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Minutes of The Ninth Meeting of Haemophilia Reference Centre  
Directors held at the Oxford Haemophilia Centre on Monday 15th  
October 1979

Present:-

Professor Arthur Bloom - Chairman  
Dr. C.R. Rizza  
Dr. J.M. Matthews  
Dr. P. Jones  
Dr. P. Hamilton  
Professor E.K. Blackburn  
Dr. F.E. Preston  
Dr. I.W. Delamore  
Dr. R.T. Wensley  
Dr. P. Kernoff  
Dr. E. Tuddenham  
Dr. G. Savidge  
Dr. C. Prentice  
Dr. C. Forbes  
Dr. C. Ludlam  
Dr. J. Craske (Chairman Hepatitis, Working Party)  
Miss R.J.D. Spooner

Professor Bloom said that Professor Ingram and the Department of Health and Social Security had asked for the approval of the Reference Centre Directors regarding the appointment of Dr. Savidge as Director of the St. Thomas' Hospital Haemophilia Reference Centre following Professor

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Ingram's retirement. Professor Bloom thought that this matter should be taken as the first item on the Agenda and that the position regarding Dr. Christopher Ludlam should be considered at the same time. Dr. Savidge and Dr. Ludlam were asked to leave the meeting for a few minutes. Professor Bloom said that the Department of Health had reviewed the position of St. Thomas' Hospital as a Haemophilia Reference Centre on the retirement of Professor Ingram. It was felt that St. Thomas's should continue to be a Haemophilia Reference Centre, but the Department of Health felt that the Haemophilia Centre Directors of the UK should be asked to approve the appointment of Professor Ingram's successor as Haemophilia Reference Centre Director. Dr. Geoffrey Savidge had been appointed to the post at St. Thomas' Hospital. Professor Blackburn outlined Dr. Savidge's background and Professor Bloom asked whether Dr. Savidge's appointment as Reference Centre Director at St. Thomas' Hospital met with the approval of the Reference Centre Directors. This was agreed.

Professor Bloom said that a similar situation had arisen over the appointment of Dr. Christopher Ludlam as Dr. S.H. Davies's successor at the Edinburgh Royal Infirmary Haemophilia Reference Centre. Dr. Davies thought that the appointment of his successor should be approved by both the Scottish Home and Health Department and the Haemophilia Reference Centre Directors. Dr. Davies had contacted the Scottish Home and Health Department about this matter but had received no reply. Officially there were no Haemophilia Reference Centres in Scotland though unofficially the Glasgow and Edinburgh

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Centres acted as Haemophilia Reference Centres. Dr. Delamore and it was agreed suggested that Professor Bloom should write to the Scottish Home and Health Department saying that the Haemophilia Reference Centre Directors of the UK had discussed the appointment of Dr. Ludlam and the situation of the Edinburgh Haemophilia Centre and approved the appointment of Dr. Ludlam as Dr. Davies's successor.

Dr. Savidge and Dr. Ludlam were welcomed back to the Meeting.

2. Minutes of the previous meeting

Professor Ingram intimated by letter that he wished to make an amendment with regard to the record in the minutes of his conversation with Mr. Berry of Immuno. The Minutes were altered accordingly.

The Minutes of the Eighth Meeting of the Haemophilia Reference Centre Directors were approved and signed.

3. There was some discussion regarding the two types of Immuno material on the market a "Blue" material and a "Red" material. Dr. Craske suggested that the Directors should perhaps look at the different types of Immuno products to find out how much "Red" and "Blue" material was used and to assess the difference, if any, between these two types of material. It was agreed that the question of "Red" versus "Blue" Immuno material should be referred to the Hepatitis Working Party. The question of the source of plasma used by Immuno for factor VIII production was raised and there was a feeling that the plasma came from places other than Europe and USA. There was

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some suspicion that African plasma was being imported to Austria.

4. Haematuria Working Party

Drs. Forbes, Prentice and Kernoff had been asked to look into the feasibility of a Haematuria Working Party being set up. Dr. Peter Kernoff said that he had been very doubtful about this project. Some work had been done several years ago on the problems of haematuria and the results had been published. He thought that the situation remained unchanged.

Dr. Forbes said that he thought that it would possibly be worthwhile for Directors to look at the blood pressure of patients on home therapy when they came for follow-ups. Dr. Prentice's feeling was that this was the type of project best done by individual Centres rather than by an organised Directors Working Party. Dr. Delamore, however, thought it would be better to do this type of study on a National basis as individual Centres would not have enough cases.

A decision on a Haematuria Working Party was deferred until after the November Meeting of Haemophilia Centre Directors. Professor Bloom suggested that the Haemophilia Centre Directors should be asked if there was anybody who would be willing to set up a detailed study. If there was someone willing to organise this study, he should send a detailed proposal for the Reference Centre Directors consideration.

Dr. Forbes commented that he had the impression that haematuria was less common now in severe haemophiliacs than

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it had been some years ago and this was possibly related to the introduction of home therapy. Several Directors present at the Meeting had the same impression. It was agreed that the question of a Haematuria Working Party being formed should be raised at the November meeting of Haemophilia Centre Directors.

5. Trial of FEIBA or AUTOPLEX in the UK

Professor Bloom read a letter from Mr. Norman Berry of Immuno UK which set out the background to this item on the Agenda. Immuno were applying to the Committee on the Safety of Medicines for a Clinical Trial Certificate to enable them to set up a trial of FEIBA in the UK. There were at the present time two trials being undertaken already, one in the USA and the other in Holland.

Dr. Prentice said that he had presented the UK data on the treatment of Inhibitor patients at the Vienna Meeting earlier in 1979 and the consensus at that Meeting was that a properly controlled prospective trial was the only way to find out if FEIBA or AUTOPLEX were clinically effective. He wondered whether selected Centres in the UK would be prepared to join in a trial which Immuno were endeavouring to organise in the United States.

Dr. Preston said that some Sheffield patients were convinced that FEIBA was beneficial to them and were to some extent putting pressure on doctors to use it. Dr. Prentice said that he would not like to take on the organisation and

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running of such a trial and he would much prefer if a trial was to be run in the UK that it should be combined with the trial in the United States. The trial in the United States was to be on "closed" and not "open" bleeds. There was a general feeling that the assessment of results in "closed" bleeds would prove very difficult.

Dr. Delamore said that FEIBA and AUTOPLEX were very expensive materials and this made it even more important to know how effective it was in controlling bleeding. The price was thought to be in the region of 30-40p/unit. He would want to know very much more about what the American trial was doing before he would agree to join it.

Dr. Prentice saw no problems over sending data and samples to the United States. Dr. Kernoff said that he wondered what the present position was regarding supplies of AUTOPLEX as he understood that there was a shortage. Professor Bloom replied that he had received information very recently from Travenol on AUTOPLEX. A trial had been carried out in the USA but he had not been given the detailed results although they were alleged to be good. Travenol however were now running into production problems with the product, in particular with regard to standardizing the units of activity in each batch. Dr. Prentice thought that if a trial was undertaken in the UK the materials would be supplied free of charge.

Professor Bloom said that he felt that most UK Haemophilia Centres lacked both the staff and the time to do detailed studies with lengthy protocols. Dr. Rizza said that

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he was not convinced by the literature that FEIBA was a useful material. He had obtained good results with Factor VIII concentrates and had not used FEIBA at all. He would be most reluctant to take part in a trial of FEIBA.

Professor Bloom suggested that the matter should be referred back to the Inhibitor Working Party and that Dr. Prentice should get details from Professor Klimt and Dr. Sixma concerning their trials. The Working Party should then report back to the Reference Centre Directors with their proposals.

Dr. Rizza said that there were problems also regarding the assay of factor VIII antibodies as there was much variation from Centre to Centre. It was agreed that a trial of FEIBA would be desirable and that Dr. Prentice should get details of the Dutch and American trials and report to the next Reference Centre Directors Meeting.

6. Pain Relief

Dr. Rizza had received a letter from Professor Ingram in which he referred to a paper by Dr. Budd of Bradford of the Intractible Pain Society (Ref.: Budd, K. (1979) The Concept of chronic pain relief. Health Trends 11, 69.) Professor Ingram thought that it might be valuable for the Haemophilia Centre Directors to make contact and to liase with the Intractible Pain Society but as he was on the point of retirement he did not think it would be right for him to make the approach to the Society.

Dr. Tuddenham said that none of his patients had

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intractible pain of the kind usually dealt with by the Intractible Pain Society and Professor Bloom, Dr. Rizza and Dr. Forbes agreed with this comment.

Dr. Prentice added that he thought it was important to convince haemophilic patients that they did not have intractible pain. Dr. Delamore said that some of his patients complained of much pain and felt that their pain was intractible, even if the medical staff did not regard it as such.

Professor Bloom suggested that the Reference Centre Directors should read the article quoted by Professor Ingram and defer further discussion until the next meeting of Reference Centre Directors. This was agreed.

#### 7. Collection of data for Haemophilia Centre Directors

Professor Bloom said that some Directors were worried about the amount of information at present requested from Haemophilia Centres. The collection of data over the last ten years had been invaluable and had helped considerably with haemophilia management. In particular the Directors were able, by means of those statistics, to show the DHSS that the supply of NHS freeze dried concentrate fell far short of the UK requirement. It was felt that Haemophilia Reference Centre Directors should from time to time review the system for collecting data and the type of data they felt it was useful to collect. Some Centres had difficulties over compiling the Annual Returns in their present form but Professor Bloom felt that this was largely a matter of local problems with record-keeping which needed to be resolved by the Centres.



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concerned. The problems over record-keeping arose from the many variations on the way the Centres' clinical practices were run and a system which worked well at one Centre would not be practicable at another. Each Centre had the responsibility for ensuring a good records system which would provide information on all the patients registered, seen and treated by the Centre, with details of the amount and type of materials the individual patients received.

Professor Bloom felt that the type of data collected fell into two groups:-

1. Basic data including name, diagnosis, factor VIII level, inhibitor status of known haemophiliacs in the United Kingdom. This basic information would be updated regularly.
2. Information regarding the materials used to treat these patients annually.

He invited Dr. Jones to speak regarding a short report he had circulated to the Reference Centre Directors about the collection of data.

Dr. Jones presented his document which showed that the majority of Reference Centre Directors were in favour of a review system of data collection. This was discussed in detail, and Dr. Rizza gave the Directors a memorandum from Miss Spooner which outlined the data at present stored in the Computer File in Oxford. Examples of the type of information which was at present available from the computer file were shown and discussed. It was suggested that the names of the patients should be entered into the computer file, subject to the approval

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of all Haemophilia Centre Directors at the November Meeting, to make easier the checking of data by the Directors. At present the patients are identified in the computer by code numbers only. Some concern was expressed over the possibility that much valuable data would be lost if the proposed new scheme was implemented. Under the proposed new scheme information would no longer be collected on named patients treated each year or on the materials received by individual patients.

It was agreed that Dr. Jones, Dr. Rizza and Miss Spooner should present a paper to the November meeting of all Haemophilia Centre Directors outlining the proposals for a new simplified scheme for collecting data and the computer scheme in Oxford.

Dr. Prentice asked whether the Haemophilia Society had been consulted about the use of computers. Dr. Rizza replied that they had not been consulted about this matter but that representatives would in any event be present at the November Directors meeting.

Dr. Craske said that the Hepatitis Working Party would like data to be collected for 1979 in the same way as it had been collected for 1977 and 1978. It was important to collect information on the type of materials received by patients. There was some discussion regarding von Willebrand's disease and Carriers. Dr. Craske said that he would like data to be collected for the carriers and von Willebrand's patients treated during 1979 in the same way for patients treated during 1977 and 1978. If data was not collected in detail on the patients treated during 1979, there would be difficulties

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for the Hepatitis Working Party. Dr. Jones requested that carriers should be deleted from the computer file. He said that it was a recommendation of the Clinical Genetics Society Working Party that carriers should only go into genetic registers if the patient concerned had given his or her approval (Ref.: Lancet I, 253 (1979)). It was therefore agreed that data on Carriers of Haemophilia A or B should no longer be collected on a National basis. With regard to collecting data on von Willebrand's disease patients, Professor Bloom suggested that the von Willebrand's Working Party (see Item 8f) should consider the criteria for the diagnosis of von Willebrand's disease and review the data in the computer file in 1981. The data on treated von Willebrand's patients should be collected in the meantime.

Dr. Rizza presented a brief report on the 1978 Annual Returns which had been received to date. There was some discussion as to whether or not the Directors wished to continue to collect data on the different material used for the treatment of Inhibitor patients. It was agreed that slightly amended data should continue to be collected on these patients in the future.

8a) Hepatitis Working Party

Dr. Craske presented the report that had been pre-circulated to all the Reference Centre Directors and there was some discussion regarding the details in the report.

Professor Bloom commented that one of the difficulties which many smaller Haemophilia Centres were encountering was

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in collecting the individual patient treatments day-by-day in a way which would allow easy retrieval of information at a later date, should the patient develop Hepatitis.

Dr. Jones suggested that Dr. Craske should write to the Reference Centre Directors and spell out precisely what type of information the Hepatitis Working Party required in the future. Dr. Craske agreed to do this.

Dr. Craske presented a draft Form C3 which he proposed to circulate to all Haemophilia Centre Directors asking for information on patients thought to have developed chronic hepatitis. He invited the Reference Centre Directors to let him have their comments on the Form.

8b) Home Treatment Working Party

Dr. Jones commented briefly on the activities of his Working Party (See Appendix A).

8c) Factor VIII Antibodies Working Party

Dr. Prentice presented a table giving a list of numbers of Haemophilia A patients with inhibitors who were treated at Centres during 1977 and a table summarising some of the detailed information he had obtained on these patients. Dr. Prentice said that in the light of experience he wished to modify the data collecting forms used during 1977.

Professor Bloom asked if any progress had been made in looking into the question of the Inhibitor assays and their standardisation. Dr. Rizza said that an International Study of antibody assays was being considered by the ICTH Working Party chaired by Dr. Lechner. It was therefore

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decided to wait and see what progress was made by the ICTH Working Party, before undertaking a study in the United Kingdom.

8d) Factor VIII Assay Working Party

Dr. Rizza presented a written report from the Working Party and drew particular attention to Item 3 on page 4 of the report. Many laboratories in the UK were interested in using a freeze-dried plasma standard for factor VIII assay but because of the large number of ampoules required (25,000 per annum) an approach had been made to Blood Products Laboratory at Elstree and to Protein Fractionation Centre in Edinburgh to see if these establishments would in principle be prepared to help with freeze drying the Standard. NIBSC did not have the capacity to freeze-dry such a large quantity of material.

8e) Detection of Carriers Working Party

Professor Bloom said that his Working Party had not met and had not done any work. He wondered at one time whether the Working Party could produce a broadsheet on carrier detection but felt that it would be very hard to better the W.H.O. broadsheet. He therefore queried what the remit of the Working Party was. Also as he had now assumed Chairmanship of the Haemophilia Centre Directors he did not think that he personally would have sufficient time available to be Chairman of the Carrier Working Party as well.

Professor Bloom suggested that the detection of Carriers Working Party should be disbanded and this was agreed.

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8f) Von Willebrand's Disease Working Party

Professor Bloom said that there had been some discussion previously regarding the possibility of a Von Willebrand's Disease Working Party being formed. Dr. Tuddenham had indicated that he would be willing to be Chairman of such a Working Party. The main aim of the Working Party would be to establish diagnostic criteria for the disease. It was agreed that a Von Willebrand's Disease Working Party should be set up under Dr. Tuddenham's Chairmanship.

9. Arrangements for the November Meeting of All Haemophilia Centre Directors

Dr. Rizza reported that all the people invited to speak at the Scientific Session on 21st November had accepted the invitation.

The plan was that the afternoon of 20th November would be a business meeting. The morning of the 21st would be reserved for the presentation and discussion of the reports of the Working Party Chairmen and the afternoon of the 21st would be a Scientific Session with invited speakers. The meeting would be held in the Board Room of the Oxford Regional Health Authority Offices. There was some discussion regarding the number of people expected to attend this meeting. It was estimated that there would be around 100 people present on both days and this was about the number that the room at the Oxford R.H.A. Offices could hold. It was suggested that the venue for the main meeting of Haemophilia Centre Directors should be changed from time to time and Dr. Charles

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Forbes proposed that the 1980 meeting should be held in Glasgow. This was agreed.

10. Any Other Business

Dr. Jones reported that the Darlington Associate Haemophilia Centre no longer wished to be recognised as a Centre.

Dr. Rizza referred to a letter he had received from Dr. Lane suggesting that there should be joint meetings between representatives of the National Blood Transfusion Service and the Haemophilia Reference Centre Directors.

Dr. Prentice raised the possible problem in that if Dr. Lane was invited to the Meeting a representative from the Edinburgh Protein Fractionation Laboratory should also be invited to attend. Although it was felt that the proposed meetings between representatives of Haemophilia Reference Centre Directors and NBTS Directors were important and desirable, there was some discussion about the desirability of Dr. Lane attending all Meetings of Reference Centre Directors and it was suggested that probably there should be a separate meeting of representatives of the Transfusion Service and Reference Centre Directors. It was agreed that Professor Bloom and Dr. Rizza should meet with Dr. Lane to find out the best way of promoting such Meetings.

Date of Next Meeting of Haemophilia Reference Centre Directors

It was agreed provisionally that the next meeting would be held on Tuesday 26th February 1980 at the Royal Free Hospital.

The Meeting closed at 5.00 p.m.