Minutes of the 10th Meeting of the U.K. HAEMOPHILIA CENTRE DIRECTORS HEPATITIS WORKING PARTY held at OWENS PARK, MANCHESTER UNIVERSITY ON SEPTEMBER 13th, 1982

Present:-

Dr. J. Craske (Chairman)

Dr. C.R. Rizza,
Oxford Haemophilia Centre.

Dr. P.B.A. Kernoff,
Royal Free Hospital, London.

Dr. C. Ludlam,
The Royal Infirmary, Edinburgh.

Dr. R. Lane,
Director, Blood Products Laboratory, Elstree.

Dr. F.E. Preston,
Hallamshire Hospital, Sheffield.

Miss R.J.D. Spooner,
Research Assistant, Oxford Haemophilia Centre.

By Invitation:

Dr. Terence Snape,
Blood Products Laboratory, Oxford.

Apologies for Absence were received from:-

Mrs. Mary Fletcher,
Oxford Haemophilia Centre.

Dr. Joan Trowell,
John Radcliffe Hospital, Oxford.

1. **The Minutes of the 9th Meeting of the Working Party held at Oxford on September 11th, 1981 were tabled by Dr. Craske.** He apologised for not being able to circulate these before the meeting, but this was due to a shortage of secretarial staff at the Manchester Public Health Laboratory. It was agreed that Working Party members would let Dr. Craske have any comments about the Minutes at a later date.

2. Matters Arising from the Minutes

a) Results of the four-year retrospective study 9/167

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Dr. Craske said that this was still being analysed. Approximately half the cases since 1974, had been reviewed and the data was now on the Oxford Computer files. The results would be available in about six months time.

b) Prospective study of factor VIII and factor IX associated hepatitis

Dr. Craske said that the application to the Medical Research Council had been refused owing to the Council's withdrawal from support of projects in the applied clinical research field. The DHSS had no longer any funds available owing to the reallocation of monies to the MRC, as a result of the Rothschild recommendations in 1981. Despite this a preliminary study with the help of funds from the Haemophilia Society had been carried out at Oxford. 32 patients had so far been enrolled and 28 of these had been followed for a period of at least six months. These were patients with mild coagulation defects who had had less than two transfusions of factor VIII or IX concentrate during the previous year. Nine out of nine patients treated with one batch of concentrate who had had no previous transfusions of factor VIII or IX developed non-A, non-B hepatitis with incubation periods of between 25 and 111 days. Some of these patients had received NHS factor VIII, one US commercial factor VIII and the last patient NHS factor IX.

The pool sizes of the batches of NHS concentrate administered varied from 1,436 to 2,504 plasma donations. This work implied that there was more than a 90% chance of contracting non-A, non-B hepatitis after first treatment with NHS or US commercial factor VIII concentrate. No cases of hepatitis B had so far occurred. Dr. Craske said that it was

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proposed to extend this project to other Centres to compare the attack rates of non-A, non-B hepatitis occurring after transfusion with different brands of factor VIII concentrate, and to prospectively follow-up patients with a view to determining the long-term sequelae. It was also hoped to collect suitable sera to develop tests similar to the marker test developed at the Royal Free Hospital which looked a possible candidate test for at least one sera type of non-A, non-B hepatitis. A project application would be made to Action for the Crippled Child to undertake this work.

Dr. Lane suggested that a prospective study such as that proposed would provide an opportunity of evaluating new brands of factor VIII or IX where attempts had been made to reduce the amount of virus contaminating the products by biophysical methods. This could easily be assessed if the higher attack rate observed in cases with no previous transfusion of concentrate was confirmed. He proposed that special batches of Oxford's factor VIII might be prepared from plasma obtained from a special approved donor panel which was used to prepare radioactively labelled fibrinogen for invivo studies in patients. There was also the "hepatitis reduced" brand of Hemofil, manufactured by Travenol Laboratories Limited. Biotest Laboratories in Germany had recently patented a method for the pasturisation of factor VIII and IX by heat in the presence of polysacharrides. The only way to evaluate the preparations for freedom from non-A, non-B hepatitis viruses was by chimpanzee inoculation, or in a prospective study in susceptible human subjects.

Dr. Kernoff said that he thought that the risk of contracting non-A, non-B hepatitis after transfusion with NHS

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factor IX concentrate might not be so high as that reported for factor VIII. He agreed to follow-up patients records at the Royal Free Hospital, London to see if further information was available.

Dr. Craske agreed to revise the prospective study protocol and to circulate it for Working Party Members comments. It will be open to any Haemophilia Centre Director to use this protocol when evaluating any of the new concentrate products. Directors would be invited to report the results in a standardised way to the Working Party and they would be asked to retain serial samples of each patient's serum so that a collection would be available to evaluate any new marker tests for non-A, non-B hepatitis viruses.

4. Hepatitis B Vaccine

Dr. Craske said that the Merck, Sharpe and Doehme vaccine had now been licenced for use in persons for pre-exposure immunisation by the intramuscular route. This was for persons above the age of six months. At present it was contraindicated in pregnancy. It was not yet licenced for subcutaneous injection and a comparison was under way at the Oxford Haemophilia Centre of the two routes of injection to see if the ingenicity of the vaccine by these two methods showed any difference. Any Director could prescribe the vaccine on a named patient basis in the normal way for unlicenced products if they wishedto use subcutaneous inoculation. Preliminary results suggested that the vaccine was equally immunogenic by either route.

Facilities for screening staff or patients for anti-HBs antibody were available at Manchester if other Centres found it difficult to arrange testing locally. It was essential

that anti-HBs should be measured by radioimmunoassay as other tests were not sufficiently sensitive. Categories of patients who would require vaccine were, the wives, girl-friends or consorts of patients and parents who administered concentrate to their children. Patients who would benefit from immunisation would be mildly affected haemophilia A and B and von Willebrand's disease patients and carriers of the haemophilia A and B genes. Preliminary evidence suggested that the vaccine was highly immunogenic in children below the age of one year.

5. Acquired Immune Deficiency Syndrome (AIDS)

Following discussions at the Annual General Meeting of the Haemophilia Centre Directors, it was agreed by the Working Party that as the AIDS Syndrome had similarities in its epidemiology to that of hepatitis B virus infection, enquiries would be made by members of the Working Party to ascertain the likelihood of transmission of the disease by blood or blood products. A further meeting of the Working Party would be held when more information became available.

6. Any Other Business

There was none.

7. Date of the Next Meeting

To be notified later.

J. Craske
8.1.83

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