0005

MINUTES OF THE ELEVENTH MEETING OF U.K. HAEMOPHILIA CENTRE DIRECTORS HELD IN GLASGOW ON THE 30th SEPTEMBER 1980

Chairman: Prof. A. Bloom

Apologies

Dr. S. Ardeman,
Edgware General Hospital, Middlesex.

Dr. A.M. Barlow,
The Royal Infirmary, Huddersfield.

Dr. A.J. Barrett,
Westminster Medical School, London.

Dr. T.W. Barrowcliffe (Factor VIII Assay Working Party),
NIBSC, Holly Hill, London.

Prof. A.J. Bellingham (represented by Dr. B.A. McVerry),
Royal Liverpool Hospital, Liverpool.

Dr. Ethel Bidwell (represented by Mr. T. Snape),
P.F.L., Oxford.

Prof. E.K. Blackburn,
Hallamshire Hospital, Sheffield.

Dr. J.M. Bridges (represented by Dr. Elizabeth Mayne),
Royal Victoria Hospital, Belfast.

Dr. D. Burman,
Royal Hospital for Sick Children, Bristol.

Dr. P.M. Chipping,
Hammersmith Hospital, London.

Dr. Morag Chisholm,
Royal South Hants Hospital, Southampton.

Mrs. M. Fearns (Home Treatment Working Party),
The Royal Victoria Infirmary, Newcastle-upon-Tyne.

Dr. P. Hamilton,
The Royal Victoria Infirmary, Newcastle-upon-Tyne.

Prof. R.M. Hardisty,
Hospital for Sick Children, London.

Dr. C.A. Holman (represented by Dr. Judith Kemp),
Lewisham Hospital, London.

Dr. J.F. Horley,
Royal Sussex County Hospital, Brighton.

Dr. R.M. Hutchinson,
The Royal Infirmary, Leicester.

Mr. T. Kirkwood (Factor VIII Assay Working Party),
NIBSC, Holly Hill, London.

Dr. R.S. Lane (represented by Dr. J. Smith),
BPL, Elstree.

Dr. J.R. Mann,
The Children's Hospital, Birmingham.

Dr. J. Martin,
Alder Hey Children's Hospital, Liverpool.

Dr. J.R.H. Pinkerton,
General Infirmary, Salisbury.

Dr. D. Samson,
Northwick Park Hospital, Harrow,

Dr. J.A. Shirley,
Frimley Park Hospital, Camberley.

Dr. H. Sterndale,
Isle of Thanet District Hospital, Margate.

Prof. J. Stuart (represented by Dr. F. Hill),
Queen Elizabeth Hospital, Birmingham.

Dr. H.T. Swan,
Hallamshire Hospital, Sheffield.

Dr. D.S. Thompson,
Luton and Dunstable Hospital, Luton.

Dr. Joan Trowell (Hepatitis Working Party),
John Radcliffe Hospital, Oxford.

Dr. G.R. Tudhope (represented by Dr. D. Shaw),
Ninewells Hospital, Dundee.

Prof. R.L. Turner (represented by Dr. D.R. Norfolk),
The Royal Infirmary, Bradford.

Dr. J.M. Webster,
Ashford Hospital, Middlesex.

Professor Bloom welcomed the Directors to the Meeting especially the new Directors who were attending a Haemophilia Centre Directors Meeting for the first time since taking up their appointments (Dr. C. Ludlam, Edinburgh; Dr. J. Kemp, Lewisham; and Dr. A.J. Barnett, Westminster Hospital). Professor Bloom also mentioned that two other recently appointed Directors were not able to be present. These were Dr. Janet Shirley of Frimley Park Hospital, Camberley, who had taken over on the retirement of Dr. Thomas, and Dr. P.M. Chipping of Hammersmith Hospital, who had succeeded Dr. Hilgard. Professor Bloom said that Professor Blackburn was unable to attend the meeting due to ill health and he was sure that all the Directors present at the meeting would wish to join him in

sending Professor Blackburn very best wishes for a speedy recovery.

2. Minutes of the last Meeting

The Minutes were approved and signed.

3. Matters Arising from the Minutes

One item, regarding the supplies of factor VIII, was raised by Professor Stewart and deferred until later on the Agenda.

4. Report on Meetings of Haemophilia Reference Centre Directors

Professor Bloom summarised some items which had been dealt with at recent meetings of Haemophilia Reference Centre Directors.

(a) Letter from the Haemophilia Society Regarding Prescriptions from General Practitioners for haemophiliacs to obtain supplies of Factor VIII Concentrate direct from local chemists.

This letter had been discussed in detail by the Reference Centre Directors and the Haemophilia Society had been informed that the Reference Centre Directors did not think that this was a good idea because it would mean that there was no control by the Haemophilia Centre of the materials supplied and used by the haemophiliac and also it would increase the cost of factor VIII if this practice became widespread.

(b) Dr. Poller's Quality Control Study

The Reference Centre Directors had discussed Dr. Poller's Quality Control Study and agreed that it was performing a very useful function particularly since it also involved hospitals which did not have a haemophilia centre. Dr. Poller's study

has disclosed a number of laboratories other than Haemophilia Centres which were undertaking factor VIII assays and the Reference Centre Directors thought that he should be encouraged to undertake this exercise from time to time. There was some discussion regarding Dr. Poller's studies and the question as to whether or not Dr. Poller should be invited to attend a meeting of Haemophilia Centre Directors was raised. Dr. O'Brien thought that the Haemophilia Centre Directors should have a report back from Dr. Poller regarding his study. There was some criticism of the way in which the results of Dr. Poller's study were reported. It was also noted that no standard was provided in these studies. It was generally agreed that Dr. Poller's study did not conflict with work being carried out at NIBSC or by the Directors Working Party on Factor VIII Assay, and it was agreed that Dr. Poller should be invited to the 1981 Annual Meeting of all Haemophilia Centre Directors to present a report on his study.

(c) Professor Bloom said that the rest of the business discussed at the Haemophilia Reference Centre Directors Meetings would be covered by the Agenda for the meeting.

5. Report on the 1979 Annual Returns from Haemophilia Centres

Dr. Rizza presented the report on the 1979 Annual Returns which had been pre-circulated.

Table 1 Dr. Rizza pointed out that the total amount of Factor VIII used annually at Haemophilia Centres had now reached 50 million units. Half of the material used was Commercial factor VIII concentrates. Dr. Prentice asked if a regional breakdown of the amount of materials used could be given. Miss Spooner said that a regional breakdown had previously been

prepared for Haemophilia Centre Reference Directors and could certainly be prepared again if it was the wish of the Directors. Professor Bloom thought that the publication of Regional usage would be a two-edged sword, some Regional Authorities would try to keep their Region to the lowest figures published. Dr. Rizza said that there appeared to be total inconsistency between the usage in various Regions. Professor Stewart said that there were difficulties about getting any material at all. Regional Health Authorities were reluctant to pay for Commercial materials and there was a high charge to foreign visitors to the U.K. for any cryoprecipitate used: about £3.50p per pack. Dr. Cash thought that £3.50p was a "give away" price. Professor Stewart said that he was worried about the increasing usage of Commercial factor VIII and he suggested that the Department of Health should look into the question of licensing a commercial firm or firms to make NHS material. Dr. Diana Walford said that the Department of Health at the moment, was actively discussing this question. She also said that there was a hope of increased supplies of factor VIII being available in the future as over 1 million pounds had been authorised by Ministers to improve the facilities of the BPL at Elstree. Dr. James Smith said that BPL's aim was to double their present output. Professor Bloom said that all the Directors were aware of the very severe short-fall in National Health concentrate which was a worrying situation. One of the Directors commented that he was not sure that the idea of a commercial firm taking over the manufacture of factor VIII would be a good idea because the situation might change with a change in the government. He thought that it would be better to recommend that the Department of Health look urgently into increasing the production of factor VIII concentrates in NHS

laboratories. Dr. Cash thought that there was no immediate solution to the problem and said that very considerable effort was being made by the Department of Health. The licensing of commercial firms was one of the things actively open to discussion. It was his opinion that commercial firms were not more competent than National Health Service fractionation laboratories. Professor Bloom proposed that the meeting should press the Department of Health to provide more factor VIII. It was agreed that a strong resolution should be sent from the meeting to the Department of Health that the Department view with grave concern the increasingly inadequate supplies of NHS factor VIII concentrate. Professor Stewart commented that Centres at present only bought commercially that amount of material which was required as a dire necessity by the Centre. This was the minimum need. It was not possible to assess optimum amounts which would be required but it must be much more than the present amount used. Dr. Cash thought that the Directors should put a figure to the Department of Health for the optimum amount of factor VIII that they would require in the future. Professor Bloom said that there were changing patterns of treatment. Dr. Aronstam said that a few years ago 50 million units was set as the target but even this amount of material was not available from NHS sources therefore what was the point in setting a new target if the original target had not been achieved. Dr. Willoughby said that from his experience of working with children it was clear that using factor VIII concentrates would give the possibility of non-crippled adults. How could one assess the cost of this? Dr. Swinburne pointed out that although the usage of factor VIII was increasing, some patients were still remaining undertreated. She thought that the

revised target should be for about one-third as much again as the present amount used. Dr. Mibashan pointed out that there had been three months' difficulty at the BPL which has caused many problems. He had been assured that the deficit of factor VIII supplies would be made up and he wondered if this was correct. Dr. Hill thought that until the Regions got back to a pro rata factor VIII for plasma supplied system, there would continue to be problems. Dr. Walford replied that she hoped that by April 1981 pro rata returns of factor VIII concentrate would be made to the Regions with a few exceptions in the case of Regions with extra responsibilities, such as Wessex where the Lord Mayor Treloar College was situated and which would receive an additional allocation of F.VIII above the pro rata entitlement. It would require a major effort to gear up the National Health Service to make 50 million units of concentrate even if an additional fractionation plant were available to go into production. Professor Bloom wondered whether the Haemophilia Centre Directors might like to give their own estimates of their requirements. Some Haemophilia Centres might be penalised by the short-falls in the plasma collected by the Blood Transfusion Service in their Region. Dr. Mayne enquired whether any way could be found of fractionating plasma collected from Northern Ireland. Dr. Walford said that this problem was being looked into. It was suggested that it would be useful to the Directors if the average amount of material used per patient could be divided into severity groupings, but Miss Spooner pointed out that this could only be done if the Haemophilia Centre Directors were willing to provide Oxford with more detailed breakdowns of the amount of materials used. It was agreed that a table showing the amount of material used in the Supraregions would be

provided for the Haemophilia Reference Centre Directors but would not be published widely.

Professor Stewart said that he would like to congratulate the Plasma Fractionation Laboratories on the good quality and adequate amounts of factor IX concentrate which were produced.

Table 3 - Materials used to treat Haemophilia A patients who had factor VIII antibodies. Professor Bloom pointed out the high cost of FEIBA and AUTOPLEX and that the increasing use of these materials would increase the cost of treatments. The results of a trial of FEIBA carried out in Holland would be reported at the Symposium. If Haemophilia Centre Directors in the U.K. increase their use of the FEIBA/AUTOPLEX-type materials following the publication of the Dutch report, the cost of treatment would be very high indeed. He suggested that if the experience in Holland shows that FEIBA was of benefit in the treatment of factor VIII inhibitor patients, that the U.K. Fractionation Laboratories might like to look into the possibility of making an NHS material of this type.

Table 5 - Dr. Rizza pointed out that there had been no change in the percentage of factor VIII and factor IX patients with antibodies over the last ten years.

Table 6 - Deaths. It was pointed out that half of the patients known to have died during 1979 were in the 60+ age group. Dr. Jones said that he felt it was very important that more details of mortality should be given. This was agreed and Directors were asked to send in as many details as possible regarding deaths in their patients and to send in also post-mortem reports where these were available. Dr. Rizza pointed out, however, that there were problems in obtaining post-mortem reports on haemophiliac patients because some Pathologists were

not keen to undertake post-mortems on haemophiliacs because of the possible risk of hepatitis.

Tables 7 and 8 - Age/Severity Groupings. There was some discussion regarding the Tables. A relatively small percentage of patients were in the under 10 age group and there was some speculation as to whether the reason for the low figure was that many patients under 10 years of age had not yet been to a Haemophilia Centre for diagnosis. It was pointed out that the numbers were still low even in the severely affected group who would almost certainly have attended hospital for treatment before reaching ten years of age.

Professor Bloom thanked Dr. Rizza and Miss Spooner for preparing the report.

6. Reports from Working Party Chairmen

(a) Hepatitis

Dr. Craske presented a short written report, outlining the findings of the Working Party during the last year, and described future plans of work to be undertaken by the Working Party. Various projects were progressing in Oxford, London and Sheffield. Liver biopsy studies were being undertaken at the Royal Free Hospital and at Sheffield, the preliminary results of these studies would be presented at the Symposium during the afternoon. No secondary cases of Non-A, Non-B hepatitis had been observed, but there had been a few cases of secondary hepatitis B. Hepatitis B vaccine was still unlicensed for use in the United Kingdom but was under trial in the United States. Use of immunoglobulin was being looked into by the Working Party and further information about this would be given at a later date. The Working Party planned to continue with the National

Surveillance for Hepatitis and symptomless cases of hepatitis were being studied in detail at the Royal Free and at Oxford. Large pool concentrates appeared to give a higher risk of hepatitis than small pooled concentrates and Dr. Craske felt that increased usage of small pooled concentrates would help to reduce the incidence of hepatitis in the haemophilic population. First-time exposure to large pooled factor VIII concentrate resulted in many cases of hepatitis, especially in von Willebrand's disease patients. Professor Bloom wondered whether cryoprecipitate would be a better product to use for mild haemophiliacs and von Willebrand's disease but pointed out that there was a problem over the amount of factor VIII in these materials. Dr. Creaske agreed and he said that the NHS product was certainly better than the Commercial products because of the screening of the blood donors and the regular donor panels which were used in the U.K. The screening procedures used for donors of plasma used to make Commercial factor VIII is radioimmunoassay but because of the unstable population and the poor social background, it is more likely that there will be a higher incidence of carriers of the hepatitis virus than in the U.K. volunteer blood donors.

(b) Home Treatment

Dr. Jones gave a verbal report outlining the work of the Home Treatment Working Party during the last year. The Working Party remained the same as in previous years but had received much co-operation from Dr. Aronstam and Mr. MacNay. The paper on the employment of the haemophiliacs had now been published (BMJ 1, 1169 (1980)) and a Manpower Services Commission booklet on the subject would shortly be available. The Home Treatment Working Party was planning to carry out a trial of prophylactic

therapy at Alton and at Newcastle. There were an increasing number of haemophiliacs on prophylactic therapy and four Haemophilia Centres had ten or more patients on prophylaxis. Dr. Jones outlined Newcastle's results. The average amount of material used for home therapy for haemophilic patients had remained the same in 1979 as in 1978 (i.e. approximately 23,500 units per patient) but there had been an increase in amount of cryoprecipitate used for home therapy. Most patients who were on home therapy were on low dosage, 250 or 500 units per dose. Dr. O'Brien asked if the cost effectiveness of prophylactic therapy could be looked into during the trial and Dr. Hill asked if active physiotherapy was also given to patients who were on prophylactic therapy. Dr. Jones agreed that physiotherapy was extremely vital to haemophilic patients on prophylactic therapy. The prizes which the Home Therapy Working Party had organized in conjunction with the Haemophilia Society had met with moderate success. Dr. Jones said that he would be grateful if Haemophilia Centre Directors would draw their patients attention to the availability of the prizes so that the patients could be encouraged to enter this scheme.

(c) Treatment of patients who have Factor VIII Antibodies

Dr. Prentice said that the Working Party remained the same, with the addition of Professor Bloom and Dr. Rizza. The Working Party had held one meeting in June when the possibility of a trial of FEIBA material had been discussed. The Dutch experience was being looked at by the Working Party. Dr. Prentice presented figures from the 1979 Annual Returns sent to Oxford. 119 Haemophilia A patients with factor VIII antibodies had been treated during 1979 in the U.K., 17 of these patients were on home therapy. 117 patients had been treated with Factor VIII

concentrates, 19 patients were treated with FEIBA and 6 patients were treated with other materials. Dr. Prentice thought that possibly the cost of FEIBA had influenced the Haemophilia Centre Directors against using this material. The present cost of Autoplex was 56p per unit. The results of recent trials using Prothrombin concentrates sounded impressive. The Working Party had received preliminary information regarding the Dutch trial in which 15 patients were treated with either FEIBA or a placebo. A report would be given by the Dutch group at the Symposium on the 1st October. A trial had recently started in the United States using these materials. The Working Party planned to meet again soon and would look into the possibility of organizing a U.K. trial of FEIBA or FEIBA-like materials. Dr. Colvin asked if any information was available regarding the patients with factor VIII antibodies who were on home therapy and wondered what the policy of Directors was. Dr. Rizza replied that all the factor VIII antibody patients treated in Oxford, were receiving treatment with factor VIII concentrates and some of them were put on home therapy. The patients selected for home therapy were usually those with less than 20 New Oxford units of inhibitor. 6 patients had lost their inhibitors while receiving regular factor VIII therapy. In Oxford approximately twice the amount of factor VIII was used for inhibitor patients as was used for non-inhibitor patients. There was further discussion regarding the treatment regimes adopted at Haemophilia Centres. Dr. Prentice concluded that there did not appear to be sufficient enthusiasm in the United Kingdom at present for a FEIBA versus Placebo trial to be carried out. It was suggested that the Directors should wait for results of the trial in the U.S.A. before proceeding with a U.K. trial.

(d) Factor VIII Assay Working Party

Dr. Rizza presented the report of the Working Party, the membership of which remained the same. The remit of the Working Party was to look into ways of improving the factor VIII clotting assays and standardisation. The results of the initial questionnaire concerning assay of factor VIII in the U.K. had been analysed and submitted for publication. The Working Party hoped to hold a workshop in Oxford sometime next year to study in more detail the assay of factor $VIII_C$. Haemophilia Centre Directors would be receiving information about the Workshop at a later date. Further work involving calibration of the 9th British Standard was underway. Dr. Barrowcliffe was looking into the question of an International Reference Plasma for factor $VIII_C$ and factor VIII R:ag and would report on this at the next Haemophilia Centre Directors Meeting.

(e) von Willebrand's disease

Dr. Tuddenham said that one of the main problems in the study of von Willebrand's disease was the need to define the criteria for diagnosis and the remit of the Working Party in the first instance was to clarify the situation. The Working Party were considering undertaking a new survey with the collaboration of Haemophilia Centre Directors and were actively discussing the proposal at the present time.

7. Provisional date and place for the next meeting of all Haemophilia Centre Directors

Professor Bloom suggested that the Haemophilia Centre Directors should let him have their suggestions regarding the venue for the next meeting of Haemophilia Centre Directors so that the possibilities could be considered by the Reference

Centre Directors at their next meeting, which would be held in February 1981.

8. A.O.B.

i) Hyland Low Potency Factor VIII Concentrate

Dr. Evans raised the question as to whether it was sensible to encourage the manufacture of the new low potency factor VIII concentrate, which was cheaper but not so "clean" as the other products. There was some discussion regarding the factor VIII content and the hepatitis risk with all concentrates and it was agreed that the new Hyland product was just as good as any other product for everyday use, even though the volume of the made-up dose was greater than with some other products. It was suggested that it might be useful if the usage of the two types of Hemofil were recorded in the Directors' Annual Returns but it was agreed that this was impracticable.

ii) Egg White

Dr. Walford said that it had been suggested to the DHSS that egg white preparation was very beneficial to haemophiliacs when taken either orally or intravenously. She asked if any Haemophilia Centre Directors would be willing to undertake a trial of an egg white preparation; no material was at present available so if a trial was to take place the material would have to be prepared. She suggested that any Director who was interested in the possibility of a trial of the product should speak to her after the meeting.

iii) HLA Types

Dr. Jones said that Dr. Hamilton was looking at HLA types and would like samples from other Centres, especially from patients with antibodies.

Professor Bloom thanked Dr. Charles Forbes for making the arrangements for the meeting. The meeting closed at 12.30 p.m. and was followed by a 1½-day Symposium entitled "Unresolved Problems in Haemophilia", organised by Dr. Charles Forbes and the Royal College of Physicians and Surgeons of Glasgow, and Sponsored by Travenol Laboratories Ltd. The Symposium proceedings will be published later in 1981.