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MINUTES OF THE FIFTEENTH MEETING OF HAEMOPHILIA REFERENCE CENTRE DIRECTORS held at St. THOMAS'S Hospital on MONDAY 6th SEPTEMBER, 1982

Present:-

Professor A. Bloom (Chairman)

Dr. C.R. Rizza
Dr. C. Forbes
Dr. P. Jones
Dr. P. Kernoff
Dr. C. Ludlam
Dr. J.M. Matthews
Dr. Elizabeth Mayne
Dr. C. Prentice
Dr. F.E. Preston
Dr. G. Savidge
Dr. E. Tuddenham
Dr. R.P. Wensley
Dr. J. Craske
Dr. R.F. Stevens
Dr. A. Aronstam
Miss R.J.D. Spooner

1. Apologies for Absence were received from Dr. I. Delamore (represented by Dr. Stevens) and Dr. P. Hamilton.

2. Minutes of the Last Meeting

Professor Bloom said that a letter had been received from Dr. Peter Hamilton raised a point by letter regarding the item on Staffing of Reference Centres (page 4 of the Minutes, line 6 onwards) where Dr. Ludlam suggested that a statement should be included saying that the Director of the Haemophilia Centre should have responsibility for the clinical and laboratory resources at the Haemophilia Reference Centre. Dr. Hamilton said that he had at the time made clear his reservations about this. He said that where the laboratory of a Haemophilia Reference Centre is part of an established

Haematology Department this may lead to problems, particularly if the Director of the Haemophilia Centre is not a Haematologist. Professor Bloom asked the Directors attending the meeting their views about this and whether they felt that the Minutes as recorded required amendment. After some discussion it was agreed that the Minutes gave an accurate record of the Meeting and that no amendments should be made. The Minutes were approved and signed.

3. Matters Arising from the Minutes

(a) Reference Centres in Scotland

Dr. Forbes said that a form of words had been agreed with the Scottish Home and Health Department regarding the Haemophilia Centres in Edinburgh and Glasgow and the Scottish Home and Health Department had now agreed that these Centres should be recognised as Haemophilia Reference Centres.

(b) Criteria for the designation of Haemophilia Centres/Associate Centres

Dr. Jones had pre-circulated to the Haemophilia Reference Centre Directors a revised draft document. Dr. Jones said that a few points had not been dealt with in the revised draft and he said that he would ensure that these were dealt with before the document was distributed to all Haemophilia Centre Directors. He particularly mentioned that paragraph 7 referring to Special Centres would be deleted and the Isle of Man would be taken from the list of the areas covered by Haemophilia Reference Centres. Dr. Forbes said that he was a little concerned that the wording of paragraph 1 might imply a change in the function of the Haemophilia Reference Centres ~~Directors~~ which would cause the Scottish Home and Health Department to query again the recognition of the Reference

Centres in Glasgow and Edinburgh. He felt that it was very important that the functions of the Haemophilia Reference Centres should not be too tightly defined. This was agreed. Dr. Ludlam suggested that a better title than Haemophilia Centre might be considered, for example "Haemophilia and Haemostasis Centre". Professor Bloom agreed that the title Haemophilia Centre could be misleading and might worry some patients, especially those who did not have classical haemophilia. Dr. Forbes said that he thought there would be further problems with the Scottish Home and Health Department if there was any suggestion that the title of Haemophilia Centre should be changed. He did not think that this was necessary. Dr. Rizza agreed with Dr. Forbes and pointed out that haemophilia was the main problem dealt with by Centres. Dr. Mayne said that if there was to be a change in the name "Haemophilia Centre" she would favour the title "Haemophilia and Coagulation Unit" rather than "Haemophilia and Haemostasis Unit". Professor Bloom said that he thought that "Haemophilia and Haemostasis Centre" might be a good idea from the point of view of the Department of Health and Social Security because the DHSS seemed to think that there were no problems now with haemophilia. Dr. Savidge thought that it might help to get more staffing and funds available at Centres if there was a change of title. Professor Bloom suggested that the question of the title of Haemophilia Centre should be left open at the moment and be discussed at the next meeting of Haemophilia Reference Centre Directors.

Page 2, last line: Dr. Kernoff queried the word "their" in the draft. He pointed out that Haemophilia Reference Centres frequently dealt with patients who were also registered

at other Centres and wondered whether the use of the word "their" would cause problems because of the definition of which patients were "their patients". It was agreed that the word "their" should be deleted from the draft. Page 3: Dr. Kernoff asked what was meant by Item 10 "to coordinate meetings and research programmes". It was agreed that the wording of this paragraph should be amended. Page 5, Section 5: After discussion it was agreed that it was thought to be no longer appropriate to recognise hospitals treating less than 10 severely affected patients.

Dr. Ludlam asked whether all Reference Centre Directors really wanted to see all the patients in their Supraregion. Professor Bloom said that he thought that ideally all patients should be referred to the Haemophilia Reference Centre Director, especially for Carrier Detection. Dr. Aronstam felt that this might not be feasible for the Alton Centre because the boys at Lord Mayor Treloar College were registered with many different Haemophilia Centres throughout the U.K. and it would not be appropriate for all the boys at the College to be registered with the Oxford Centre. It was agreed that the Alton Centre should liaise with the boys home Centre as they do at present and that there was no necessity for all the boys at the College to also be registered with the Oxford Centre.

The question of the responsibility for the issuing of green cards was discussed. Dr. Jones said that it had been agreed at the last meeting that the Haemophilia Reference Centres should be responsible for the issuing of green cards. The arrangements for this would be dealt with by individual Reference Centres in collaboration with the Centres in their

Supraregion. Dr. Savidge referred to Dr. Poller's studies and the wide range of results for VIII:C assays and wondered whether the results from other hospitals could be relied upon by Haemophilia Reference Centre Directors and if they should be prepared to issue Haemophilia cards without doing an assay themselves. Dr. Rizza said that he would be unhappy to issue a card for a patient he had not seen. He said that there were difficulties in knowing if particular hospitals gave a good service and were competent. Dr. Ludlam said that he felt there should be provision on the cards for the cards to be signed by the person issuing the cards; at present this was not the case and there was no indication as to who had authorised the issuing of the card. It was agreed that this would be a good idea and that the DHSS should be asked to consider amending the card in this way when a new stock was to be printed. Professor Bloom pointed out that if the criteria for the designation of a Haemophilia Centre was adhered to, the hospitals recognised as Haemophilia Centres should be competent to diagnose coagulation defects and therefore it would be superfluous for the cards to be issued by the Haemophilia Reference Centres. Dr. Preston said that he thought that there might be difficulties with the diagnosis of rarer coagulation defects at Centres other than Reference Centres. The smaller Centres could not be expected to do all types of assays. Page 6, paragraph 2: Dr. Kernoff said that he thought that this paragraph was superfluous, the arrangements for the storage of materials varied considerably from place to place and it was obvious that Centres should be careful to ensure that materials were used before their shelf-life expired. Dr. Jones wondered whether

the smaller Haemophilia Centres were fully aware of this situation and also whether G.P.'s who held home therapy stocks were aware of the need for ensuring that the material was within its expiry date. It was agreed that the second sentence should be deleted.

The staffing of Haemophilia Centres was discussed and Dr. Jones said that he had deliberately not put staffing requirements down for Haemophilia Centres. It was suggested that this was a topic which might be raised at the Manchester meeting.

Dr. Preston said that he was worried that the question of surgery for haemophiliacs was not dealt with in the document. He felt that Section 5, paragraph 2 would allow operations to be carried out at all Haemophilia Centres and he did not think that this was advisable. Professor Bloom said that any designated Haemophilia Centre should be competent to deal with any emergency situations which arose, including emergency surgery. He thought that it was the responsibility of the Director to decide if the Haemophilia Centre was competent to deal with any problems or whether the patient should be referred to a Reference Centre. Dr. Preston said that he felt the main worry was about giving guide lines for new Haemophilia Centres. Dr. Kernoff suggested that this was a matter which should be discussed in detail at the Manchester meeting and that it should be dealt with in a covering letter with the suggested revised draft.

It was agreed that Dr. Jones would prepare a revised draft document for circulation and discussion at the Manchester meeting of all Haemophilia Centre Directors and that Dr. Jones and Professor Bloom would discuss the matter before the

Manchester meeting.

4. Haemophilia Centre Directors' Annual Returns

Dr. Rizza presented a document which had been prepared by Miss Spooner and himself regarding the Annual Returns from Haemophilia Centres for 1981. He said that one of the main points of interest was the increased amount of NHS concentrate which had been used by Centres during 1981. He felt that this was an encouraging sign and hoped that the increased supplies would continue to be available to Centres. During discussion regarding the treatment of patients with Factor VIII or IX antibodies, Dr. Prentice said that he wondered what had happened to the "missing" patients, as about 100 patients who had at some time had Factor VIII inhibitors were not treated during 1981. It was pointed out that some patients did not attend hospital for treatment once their antibodies were detected and that a few patients who had previously had antibodies were no longer classified as antibody patients during the treatment year. Dr. Preston wondered whether there were any undetected cases of Christmas disease patients with Factor IX inhibitors; it was thought that this was very unlikely. Dr. Savidge asked whether the number of new severely affected haemophilic patients registered each year was available. Dr. Rizza said that he and Miss Spooner had already looked at this information but felt that it was very difficult to interpret so had not included it in reports to Directors. It was agreed that this information would be given to the Haemophilia Reference Centre Directors at their next meeting.

There was much discussion regarding the deaths reported for 1981. Dr. Preston said that he felt that much valuable

information was lost as there was no post-mortem information available. He suggested that a special form should be drawn up for Haemophilia Centre Directors to use to record the post-mortem details on patients known to have died. After discussion, it was agreed that Dr. Preston would draw up a form for circulation to the Haemophilia Centre Directors and Dr. Preston agreed to have a draft form available for discussion with the Reference Centre Directors at their next meeting. Dr. Wensley suggested that liver biopsy should always be done when a haemophilic patient had a laparotomy. This suggestion was discussed and it was agreed that the decision should be left to the discretion of the Haemophilia Centre Director concerned.

Dr. Kernoff wondered whether the Haemophilia Centre Directors estimated requirement for Factor VIII concentrate should be revised in the light of the 1981 annual returns. It was agreed that it was not necessary for the estimate to be revised at the present time but that the matter would be reviewed again next year. Dr. Aronstam suggested that the levelling out of the amount of commercial factor VIII concentrate used reflected budgeting restrictions to Haemophilia Centres.

5. Reports from Working Party Chairmen

(a) Hepatitis Working Party

Dr. John Craske said that no written report was available at present. A lot of data had come from the various surveys conducted by the Working Party and this was being analysed. It was hoped that a written report would be available in time for the next meeting. The Working Party would be holding a meeting in Manchester following the Business Meeting of the

Haemophilia Centre Directors. The two main topics which required consideration at the present time by the Reference Centre Directors were:- (1) Hepatitis Vaccine. Dr. Craske thought that discussion on this topic should be left until later in the meeting. (2) Survey which he was conducting in collaboration with the Oxford Haemophilia Centre on the use of commercial and NHS concentrates for first time or seldom treated patients. 28 patients had been entered into the study to date and followed for a period of six months or more after treatments. 9 of these patients had developed Non-A, Non-B hepatitis. It appeared that there was 100% attack rate for first time treated patients who received NHS factor VIII concentrate and more than 80% chance of contracting hepatitis following treatment with any type of concentrate. Dr. Craske had held several meetings with Dr. Richard Lane to discuss this problem. He thought that there were two viral agents in the commercial concentrate and that these were of probably different varieties. The NHS factor VIII had a low contamination rate with Hepatitis B. Dr. Craske thought that further trials of the type which had been conducted in Oxford should be carried out and that the protocol used for the Oxford study could be made available to any Directors who would like to conduct similar studies. He had discussed with Dr. Lane the possibility of concentrates being made from pools of "accredited donors" for the treatment of first time or seldom treated patients.

Dr. Craske said that he would advise caution with regard to the claims for hepatitis B-free materials which had been made by the commercial firms. The only way to check this material was to test it in patients who were treatedfor the

first time along similar lines to the way that the Oxford study had been conducted. Dr. Wensley felt it was important to point out that hepatitis B had not entirely disappeared; there had been two new cases of hepatitis B in Manchester during the current year. Professor Bloom said that he felt that the Hepatitis Working Party should give definite advice to the Haemophilia Centre Directors about the use of the "Hepatitis-free concentrates". He asked that the Working Party should give priority to the drawing up of guide-lines for use by the Haemophilia Centre Directors at their next meeting. It was agreed that the Hepatitis Working Party would give priority to the consideration of this problem.

The Chairman decided that it would be appropriate for Item 7 of the Agenda "Hepatitis B Vaccine" to be dealt with at this stage as it followed on from the work of the Hepatitis Working Party. Dr. Craske said that a vaccine manufactured by Merck, Sharpe and Dome had been licensed for use in people aged 6 ~~years~~ months or over. The vaccine was normally given by intramuscular injection. The Department of Health had drawn up the recommended list of high priority people for receiving the vaccine and the list included haemophilia patients. The vaccine would be released on the 20th September without a publicity campaign; only 15,000 courses of vaccine were available for the whole of the United Kingdom. A trial was shortly to be started in Oxford using this material in first time or seldom treated haemophilic patients. The material was to be given subcutaneously to the Oxford patients. Professor Bloom asked whether the staff and families at risk were to be given the vaccine. Dr. Craske said that he did not feel that the risk to staff was high. He suggested, however, that

the staff working with haemophilia patients should have their antibody levels checked anonymously at regular intervals. Professor Bloom felt that staff might demand the vaccine when they knew it was available and he also thought that the Haemophilia Centre Directors would soon be approached by the drug company representatives. Dr. Craske thought that it was possible that more vaccine might become available next year. Professor Bloom wondered what value the giving of the vaccine was as it was only for Hepatitis B when Non-A, Non-B Hepatitis seemed to be the larger problem for the haemophilic patients. Dr. Craske pointed out that there was still a small risk of hepatitis B from all blood products and that a vaccine for Non-A, Non-B Hepatitis would not be available for some time.

Professor Bloom asked Dr. Craske if he had any information about the acquired immune-deficiency syndrome following reports from the United States and the possible relationship of this syndrome with bloodproducts and hepatitis. Dr. Craske said that he would find out more about this and agreed to try to have some information available for the Haemophilia Centre Directors at the Manchester meeting.

5. (b) Factor VIII Antibodies Working Party

Dr. Colin Prentice reported on the progress with the trial of Factor VIII versus Autoplex which the Working Party was organising. The protocol was outlined and a summary of the study was presented to the Reference Centre Directors. 10 patients were included in the trial at the present time; it was hoped that about 30 patients would eventually be included in the study. Only patients who had at some time been recorded to have had more than 5 Bethesda units of inhibitor

were to be included in the study. Dr. Wensley asked if any of the Directors who had used Autoplex for the treatment of patients with factor VIII antibodies had observed side-effects; 3 out of the 4 patients treated in Manchester had had violent reactions with the material. Dr. Aronstam said that he had not had any problems with the boys at Alton who had received the material and Dr. Savidge said he had had a few problems but these were easily resolved by careful administration of the material.

Dr. Prentice said that in March 1983 he would take up an appointment as Professor of Medicine in Leeds. He would very much like to continue as Chairman of the Haemophilia Centre Directors Working Party on the Treatment of Patients with Factor VIII Antibodies until the trial had finished. It was agreed that Dr. Prentice should continue for the time being as Chairman of the Working Party.

5. (c) Factor VIII Assay

Dr. Rizza said that no meetings had been held of the Factor VIII Assay Working Party since the last meeting of the Haemophilia Reference Centre Directors. The members of the Working Party had been busy with several projects including an International Study and calibrating the new International Plasma Standard. Dr. Barrowcliffe would report in detail on this project at the Manchester meeting.

Dr. Kernoff asked Dr. Rizza for his comments on the differences between the results of the one- and two-stage factor VIII assay. Dr. Rizza said that Oxford found higher two-stage assay results when assaying the concentrates. There was some discussion about the value put on the bottles of

factor VIII concentrate which were purchased from commercial firms. Dr. Rizza said that the Oxford Centre was receiving samples from batches which they were considering purchasing and assaying the material before placing an order. He did not find now that there was wide discrepancy between the results of the assays at the Oxford Haemophilia Centre and the values put on the material by the commercial firms.

5. (d) Von Willebrand's Disease Working Party

Dr. Tuddenham said that to date information had been received for the von Willebrand's disease Survey on 557 different von Willebrand's disease patients. He would report in detail on the results at the Manchester meeting. Dr. Mayne asked Dr. Tuddenham whether von Willebrand's disease patients who had thrombocytopenia should be included in the survey and whether many Directors had patients with this complication. Professor Bloom said that some families certainly do have thrombocytopenia and Dr. Tuddenham said that he would be very pleased to receive information about these patients from the Haemophilia Centre Directors.

6. Register of Patients with Inherited Platelet Disorders

Dr. Preston said that he thought that patients with Inherited Platelet Disorders were a neglected group of patients. He had no idea how many patients there were in the U.K. with platelets disorders, the severity of their problem, how they were classified by Haemophilia Centre Directors, etc. He suggested that a Register should be set up by the Haemophilia Centre Directors, similar to the Register now being set up for von Willebrand's disease patients. Professor Bloom said that a survey could be interesting but these patients did not seem to have any severe haemostatic problem. He wondered whether

the Haemophilia Centre Directors might like to consider the setting up of a Working Party to look into the Inherited Platelet Disorders. He suggested that Dr. Preston should write a paper stating his proposals for discussion at the next Reference Centre Directors meeting. This was agreed.

8. Arrangements for the 1982 meeting of all Haemophilia Centre Directors

Dr. Wensley said that approximately 70 people had registered for the Business meeting (Day 1) and 140 people for the Symposium (Day 2). The Symposium was to be recorded and it was hoped that the proceedings would be published as soon as possible. The Agenda for the meeting had been sent to all participants.

9. Arrangements for the 1983 meeting of all Haemophilia Centre Directors

It was agreed that the 1983 meeting should be a one-day meeting, held in Oxford in October and Professor Bloom said that he would be very pleased to organise a two-day meeting in Cardiff in 1984.

10. Date and Place of next meeting of Reference Centre Directors

The next meeting of the Reference Centre Directors would be held on Monday 14th February, 1983 at the Royal Free Hospital.

11. Any Other Business

a) Professor Bloom said that Dr. Shinton had written to him regarding home therapy packs of the Factor VIII and IX concentrates made by the Blood Products Laboratory at Elstree. Professor Bloom had been in touch with Dr. Lane, who said that the production of home therapy packs containing water as well as concentrates was under active consideration by the B.P.L.

but that there would be no space available at B.P.L. for the storing of these packs until 1985. Dr. Lane would shortly be taking the views from the Haemophilia Centre Directors regarding the type of packaging the Directors required.

b) Professor Bloom said that he had received a letter from Dr. Swan about the Directorship of the Haemophilia Centre in Sheffield. This had brought to the surface a problem which he felt had arisen in many Haemophilia Centres. He felt that the Reference Centre Directors should give some consideration to the question of how many Directors there should be for Haemophilia Centres. Professor Bloom would like to see only one designated Director for every Centre, with a nominated deputy Director. He felt that the choice of the Director for an individual Centre was up to the Centre concerned and that the Haemophilia Reference Centre Directors could not arbitrate in this matter. There was some discussion about the number of designated Directors which was thought to be appropriate for Haemophilia Centres. Dr. Ludlam thought that one of the functions of the Haemophilia Reference Centre Directors was to approve the appointment of individual Directors; he recalled that at the time of his appointment to his present post in Edinburgh, his appointment had been discussed by the Reference Centre Directors and approved by them before he was invited to attend the meeting of Haemophilia Reference Centre Directors. It was agreed that the Reference Centre Directors should feel free to review the designation of a Reference Centre when there was a change of Directorship.

Professor Bloom said that he also queried whether two representatives from each Reference Centre should attend the Reference Centre Directors meeting. He thought that possibly

only one representative should come from each Reference Centre and that where there were two designated Directors these Directors could take it in turn to attend the meetings. Dr. Jones said that in Newcastle the situation was quite clear; Dr. Jones was the Director of the Centre and Dr. Hamilton was the Co-Director and was laboratory orientated. He would not like his Co-Director to be excluded from the meeting of Haemophilia Reference Centre Directors; he and Dr. Hamilton had totally different responsibilities regarding the running of the Haemophilia Centre. Dr. Kernoff said that he thought that all designated Directors/Co-Directors should attend the meetings as they made useful contributions to the meeting. There were lengthy discussions regarding the attendance at the Reference Centre Directors meetings but it was agreed to leave things as they were for the time being and that the situation in Sheffield should be sorted out locally. Professor Bloom pointed out that the Hallamshire Hospital was the Reference Centre and therefore Dr. Preston was the Director of the Reference Centre in Sheffield.

Professor Bloom said that he would like to advise that there should be only one Director for each Haemophilia Centre in the United Kingdom. There was some discussion about this but it was agreed that the priority should be for sorting out the criteria for the designation of Haemophilia Centres before the question of the number of Directors of the Centres was raised.

c) Professor Bloom had received a letter from Dr. Colvin referring to correspondence he had had from Germany asking for information about the usage of factor VIII by his Haemophilia Centre. Dr. Colvin and other Directors had been

rather concerned about this letter and wondered what reaction there had been from the Haemophilia Reference Centre Directors. The Reference Centre Directors agreed that they had replied to the letter but had not given as much detailed information as had been requested.

d) Dr. Kernoff had raised the possibility of nurses being invited to attend the Haemophilia Centre Directors meeting. It was agreed that this matter should be left for the time being and that the Haemophilia Reference Centre Directors would consider the matter again at a future date.

e) Dr. Savidge said that he would like to discuss with the Reference Centre Directors their policy regarding Dr. Poller's work especially as he was required to report to the Haemophilia Centre Directors at the Manchester meeting regarding the activities of Dr. Poller's Committee. Dr. Poller seemed to have moved into the field of testing for the diagnosis of mild Haemophilia A, assays for Factor VIII:C and VIII:RAg. Dr. Savidge wondered whether Dr. Poller's monitoring of the performance of laboratories was very useful. He queried the way Dr. Poller's results were presented and he wondered whether Dr. Poller should notify the persistently poor results. Dr. Savidge wondered if there was an overlap between Dr. Poller's work and the work of the Haemophilia Centre Directors Factor VIII Assay Working Party. Dr. Rizza said that he understood that Dr. Poller did not want to be involved with the work of the Factor VIII Assay Working Party. Dr. Savidge was a little concerned how far Dr. Poller was going into the methodology used by the Haemophilia Centre Directors. It was agreed that there was no need for concern at the present time but that the situation would be reviewed at a later date.

f) Chairmanship of the Haemophilia Centre Directors

Professor Bloom said that when he had been appointed as Chairman of the Haemophilia Centre Directors, on the retirement of Professor Blackburn, he had agreed to take on the job for three years and the three-year period was now completed. It was unanimously agreed that Professor Bloom should be invited to continue as Chairman for three more years and that this proposition should be put to the Meeting of Haemophilia Centre Directors in Manchester.

Professor Bloom thanked Dr. Savidge for his hospitality and the meeting finished at 4.00 p.m.

GRO-C: Bloom

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