MINUTES OF THE 14TH MEETING OF THE U.K. HAEMOPHILIA CENTRE DIRECTORS' HEPATITIS WORKING PARTY HELD AT THE OXFORD HAEMOPHILIA CENTRE ON FEBRUARY 6TH 1985

PRESENT: Dr. J. Craske, Chairman
Dr. Charles Rizza
Dr. Eric Preston
Miss Rosemary Spooner
Mrs. Mary Fletcher
Dr. Peter Kernoff
Dr. Joan M. Trowell
Dr. C. Ludlam
Dr. J. Smith representing Dr. Lane

Apologies for absence were received from Dr. Richard Lane and Professor H.C. Thomas.

1) Minutes of the previous meeting held on September 15th 1984 were approved.

2) Matters arising from the Minutes:

a & b) Introduction of Heat Treated factor VIII

The present position regarding supplies of heat reated factor VIII was reviewed. In April 1985 it was hoped to introduce NHS factor VIII heat treated by a dry heat process (68^{o}F 72 hrs) as it became available. Each Region would be given supplies according to the amount of plasma received at the Blood Products Laboratory at Elstree. Distribution would be via the Regional Transfusion Centres. The names and numbers of patients treated would be recorded. While no formal follow up was being carried out, it was hoped that Directors of Haemophilia Centres would be willing to supply case reports of any possible side effects or lack of efficacy of the product. The yield of VIIIc was slightly lower than previously thought. The range of factor VIII clotting activity fell from 230-240 units/ampoule to 165-185 units after heating.

High Purity Factor VIII (NHS factor VIII concentrate)

This product was under development and was a new product requiring a new product licence, and therefore, would have to undergo formal clinical trials, both for safety and efficacy.

This was a high yield product, containing about 10 times the specific factor VIII activity of previous products. The product was more heat stabile than previous products, and would withstand 72^{o}C for 24 hours without significant loss of activity. A formal trial of the product would start at some Haemophilia Centres in late March and would last for one year.

Other Heat Treated Factor VIII's Hepatitis Risk

In discussion it was reported that trials of heat treated prophylate (a 'wet' heat treated factor VIII) had so far produced no hepatitis after 5 months, and no sero-conversions to HTLV-3 positive. The Armour heat treated product had been associated with non-A, non-B hepatitis in 2 patients given the batch at one Haemophilia Centre. Two other cases were possibly related to a second batch. Experiments with dry heat treated factor VIII had shown minor abnormalities of ALT results after administration intravenously in chimpanzees.

Trials of a small pool heated factor VIII at Oxford had produced no hepatitis 3 months after being given to 3 patients who had received few products before. The pool size was 300 - 1,000 donors.

Dr. Craske said that it was important to encourage reports of hepatitis after use of heat treated factor VIII. It would give Directors the best indication as to whether there was any reduced risk of hepatitis after first exposure to heat treated factor VIII. Present evidence showed this to be unlikely.

c) Surveillance of chronic hepatitis B

This item was deferred until the next meeting. Dr. Craske said he had had no time to prepare plans.

3) HEPATITIS B VACCINE

Recent developments. There were no significant items to report.

4) ANY OTHER BUSINESS

Chronic non-A, non-B hepatitis. At the invitation of Dr. Craske, Dr. Preston presented the results of the Sheffield experience of the use of liver biopsy in the assessment of chronic liver disease in haemophilia. These have since been published (see

In all 43 biopsies had been carried out on 34 patients. The indications for biopsy in the first instance had been persistently raised transaminases for at least 6 months. The results of the first biopsies revealed histological changes compatible with 'chronic persistent hepatitis' in 21 patients; 'chronic active hepatitis' in 9 patients and cirrhosis in 4 patients. Ten patients had undergone a second biopsy 2 - 6 years after the first. The main indication had been persistently abnormal liver function tests. Of the 10, the second biopsy showed that only 2 had not shown progression of their liver disease.

The results of second biopsies were as follows:-

Biopsies

1st		2nd	
2 CPH	-	2 CPH	) Final features
1 CAH	-	1 CPH	) 3CPH/2CAH/5 cirrhosis
2 CPH	-	2 CAH	)
2 CPH	-	2cirrhosis	)
3 CAH	-	3cirrhosis	)

Two patients had died in liver failure. Both had been elderly. One patient had oesophageal varices and 2 patients spider naevi.
One patient in the group had Haemophilia B.

These results indicated that about 20% of haemophiliacs contracting non-A, non-B hepatitis were likely to contract chronic liver disease. It was also doubtful whether the conventional interpretation of chronic persistent hepatitis as a histological diagnosis was applicable to non-A, non-B hepatitis.

HTLV-3 Infection

It was reported that 8 out of 59 Haemophilia B patients treated with NHS factor IX concentrate had been found to be HTLV-3 antibody positive. The transfusion records of 5 of these patients had been reviewed, and no common batch of factor IX could be found. Dr. Ludlam said that in Edinburgh a batch of factor VIII had been associated with HTLV-3 antibody sero-conversion in 16/32 patients receiving the material. Factor IX prepared from the same pool of plasma had produced no sero-conversion in 8 recipients in four months after transfusion.

It was hoped that heat treated NHS factor IX would be available from June 1985.

DATE OF NEXT MEETING

September 11th 1985, 11-0a.m. at the Oxford Haemophilia Centre.

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31st August, 1985

Our ref JC/PH Your ref

Dr. C.R. Rizza,
Haemophilia Centre,,
Churchill Hospital,
Headington,
Oxford, OX3 7LJ

Dear Dr. Rizza,

Reference omitted from the Minutes of the U.K. Haemophilia Directors Hepatitis Working Party held on the 6th February, 1985, :

Page 2, Any Other Business: (see C.R.M. Hay, Preston, F.E., et al Lancet 1985, i, 1495 - 1497: Progresive liver disease in haemophilia; an understated problem?)

Kind regards,

Yours sincerely,

GRO-C

J. Craske
Consultant Virologist