Hepatitis-associated-antigen-positive hepatitis in a tuberculosis unit

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SUMMARY An outbreak of hepatitis-associated-antigen-(HB Ag)-positive hepatitis in a hospital unit for the care of male patients with pulmonary tuberculosis is described. Sixty-four patients were studied of whom 37 were HB Ag positive. Hepatitis developed in at least 20 and was icteric in 11. The illness was mild, without fatality due to hepatitis and persistent jaundice did not occur. A carrier state developed in 15 of 24 HB Ag-positive patients followed up for more than six months and was unrelated to the presence or absence of initial hepatitis. Spread of HB Ag to domestic and medical staff occurred and following the discharge of the patients, household contacts became positive. Five, all wives of patients, developed jaundice. Faeces and sputum were HB Ag negative in seropositive cases. The origin of the outbreak remains undetected. The probability of non-parenteral transmission of HB Ag in this outbreak is discussed. Closure of the unit, isolation of HB Ag-positive cases with separate toilet and kitchen facilities, and discharge of patients when their respiratory condition allowed, resulted in prevention of further spread and eventually all patients were discharged from the unit.

Virus hepatitis is separated into two types on the basis of associated antigens and incubation period. Virus A hepatitis (acute infective, epidemic, IH MS-1) occurs in pinpoint epidemics, has a short incubation period (Krugman, Giles, and Hammond, 1967; Berg, Vellar, and Nesvoid, 1971; Ajdukiewicz, Fox, Dudley, Doniach, and Sherlock, 1972), and may be associated with Milan antigen HB Ag (Del Prete, Constantino, Doglia, Graziina, Ajdukiewicz, Dudley, Fox, and Sherlock, 1970; Ajdukiewicz *et al*, 1972). Virus B hepatitis (serum, SH, MS-2) follows parenteral infection, but also occurs in sporadic cases in adults, particularly in urban areas (Cossart and Varhman, 1970; Prince, Hargrove, Szmuness, Cherubin, Fontane, and Jeffries, 1970). The incubation period is longer (Krugman *et al*, 1967) and Australia antigen (HB Ag) is detected in the preicteric and early icteric phases. Anicteric forms of both types occur (Krugman *et al*, 1967).

Virus B hepatitis may be acquired by ingestion of serum (Krugman *et al*, 1967; Prince *et al*, 1970).

Other suggested non-parenteral modes of transmission include airborne spread with inhalation or ingestion of HB Ag (Almeida, Kulatilake, Mackay, Shackman, Chisholm, MacGregor, O'Donoghue, and Waterson, 1971) and venereal spread (Hersh, Melnick, Goyal, and Hollinger, 1971; Jeffries, James, Jefferiss, MacLeod, and Willcox, 1973). Prince (1971) reported that all patients in an institution for the mentally retarded became infected with HB Ag within one year of entering the hospital. He also found HB Ag in 10% of families of HB Ag carriers. Family spread and spread to close contacts of virus B subjects has been described by Mirick and Shank (1959), Blumberg, Melartin, Guinto, and Werner (1966), and Wright, Perkins, Bower, and Jerrome (1970). HB Ag has also been found in the saliva and semen of HB Ag-positive patients (Heathcoate, Cameron, and Dane, 1974).

Smooth muscle antibodies, although usually associated with chronic liver disease, have been noted in virus A and virus B hepatitis (Walker, Doniach, Willette, Cameron, and Dane, 1970; Ajdukiewicz *et al*, 1972). Antinuclear and antimitochondrial antibodies were not found in their patients.

The discovery of HB Ag-positive hepatitis in an

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Patient No. (Age yr)	Date of Admission to Unit	HB Ag Tests										Latest HB Ag Test	Start of Injections
		1971					1972						
		Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.			
01 (79)	28.8.61			-	-				-	-	- 21.5.73 Died July 1973	None	
02 (42)	2.6.70 (1966,67,69)	+	+								+ 20.9.71	S 1966, 1967, 1969	
03 (61)	2.9.70 (Unknown)	+	+								+ 17.8.73	Unknown	
04 (69)	9.3.71	+	+	+	-	-	+	-			- 6.12.72	S 12.3.71	
05 (60)	12.3.71		+	+	+						+ 8.11.71	S 12.3.71	
06 (66)	7.5.71			+	+		-		+		+ 3.3.72	S 8.5.71	
07 (70)	12.5.71 (1969)		+	+		+					Died Dec. 1971	S 10.2.69 14.11.69	
08 (57)	17.5.71			+	+						+ 20.10.73	S 18.5.71	
09 (16)	19.5.71		+	+	-	-					- 17.12.71	S 20.5.71	
10 (73)	21.5.71		+	+	-	-	-				- 17.8.73	S 21.5.71	
11	24.5.71		*	+				+			+ 9.3.72	S 24.5.71	
12 (75)	27.5.71		+	+							+ 2.10.73	S 27.5.71	
13 (55)	11.6.71			+		+					+ 20.10.73	S 2.6.71	
14 (32)	8.6.71			+	+	+	-	-	-		- 21.5.72	None	
15 (50)	12.6.71	*		-	+	+	+	+	+		+ 5.6.73	None	
16 (65)	14.6.71		+	+	+	-	+	-	+	+	- 7.8.73	14.6.71	
17 (54)	21.6.71	+	+	-	-	-					- 17.8.73	S	
18 (48)	24.6.71	-	-	*							- 17.8.73	None	
19 (51)	26.6.71	-	*								- 4.9.71	None	
20 (58)	30.6.71		+	*					-		- 17.8.73	S 30.6.71	
21 (63)	8.7.71		+								Died Nov 1971	S 30.6.71	
22 (27)	12.7.71		-	*		-					- 3.7.73	S 12.7.71	
23 (27)	19.7.71		-	-	+	+					+ 15.11.72	S 19.7.71	
24 (26)	3.8.71		-	*							- 9.10.71	S 5.8.71	
25 (30)	23.8.71		-	-	*					+	+ 5.4.72	S 24.8.71	
26 (58)	27.8.71		-	-*	+	H			-		- 17.8.73	S 28.8.71	
27 (60)	27.8.71	-	+	-	-	-	-			-	Died Jan 1973	S 28.8.71	
28 (52)	30.8.71		-	-	-	-		-	-		- 10.7.72	None	
29 (82)	30.8.71		-	-	+	+	+				+ Died Feb 1972	S 30.8.71 Blood 2.9.71	
30 (68)	30.8.71		-*	-	+						- 18.5.72	S 1.9.71	
31 (56)	6.9.71	+	*								+ 19.10.73	S 1970	
32 (70)	13.9.71	-	-	-	+	+		+	+		+ Died Jan 1973	S 13.9.71	
33 (64)	22.9.71	-	-	-	+	-	-	-	+	+	- 9.10.73	S	
34 (66)	1.10.71	-	-	-	+	+	+	+		+	+ Died June 1973	S 1.10.71	

Table I Details of patients admitted to the unit, dates of admissions, the dates on which HB Ag tests were done and on which hepatitis occurred are indicated together with the initial injections received by the patients

isolated unit for the therapy of tuberculosis provided an opportunity to examine the incidence of HB Ag hepatitis and anicteric hepatitis, the mode of transmission, the incubation period, the persistence of HB Ag, family spread of HB Ag, and the occurrence of autoantibodies in the infected patients.

Materials and Methods

Eight HB Ag-positive cases were detected from a total of 272 patients' sera submitted to the laboratory of the Regional Hospital, Galway, for routine biochemical investigations in August 1971. Six of the eight were patients in a 50-bed tuberculosis unit in

another hospital, while the remaining two (code nos. 02, 03, table I) were expatriants of that unit. Occasional cases of jaundice had been noted in the unit in the previous two years, and at the time of discovery of HB Ag-positive sera, three patients (codes 04, 10, 17, table I) were jaundiced, while the two expatriants (codes 02, 03) were jaundiced in another hospital. From 1 September 1971 all patients (aged 16-82 years; mean age 58) and staff of the unit had HB Ag, serum aspartate aminotransferase (SGOT) and serum bilirubin levels monitored at two-weekly intervals, where possible. All routine blood specimens sent to the laboratory from all other units in the hospital, including the female tuberculosis unit

Patient No. (Age yr)	Date of Admission to Unit	HB Ag Tests								Latest HB Ag Test	Start of Injections
		1971					1972				
		Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	
35 (63)	2.10.71		-H	+						- Died Dec 1971	S 12.7.71
36 (56)	5.10.71		-	*	-	-H	-			- 17.8.73	S 5.10.71
37 (79)	6.10.71		-*			-				- 17.8.73	S 8.10.71
38 (70)	11.10.71		-							- Died Nov 1971	S 12.10.71
39 (74)	12.10.71		-	-	-	-		-	-	- 21.8.72	None
40 (78)	18.10.71		-		*			-		- 17.8.73	S
41 (27)	19.10.71		-	-	-					- 17.1.72	S 19.10.71
42 (67)	26.10.71			-						- Died Dec 1971	S 28.10.71
43 (46)	28.10.71		-	-	-					Died Dec 1971	S 29.10.71
44 (53)	29.10.71 1969, 70			+	+	*		+H	+	+ 21.9.73	S 1969, 70, 71
45 (28)	29.10.71			-	-*	-		+		- 17.8.73	S 30.10.71
46 (58)	1.11.71			+	*	-		-		- 9.3.72	None
47 (57)	4.11.71			-*					+	+ 7.3.72	None
48 (59)	5.11.71			-	-*	-				- 17.8.73	S 16.11.71
49 (56)	11.11.71			-	-	-*				- 17.8.73	None
50 (76)	12.11.71			-	-*				+H	+	+ 14.12.72
51 (43)	12.11.71			-	-	-*				- 17.1.72	S 13.11.71
52 (78)	15.11.71			-	-	-	-	+	+H	+ 1.2.72	S 16.11.71
53 (70)	18.11.71			-	-	-	-	+	+	+ 26.2.74	S
54 (55)	18.11.71			-	-	-	-	+	+	+ 17.8.73	S 20.11.71
55 (65)	19.11.71			-	-	-	-*			- 17.8.73	S 20.11.71
56 (53)	20.11.71				-	-	-*	-		- 17.8.73	None
57 (74)	22.11.71				-	-*	-	-	-	- Died 1973	S 16.12.71
58 (50)	23.11.71				-	-	-*			- 16.10.72	None
59 (81)	25.11.71				-					Died	S 28.11.71
60 (40)	3.12.71					-	-	-*		6.1.72	
61 (58)	7.12.71				-		-	-		- 17.8.73	None
62 (54)	8.12.71									- 17.1.73	None
63 (45)	10.12.71				-*					- 16.12.71	None
64 (75)	16.12.71				-	-	-	-	H	+ 16.8.72	S 18.12.71

* Patient discharged from unit
+ or - indicates result of test for HB Ag
H = The occurrence of hepatitis either icteric or anicteric
S = Streptomycin
I = Iron injection

Table 1 Details of patients admitted to the unit, dates of admissions, the dates on which HB Ag tests were done and on which hepatitis occurred are indicated together with the initial injections received by the patients—continued

were screened for HB Ag during the period studied. Household contacts of discharged patients had HB Ag, SGOT, and bilirubin checked once after the patient's discharge from the unit in March and April 1972. Because of the large area of western Ireland in which the patients resided and the remoteness of their dwellings it was only possible to follow small numbers of the patients outside hospital. Domiciliary samples were collected by the authors, the family doctor, and the public health authorities of the appropriate areas. Liver biopsy was performed on one patient (no. 27) because his abnormal liver enzyme pattern was not suggestive of acute hepatitis.

Fifteen HB Ag-positive patients (code nos. 4, 6, 10,

15, 16, 17, 26, 27, 32, 33, 34, 35, 39, 48, 57) had anti-nuclear, smooth muscle, and antimitochochondrial antibody tests done at the time of HB Ag positivity. Faeces from 13 HB Ag-positive patients and sputum from 10 HB Ag-positive patients were examined for HB Ag.

The tuberculosis unit accepts male patients from the West of Ireland who have pulmonary tuberculosis proven or suspected. It is divided into four eight-bed wards, one seven-bed ward, one six-bed ward, and five single rooms. There is a corridor, sitting-room, and canteen shared by the ambulant patients. Toilet facilities are also shared by ambulant patients. Cutlery and tableware are interchangeable among patients after being washed in the unit's kitchen.

Laundry from the tuberculosis unit and from the other eight units of the hospital are dealt with by a central laundry in the grounds of the hospital. Shaving equipment and other personal toiletries were not shared at any time. All the patients have their own towels, and no others are provided. The water supply is that common to other units in the hospital.

The unit is staffed by doctors and nurses, a minority of whom have duties in other parts of the hospital. The domestic staff does not rotate to other units. There is a central x-ray department common to all units and this is visited by the ambulant patients when necessary. Disabled patients are radiographed with portable equipment. Blood specimens are sent to the Regional Hospital Laboratory. The patients receive visitors freely. The female tuberculosis unit is situated a quarter of a mile away in a separate building.

Techniques for phlebotomy and injections are similar. Disposable syringes and needles are used at all times and the patients do not have access to the used materials. Where streptomycin is used it is taken from a multiple-dose vial. All other parenteral drugs used are from single-dose ampoules. Most of the drugs used in the unit, eg, isoniazid, PAS, are given orally. All patients admitted have blood drawn for investigations within 24 hours of arrival at the unit. Erythrocyte sedimentation rates were not done in the unit after the outbreak was noticed. Parenteral drugs and the route of administration as well as the commencing date of therapy are noted in table I.

Criteria for diagnosis of hepatitis were those of Krugman *et al* (1967).

Serum from patients was frozen until tested, or was immediately screened for HB Ag by immuno-electro-osmophoresis. Samples were heated at 55°C for 15 minutes before testing. A Hepascreen HB Ag detection kit marketed by Becton Dickinson was used with agar plates containing pre-cut wells 3 mm in diameter with 5 mm centre-to-centre spacing. Antibody (human, 20 μ l) was placed in the anodal wells and 20 μ l of HB Ag or test serum in the cathodal wells. Oxid barbitone acetate buffer, pH 8.6, ionic strength 0.1, was placed in the electrophoretic chamber and a voltage of 200 volts was applied for two hours. Visible precipitin lines between the anodal and cathodal wells were indicative of the presence of HB Ag.

Faecal HB Ag was examined by the technique of Grob and Jemelka (1971). Faeces (1g) was thoroughly mixed with 3 ml of balanced Hart's solution containing 1 g of streptomycin, 1 g of chloramphenicol, and 2 million units of penicillin per 100 ml. The mixture was centrifuged at 3000 rpm for 15 minutes

and the supernatant tested for HB Ag. Sputum was tested directly unless it was too viscous, in which case it was thoroughly shaken with an equal volume of 0.9% saline, and the resulting solution tested. Total bilirubin, alkaline phosphatase, and aspartate aminotransferase were assayed in serum using the Technicon SMA 12/30 AutoAnalyzer.

Antinuclear, smooth muscle, and mitochondrial antibodies were detected by an immunofluorescent technique. Unfixed, 4 μ -thick cryostat sections of rat liver (for antinuclear antibodies), of mouse kidney (for mitochondrial antibodies), and of mouse stomach (for smooth muscle antibodies) were used. Sections were covered with the patient's serum for 30 minutes at room temperature, washed twice in phosphate-buffered saline (Difco Bacto FA buffer, pH 7.2) for 10 minutes. Specimens for antinuclear antibodies were partially dried and fixed for five minutes in ethanol and partially dried again. Sections were then covered with fluorescein-conjugated anti-human immunoglobulin serum (AHG horse origin fluorescein conjugate obtained from Roboz Surgical Instrument Co, Inc, Washington DC 2000E) for 30 minutes, washed in buffered saline as before, partially dried and mounted in buffered glycerol (Difco Bacto FA mounting fluid). Samples were examined microscopically using a Leitz microscope with ultra-violet source.

Results

Sixty-two patients who were in the unit in September 1971 or were subsequently admitted (until closure of the unit to new admissions in December 1971) were assessed, as well as two recent expatriates of the unit who presented at another hospital with jaundice (codes 02, 03, table I). By April 1972, 37 were HB Ag positive (codes in table I, 02 to 17 inclusive, 20, 21, 23, 25, 26, 27, 29 to 35 inclusive 44 to 47, 50, 52, 53, 54, and 64). Five of these (nos. 11, 15, 23, 25, 26) became HB Ag positive shortly after discharge from the unit. The outcome in all the patients is shown in table II. Two patients (nos. 36 and 61), who became jaundiced, were (HB Ag) negative when tested.

HB AG IN OTHER HOSPITAL UNITS

HB Ag was not detected in any other unit of the hospital. No cases of hepatitis were seen in the other units.

SPREAD OF HB AG TO STAFF

Four doctors, 13 nurses, five domestics, and one attendant were examined. One doctor and one nurse got hepatitis. Both had accidentally pricked themselves with needles used to take blood from HB Ag-positive patients. A barber who visited the unit

Patient Code	No. of Patients	Early Outcome (0-6 mth)	Late Outcome (6-24 mth)		HB Ag-negative Clinically Normal	Died during Study	Unknown
			Persistent Jaundice	Persistent Carriers Clinically Normal			
02,03,04, 05, 10, 15 17, 23, 26, 44, 50	11	Jaundice	0	5	4	0	2
06, 09, 16, 31, 33, 34, 35, 52, 64	9	Anicteric hepatitis	0	5	0	1	3
01, 07, 08, 11, 12, 20, 27, 29, 31, 45, 53, 54	12	No jaundice (possible anicteric hepatitis)	0	5	3	3	1
13, 14, 21, 25, 46, 47	6	Lost to follow-up	0	0	0	1	5
Total 38			0	15	7	5	11

Table II Early and late outcome in 38 HB Ag-positive cases

weekly was persistently negative. One laboratory technician who frequently handled blood from the unit presented at another hospital with HB Ag-positive hepatitis. One other nurse and one domestic were transiently HB Ag positive without evidence of hepatitis.

Patient No.	Relatives Tested	HB Ag	Jaundice
05	Brother (A)	+	No
	Brother (B)	-	No
	Wife of A	-	No
	Wife of B	-	No
10	Wife	-	No
14	Wife	-	Yes
15	Wife	-	No
17	Wife	+	Yes
	Lodger	-	No
19	Wife	-	Yes
Negative ¹	Son	-	No
	Son's wife	-	No
20	Wife	+	Yes
	Son	-	No
	Daughter	-	No
22	Father	+	No
Negative	Mother	+	No
	Wife	+	Yes
24	Mother	-	No
Negative	Father	-	No
	Brother	-	No
25	Brother	-	No
26	Wife	-	No
	Brother	-	No
36	Wife	-	No
Negative	Lodger	-	No
	Wife	-	No
40	Wife	-	No
Negative	Wife	-	No
	Wife	-	No
41	Wife	-	No
Negative	Wife	+	No
	Wife	-	No
45	Wife	-	No
46	Brother	-	No
	Brother's wife	-	No

Table III Spread of HB Ag to relatives of patients

¹Negative indicates patients who were HB Ag negative on all occasions on which the test was done.

SPREAD OF HB AG TO FAMILIES AND CLOSE CONTACTS OF PATIENTS

Thirty-one close contacts of 17 patients were examined for HB Ag, jaundice, and biochemical liver abnormalities in March and April 1972. Six of the 17 patients were HB Ag negative while they were in hospital (table III). Seven of the 31 contacts were HB Ag positive. Three of these were jaundiced. Two other relatives presented to another hospital with jaundice, but blood was not available at the optimum time for HB Ag testing. Relationships are shown in table III. It is noticeable that all relatives who became jaundiced are wives of patients. Spread to relatives could not be correlated with the presence or absence of the HB Ag carrier state in the contact patient (see tables III and IV). Wives became jaundiced on average 16 weeks after their husbands' discharge from the unit. It is interesting that the father and mother of one HB Ag-negative patient (case 22) were found to be HB Ag positive. Insensitivity of the method used for detecting HB Ag or inappropriate timing of the tests on this patient who was tested on two occasions only may account for this unexpected finding.

INCUBATION PERIODS

It was possible to measure the incubation period (time from admission to the units to onset of hepatitis) in 16 patients (code numbers 04, 05, 10, 15, 16, 17, 23, 26, 32, 33, 34, 36, 44, 50, 61, 64). This varied from 14 to 34 weeks, being 14 to 21 weeks in 14 of these. Measurement of the interval between admission to the unit and development of HB Ag positivity revealed a wide range, four to 26 weeks (14 patients—code numbers 11, 15, 23, 26, 27, 29, 30, 32, 33, 34, 35, 52, 53 and 64), and HB Ag positivity was

followed by hepatitis within 0 to 11 weeks (seven patients—codes 15, 23, 26, 32, 33, 34 and 64). Abnormal liver function tests preceded detection of HB Ag in two patients (code nos. 15, 35). Hepatitis and the first detection of HB Ag occurred simultaneously in two patients (code nos. 23, 64).

MORTALITY AND MORBIDITY

There was no mortality from hepatitis in the unit. No episodes of hepatic failure occurred in any patient. Patients who died during the study (see table II) had no clinical evidence of liver disease. No necropsies were performed because of the health risks involved.

PERSISTENCE OF HB AG

As of August 1973 it has been possible to follow 24 HB Ag-positive patients for a period exceeding six months (table IV). This shows a high frequency of HB Ag carriers in the patients studied. Persistence of HB Ag cannot be definitely related to the presence or absence of initial hepatitis, overt or biochemical. Some patients who were HB Ag positive and had subsequently been negative, developed positivity again (codes 04, 06, 16, 23). This may reflect the sensitivity of the techniques employed or alternatively reinfection with HB Ag. Patients 04 and 06 had been sent home HB Ag negative but subsequently became positive at home. Of 24 patients followed up for

more than six months, 15 are persistent carriers (nos. 03, 08, 12, 15, 16, 23, 31, 32, 33, 34, 44, 50, 52, 53, 54). No patients who remained positive for six months initially have become negative on further follow-up (table IV).

ANTIBODIES

Sixteen HB Ag-positive patients were examined for antinuclear, antimitochondrial, and antismooth muscle antibodies, before, during, and after hepatitis where possible. All antibody tests were negative in seven cases with jaundice (code nos. 4, 10, 15, 17, 26), in six with anicteric hepatitis (code nos. 6, 16, 32, 33, 34, 35, 37), and in three with no abnormality (code nos. 27, 39, 48).

HB AG IN FAECES AND SPUTUM

All tests for HB Ag in faeces and sputum were negative, although the serum was positive for HB Ag when faeces and sputum were collected.

Discussion

The occurrence of virus B hepatitis in long-term-stay institutions has been emphasized in recent years (Krugman and Giles, 1970; Prince, 1971), and is known in the general population in the area (Fitzgerald, Reynolds, Grimes, and McCarthy, 1973). It is clear that the outbreak of hepatitis is due to the

Patient	Follow Up (mth)	Duration of HB Ag Positivity (mth)	Hepatitis	Jaundice or HB Ag in Relatives
03	24	24	+	
04	16	4	+	
08	22	22	—	
10	23	2	+	
14	7	2	—	+
15	11	11	+	
16	20	19	+	
17	23	1	+	+
20	22	5	—	+
23	11	11	+	+
26	22	2	+	
27	8	1	(+) ¹	
30	6	5	—	
31	23	23	—	
32	11	11	+	
33	20	13	+	
34	18	18	+	
44	13	13	+	
45	17	1	—	
50	9	9	+	
52	11	11	+	
53	16	16	—	
54	17	17	—	
Also				
12	24	24	—	

Table IV HB Ag persistence in positive patients followed up for a period exceeding six months from initial HB Ag detection

¹Enzyme pattern not typical of hepatitis. Liver biopsy showed amyloidosis and alpha-1-antitrypsin deficiency changes.

presence of HB Ag in the unit, because of the known association between the two, the high number of cases of hepatitis in the HB Ag-positive patients compared with the HB Ag-negative patients, the absence of HB Ag and hepatitis in the female tuberculosis unit (where the patients receive the same chemotherapy), the temporal relationship between the patient's admission to the unit and his subsequent hepatitis, and the occurrence of HB Ag and jaundice in the patient's relatives at home following his discharge from the unit.

The exact mode of transmission of HB Ag cannot be defined. It is probable that several modes were operative in this outbreak. The infection of the doctor, the laboratory technician, and the two nurses can be assumed to be parenteral. Likewise, patients 29 and 44 may have originally been infected through previous blood transfusions. Most patients in the study had received streptomycin by intramuscular injection, and on assessment of this route as a possibility in transmission can be made from our data (table I). Thirty-one patients of 47 who received streptomycin injections became HB Ag positive as against five of 16 patients who did not receive streptomycin. HB Ag-positive patients nos. 14, 15, 46, 47, and 50 did not have streptomycin at any time (nor any other intramuscular or intravenous injection). Although multiple-dose vials of streptomycin were used, only sterile disposable needles and syringes were employed. No instance of HB Ag-positive hepatitis was found in the female tuberculosis unit of the same hospital, although similar injection techniques and streptomycin vials are employed. The parenteral route of transmission also fails to explain the occurrence of HB Ag in the domestic staff and the relatives of patients. Close contact of the patients appears to be important in transmission and this is borne out by the spread of HB Ag in the domestic staff and the relatives of patients. Close contact of the patients appears to be important in transmission and this is borne out by the spread of HB Ag to the patients' wives. The latter may, however, be due to sexual spread as suggested by Hersh *et al* (1971) and by Jeffries *et al* (1973). A high incidence of HB Ag carrier state in patients with tuberculosis or chronic bronchitis (Peters, Vesely, Kulich, and Dura, 1972) suggests either an easy portal of entry of HB Ag or an immunological abnormality leading to the carrier state, or both. The absence of HB Ag in faeces could suggest a route of non-parenteral transmission other than the gastrointestinal tract. It is possible that airborne spread, with entry of the virus through a damaged respiratory tract, may have occurred but this cannot be shown. There was no case of massive haemorrhage or of blood spillage in the unit in the previous year to

account for considerable aerial contamination, and the timing of such aerial contamination would not account for later infection of patients not yet admitted to the unit. Detailed efforts to relate spread to haircutting, shaving, laundry, lavatories, and water supply were not successful. The use of contaminated cutlery and kitchenware as a source of infection could not be ruled out. As urinary HB Ag was not examined, the possibility of this route contributing to infection cannot be commented upon. Sputum excretion of HB Ag was not found. HB Ag sub-determinants may be helpful as markers of the mode of transmission (Mosley, Edwards, Meihaus, and Redeker, 1972) and it is planned to study them in relation to this outbreak.

The origin of the outbreak is not clear. Staff in the unit have noted frequent cases of jaundice since 1969. From our data it can be seen that seven patients had previous admissions to the unit (code nos. 02, 07, 10, 31, 35, 44 and 61). Case 31 had HB Ag on admission to the unit and had previously been admitted in 1970, suggesting previous infection in the unit then. Case 02 had acute viral hepatitis in 1970, having been in the unit on several previous occasions. These pointers suggest that continuing HB Ag infection was present since 1969 or 1970. The extent of this may not have been evident as many of the patients would still be in the hepatitis incubation period on discharge from the unit, later developing jaundice at home.

Search for a long-term carrier of the infection in the unit was unrewarding. No member of the staff had persistent antigenaemia and the only long-term patient (code 01) was not found to be HB Ag positive. Incubation periods in the study of 14 to 34 weeks is longer than that of four to 15 weeks in the Willowbrook State School experiment (Krugman *et al*, 1967). However, the modes of transmission cannot be strictly compared.

The fact that we did not detect faecal HB Ag is in contrast to the findings of Grob and Jemelka (1971) who found faecal HB Ag in each of 11 patients with sporadic acute hepatitis.

Autoantibodies were found in none of the patients examined, in contrast to the findings of Walker *et al* (1970) and Ajdukiewicz *et al* (1972).

The high incidence of carriers of HB Ag for periods of more than six months is notable and confirms the findings of Peters *et al* (1972) in tuberculous patients. It is of interest that all 15 patients with HB Ag persisting for periods exceeding six months have remained carriers for the duration of follow up. The very high incidence of HB Ag positivity in the unit as opposed to that in the general population, combined with the high carrier state, suggests that the unit may be the main reservoir for HB Ag infection in the west of Ireland. The fact that there has been no

notable increase in HB Ag-positive hepatitis in this area recently and the small number of contacts infected is suggestive of low infectivity outside hospital. It is not yet possible to say what the incidence of chronic hepatitis will be among the patients studied.

The unit was closed to all new admissions in December 1971 and HB Ag-positive cases were kept in isolation from others. Nursing and kitchen facilities were divided between the two groups. By July 1973 the unit was empty. Before this HB Ag-negative cases of tuberculosis were being admitted to a new unit in the hospital grounds. No recent inpatient jaundice has occurred and only one patient, who was previously in the original unit, has been found positive in recent months. Since the study was completed a report from an oncology unit confirms the danger of spread to personnel in contact with HB Ag-positive patients (Wands, Walker, Davis, Waterbury, Owens, and Carpenter, 1974). The demonstration of HB Ag in the saliva of 76% patients with acute hepatitis and 86% of HB Ag carriers (Villarejos, Visoná, Gutiérrez, and Rodríguez, 1974) suggests that spread of infection is particularly likely to be brought about by droplet spread during coughing.

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