Minutes of the sixth meeting of the U.K. Haemophilia Centre Directors' Hepatitis Working Party, which was held at the Oxford Haemophilia Centre on Wednesday 20th February, 1980.

PRESENT:	Dr. J. Craske (Chairman) Miss R.J.D. Spooner Dr. Joan Trowell Dr. Susanta Ghosh	Oxford
	Dr. Peter Kernoff Dr. H.C. Thomas	Royal Free Hospital, London
	Dr. Howard Davies	Edinburgh - by invitation

1. Apologies for absence; none.

2. Minutes of previous meeting held at Oxford on Monday Auguat 8th, 1979 were approved.

Matters arising from the Minutes:-

(a) Hepatitis Surveillance. Dr. Craske said that the first report to the D.H.S.S. on the research project started in September 1978 had been submitted in October 1979. Copies had already been circulated to members of the Working Party. The aim was to analyse the cases of hepatitis reported to Oxford for the years 1977-79 inclusive. Preliminary analysis of the figures was available for 1977 and treatment returns for 1977 and 1978 were presented at the meeting. One surprising outcome had been that at least 33% of patients treated in 1977 and 1978 received only one product. Further analysis of the results for 1977 and 1978 would shortly be available. Dr. Craske had received a letter from the D.H.S.S. expressing satisfaction with the way the project was progressing.

It had been agreed at the Directors' annual meeting that hepatitis returns to Oxford should continue as at present after the end of the 3 year project subject to annual review.

Dr. Howard Thomas and Dr. Kernoff described a prospective study they had carried out on patients receiving concentrate for the first time. Eleven patients had been followed for periods of upto four years. All of these had evidence of chronic hepatitis as judged by persistently abnormal serum transaminases unrelated to hepatitis B. A few patients had undergone a liver biopsy and this showed changes ranging from acute hepatitis to chronic persistent hepatitis with some suggestion of early progression to chronic active hepatitis. Eight of these patients had had no overt evidence of acute hepatitis. Most of the Royal Free patients had received commercial concentrate.

Dr. Ghosh said that similar results had been seen at Oxford in patients receiving mainly NHS concentrate for the first time. It was agreed that more information was needed on the risk to patients of developing chronic non-A, non-B hepatitis by prospectively following patients first exposed to concentrate or other products, e.g., mild haemophiliacs undergoing non-emergency surgery. The value of other methods of treatment to cover operations needed reassessing.

Dr. Craske said it was hoped to publish a paper shortly on the significance of serological tests for hepatitis A and B in haemophiliacs.

(b) Study of hepatitis B in family contacts of haemophiliacs and mildly affected patients. Dr. Ghosh described preliminary results of the clinical assessment of 20 close relations of severe haemophiliacs on home treatment for evidence of past hepatitis B infection and abnormal liver function tests as an index of possible transmission of non-A, non-B hepatitis. Many of these relatives give treatment to the index patient in their own homes.

Of 20 relatives so far studied only one had abnormal transaminases. She was the mother of a haemophiliac, but was herself a carrier of the haemophilia gene, and had had transfusions of factor VIII in the past. Tests for hepatitis A antibody were being done as a control.

Dr. Kernoff said that a similar study was in progress at the Royal Free.

(c) Chronic Hepatitis (including agenda item 4)

i) As a result of the report of the experience at the Royal Free, a wide ranging discussion followed on the value of liver biopsy in assessing acute and chronic liver disease in haemophilia. Dr. Trowell said it was likely that they would consider biopsy on patients at Oxford with chronic liver disease with a view to improving their clinical management.

Dr. Thomas said that the Royal Free had received a letter from a similar unit in France suggesting an international collaborative project to obtain more information on the significance of findings of liver biopsy in haemophiliacs. It was agreed that a more valuable course would be to undertake a collaborative study between interested Haemophilia Centres in the U.K., using liver biopsy and clinical criteria. The aim would be to try and obtain epidemiological information about the risks of different forms of treatment to the patient and also the value of non-invasive techniques and other new tests of liver function e.g., the presence of procollagen peptides in serum. Further discussions were needed and Dr. Craske said he would be visiting Sheffield Haemophilia Centre to have discussions with Dr. Preston and his colleagues. It was suggested that the Edinburgh Centre should be included in this study. Dr. Davies agreed to suggest this to Dr. Ludlam.

ii) Natural History of Non-A, non-B Hepatitis

It was agreed that answers were needed on the following questions:-

1) The incidence of post transfusion hepatitis both overt and symptomless, especially non-A, non-B following first exposure to treatment with factor VIII and IX concentrates, particularly if there is any difference between different products. (Commercial, NHS concentrate and cryoprecipitate).

2) What is the chance that symptomless or overt non-A, non-B hepatitis may become chronic and lead to chronic active hepatitis or cirrhosis. This would include the natural history of the disease and whether re-exposure or immunosuppressive drugs such as steroids predisposed to recondescence of the disease.

3) Is there any risk of spread of non-A, non-N hepatitis to close household contacts or spouses of the affected patient?

It was important to obtain the answers to these questions as they will affect the management of patients requiring replacement therapy for the first time, particularly large pool concentrate to cover operations.

The answers to these questions may be obtained by:-

a) A study of the incidence of hepatitis A and B antibody and abnormal liver function tests in the families of haemophiliacs on home treatment.

b) Prospective studies of the incidence of hepatitis in haemophiliac patients coming to operation, with particular reference to the incidence of abnormal serum enzyme levels following acute hepatitis.

4. Collaborative Study of Chronic Hepatitis.

This was dealt with under item 3 (c)

5. Analysis of Data in the Computer File.

Jean Spooner said that she hoped to have estimation of the incidence of hepatitis related to different products in 1977 and 1978 by the next meeting. She showed tables detailing the proportion of patients who were treated with each product in these years and also the number receiving one product only. With some products this reached about 50% of the patients who received that product in a treatment year. It was also hoped to obtain an estimation of the attack rates for patients receiving concentrate for the first time in 1978.

6. Any other business.

Proposed Trial of Hepatitis B Vaccine in Haemophiliacs.

Dr. Craske reported that he had had a meeting with Dr. Reichle, Associate Medical Director in Europe of Merck, Sharp & Dohme, regarding the possibility of carrying out a trial of Hepatitis B vaccine in Brisith Haemophiliacs. Two groups of patients were thought suitable.

a) Newly diagnosed haemophiliacs.

b) Mild haemophiliacs who normally require little, if any treatment, about to undergo elective surgery. It had been agreed that further information would be obtained regarding the prevalence of Anti-HB_s in U.K. haemophiliacs, with particular reference to the proposed group of patients for this trial. It seemed likely that Dr. Reichle would attend a meeting of the Working Party in July to discuss this further when details of the preliminary trials in the U.S.A. would be available.

Date of Next Meeting.

To be arranged.

J. Craske.
Chairman