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Minutes of a Joint Meeting of Directors of Haemophilia Centres and Blood Transfusion Directors held at the Regional Blood Transfusion Centre in Sheffield on 31.1.74

Those present at the Meeting were:-

Prof. E.K. Blackburn (Chairman)(Sheffield Haemophilia Centre)

Dr. P.G. Arblaster (Treloar Haemophilia Centre)

Dr. A. Aronstam (Treloar Haemophilia Centre)

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

Dr. Ethel Bidwell (Oxford Blood Products Laboratory)

Dr. Rosemary Biggs (Oxford Haemophilia Centre)

Dr. A.L. Bloom (Cardiff Haemophilia Centre)

Dr. T.H. Boon (Newcastle Haemophilia Centre)

Dr. C.C. Bowley (Sheffield Blood Transfusion Centre)

Dr. D.G. Chalmers (Representing Prof. Hayhoe)(Cambridge Haemophilia Centre)

Dr. T.E. Cleghorn (North London Blood Transfusion Centre)

Dr. J. Darnborough (Cambridge Blood Transfusion Centre)

Dr. S.H. Davies (Representing Prof. Girdwood)(Edinburgh Haemophilia Centre

Dr. I.W. Delamore (Manchester Haemophilia Centre)

Dr. Katherine Dormandy (Royal Free Hospital, London)

Dr. J.O.P. Edgcumbe (Exeter Haemophilia Centre)

Dr. D.I.K. Evans (Manchester Children's Hospital)

Prof. P.T. Flute (St. George's Hospital, London)

Dr. C. Forbes (Glasgow Haemophilia Centre)

Dr. Jean Grant (Oxford Blood Transfusion Centre)

Dr. J. Guyer (Sheffield Children's Hospital)

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

Dr. J.P. Hayes (Representing Prof. Humble)(Westminster Hospital, London)

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

Dr. A. Inglis (Carlisle Haemophilia Centre)

Prof. G.I.C. Ingram (St. Thomas' Hospital, London)

Dr. G.C. Jenkins (London Hospital, London)

Dr. P. Jones (Newcastle Haemophilia Centre)

Dr. D. Lehane (Liverpool Blood Transfusion Centre)

Dr. J. Leslie (Southampton Haemophilia Centre)

Dr. M. Lewis (Representing Prof. Davidson)(Kings' College Hospital, London)

Dr. W.d'A. Maycock (Blood Products Laboratory, The Lister Institute, Elstree)

Dr. E. Mayne (Representing Prof. Nelson)(Belfast Haemophilia Centre)

Dr. M.J. Meynell (Birmingham Haemophilia Centre)

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

Dr. J.R. O'Brien (Portsmouth Haemophilia Centre)

Dr. C.R.M. Prentice (Glasgow Haemophilia Centre)

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

Dr. J.D.M. Richards (Representing Prof. Prankerd) (University College Hospital, London)

Dr. C.R. Rizza (Oxford Haemophilia Centre)

Dr. D. Stern (Bournemouth Haemophilia Centre)

Prof. J.W. Stewart (Middlesex Hospital, London)

Dr. J. Stuart (Birmingham Haemophilia Centre)

Dr. H. Swan (Sheffield Haemophilia Centre)

Dr. L.M. Swinburne (Leeds Haemophilia Centre)

Dr. A.S. Todd (Representing Dr. Tudhope)(Dundee Haemophilia Centre)

Dr. R.L. Turner (Bradford Haemophilia Centre)

Dr. Sheila Waiter (Department of Health and Social Security)

Dr. C.R.R. Wylie (Derby Haemophilia Centre)

Apologies for absence were received from:-

Dr. T. Black (Liverpool Haemophilia Centre)

Dr. I.A. Cook (Inverness Haemophilia Centre)

Prof. W.M. Davidson (Represented by Dr. M. Lewis)

Dr. A.A. Dawson (Aberdeen Haemophilia Centre)

Col. P.E. Field (Northern Ireland Blood Transfusion Centre)

Prof. Girdwood (Represented by Dr. S.H. Davies)

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

Prof. J.G. Humble (Represented by Dr. J.P. Hayes)

Prof. M.G. Nelson (Represented by Dr. E. Mayne)

Prof. T.A.J. Prankerd (Represented by Dr. J.D.M. Richards)

Dr. G.L. Scott (Bristol Haemophilia Centre)

Dr. H. Sterndale (Margate Haemophilia Centre)

Dr. G.R. Tudhope (Represented by Dr. A.S. Todd)

Mr. J.G. Watt (Edinburgh Protein Fractionation Centre)

1. An opening address of welcome was given by Dr. C.C. Bowley.

2. Matters arising from the Minutes.

(a) Progress of the Haemophilia Centre Directors report on Jaundice, Antifactor VIII and Antifactor IX in patients with Haemophilia and Christmas disease. Dr. Biggs noted that the paper on this subject had been accepted for publication in the British Journal of Haematology and that page proof was included in the papers of the meeting for the information of Haemophilia Centre Directors.

ACTION. Dr. Biggs asked that survey returns be made on the 1972 forms by all those Directors who had not yet completed the data for 1972. Dr. Biggs also asked that in making the 1973 returns, Directors should record the numbers of bottles or ampoules of concentrates used and make no attempt to convert these to any notional number of donor units.

(b) Report on the Progress of the Survey of Au Antigen in House Contacts of Haemophiliacs.

Dr. Ingram said that in all 43 family groups had been studied. 72 samples from patients and 63 from contacts had been tested. Of the samples from patients, 2 were Ab and Ag positive, 1 was Ag positive and Ab negative, 43 were Ab positive but Ag negative and 26 were both Ag and Ab negative. Of the contacts 1 was Ag positive and Ab negative and ~~only~~ 5 were Ab positive and Ag negative and 57 were Ab and Ag negative.

Discussion about this paper included the following topics:-

(i) Distinction between the various categories of HbAg positive patients (Dr. Evans, Dr. Davidson, Dr. Delamore)

(ii) The idea that enzyme studies should more often be made (Dr. Davies)

(iii) A report was made of the tests made at the Alton Centre (Dr. Rainsford)

(iv) A test based on lymphocyte transformation was

described (Dr. Forbes).

ACTION. Dr. Ingram said that more samples from patients and also from house contacts of patients were required. Dr. Ingram said that the virologist at St. Thomas's offered to assay antigen for those Directors with antigen positive patients and who do not have assay facilities. It was stressed that more follow-up samples from all patients and their known contacts were required.

(c) Trial of prophylaxis at Alton - an Interim report.

Dr. Arblaster described the aims of the trial and outlined some of the practical difficulties which they had come across early in the trial.

Dr. Aronstam then described the results of the first two terms of the trial. He stressed that the trial was still 'double blind'.

3. The present and future supply of Factor VIII.

Dr. Biggs introduced Appendix B which was an M.R.C. Working Party report mainly concerning the numbers of patients with Haemophilia and the amounts and varieties of Factor VIII likely to be needed for that treatment. Dr. Biggs noted that this report had now been approved by the M.R.C. and accepted for publication in the British Journal of Haematology. Dr. Biggs said that there were three main questions for discussion.

(a) How many Haemophiliacs are there in the United Kingdom?

(b) What kind of material was best for their treatment?

(c) How much of it was likely to be needed?

Dr. Biggs said that the report suggested a need for material derived from 500,000 to 750,000 donations annually.

These subjects were then discussed as follows:-

(a) On how many haemophiliacs are there in the United Kingdom?

(i) Dr. Jones reported on a survey that he is making in the Newcastle area. He said that he had encountered a number of haemophilic patients who had no haemophilia cards and whose blood had never been tested at a coagulation laboratory. He suggested that any count of patients known at haemophilia centres was likely to underestimate the total number of such patients. He had encountered 287 diagnosable bleeders in a population of 3 million, an incidence of 9.6 per 100,000 of the population.

(ii) Dr. Prentice suggested that it might be profitable to employ a doctor full time to carry out a survey of the number of haemophiliacs in the United Kingdom and to gather any other similar information.

(iii) Dr. Ingram spoke on the long term forecast of factor VIII requirements (paper circulated at the meeting) and stressed that the incidence of haemophilia is likely to rise as treatment improved. Any assessment of amount of A.H.G. required for therapy must take this into account.

(b) What kind of material was best for treatment?

There was a wide ranging discussion about the relative merits of cryoprecipitate and freeze dried concentrates with regard to ease of manufacture, recovery from the original plasma, ease of administration and recovery of activity in the patients. It was generally felt that larger supplies of concentrated preparations were required now and urgently and some felt that it was rather meaningless to ask doctors if they would prefer freeze dried concentrate to cryoprecipitate when no freeze dried concentrates were available to them. When the discussion was completed the meeting was asked to

indicate whether anyone would in fact prefer to have cryo-precipitate if freeze dried concentrate were freely available. It was clear that none of those present would prefer cryo-precipitate.

(c) How much material was likely to be needed?

Dr. E. Mayne gave statistics for Belfast and said that they use material prepared from approximately 10,000 donors for the management of their patients. They keep a stock of commercial concentrate which they find invaluable in the present troubled times.

Dr. Bowley presented a paper (circulated) in which he analysed the use of cryoprecipitate in the Sheffield Region. From local figures, he concluded that the calculated national requirements of factor VIII as reported in Appendix B were probably an over-estimate. Dr. Blackburn questioned the data on which these conclusions were based.

Dr. Maycock said that from his own survey of the amount of material required for the treatment of haemophilia, he obtained figures very similar to Dr. Biggs's figures and he pointed out that in 1971, B.T.S. Centres were already supplying 3x more cryoprecipitate than calculated by Dr. Bowley for 1973. Even more must be required now.

Dr. Rizza presented a paper analysing the use of cryo-precipitate, British freeze dried concentrates, and commercial concentrates in Oxford during the year 1973. The Oxford figure showed that the recovery of factor VIII activity from plasma by the cryoprecipitate method and by the alcohol fractionation method were similar and that the recovery of factor VIII activity in the patient' plasma was marginally better when freeze dried fractions were used.

In view of all that had been said, the Chairman concluded

that with one exception, the Meeting supported and wholeheartedly endorsed the Appendix B Document. Again it was stressed that the estimates in Appendix B are just for present and that in five years time there may be a need for more material.

ACTION. The Chairman agreed to write to the D.H.S.S. saying that the meeting of Haemophilia Centre Directors and Transfusion Directors, approved the contents of Appendix B and recommended that this document be used as the basis for planning the future requirements for factor VIII in the United Kingdom.

The meeting then went on to discuss problems which would arise in trying to increase the supply of factor VIII freeze dried concentrates.

It was felt that once the new fractionation laboratories in Edinburgh and at the Lister Institute were in full production they should be able to meet the needs of the country provided sufficient plasma was available.

Some Blood Transfusion Directors felt that plasmaphoresis which was already being carried out on a large scale in some Centres might be the answer to the problem of plasma supplies. Dr. Cleghorn described his procedure and said that his donors found it acceptable and not distressing.

There was no doubt that the 'processing' of more blood to obtain plasma for manufacture of factor VIII would require more staff, equipment, mobile vans with cold storage facilities, etc., and that this would add to the Blood Transfusion Centres' costs.

Dr. Waiter could give no statement as to how this extra expense would be met but she said that it should in the first instance be referred to the D.H.S.S. She made the point that the purchase of commercial A.H.G. was already costing the D.H.S.S. a lot of money.

The meeting digressed for a short time to discuss the problems of genetic counselling and how newer techniques such as ante-natal sexing and amnioscopy to obtain samples of cord blood might help in counselling prospective parents.

Several Directors said that they did not treat all the patients at their Centres since this was too inconvenient for the patient and too difficult. On the other hand, they were aware that the materials might not be used properly. This raised the question of home therapy. It was stressed that home therapy was becoming more accepted and widespread and was improving the quality of the patients' lives. Cryo-precipitate was not ideal for home therapy from many points of view. Some Directors were buying commercial A.H.G. for use in home therapy.

5. <u>The Organisation of Haemophilia Centres.</u>

Professor Blackburn summarised for the meeting the document drawn up by Dr. Biggs and Rizza on the reorganisation of Haemophilia Centres in the United Kingdom. The document was sent to the D.H.S.S. in January 1972 but the D.H.S.S. had been unable to make any comment on it yet because of the reorganisation of the Health Service which was to come into effect in April, 1974. Dr. Waiter said that some decision about the reorganisation of Haemophilia Centres would be arrived at after April, 1974.

Dr. Biggs said that she had sent to the D.H.S.S. another memorandum about reorganisation of Haemophilia Centres. This document suggested that the role of the Major Haemophilia Centres should in the future be changed.

This document envisaged each Major Centre as playing a more important role in supporting the Haemophilia Centres, grouped around it. The sort of things that were proposed as important for the Major Centres in the future were:- the supply of therapeutic materials, medical cover during holiday periods, a reference laboratory service and a training service for medical, ancillary staffs and patients, a specialist reference centre for advice by telephone and consultation and finally a centre for the organisation of local research.

The Directors felt that such a reorganisation could well help them to control the use of Factor VIII concentrates in peripheral hospitals which should in turn promote better management and more economical use of rare resources.

Most Directors found great difficulty in obtaining medically qualified staff for their Centres, especially at S.H.O. grade. Furthermore, although it was desirable to have haemophiliacs examined and assessed by doctors of the rank of registrar and above, this was rarely possible.

Some regions were still having difficulty in getting nurses to help with infusions.

It was felt that the orientation of the Haemophilia Centres to the Major Centres on a more definite administrative basis might help Directors to obtain the therapeutic materials and staff they need and might contribute substantially to improving the treatment of patients in the United Kingdom.

ACTION. Dr. Waiter was asked to continue with her work in promoting the drafting of a new H.M. on the roles and duties of Haemophilia Centres recognising and laying the foundation for a new view for the Major Centres.

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Blood Product Evaluation Studies

A – Edinburgh Concentrate (INTERMEDIATE)

Date	Patient	Batch No.	Solubility	Particles	Factor VIII content Stated	Factor VIII content Assayed	Actual dose	Observed Rise	Expected Rise	% Recovery	Temp.	Othe Reac
6.11.73	[redacted]	34	Good	Nil sig.	4 u/ml (3.6 dry)	2.2 u/ml	429 u.	0.15 u/ml	0.16 u/ml (0.14)*	94% (107%)*	Nil	N
8.11.73		343	Good	Nil sig.	7 ↓ 4 u/ml ↑ (4.4 dry)	2.15 u/ml	249 u.	0.09 u/ml	0.09 u/ml (0.07)	100%(128%)	Nil	Sligl head
9.11.73		33	Good	Nil sig.	7 u/ml	1.95 u/ml	226 u.	0.06 u/ml	0.08 u/ml (0.07)	75%(86%)	Nil	Sligl head

* Figures in brackets calculated by formula:- Plasma volume = (1 – PCV) x 77.7 x bodyweight)

Others calculated from formula :- Expected rise (%) = $\frac{\text{Dose given (units)}}{\text{Bodyweight x 0.4}}$

Patient gets matches & AF and cryo
Sometimes gets Humafil

CRYOPRECIPITATE

ca 60 donations

Date	Patient	Factor VIII content assayed	Actual dose given	Observed rise	Expected rise	% Recovery	Temp.	Reactions
5.11.73	[redacted]	2.5 u/ml	2236 units 50	.69 u/ml	1.07 u/ml (.97)*	64 (71)*	N	Nil
6.11.73		3.2 u/ml	1082 units 30	.33 u/ml	0.52 u/ml (.45)	63 (73)	N	Nil
7.11.73		3.4 u/ml	806 units 15	.19 u/ml	0.38 u/ml (0.34)	50 (56)	N	Nil
8.11.73		1.8 u/ml	436 units 15	.19 u/ml	0.21 u/ml (0.18)	90 (105)	N	Nil
9.11.73		1.8 u/ml	329 units 15	.20 u/ml	0.16 u/ml (0.14)	125 (142)	N	Nil

*Figures in brackets calculated by formula:- Plasma volume = (1 - PCV) x 77.7 x bodyweight)

Others calculated from formula: Expected rise (%) = $\frac{\text{Dose given (units)}}{\text{Bodyweight x 0.4}}$

1 cryo = 200 ml plasma standardised

INTERMEDIATE FACTOR VIII TRIAL (EDINBURGH)

PATIENT:..... DATE OF BIRTH:..... BLOOD GROUP:.....

FACTOR VIII LEVEL:..... HEIGHT:..... DOSE: ..... units

FACTOR VIII INHIBITOR:..... WEIGHT:..... DURATION OF INFUSION: ..... mins

IN VIVO

TIME	VIII (B)	VIII (I)	Fibr	Eth Gel	S FDP	P/let Ct.	Hb	RBC	MCV	Hct	WBC	Retics	ESR	Plasma Hb	Met Hb	Hapt glob	Direct Coombs	HB-Ag HB-Ab	C_3	Lymph Blast	Urine	Bld Film
PRE-INF																						
10 mins																						
1 hr.																						
3 hrs.																						
6 hrs.																						
24 hrs.																						
6 months																						

IN VITRO (CONCENTRATE)

PARTICLE COUNT:..... ANTI-A TITRE:.....

VIII CONTENT(B):..... ANTI-B TITRE:.....

VIII CONTENT(I):..... Na^+ CONTENT:.....

VIII CONTENT(B):..... BATCH NO:..... VOL. DIST. AQ ADDED:.....

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