Minutes of the 13th Meeting of the U.K. Haemophilia Centre Directors Hepatitis Working Party held at the Oxford Haemophilia Centre at 11.00 a.m. on September 15th 1984

Present: Dr. J. Craske - Chairman
Miss R. Spooner
Dr. P. Kernoff
Dr. J. Smith (representing Dr. Lane)
Blood Products Laboratory
Mrs. M. Fletcher
Dr. C. Ludlam
Dr. C. Rizza

1. Apologies for Absence were received from:

Dr. R. Lane
Dr. J. Trowell
Dr. H.C. Thomas
Dr. E. Preston

2. The Minutes of the 12th Meeting held on September 14th 1983 were approved.

3. Matters arising from the Minutes

a) Trials of heat treated factor VIII. The results of trials of heat treated commercial factor VIII were reviewed.

i) Dry heat. The Hemofil HT trial showed a 63% incidence of elevated transience in patients who had previously not received factor VIII concentrate. One patient had also had CMV infection, though it was not known if this was related to factor VIII treatment. The trial of the Armour heat treated product had been suspended by the Company after the occurrence of 2 cases of symptomatic short incubation, Non-A, non-B hepatitis in one Haemophilia Centre. The results so far suggested that 'dry' heat treatment of factor VIII has little effect (if any) on the incidence of Non-A, non-B hepatitis in first time treated patients.

Dr. Smith reviewed the progress of studies of small pool NHS factor VIII at Oxford. The plasma was obtained for plasma-

pherised donors who were carefully chosen and had regular liver function tests, and had previous clean records with respect to freedom from hepatitis in the recipients of their donations. The batches made from 1200 donors had been associated with mild anicteric Non-A, non-B hepatitis with incubation periods of 10-16 weeks in 4/10 recipients. Two batches of 300 donors had both been given to two patients, so far with no hepatitis in the recipients. There was a limit on the pool size as the small quantity of factor VIII produced with these batches was associated with a big rise in costs.

It was planned to produce 'dry' heated NHS factor VIII for use shortly.

ii) Wet heat. One commercial manufacturer was producing a 'wet' heat material where the final concentrate was heated before freeze-drying. Problems with heat treatment might arise from a reduced yield of factor VIII clotting activity, the production of neoantigens associated with denaturation of proteins, and especially with factor IX, with the activation of clotting activity in vivo. The Edinburgh PFL was investigating a 'wet' heat preparation of factor VIII and had produced a trial batch. One recipient had a reaction after receiving some of the material, but investigations were still proceeding. Trials of 2 'wet' heat preparations have been carried out in Germany, but the results have not yet been published. The lower yield of factor VIII clotting activity would make this very expensive.

4. Factor VIII and IX associated hepatitis

Tables summarising the reported cases in the years 1980-1983 were circulated. A paper showing the relationship of

hepatitis to the number of patients receiving different brands of concentrate was rejected on the grounds that the calculated incidence of hepatitis was unexpectedly low, and it was decided to check these findings by another method.

5. Chronic Hepatitis

The problems with the present report form were reviewed. The lack of a definition of chronic Non-A, non-B hepatitis, other than the histological appearances on liver biopsy in the absence of a specific laboratory test made it impossible to devise suitable criteria to form the basis of a report form. It was decided to recommend to the Haemophilia Centre Directors that the form should be discontinued. This question would be reviewed when more information was available.

Dr. Craske would consider proposals for collecting information about Hepatitis B carriers.

6. Oxford Hepatitis B vaccine study

Fourteen patients and 10 staff so far found to be susceptible to hepatitis B infection by antibody screening had received a course of 3 injections of Hep B Vax (Merck), dose 20 µg, at 0,1 and six months either subcutaneously (patients) or intramuscularly (staff) and had been followed up for 9 months.

The results showed no significant difference in immune response between the staff and patients. A satisfactory response was defined as sero-conversion to Anti-HB_S+ at any time during the 9 month follow-up to produce an antibody titre of $\geq$ 50 MIUS/ml. A satisfactory response was observed in 17 out of 24 subjects (71%). The main factor affecting the immune response was the age of the recipient. In subjects over 40

years of age or over a satisfactory response was observed in 6 out of 11 subjects (55%).

These results suggested that careful consideration should be given before the vaccine was used in persons over 40 years. If immunisation was carried out, follow-up at 6 and 9 months after the first dose of vaccine should be done to confirm the response to vaccine. The experience in renal dialysis units showed that the production of anti-HB_s in immunosuppressed patients were not always associated with immunity to hepatitis B.

7. Any Other Business

There was none.

8. Date of Next Meeting

February 6th at 11.00 a.m. at the Oxford Haemophilia Centre.

J. Craske
15.01.85