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Minutes of the THIRTEENTH MEETING OF HAEMOPHILIA REFERENCE CENTRE DIRECTORS held at St. Thomas's Hospital on MONDAY 14th SEPTEMBER, 1981.

Present:-

Prof. A. Bloom (Chairman)
Dr. C.R. Rizza
Dr. I. Delamore
Dr. C. Forbes
Dr. P. Hamilton
Dr. P. Jones
Dr. P. Kernoff
Dr. C. Ludlam
Dr. Elizabeth Mayne
Dr. F.E. Preston
Dr. G. Savidge
Dr. E. Tuddenham
Dr. R.T. Wensley
Dr. J. Craske
Miss R.J.D. Spooner

1. Apologies for Absence were received from Dr. G. McDonald, Dr. J. Matthews, Dr. C. Prentice and Dr. H.T. Swan.

2. The Minutes of the last meeting of the Reference Centre Directors were approved and signed.

3. Matters arising from the Minutes

(a) Northern Ireland and Scotland

Scotland. There was no further information regarding the formal recognition of the Haemophilia Centres in Glasgow and Edinburgh as Haemophilia Reference Centres. Drs. Forbes and Ludlam both thought that the hold-up was administrative and that the recommendation would shortly be approved by the Scottish Home and Health Department.

Northern Ireland. Professor Bloom said that he had received

a letter from Dr. Thornton of the DHSS Northern Ireland Office confirming the designation of the Royal Victoria Hospital in Belfast as a Haemophilia Reference Centre.

(b) Dr. Poller's Factor VIII Quality Control Study

Professor Bloom said that it had been agreed at the last meeting of Haemophilia Reference Centre Directors that the Reference Centre Directors felt that they should be represented on Dr. Poller's Study Group and Dr. Savidge had kindly agreed to be the representative. It was also agreed at that time that Dr. Poller should be invited to attend the next meeting of all Haemophilia Centre Directors but it was felt that now Dr. Savidge was the Reference Centre Directors representative on Dr. Poller's Group it would be more appropriate for Dr. Savidge to report back to the Haemophilia Centre Directors about the work of the Group. It was agreed that the Reference Centre Directors would wait for Dr. Savidge's advice after he had had a chance to meet with Dr. Poller's Group before inviting Dr. Poller to attend any meeting of Haemophilia Centre Directors.

(c) Report from Mr. Rosenblatt

It was agreed that the Reference Centre Directors would wait and see what developments there were in the insurance field.

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

Professor Bloom suggested that Item 8 on the Agenda should be included with this item. Professor Bloom referred to a letter he had received from the Haemophilia Society's Co-ordinator concerning the problem one of the Society's members had encountered when he turned up at a Haemophilia

Centre unexpectantly and was not, in his view, dealt with adequately. The patient had complained to the Society and also to the Health Authority concerned. The Society had written to the patient concerned about this and also to the Haemophilia Centre. Dr. Kernoff expressed his concern at the proliferation of Haemophilia Centres, many of which had very few patients. Professor Bloom referred to a letter he had received from Dr. Shinton regarding the treatment of haemophilic patients at hospitals without a Haemophilia Centre. Dr. Shinton had said that he wished to raise these points at the next meeting of all Haemophilia Centre Directors. Dr. Jones said that at the last meeting of the Reference Centre Directors he and Dr. Kernoff had agreed to draw up a memorandum regarding the designation of Haemophilia Centres/Associate Centres. He had drawn up a short memorandum for consideration by the Reference Centre Directors at this meeting regarding the designation of a "Haemophilia Centre" and this memorandum was circulated to those present. He suggested that the title of "Associate Centres" should be removed and that in the future only Haemophilia Centres and Reference Centres should be designated. The matter was discussed at some length. Dr. Preston felt that the clinical cover required at Haemophilia Centres should be spelt out in greater detail. Dr. Mayne felt that a Consultant or Registrar should be available at all times, but that there would be difficulties if it was compulsory for a Consultant to be available at all times. Dr. Forbes suggested that all surgery should be restricted to Haemophilia Reference Centres as was the case some years ago. After further discussion it was agreed that Dr. Shinton would be told that the questions he had raised in his letter were

under review and that Dr. Jones could re-evaluate the current status of the DHSS memorandum and circulate possible suggestions for inclusion in any revised version to the Reference Centre Directors for consideration at their next meeting.

3(e) Mortality in haemophiliacs

Dr. Forbes reported that he had now gathered data on causes of death in haemophiliacs over the past 25 years and he was proposing to publish this shortly. Dr. Forbes suggested that autopsy reports should be requested from Haemophilia Centres when deaths were reported and possibly that some postmortem specimens might also be made available for analysis. Dr. Rizza reminded the meeting that Dr. Craske had already asked the Directors for autopsy liver specimens. It was agreed that Dr. Forbes would raise at the October meeting of all Directors the question of more detailed information regarding deaths being obtained from Haemophilia Centre Directors.

3(f) Publishing of Data

Dr. Rizza said he had approached the DHSS's Medical Editor of "Health Trends" (Dr. Hunt) regarding the possibility of the Directors Annual Returns being published in "Health Trends" and had been told by Dr. Hunt that "Health Trends" would be prepared to publish the reports subject to their being accepted by the Journal's referees. Dr. Hunt could not promise that the reports would be published annually on a long-term basis. Some concern was expressed that the DHSS's "Health Trends" circulation was rather limited. It was agreed that the five-year report should be published in "Health Trends" and, if possible, also in another medical journal for wider circulation.

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3(g) Supplies of Commercial Factor VIII

Professor Bloom said that a Company called Interpharm had approached Dr. Savidge regarding the marketing of factor VIII and Professor Bloom had taken the matter up with the Medicine's Division at the Department of Health. The Department confirmed that any imported material must be cleared by NIBSC through the usual channels and that these channels could not be by-passed.

4. Haemophilia Centre Directors' Annual Returns

Dr. Rizza presented tables and graphs giving the data from the 1980 Annual Returns and the information was discussed in detail. Dr. Rizza drew attention in particular to table 1 and figure 1 which showed that the amount of factor VIII used in 1980 had again increased, especially the Commercial materials. It was noted from table 9 that more deaths in haemophiliacs had been reported but it was thought that this probably related to better reporting from Centres rather than a real increase in the number of deaths. Dr. Rizza proposed that tables 1-11 and the two graphs should be circulated to all Haemophilia Centre Directors before the October meeting. This was agreed.

5. Distribution of Factor VIII and other Blood Products

Professor Bloom referred to a meeting in April which the Department of Health had called and to which representatives of the Plasma Fractionation Laboratories, Haemophilia Reference Centre Directors and Blood Transfusion Services were invited. The main problem for the Haemophilia Centre Directors was a recommendation from the Department of Health that Blood Transfusion Centres should purchase, hold,

distribute and control the stock of all blood products, including factor VIII supplies. The Department of Health claimed that the Haemophilia Centre Directors would still have a say in which materials were purchased and that this system would enable the Department of Health and the Blood Transfusion Service to have monthly returns on the amounts of materials which were purchased and used. The Reference Centre Directors were most concerned about the effects of the DHSS's proposals on the day to day running of their clinical practice and it was felt that the scheme would result in loss of flexibility in purchasing factor VIII and distributing it to patients. The worry was also expressed that if the new scheme was implemented there would be problems with budgetary restrictions regarding the purchase of commercial factor VIII concentrates. After much discussion it was agreed that the Haemophilia Centre Directors would resist strongly the transfer of factor VIII stock control to the Blood Transfusion Service.

6. Designation of the Treloar Haemophilia Centre

The question of designation of Treloar Haemophilia Centre as a Reference Centre was raised by Dr. Savidge. He drew attention to the fact that the Centre had very special and wide experience in the management of haemophilia in adolescents and played an important role in introducing the boys who attended the College to home therapy. It was pointed out in discussion that Treloar Haemophilia Centre was not in the same situation as the Haemophilia Reference Centres who had patients referred to them from wide areas and who provided a comprehensive service all the year round. The Treloar Haemophilia Centre was closed down during the College holidays

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and patients had to go to Basingstoke for treatment. Professor Bloom thought that there might be serious problems if Treloar was designated as a Reference Centre, and he wondered whether perhaps it would be better for Dr. Aronstam to be invited to attend the Haemophilia Reference Centre Directors meetings without the official designation of Treloar as a Reference Centre. Dr. Jones suggested that Dr. Aronstam should be co-opted to attend the Haemophilia Reference Centre Directors meeting as the Expert in Adolescent Haemophilia Management in the same way as Dr. Craske was invited to attend the meeting as the expert in Hepatitis. It was agreed Treloar Haemophilia Centre could not be designated as a Reference Centre but that Dr. Aronstam should be invited to attend the meeting of Reference Centre Directors on account of his special experience of managing haemophilic boys at the College.

7. Reports from Working Party Chairmen

(a) Hepatitis Working Party

Dr. Craske presented the results of the Working Party's activities during the last three years. The cases of hepatitis reported by Haemophilia Centre Directors, had been mild in most instances and no acute case in recent years had resulted in death. Several questions were still to be answered regarding hepatitis in haemophiliacs. One was whether acute attacks of hepatitis in haemophiliacs would result in chronic liver problems in a few years time. Table 4 gave the results of the survey of patients who had received a "suspect" batch of Kryobulin earlier this year. Table 5 gave the results of the Hemofil Study in 1974 and compared these results with more recent results with Kryobulin and other materials. Table 6 gave information about the multiple attacks of Non-A, Non-B

hepatitis in haemophiliacs. Dr. Craske thought that the fractionation methods used might be relevant to the incidence of hepatitis in patients treated with Commercial and NHS concentrates. He thought it was possible that the intermediate products might have two viruses and the US commercial products one virus. A prospective study of post-transfusion hepatitis in previously untreated or infrequently treated patients was being undertaken in Oxford and in two other Centres in the U.K. It was hoped that a grant from the Medical Research Council would be obtained to finance this project. Dr. Craske drew attention to a hepatitis B vaccine prepared by Merck, Sharp and Dohme and to a proposed trial to be conducted in the United Kingdom. Dr. Wensley asked whether the Working Party had considered the status and value of VIII/IX materials which are claimed to have been made with reduced Non-A/Non-B hepatitis risk by various forms of chemical and physical treatment. Dr. Craske replied that Biotest Laboratories had published results in which it was claimed that a hepatitis-free factor IX concentrate was available. The claim was that there was 95% reduction of Non-A, Non-B hepatitis, but he did not think that the claims were yet proven. Professor Bloom mentioned that three firms were now claiming that they had produced hepatitis-free concentrates. Dr. Craske said that the laboratory tests show that hepatitis B virus was reduced, but it was not possible to test for Non-A/Non B Hepatitis virus at present. Professor Bloom said that NIBSC would expect the manufacturers to prove the claim for each batch of concentrate produced, but it could not prohibit the use of the material for named patients. Dr. Craske said that Dr. Lane of the Elstree BPL was looking into the possibility of preparing "hepatitis-reduced risk" material

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at BPL and PFL. Dr. Savidge suggested that hepatitis-free commercial material should be used for anticoagulant reversal in preference to the NHS factor IX concentrate. In answer to a question from Dr. Hamilton, Dr. Craske said that there was no evidence that there were any cases of halothane hepatitis amongst the haemophiliacs studied.

(b) Home Treatment Working Party

Dr. Jones reported on a recent collaborative study with the Treloar Haemophilia Centre on the claim that high potency factor VIII produced by Revlon had a longer in vivo ½-life than other materials. Their study showed that there was no difference in the ½-life of the Revlon material compared with other materials, therefore there was no reason to recommend the use of the high potency material. It was hoped that the results of the Alton study would be published soon. Dr. Jones was analysing the data on prophylaxis and would report on this next summer.

(c) Factor VIII Antibodies

Dr. Prentice was not present at the meeting but had sent a document to the meeting regarding the proposed trials of materials for the treatment of patients with factor VIII antibodies. He hoped to get a trial under way very soon. Dr. Delamore said that there had been a meeting with the manufacturers of Autoplex and a protocol had been drawn up. This was being revised but he had not yet seen the revised draft. Dr. Mayne thought that FEIBA had only a small place in the treatment of haemophiliacs with factor VIII inhibitors. The worry was expressed that if a British trial showed good results with a very expensive material then all Haemophilia Centre Directors in the U.K. might wish to use this material

to treat their patients and the cost of patient treatment would considerably increase. Dr. Kernoff referred to published reports describing the clinical effectiveness of FEIBA. He wondered what the advantages of the U.K. study would be. Dr. Kernoff said that he would have thought that a small scale trial with only a few Centres involved would be the best plan. Professor Bloom agreed that the Working Party should go ahead with producing a protocol for consideration by the Directors. Dr. Rizza outlined Oxford's experience using factor VIII concentrates to treat patients with factor VIII antibodies. Dr. Jones suggested that the Working Party should draw up recommendations regarding the treatment of patients with factor VIII antibodies and a synopsis of their results should be available to all Haemophilia Centre Directors. It was agreed that Dr. Prentice should be asked to arrange a meeting of the Factor VIII Antibodies Working Party as soon as possible and that the Working Party should draw up a protocol for a trial and arrange for the trial to be got under way without further delay.

(d) Factor VIII Assay Working Party

Dr. Rizza said that there had been no meetings since the February meeting of Haemophilia Centre Directors but one was shortly to be held. The Working Party had collaborated with NIBSC in the standardization of the Internal Reference Plans and the British Standard. In addition work was still going on into the effect of alumina and $BaCl_2$ as absorbents in the two stage assay of factor VIII:C. They were looking into several aspects as a result of this and a written report would be available for the Haemophilia Centre Directors at their next meeting.

(e) Von Willebrand's Disease Working Party.

Dr. Tuddenham said that the Working Party had met on the 4th September at the Royal Free Hospital and gave the Reference Centre Directors a copy of the draft minutes of that meeting at which guidelines for the criteria for diagnosing von Willebrand's disease had been drawn up. The Working Party felt that a central register should now be established which would include the results of the essential laboratory tests on the von Willebrand's disease patients. Only patients who had been issued with special medical (green) cards should be included in the register and only patients who had a definite risk of bleeding should be issues with green cards. Dr. Tuddenham said that the Working Party would like the central register of von Willebrand's disease patients to be held in Oxford if possible and Miss Spooner agreed to look into the possibility of this being done. It was agreed that the Working Party's recommended criteria for the diagnosis of von Willebrand's disease and proposals for the setting up of a central register of von Willebrand's disease patients should be circulated to the October meeting of all Haemophilia Centre Directors for consideration and approval.

8. Hammersmith Hospital

Dr. Tuddenham reported that the post of Director of the Haemophilia Centre at the Hammersmith Hospital had been frozen for some time and that a Locum was acting as Director and organizing the haemophilia service. Professor Luzzatto had recently been appointed as Professor of Haematology at the Post Graduate Medical School, but the situation was still as it had been for some months and everyone was rather worried

about the long-term situation at the Hammersmith Hospital if the post of Haemophilia Centre Director continued to be frozen. It was generally agreed that it was difficult for the Reference Centre Directors, as a group, to be involved with local arrangements and it was felt that problems such as those at the Post Graduate Medical School were best dealt with on a Supraregional basis by the Reference Centre in collaboration with the Haemophilia Centre concerned.

9. Armour Research Grants

Professor Bloom said that the Armour Pharmaceutical Company were considering setting up an Armour Research Fellowship and had asked if the Haemophilia Reference Centre Directors would be prepared to play some part in refereeing applications for the Fellowships. There was some discussion about this. Most Directors were against this suggestion. It was agreed that the Haemophilia Reference Centre Directors did not think it appropriate that they should handle the Armour Research Fellowships and that Professor Bloom should suggest to Armour that they might if they wished make a contribution to the Haemophilia Society for the express purpose of funding research.

10. Arrangements for the next meeting of all U.K. Haemophilia Centre Directors

The Agenda for the meeting, which was to be held at the Royal Free Hospital on Friday 9th October, was approved. Arrangements for the meeting were well in hand.

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

Dr. Delamore and Dr. Wensley said that they would be very pleased for the 1982 meeting of all Directors to be held in Manchester. It was agreed that the Meeting in 1982 would be a two-day meeting held in Manchester, the first day being a Business Meeting and the second day a Scientific Symposium with invited speakers. The suggested dates for the meeting were Monday and Tuesday September 13th and 14th. It was pointed out that these dates might cause administrative difficulties in that there would be little time for the Reference Centre Directors to meet before then. Dr. Wensley and Dr. Delamore said that they would look into the possibility of an alternative date towards the end of September or early in October. Dr. Wensley said however that the choice of dates was governed by the availability of the lecture hall and the availability of accommodation in the University Hall of Residence.

13. Any Other Business

(a) Dr. Craske said that the question of reporting back to Commercial firms regarding cases of hepatitis in patients who had been treated with Commercial Factor VIII concentrates had been raised. Dr. Rizza had written to the Reference Centre Directors to ask if they would be agreeable for data to be passed on to the Commercial firms and all the Directors had agreed to this proposal. Dr. Craske wondered, however, whether the Directors would like the names of the patients to be withheld or whether they would be willing for names to be disclosed to Commercial firms. Following some discussion

it was agreed that the names of patients would not be passed on to Commercial firms.

(b) The Haemophilia Nurses Association

Professor Bloom had written to Sister Fearns following the last meeting of Haemophilia Reference Centre Directors saying that the Reference Centre Directors were pleased to hear of the formation of the Haemophilia Nurses Association and had invited Sister Fearns to present a brief report on the activities of the Nurses at the October meeting of all Haemophilia Centre Directors at the Royal Free Hospital. Dr. Jones said that the British Association of Social Workers wished to have a Haemophilia Association similar to that of the nurses and sought the approval of the Haemophilia Reference Centre Directors. The Social Workers would like to send a representative to the Haemophilia Centre Directors annual meetings to give a report on activities. It was agreed that Professor Bloom would write to the representative of the British Association of Social Workers in Newcastle inviting her to attend the October meeting of all Haemophilia Centre Directors at the Royal Free Hospital.

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

It was agreed that the next meeting of Haemophilia Reference Centre Directors would be held at the Royal Free Hospital on the 1st March 1982.

Professor Bloom thanked Dr. Savidge for his hospitality and the excellent lunch and the meeting closed at 4.30 p.m.