Revised July 1975

Minutes of the Haemophilia Centre Directors Meeting held in Oxford on 1.11.74

Chairman: Professor E.K. Blackburn

Those present at the Meeting were:-

Dr. P.G. Arblaster
Treloar Haemophilia Centre, Alton.

Dr. E. Bidwell
Plasma Fractionation Laboratory, Oxford.

Dr. R. Biggs
Oxford.

Professor A.J. Bellingham
Liverpool.

Dr. T. Black
Liverpool.

Dr. T.E. Blecher,
Nottingham.

Dr. A.L. Bloom
Cardiff.

Dr. I. Burton
Bradford.

Dr. D.G. Chalmers
Cambridge.

Dr. I.L. Chrystie
St. Thomas's Hospital, London.

Dr. J. Craske
Poole Public Health Laboratory.

Dr. S.H. Davies
Edinburgh.

Dr. A.A. Dawson
Aberdeen.

Dr. I.W. Delamore
Manchester.

Dr. Helen Dodsworth
St. Mary's Hospital, London.

Dr. K.M. Dormandy
The Royal Free Hospital, London.

Dr. J.O.P. Edgcumbe
Exeter.

Dr. D.I.K. Evans
Manchester.

Dr. E.A. French
Nottingham.

Professor P. Flute
St. George's Hospital, London.

Dr. Jean Grant
Blood Transfusion Service, Oxford.

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Dr. F. Hill
Hospital for Sick Children, London.

Dr. C.A. Holman
Lewisham Hospital, London.

Dr. A. Inglis
Carlisle.

Dr. N. Islam
St. Thomas's Hospital, London.

Dr. G.C. Jenkins
The London Hospital, London.

Dr. P. Jones
Newcastle.

Dr. P.B.A. Kernoff
Leeds.

Dr. J. Leslie
Southampton.

Dr. M.L. Lewis
Kings College Hospital, London.

Dr. W. d'A Maycock
Blood Products Laboratory, Elstree.

Dr. J.D. McHardy
Lord Mayor Treloar College, Alton.

Dr. R.S. Mibashan
Hammersmith Hospital, London.

Dr. J.R. O'Brien
Portsmouth.

Dr. C.R.M. Prentice
Glasgow.

Mr. K. Polton
Haemophilia Society, London.

Mr. J.L. Prothero
Haemophilia Society, London.

Dr. S.G. Rainsford
Lord Mayor Treloar College, Alton.

Dr. J.D.M. Richards
University College Hospital, London.

Dr. C.R. Rizza
Oxford.

Dr. G.L. Scott
Bristol.

Dr. D. Stern
Bournemouth.

Professor J.W. Stewart
Middlesex Hospital, London.

Dr. J. Stuart
Birmingham.

Dr. L.M. Swinburne
Leeds.

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Dr. G.R. Tudhope
Dundee.

Dr. Sheila Waiter
DHSS, London.

Dr. J.G. Watt
Protein Fractionation Laboratory, Edinburgh.

Dr. D. Whitmore
Lewisham Hospital, London.

Dr. D.A. Winfield
Derby.

Dr. A.J.J. Wood
Dundee.

Apologies for absence were received from:-

Dr. A. Aronstam
Treloar Haemophilia Centre, Alton.

Dr. P. Barkhan
Guy's Hospital, London.

Dr. I. Cook
Inverness.

Professor W.M. Davidson
(Represented by Dr. M.L. Lewis)
King's Hospital, London.

Professor R.H. Girdwood
(Represented by Dr. S.H. Davies)
Edinburgh.

Dr. R.J. Guyer
Sheffield.

Professor R.M. Hardisty
(Represented by Dr. F. Hill)
Hospital for Sick Children, London.

Professor F.G.J. Hayhoe
(Represented by Dr. D.G. Chalmers)
Cambridge.

Professor G.I.C. Ingram
(Represented by Drs. Chrystie and Islam)
St. Thomas's Hospital, London.

Dr. M.J. Meynell
Birmingham.

Professor P.L. Mollison
(Represented by Dr. Helen Dodsworth)
St. Mary's Hospital, London.

Professor M.G. Nelson
Belfast.

Professor T.A.J. Prankerd
(Represented by Dr. J.D.M. Richards)
University College Hospital, London.

Dr. H. Sterndale
Margate.

Dr. G.R. Tudhope, Dundee
(Represented by Dr. A.J.J. Wood)

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Dr. H.T. Swan
Sheffield.

Dr. R.L. Turner
(Represented by Dr. I. Burton)
Bradford.

Professor Blackburn opened the meeting by thanking Drs. Biggs and Grant for arranging the meeting and making the facilities available. He welcomed those present, in particular Dr. D.A. Winfield (newly appointed Director of Derby Centre), Mr. Prothero and Mr. Polton (representing the Haemophilia Society), and the representatives of Directors of Centres unable to attend.

Professor Blackburn also mentioned with regret Dr. Bowley's death NOT RELEVANT shortly after the January meeting and the Directors paid their respects to his memory.

Minutes of the January 1974 Meeting were approved.

MATTERS ARISING FROM THE MINUTES

(a) Progress of the Directors study of Jaundice and Factor VIII antibodies

Dr. Biggs presented the results for 1973 in the form of four tables which compared the 1973 results with those of previous years (Agenda Appendix 3a). The first showed patients treated and material used to treat them. The second table concerned the types of materials used. The third table showed the cumulated number of patients having factor VIII antibodies in relation to the total number of patients treated at the Centres during 1969-73. In reply to Professor Stewart, Dr. Biggs said that any patient who had ever had an antibody at anytime was included regardless of whether or not the antibody had ever disappeared from that patient's plasma. The fourth table showed the incidence of jaundice in terms of episodes of jaundice per patient treatment year.

ACTIONS

1. Dr. Biggs pointed out that rather a large number of Directors had made no returns for 1973. She asked for returns to be made as soon as possible.

2. Dr. Biggs suggested that the results for the years, 1972, 1973 and 1974 should be published as a follow-up report to the first report published in the British Journal of Haematology. It was agreed that this should be done.

(b) Report on Jaundice following treatment with commercial Factor VIII

Dr. J. Craske of the Public Health Laboratory, Poole General Hospital, made a report on an epidemic of Hepatitis A and B in the haemophilic patients in Bournemouth who had received one particular batch of commercial factor VIII. 6 patients had hepatitis A and 3 hepatitis B. Dr. Craske said that his report was (as far as he knew) the first record of hepatitis A being transmitted to a group of patients by one batch of therapeutic material. Dr. Craske pointed out that hepatitis A can be prevented by giving gamma globulin.

Dr. C. Rizza said that since January 1974 there had been 11 episodes of hepatitis in Oxford patients. 9 of these patients had received commercial concentrates but all of them had also had NHS concentrate and it was not easy to identify the material which had caused the jaundice. Neither was it easy to determine the incubation periods.

There was a discussion contributed to by Professor Stewart and Drs. Mibashan, Rainsford, Prentice and Biggs about the problems arising from the use of therapeutic materials which might be contaminated with various hepatitis viruses. Prof. Stewart said that he thought material identified as

containing hepatitis B antigen need not be withdrawn from use since this material could be given to patients known to have hepatitis B antibody or to have had hepatitis. Dr. Rainsford said that a report on cases treated at Alton would shortly be published. Dr. Prentice said that he was making lymphocyte transformation studies which suggested that most severely affected patients had not been exposed to antigen. Dr. Rainsford asked if any concentrate preparations had been tested for hepatitis antibody and Dr. Craske said that he thought not. Dr. Biggs said that it was not yet proved that the commercial factor VIII was much more dangerous from the point of view of causing hepatitis than other preparations and that she hoped that this material would not get an unnecessarily bad name. It was in fact clinically invaluable while the NHS supply was so limited. Dr. Craske agreed with this but said that he felt that a wholly NHS Concentrate was likely to be safer when that was available.

ACTION

Dr. Craske undertook to draw up a plan to study the incidence of various types of hepatitis at different Centres and the relationship of infection to the various types of material used.

(cd) Carriers of Hepatitis B Antigen in Household Contacts of Haemophilic Patients and Persistent Carriers of Hepatitis B Antigen

Drs. Chrystie and Islam made reports on studies progressing at St. Thomas's Hospital (Agenda Appendix 3(c) i, ii and iii). Prof. Stewart, Dr. Davies, Prof. Blackburn, Dr. Waiter and Dr. Craske contributed to a discussion on persistent carriers of hepatitis B antigen. It was generally thought that

the only real risk from a carrier of hepatitis antigen was if the carrier was bleeding. There was no need to be too concerned about normal people who were carriers but patients who were carriers should be identified by a note on their Haemophilia Cards. Dr. Waiter said that the DHSS felt that in laboratories specimens that were likely to be antigen positive should be identified and staff made aware of the risks. This topic had been raised by Professor Nelson who was unable to be present at the meeting. Professor Blackburn hoped that the discussion would have answered Professor Nelson's questions. Dr. Craske thought that a study of the carrier was being undertaken.

(d) Report of the trial of prophylactic therapy with factor VIII at Alton

Dr. Arblaster said that he had little to report. There had been a good many difficulties in conducting the trial, such as withdrawal of boys from the trial for various reasons. The results to date were being examined statistically and he hoped that it would be possible to make a full report to the next meeting.

REORGANISATION OF HAEMOPHILIA CENTRES

Dr. Waiter introduced the DHSS draft document on the reorganisation of Haemophilia Centres. She said that advice on the treatment of Haemophilia had been sought from an Expert Group which had met twice to advise the Department. As a result of discussions with this Group the concept of a three-tier system of haemophilia centres had evolved. The roles of the old Major Treatment Centres had changed, they now have administrative duties and additionally give support to other Haemophilia Centres in various ways. She

said that the new document had defined more clearly the duties of the Haemophilia Centres and the major centres. It was felt that some hospitals where patients were now treated would be excluded from designation as Haemophilia Centres by the new definition and it was for this reason that a new category of Associate Centres was proposed. These Associate Centres would be visualised as satellites to the Haemophilia Centres.

Dr. Black asked if the DHSS envisaged any particular staffing structure for the administration of the duties of the Treatment Centres. He felt that the minimum requirements were a Clinician with interest in haematology and a laboratory Haematologist working in partnership. Prof. Blackburn said that if the minimum staffing could not be provided then a Haemophilia Centre should not be established. Dr. Biggs supported Prof. Blackburn in saying that the service for haemophilic patients in the regions was in competition with other services and unless the Regional Authorities were prepared to provide for the service a Haemophilia Centre could not be established. She thought that the Directors should assess their needs and perhaps inform their Reference Centres or report to the next Directors meeting.

There were discussions about the role of Reference Centres and Associate Centres. Professor Stewart, Professor Flute and Dr. Holman felt that there was no need to designate Reference Centres. They particularly objected to the idea that the distribution of therapeutic material should be co-ordinated by Reference Centres. They felt that patients would be better treated if all of the available therapeutic material was sent out by the Transfusion Service to any hospital doctor who asked for it. There was also discussion about the designation of Associate Centres. One argument in favour was that the existence

of these Associate Centres would provide a service nearer to patients home than the designated Haemophilia Centres (Dr. Inglis, Mr. Prothero). It was felt (Dr. Edgcumbe, Prof. Flute) that patients should be able to get good treatment at any large hospital. On the other hand the advantages of the association of satellite Centres with a main Centre were emphasised by Dr. Stuart, Dr. Prentice, Dr. Rainsford and others. Dr. Waiter emphasised that it was for the various Regions to decide on the organisation which suited them best. When there had been discussions between the Regional (and Area) Health Authorities and the existing Haemophilia Centre Directors then the DHSS would be advised and a new list of Haemophilia Centres, Reference Centres and Associate Centres would be drawn up and issued by the DHSS.

From the discussion it seemed that the main objections to the designation of Reference Centres came from the London area and concerned particularly the distribution of therapeutic materials. It was suggested that there might be no organisation that was ideal for all parts of the country (Dr. Mibashan). Dr. Waiter agreed to make some changes in the wording of the section of the draft document referring to the distribution of therapeutic materials.

ACTION

The acceptance of the document provided by Dr. Waiter on the organisation of Haemophilia Centres was put to the vote and all were in favour apart from the Directors of three London Centres.

THE SUPPLY OF FACTOR VIII

(a) Plans to Increase the Supply of Factor VIII

Professor Blackburn said that following the January 1974 meeting of

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Haemophilia Centre Directors, he had written to the DHSS, as requested by the Directors, to inform the DHSS that the Directors approved the report of the MRC Cryoprecipitate Working Party (BJH 27, 391, 1974) and recommended the use of this report as the basis for future planning of supplies of factor VIII. Dr. Biggs said that the DHSS had been aware of the urgent need for more supplies of factor VIII since 1967. There was in fact very little that the DHSS could do about increasing supply if this need was not appreciate in the Regions. Dr. Biggs said that she would like to emphasise the fact that if the commercial supply of factor VIII were taken into account there was now no shortage of factor VIII in the United Kingdom. It was up to the Directors to insist in the Regions that the needs of haemophilic patients be met. If this were done, and the expense of the commercial factor VIII was appreciated, then perhaps resources would be made available for provision of adequate amounts of factor VIII within the NHS.

Professor Blackburn said that the Directors could encourage their colleagues to use packed red cells. Dr. Maycock said that about double the amount of NHS concentrate had been made in 1974 as compared to 1973. He said the Expert Group referred to by Dr. Waiter had, at its first meeting, set a target for antihaemophilic globlin to be prepared from 275,000 donations annually by 1975. Progress had been slow and much depended on allocation of money to the Blood Transfusion Service by the Regional Health Authorities. Dr. Maycock said that the present use of packed cells averaged 8% but that a 40% usage (achieved at one centre in Scotland) should be aimed at in England. The laboratory at Elstree had the capacity to increase production of factor VIII by 7-8 times but would need new equipment and must receive more plasma. Mr. Watt said that in Scotland they aimed to produce 4 million factor VIII units annually.

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Half of this would be freeze dried concentrate and half cryoprecipitate. Their aim was to fractionate 60% of the donations collected. It was stated that in Scotland twice as much money per head of population is spent on the Transfusion Service as in England. Another requirement for fractionation was the use of plastic bags and these were expensive and available from one supplier only. Half of the centres in England used plastic equipment. Mr. Watt said that all blood in Scotland was collected into plastic containers.

Dr. Mibashan said said that when required for emergency he had been able to obtain commercial factor VIII for particular patients on prescription and with the support of the hospital administration. He described the use of commercial factor VIII for four patients having factor VIII antibodies. Dr. Waiter said that Dr. Mibashan had found the local solution to the immediate supply position; a case had to be made for the use of commercial material in each locality. She said that every effort was being made to increase the supply of factor VIII within the NHS. Dr. Arblaster said that the NHS never supplied anything unless the need was proved. Dr. Jones said that doctors should certainly write prescriptions for patients and that he had allocated material costing £30,000 a year for patients on home therapy. It was felt that there could be no hesitation in writing such prescriptions for patients needing operations or having inhibitors but that there were difficulties in using money for such things as home therapy (Dr. Holman). Money used for haemophilic treatment would not be available for other essential hospital needs. Professor Stewart felt that there should be a special budget for factor VIII. Mr. Watt said the real problem was shortage of money. If £50,000 were available in a Region should it be spent on Commercial Factor VIII or on the Transfusion Service ? Clearly the long

term aim was better but the patients needed treatment today and the same money could not be spent twice. In reply to a question from Professor Stewart, Dr. Waiter said that the DHSS did not ask the Regional Authorities to spend their money in any particular way. Dr. Mibashan said that money had been withdrawn from a Development Fund to supply material at the Postgraduate School and this could not be done every year.

Dr. Chalmers asked what happened to the dried concentrate now made at the Blood Products Laboratory. Dr. Maycock said that it was distributed to those who asked for it and that it was not distributed according to the amount of plasma supplied by a Region. He said that some regions supplied plasma but had few patients.

Professor Blackburn said that the Directors should concentrate their attention on giving their patients the best treatment that was available. This was the first step to establishing priorities. Mr. Polton said that he was disturbed to think that any other consideration such as money should be envisaged.

(b) The use of factor VIII for patients having factor VIII antibodies

Dr. Dormandy said that the wide use of human factor VIII concentrate for patients having factor VIII antibodies would greatly increase the amounts of concentrates used. Dr. Rizza said that in Oxford, patients having antibodies were treated for severe bleeding episodes likely to cause crippling and not for minor bleeding. Professor Stewart said that he had found the NHS concentrate to be very useful for patients having antibodies.

(c) The use of factor VIII for the home therapy programme

Dr. Davies and Mr. Prothero both said that all haemophilic patients

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questioned by them supported self administaration of therapeutic materials. The Haemophilia Society are hoping to organise a trial of home therapy and sought the support of the Directors for this project. The Haemophilia Society were also planning to write a handbook for patients. Professor Stewart and Dr. Prentice both spoke in favour of the home therapy trial. Dr. Biggs said that a small trial of home therapy was already planned co-operatively between the Oxford and St. Thomas' Hospital Centres. She said that she hoped that the trial planned by the Haemophilia Society would be co-ordinated with that in Oxford and London.

THE PROVISION OF A BRITISH FACTOR VIII STANDARD

Professor Blackburn said that the present arrangements for making the British Standard had been discontinued. In view of the fact that all of the Haemophilia Centre Directors had expressed the wish to have the British Standard continued arrangements were being made for a new source of supply. Dr. Maycock and Dr. Bidwell spoke of plans to make this new standard co-operatively between the Oxford and Elstree Laboratories. Professor Stewart asked if it was possible to experiment with methods of making a standard plasma having about 1 u/ml factor VIII. Dr. Maycock asked Directors to estimate the number of vials of standard that they might need every year. Professor Blackburn said that he hoped the new standard would be available soon because the 4th British Standard was deteriorating. Dr. Bidwell said that according to a recent estimate the value of the 4th British Standard was 0.53 u/ml.

A PROPOSED NATIONAL SURVEY OF PATIENTS HAVING HAEMOPHILIA AND CHRISTMAS DISEASE

Dr. Biggs presented an outline proposal for a national survey of Haemophilia

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and Christmas disease patients. The aims of the survey were to find out how many patientsthere were and where and how they are at present treated. Based on a selection of patients it was also planned to discover the social problems encountered by patients having various types of treatment.

Professor Stewart thought that we already had much information. It was pointed out that patients registered at a centre were not always treated at that centre (Dr. Rainsford) and that from the present distribution of cryoprecipitate many patients were not treated at Haemophilia Centres.

Dr. Jones and Dr. Prentice supported the idea of carrying out a National Survey as did Mr. Prothero. Surveys were already being conducted by both doctors and being considered by the Haemophilia Society. Dr. Jones and Dr. Prentice both had cirticisms to make of the outline plans proposed by Dr. Biggs and thought that much of the information could be obtained in easier ways and at less cost. They said that they would write their comments down and send them to Dr. Biggs. Dr. O'Brien pointed out that if the survey were to be supported the centres would need assistance in collecting information and that the questions would have to be of the sort that could be answered by reading the patient's notes.

Dr. Biggs thanked those making suggestions and said that all comments would be taken into account in the final plans.

ACTION

The meeting approved the proposal that Dr. Biggs should go ahead to obtain funds to support the survey on behalf of the Haemophilia Centre Directors.

ANY OTHER BUSINESS

Professor Stewart suggested that a form to identify patients should be

drawn up at Oxford and supplies sent to the Haemophilia Centres Directors. This form should be completed for every new patient seen at the centres and returned to Oxford. In this way the number of patients known at the centres would be continuously updated. Dr. Biggs agreed to follow this suggestion.

Dr. Jones asked that factor VIII related protein be considered at the next meeting.

Dr. Swinburn said that she would like to include an item on the treatment of patients having haematuria.

The meeting closed at 4. 30 p. m. with thanks to Dr. Grant for providing the premises and to Miss Spooner for making the arrangements.