MINUTES OF THE FOURTH MEETING OF THE U.K. HAEMOPHILIA CENTRE DIRECTORS' HEPATITIS WORKING PARTY WHICH WAS HELD AT THE OXFORD HAEMOPHILIA CENTRE ON MONDAY, JANUARY 29th, 1979.

PRESENT: Dr. J. Craske (Chairman) Manchester PHL
Dr. Howard Davies, Edinburgh
Miss R.J.D. Spooner, Oxford
Dr. D. Ellis, Lister Institute, Elstree, Herts
Dr. J. Trowell, Oxford
Dr. S. Ghosh, (Research Fellow in Hepatitis)
Oxford Haemophilia Centre

1. The Minutes of the last meeting, held on November 7th, 1978, were approved.

2. Matters arising from the Minutes

2c) Study of chronic liver disease in patients at Oxford and elsewhere.

The protocols for the study of serum bile acids as an index of chronic liver damage, and serum enzyme levels after transfusions of factor VIII were discussed. As a first step fasting bile acid levels will be performed on 15 - 20 Oxford patients over the next year. The study of serum enzyme levels after infusion of factor VIII will be combined with the first investigation. A similar number of patients will be studied at Edinburgh. The significance of serum bile acids was discussed. Dr. Davies said that there was not enough information about the test in healthy adults. Dr. Trowell said that she thought the results would be similar to the brom sulphthalein excretion test. It was agreed that it was worthwhile proceeding as it only involved one blood sample from the patient, and there was a small chance it might be useful in the investigation of chronic hepatitis in Haemophilia. The results of the fasting bile acid levels will be reviewed and selected patients will have a post-prandial serum bile acid test done according to page 2 of Dr. Percy Robb's protocol.

Other 'non-invasive' techniques which might help assess chronic liver disease in haemophiliacs was discussed. Dr. Trowell said that techniques such as the Emiscan could detect gross changes such as the shrunken liver found in the later stages of cirrhosis, but they were unlikely to detect early chronic liver disease reliably. Dr. Ghosh said the follow-up of haemophiliacs was proceeding well at Oxford. So far 25% of patients examined prove to have persistent transaminitis.

Chronic Hepatitis Form

Form H for the reporting of cases of possible chronic liver disease was discussed. It was thought that the present draft was too complicated. It was decided that in the first instance the aim will be to collect brief details of patients thought to have chronic liver disease, with the aim of conducting a more detailed survey later this year. Dr. Trowell agreed to revise the form to include information about clinical symptoms and signs, raised serum enzyme levels, and the results of hepatitis B serology. This will enable patients to be classified into broad groups as indicated in the chronic hepatitis protocol for patients at Oxford. This information will be

reviewed in six months time at the next meeting of the Working Party. A form aimed at gathering more detailed information will be prepared in the light of the preliminary information obtained. Individual Haemophilia Centre Directors will be approached with a view to collaborating in the survey.

Prospective Survey

Dr. Craske agreed to produce a report on this project showing the relations of serum enzyme levels to the current and past treatment, and to the results of serological tests for hepatitis B infection.

2f) Hepatitis Surveillance

The draft document "A working definition of factor VIII and IX associated hepatitis" was approved with minor modifications. Dr. Ellis thought a third category of factor VIII associated hepatitis might be necessary, but it was decided to leave the present classification and review this at a later date. Dr. Craske will send copies to Dr. Lane at the Lister Institute and Dr. Diane Walford at the Medicines Commission.

Dr. Ellis also asked the meeting's opinion as to whether a batch of factor VIII possibly implicated with cases of hepatitis B could be used to treat a patient who was known to be anti-HB_s positive. It was thought likely that this would not harm such a patient, since most patients regularly receiving treatment with freeze dried concentrates received transfusions of material which was infected with hepatitis B virus. The only observable effect was a boost in hepatitis B antibody. However, some workers in the U.S.A. (1) are of the view that repeated exposure to hepatitis B virus present in factor VIII may be a factor in the causation of chronic liver disease, despite the presence of anti-HB_s in a patient's serum. It was agreed that the Haemophilia Centre Director concerned would be consulted before the use of such material was made in response to a request from a Haemophilia Centre to the Lister Institute for a supply of factor VIII.

Revised forms C1 and C2 for reporting of cases of hepatitis

These were approved. The only modification suggested was that when new batches were ordered, a space for the separate recording of the results of past tests for hepatitis B and A might be helpful.

3. Proposed trial of Hepatitis B Vaccine

Dr. Craske said that trials of one vaccine were proceeding in the U.S.A. He would find out the results of these trials before the next meeting and the Working Party might then be in a position to make recommendations to the Haemophilia Centre Directors' regarding a vaccine trial.

4. Recent Hepatitis Research

Dr. Craske said that the susceptibility of the chimpanzee to non-A, non-B hepatitis had now been confirmed. Professor Zuckerman at the London School of Hygiene had produced non-A, non-B hepatitis in one of his chimpanzees twelve weeks after the inoculation of 1,000 units of commercial factor IX, which had

been implicated in an outbreak of non-B hepatitis at King's College Hospital. Dr. Craske is due to attend a meeting of the Medical Research Council ad hoc group on non-A, non-B hepatitis to discuss future developments and likely lines of research.

Dr. Craske said that small virus particles had been seen on the electron microscope in the faeces of further cases and contacts of patients with non-A, non-B hepatitis. One of these cases had been in a haemophiliac.

5. Any other business

None.

6. Date of next meeting

To be arranged in approximately six months' time.

Reference

1) Spero, J.A. et al (1978) New Eng. J. Med. 298, 1373-8.