HAEMOPHILIA DIRECTORS HEPATITIS WORKING PARTY

HEPATITIS ASSOCIATED COMMERCIAL FACTOR VIII 1976

As a continuation of the study of Hemofil begun in 1974, it was decided to study the incidence of hepatitis after transfusions of Kryobulin in 1976 and to compare this with that due to Hemofil.

The methods used were the same as in the first Hemofil survey. Six batches of Hemofil were studied and transfusion records were available on 16 batches of Kryobulin. One out of 16 batches of Kryobulin and one of six batches of Hemofil were positive for HB_sAg when tested by Radioimmunoassay (RIA) by Dr. Dane at the Virus Laboratory, Middlesex Hospital. It is probable that this is a reflection of the introduction of the screening of donors by RIA by all commercial firms in 1975.

RESULTS

Returns were received from 24 Haemophilia Centres. There was epidemiological evidence that 2/6 batches of Hemofil and 2/16 batches of Kryobulin contained hepatitis B virus. Similarly, 4/6 batches of Hemofil and 3/17 batches of Kryobulin were associated with cases of Non-B hepatitis. Of 371 patients transfused with Hemofil in 1974-5, 111 received further transfusions in 1976. In addition 77 patients received Hemofil for the first time. A total of 101 patients were transfused with Kryobulin of whom 31 had previously received Hemofil in 1974-5.

HEPATITIS B

Table 1 summarises the cases of hepatitis detected so far. Two cases of hepatitis B occurred in patients previously known to have had transfusions of Hemofil in 1974. There were two asymptomatic cases not included in Table 1 which were detected by chance when they were found to have become HB_sAg positive. These patients received one and two bottles respectively of one batch of Hemofil in 1974, so they were probably not infected with Hepatitis B when transfused

with Hemofil. Studies at Alton show that of 14 patients susceptible before transfusion with Hemofil, 13 had hepatitis or seroconverted to Anti-HB_s positive, giving an attack rate of 92.8%. It is not possible to measure the effect of donor screening on the incidence of hepatitis B yet as more cases are needed to produce a significant result.

NON-B HEPATITIS

Cases of Hemofil associated Non-B hepatitis have continued to occur, all in patients receiving Hemofil for the first time. Evidence of specific protection conferred by a previous batch of Hemofil against contracting Non-B hepatitis is given in Table 2. With the exception of batch X, all 47 cases of hepatitis after transfusion of batches Q - W are in patients receiving Hemofil for the first time. The evidence relating to Hemofil associated Non-B hepatitis is the best we have so far that this is an infective agent which confers specific protection against re-exposure from further batches infected with the same agent, as is shown in Table 2. One case associated with batch X occurred in a patient who received 201 bottles from 7 batches, 6 of which were known to produce Non-B hepatitis in other patients. There was no other known source for his hepatitis, so that one explanation may be that a second agent is involved in transfusion associated Non-B hepatitis.

MULTIPLE ATTACKS OF HEPATITIS

Further evidence in favour of a second type of Non-B hepatitis is given in Table 3. Fourteen out of 512 patients in this survey have had multiple attacks of hepatitis; 11 had Hemofil associated Non-B + Hepatitis B; one had Lister associated Non-B hepatitis in 1973 at Alton followed by Hemofil associated Non-B in 1974. Two patients, one of whom also had Hemofil associated hepatitis B, had Hemofil associated Non-B hepatitis in 1974 followed by Kryobulin associated hepatitis in 1976, i.e. one patient had 3 attacks. This suggests that an attack of Hemofil associated Non-B hepatitis fails to protect against Kryobulin Non-B hepatitis, i.e. a second type of Non-B hepatitis is probably associated with Kryobulin transfusions, and possibly batch X of Hemofil (Table 2). Further

analysis of these data should be available shortly.

The incubation period of Kryobulin associated Non-B hepatitis has a range of 7-91 days whereas that for Hemofil is 8-60 (figure 1). Further information may be obtained during the next year when it is proposed to compare Hemofil and Kryobulin in the same way.

CONCLUSIONS

These results indicate that it is essential to continue these studies with the object of answering the following questions.

1) The effect of the RIA screening for HB_sAg of the plasma donations used to prepare plasma pools on the incidence of commercial Factor VIII hepatitis B

2) The number of types and incidence of Non-B hepatitis.

3) The incidence of sequelae after acute hepatitis. One of the first schemes to be put forward by the Hepatitis Working Party will be a project to follow up every case of hepatitis associated with commerci l Factor VIII which has been included in this survey. This will be put forward at the meeting of the Supra Regional Directors in the New Year.

Further projects proposed are as follows:

1) A study of hepatitis after NHS concentrate. Some Centres have already agreed to take part but anyone who is interested should contact me at the Public Health Laboratory, Withington Hospital, Manchester M20 8LR (Tel: 061-445-2416). It is hoped to start this project sometime in November or December, 1977.

2) A retrospective survey of the records of past years at Oxford to study the incidence of multiple attacks of hepatitis.

3) The compilation of a register of carriers of HB_sAg to be kept with the other patient data at Oxford so that this information is readily available. This might include a patient's E antigen status. Carriers who are E antigen posit are known to be far more effective transmitters of hepatitis B to contacts than E antibody positive carriers.

4) I also suggest that a collection of sera which are discarded after laboratory use be made, so that retrospective studies can be undertaken should tests for Non-B hepatitis become available. Storage facilities can be made available at the Public Health Laboratory, Manchester. This will not preclude any other interested persons making their own collections.

We are also interested in receiving faeces and urine from cases of Non-B hepatitis, if possible taken within one week of the onset of illness, to attempt isolation of possible infective agents. Specimen containers and packaging can be obtained if necessary from me at the Public Health Laboratory, Withington Hospital.

J. Craske.
22.9.77.

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TABLE 1

FACTOR VIII ASSOCIATED HEPATITIS 1973-6

YEAR	BRAND	TOTAL PATIENTS TRANSFUSED	HEPATITIS B	HEPATITIS NON-B
1973-5	HEMOFIL	371	30 (8.0)	48 (13.0)
	KRYOBULIN		NOT KNOWN	
1976	HEMOFIL	183	3 (1.6)	5 (2.7)*
	KRYOBULIN	101	6 (5.9)	8 (7.9)
1973-6 TOTAL TRANSFUSED		512		

2 CASES NON-B HEPATITIS EXCLUDED AS BRAND IMPLICATED DOUBTFUL

Figures in brackets indicate percentages.

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TABLE 2

FACTOR VIII - ASSOCIATED
NON-B HEPATITIS : PROTECTION CONFERRED
BY TRANSFUSION OF INFECTED BATCH

BATCH	TOTAL PATIENTS TRANSFUSED WITH BATCH	PATIENTS RECEIVING HEMOFIL FOR FIRST TIME WITH THIS BATCH	NON-B HEPATITIS PREVIOUS TRANSFUSION* NO	YES
P	30	30	NIL	NIL
Q	85	53	6 (11.3)	NIL
R	55	38	3 (7.8)	NIL
S	117	74	10 (13.5)	NIL
T	116	66	13 (19.6)	NIL
U	75	37	9 (23.6)	NIL
V	79	33	3 (9.0)	NIL
W	86	20	3 (15.0)	NIL
X	52	17	1	1 (2.0)
TOTAL		371	48	1

*PREVIOUS TRANSFUSION OF INFECTED BATCH OF HEMOFIL MORE THAN 60 DAYS BEFORE FIRST TRANSFUSION OF CURRENT BATCH.

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TABLE 3

MULTIPLE ATTACKS FACTOR VIII

ASSOCIATED HEPATITIS

HEPATITIS	NO. PATIENTS		TOTAL
	TWO ATTACKS	THREE ATTACKS	
HEMOFIL ASSOCIATED NON-B + HEPATITIS B	11		11
NHS FACTOR VIII NON-B + HEMOFIL NON-B	1		1
HEMOFIL NON-B + HEMOFIL HEPATITIS B + KRYOBULIN NON-B		1	1
HEMOFIL NON-B + KRYOBULIN NON-B	1		1
	13	1	14