBAG or any association with hepatitis in their units. There were no deaths among staff who developed hepatitis.

Twenty-eight of the 29 units collaborated in the survey in both years but the consultant in charge of unit 4 was unable to continue to return records in 1972. Nevertheless, another unit was included in 1972. Neither had an outbreak of hepatitis in 1972 and the substitution does not, therefore, materially affect the results.

UNITS WHERE HBAG APPEARED DURING 1971-2

HBAG was detected in one or more specimens from nine dialysis units during the two years. One unit—13—had two separate incidents.

Appearance of HBg not followed by Outbreak.—Seven of

the 10 incidents did not give rise to subsequent infections of patients or staff.

The relative insensitivity of the routine test method was involved only once (unit 17). Failure to have a specimen tested for HBAG before readmission led to an incident in unit 15. Another unit—16—was put at risk by a patient who developed hepatitis-B antigenaemia in the interval between admission and the first regular specimen. HBAG was introduced to unit 13 in 1972 by the re-admission of a home dialysis patient with hepatitis, thought to be obstructive jaundice, for two days before a specimen was sent for HBAG tests. In unit 11 HBAG was detected in a regular specimen from a patient who had regular dialysis and tests for HBAG in the unit for over two years but no blood transfusion in the year before HBAG was detected. Reexamination of earlier specimens by the most sensitive test methods available did not reveal HBAG. There was no known source of HBAG in the unit.

In each of two units—5 and 14—a patient with HBAG detected in an admission specimen was accepted for haemodialysis in isolation but the infection risk was, of course, restricted to staff who attended the isolated patients.

It appears from the records that four candidates whose sera contained HBAG were not accepted for maintenance dialysis. Nevertheless, this may be an underestimate; specimens for HBAG tests from many patients, including those with renal disease, are sent to the laboratories with routine request forms. HBAG carrier patients who later develop chronic renal failure might not appear in the survey records.

Appearance of HBAG followed by Outbreak.—In the two years outbreaks began in three units—4, 12, and 13. These were swiftly terminated and far fewer patients and staff were infected than in previous outbreaks.

The largest of the outbreaks began in 1971 in unit 4, where there had been an outbreak in 1969-70. HBAG was first detected in March 1971 in a regular specimen from a patient who had been dialysed in the unit for 15 months and who last received a blood transfusion in March 1970. Tests by sensitive methods of stored sera from this patient did not show HBAG. Subsequent tests of patients and staff of the unit showed HBAG in the serum of a nurse who had begun duty without having had a preliminary specimen taken. Subtyping showed, however, that the nurse's HBAG subtype was *ad* whereas the patient's was *ay*. During July-December 1971 nine other patients and a nurse in the unit developed HBAG infections; sera from eight were subtyped and all were *ay*. The outbreak ended in 1971 except for one nurse, who developed clinical hepatitis in May 1972. This outbreak was remarkably similar to the previous outbreak in the same unit: in both episodes 10 patients were infected but staff infection was rare. The most notable similarity was that HBAG cleared from patients'

sera relatively quickly compared with other outbreaks in which long-term HBAG carrier patients had been common and had presented a major problem in outbreak control.⁴

The next outbreak began in July 1971 in unit 12. The original source of infection was probably blood transfused to a patient before acceptance for maintenance haemodialysis. In the area served by unit 12 all blood for transfusion was not screened for HBAG at the time though screened blood was supplied for the unit. On admission in May 1971 the patient's serum did not contain HBAG but hepatitis B antigenaemia was discovered during routine testing in July; clinical hepatitis developed 60 days later. HBAG was detected in sera from three other patients in the unit two to three months later. The subtype of all four HBAG infections was *ad*. Isolation facilities were insufficient but emergency isolation accommodation—two prefabricated "homes on wheels"—were quickly erected beside the main unit and cross-infection precautions were intensified. There were no further infections. The events in unit 13 in 1971 constitute an outbreak by definition but in fact infection was not transmitted within the unit and only one patient and one doctor were infected.

OUTBREAKS CONTINUING IN 1971-2

The large outbreak in unit 2 that began in 1969 was not completely controlled by 1971. Patients beginning haemodialysis in a new unit were not infected but two patients, admitted to the original unit in 1970 before it was closed to new entrants, and four members of staff were infected in 1971. In 1972 only one person, a doctor, was newly infected.

The outbreak in unit 10 continued throughout 1971 and 1972. Unit 10 contributed more than half of the HBAG associated infections reported during this period. Control measures in this unit were reviewed in September 1972 and it was found that, because of an inadequate isolation area, there was a two way movement of patients and staff between the main unit and the isolation area. There was also opportunity for reintroduction of infection to the main unit with emergency admission of home dialysis and transplanted patients. Continued admission of new patients maintained the supply of susceptibles. Subsequently, adequate accommodation was made available and other appropriate measures were taken. The last HBAG associated infection reported from this unit appeared in the first half of 1973.

The outbreak in unit 5, in progress before the survey began in 1968, continued. This outbreak is unlike all others in the survey in that it is not associated with HBAG. The diagnosis of hepatitis is based mainly on abnormal results of serum transaminase tests, more than a third of the affected patients experienced repeated episodes of this illness, and from 1968-1972 only one member of staff developed hepatitis. All but one of the 29 "other" infections among patients in 1971-2 were reported from unit 5. Laboratory tests for hepatitis A, when available, should help to determine the cause of this outbreak.

Three persons, one associated with unit 2 and two with unit 10, though not patients or staff of the units, were reported to have developed clinical hepatitis with hepatitis B antigenaemia during the two years. They were a nurse in an outpatient clinic, a husband, and fiancé of long-term HBAG carrier patients on home dialysis.

Preliminary Information on Survey in 1973

Consultants in charge of five more units collaborated in the survey in 1973. An attempt has been made to estimate the prevalence of HB antigenaemia among all patients previously and currently treated in the units and to assess the incidence of hepatitis among home dialysis assistants and patients and staff of transplant units. Records are not yet complete but it appears that in 1973 the only remaining HBAG associated outbreak was brought under control and new out-

breaks did not arise. Thus it seems reasonable to assume that the analysis for 1973 will show a continued decline in the incidence of HBAG associated hepatitis.

Discussion

The prevention and control programme depends on regular laboratory tests to prevent the entry of HBAG to the units, and when this is not achieved, to detect any source of HBAG within the unit promptly and transfer an infected patient to dialysis in isolation. Good cross-infection precautions are needed because of the relative insensitivity of the regular laboratory test methods and the possibility of development of HB antigenaemia between regular tests. Isolation accommodation must also be available for dialysis.

The key to most problems of hepatitis B in dialysis units is the tendency of patients with chronic renal failure to respond to the infection by becoming long-term carriers of the causal agent whose infection can be detected by HBAG tests only. If these patients continue to be dialysed in the unit infection is likely to spread to other patients, some of whom in their turn will become long-term HBAG carriers. Thus, as the sources of infection within the unit increase, the risk of infection to staff increases and this risk extends to hospital staff outside the unit and home contacts of infected patients.

The programme is designed to keep the number of HBAG carrier patients on maintenance haemodialysis to a minimum and thus protect other patients, hospital staff, and home contacts of patients.

It was not feasible to include a control group in this study. Nevertheless, after initiating the prevention programme in 1970, the incidence of hepatitis B infection among patients and staff of the units declined progressively. Probably the association in time between the two events—the prevention and control programme and the reversal of the incidence trend—was one of cause and effect. Similar detailed surveys have not been reported from other countries so that direct comparisons are not possible. Nevertheless, there is evidence that a large pool of HBAG carrier patients is being created in the course of treatment in haemodialysis units in other countries. In European centres as a whole almost 1,000 patients developed HB antigenaemia in 1972.⁵ In the U.S.A., where HBAG carrier rates in the general population are similar to those in the U.K.,^{6,7} hepatitis B infection among patients and staff of dialysis units is common.⁸

The present results support previous findings that even substantial outbreaks of hepatitis B can be controlled. In one such outbreak new patients were not accepted from March 1970 until an extra unit was provided. Though two patients, who began dialysis in the original unit early in 1970 and who continued dialysis among HBAG carrier patients, became infected and five of the staff developed clinical hepatitis, patients treated in the new unit were not infected. In another outbreak infections continued to appear throughout the two years and it seemed that control measures that had been effective in other outbreaks had failed there. Nevertheless, several serious defects in the measures taken were found when the situation was reviewed in September 1972. The last HBAG associated infection appeared in 1973 some months after adequate isolation accommodation was made available and comprehensive control measures were applied.

In each of these outbreaks some long-term HBAG carrier patients were created and they remained sources of infection long after the outbreak in the unit was controlled. Human anti-HBAG immunoglobulin has recently become available, as part of a M.R.C. trial,⁹ to persons who suffer inoculation injuries, or contaminate cuts, abrasions, or the conjunctiva with material containing HBAG, or ingest it. The prophylactic value of anti-HBAG immunoglobulin used in this way is not yet established but results of preliminary studies^{10,11} are encouraging. At present there is so little hepatitis in dialysis units in the U.K. that routine prophylaxis for staff seems unnecessary. Repeated administration of anti-HBAG immunoglobulin may possibly prevent patients with chronic renal failure from acquiring the causal agent of hepatitis B and becoming carriers but, until there is clear evidence of its protective efficacy

for this vulnerable group, avoidance of the creation of a pool of HBAG carrier patients by preventing HBAG from entering and spreading in dialysis units should remain the principal means of protecting all those involved in maintenance dialysis and associated treatments. Prophylaxis with "specific" immunoglobulin, for those who sustain the injuries described above, should be used as a second line defence at present.

The results of regular HBAG tests showed that—apart from occasions when HBAG was found in the sera of candidates for treatment who were either not accepted or dialysed in isolation from the outset—there were eight instances of a unit at risk of an outbreak by the entry of HBAG. Surprisingly, in view of the relative insensitivity of the routine screening methods, there was only one instance in which it could be demonstrated by retrospective tests that a more sensitive method would have detected HBAG earlier. This incident did not lead to an outbreak. Nevertheless, the more sensitive haemagglutination methods are likely to be brought into general use for routine tests.

In two instances HBAG carriers, whose preliminary tests had been inadvertently omitted, started work in dialysis units. Both were later transferred to other duties and there were no sequelae in the units. There is no clear evidence of HBAG carrier staff members as sources of outbreaks in dialysis units in the U.K. and they may in fact present little hazard of infection to patients.

There were four instances of patients who may have developed HB antigenaemia as the result of blood or plasma transfusions: plasma given to one patient and blood given to two others had not been tested for HBAG. If the transfusions were the sources of these infections, HBAG tests by sensitive methods of all blood products should help to prevent similar episodes in the future. One patient who developed HB antigenaemia had received a transplant from a donor whose serum had not been tested for HBAG; the transplanted kidney was probably not the source of this infection but there is no doubt that serum from each transplant donor should be tested for HBAG.

Thus it seems that most of the introductions of HBAG to the units might have been prevented but two remain. Both were patients dialysed in their units for more than a year, neither had received a blood transfusion for a year, retrospective tests by sensitive methods including electron microscopy did not reveal HBAG, and no known source of HBAG was found in the two units. There are two possible explanations. Firstly, the patients could have been infected from sources outside the units. There is evidence that many patients with acute hepatitis B infections have no history of parenteral inoculation¹² and that infection may be acquired by intimate contact with HBAG carriers.¹³ The other possibility is that the patients' carrier state, existing either before entry to the unit or resulting from blood transfusions received a year before HBAG was detected, could not be detected by the most sensitive methods available. If this is the case it is reassuring that one of the patients did not cause any infection and the infections for which the other patient was the source did not appear for some months after HBAG was detectable in her serum. Probably when HBAG cannot be prevented from entering a unit the spread of infection can be prevented or limited if good cross infection precautions have been constantly maintained, frequent and regular HBAG tests of sera are made, and infected patients are promptly isolated. It has also been found possible to start HBAG carrier candidates on haemodialysis by training them in isolation in hospital for future dialysis at home.

The continuing decline in the incidence of hepatitis B infections makes treatment in haemodialysis units in the

United Kingdom safer for patients, staff, and home contacts. Probably the improvement has resulted from the application of the prevention and control measures and that, by carefully continuing the programme, the decline in the incidence of hepatitis B infections can be maintained.

We are grateful to the dialysis unit staff who completed the records and dispatched the specimens. We thank Mrs. J. Miller and other members of the staff of the Epidemiological Research Laboratory for helping with the coordination of the survey, and Dr. D. S. Dane for allowing us to quote subtyping results.

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