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MEETING OF SCOTTISH FACTOR VIII WORKING PARTY
held in Department of Medicine Library
Royal Infirmary of Edinburgh 11 August 1988

Present: Dr C A Ludlam, (Chairman), Royal Infirmary, Edinburgh
Dr G D O Lowe, Royal Infirmary, Glasgow
Dr B E S Gibson, Sick Children's Hospital, Glasgow
Dr E Mayne, Royal Victoria Hospital, Belfast
Dr D B L McClelland, Edinburgh BTS
Dr R J Perry, Protein Fractionation Centre
Dr B Cuthbertson, Protein Fractionation Centre
Dr P Foster, Protein Fractionation Centre
Dr R Stewart, SNBTS HQ Unit

Apologies were received from Professor Cash.

INTRODUCTION

Dr Ludlam welcomed the members to the meeting, introduced Dr Stewart to the group and thanked him for agreeing to act as secretary.

Minutes of previous meeting:

These were agreed as a true record of the meeting on Thursday 23 June.

Future Meetings:

It was agreed that the next meetings of the group be on 8 September 1988 and 6 October 1988.

Factor VIII Usage:

Statistics on the usage of Factor VIII in the East of Scotland were circulated (Appendix I), and those of the Edinburgh centre were reviewed. The use of Factor VIII was greater in those who are anti HIV positive. Dr Ludlam commented that their reduction in usage during 1985/86 was probably due to concern over HIV transmission, and Dr Lowe added they had similar data which showed that the reduction at this time was due to a reduction in home usage, while hospital usage was unchanged.

Dr Lowe supplied the following figures for Glasgow Royal Infirmary usage, which corresponds to appproximately 160 patients:

	1984	2.4 million units
	1985	2.1 million units
	1986	2.7 million units
	1987	3.6 million units
First half	1988	2.7 million units

Dr Lowe stated that this half-year figure included 1 million units used to cover 7 orthopaedic operations, and if this is taken out of the total, usage is the same as 1987.

Dr Lowe commented that before 1986 Glasgow usage was below the national average, in 1986 it exceeded the average and in 1987 was the same as the UK figure.

Dr Gibson gave the following figures for paediatric use in Glasgow:

	1986	600,000 units (22 patients)
	1987	920,000 units (26 patients)
First half	1988	610,000 units (26 patients)

Dr Gibson commented that they had a few patients on short term prophylactic therapy and the major increase in use is in patients on home therapy: the biggest users are anti-HIV negative, although there are some anti-HIV positive high users.

Dr Mayne said that approximately 80 patients per year are treated at the Belfast Centre.

Dr Perry requested that the Haemophilia Directors supply monthly Factor VIII usage figures and this was agreed. It also was agreed that Dr Stewart should design a form (see Appendix 2) which would be sent to the Haemophilia Directors on the 26th of each month which will request the following information on number of units issued:

Total PFC FVIII
Total cryoprecipitate
Commercial FVIII (specified by brand)
FEIBA
HYATE-C
F IX

The completed forms should be returned to Dr Stewart as soon as possible and the data shall be collated and fed back to the Haemophilia Directors and members of the Working Party by the 15th of the following month.

A copy of a draft of the form will be supplied to the members of the Working Party for their comments and Dr Ludlam will contact the Dundee, Aberdeen and Inverness Centres to discuss the data collection with them.

Previously Untreated Patient (PUP) Studies:

Dr Perry stated that a new Factor VIII product will be available for clinical trials in early 1989. This product will have a higher specific activity, being 5-10 times purer than the existing product (Z8). Dr Perry stated that more fibrinogen, fibronectin and other lower molecular weight proteins will be removed; these contaminants may be implicated in allergic reactions and immune disturbance. Dr Perry stated that this product will be a 'stepping stone' to a totally new product.

The requirements for Product Licence for the new product were discussed. Dr Perry stated that to obtain a variation, invitro virus inactivation data, and patient data including recovery, half-life data and (at least subjective) evidence of haemostasis were required. This was discussed.

The number of PUP's needed to be treated to demonstrate that a product was non-infectious was discussed, in relation to the ISTH guidelines. Dr Foster supplied a copy of a graph of the statistical power v.s. number of patients treated with zero event rate. It was agreed by the group, that in their opinion more value might be attached to the use of multiple batches in fewer patients, rather than one batch in many patients. It was agreed that this should be discussed with the Statistical Adviser, Dr R J Prescott at the October meeting.

Dr Ludlam supplied copies of the protocol for the new 8Y PUP study and agreed to write a draft protocol for the Scottish/NI to study.

It was agreed that all the Haemophilia Directors should submit the protocol to their local Ethics Committee, emphasising that the study will necessiate repeated venepuncture.

It was agreed that it would be of value to include a group of "normals," in whom prospective regular LFT's were performed, as these valuable background data are often missing. Dr McClelland suggested that a grant application be made to the SHHD to find this study in "normals."

The Haemophilia Directors were requested to supply historical LFT and product use data on patients, where available.

The inclusion of patients who had received only cryoprecipitate previously was discussed, as the group estimated that they would find only about 5 PUP per annum, and some of these may be treated elsewhere prior to referral to the centre.

It was agreed that patients treated with cryoprecipitate only be included, if they have weekly LFTs performed for the first month, but criteria must be agreed in advance to determine who should be excluded. Dr Perry stated that if it proved difficult to find sufficient PUPs, additional virucidal validation data could be supplied by demonstrating that the process was virucidal to a degree at least equivalent to that of a known acceptable product, e.g. 8Y. Dr Ludlam agreed with this point, particularly if a virus known to be very stable, e.g. parvovirus, could be shown to be inactivated.

Due to the difficulty of performing large studies in PUP population, it was agreed Dr Ludlam should telephone Dr Rotblatt and invite her to attend the September meeting to advise the group of the Licensing Authorities attitudes.

Validation of SNBTS Co-agulation Factors:

Dr Perry requested the agreement of the group with the conclusions reached in PFC paper on the above topic. Dr Ludlam said that this was a large issue and would require full discussion and it was agreed that it should be discussed at the September meeting.

The necessity to demonstrate the lack of infectivity of NANBH for a new product PL was discussed. Dr Perry being of the opinion that this was not necessary.

It was agreed that a protocol and flow chart for the half-life and recovery studies, be prepared by Dr Perry for the next meeting. The PFC will supply their optimal requirements for the protocol, and their feasibility will be considered by the Haemophilia Directors.

Availability of Commercial Factor VIII

Alpha have agreed to supply 50,000 Units per month to the RIE. Dr Lowe said they also had agreement of supplies from Alpha.

Dr Ludlam thanked the group for their contributions and the, meeting was closed.

RRC Stewart 12/8/88

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APPENDIX I(a)

EDINBURGH HAEMOPHILIA CENTRE - FACTOR VIII AND CRYO (IN UNITS)

2-5 2-5

	Severe 1	Severe 2	Mod 1	Mod 2	Mild 1
VIII & Cryo 1987	20	17	10	3	5
	880,370	1,297,535	430,020	44,530	82,160
1986	16	17	6	2	10
	611,860	836,370	114,390	101,590	324,470
1985	19	17	6	5	10
	544,840	797,110	92,750	112,760	135,760
1984	19	19	4	4	9
	740,580	1,274,970	35,040	268,160	74,980
1983	21	19	5	4	6
	716,915	1,249,350	47,460	171,240	70,300

APPENDIX I(b)

DUNDEE COAGULATION FACTOR USAGE

	FACTOR VIII	FACTOR IX
1983	359,040 i.u.	67,500 i.u.
1984	340,240 i.u.	100,500 i.u.
1985	346,000 i.u.	103,200 i.u.
1986	436,000 i.u.	168,300 i.u.
1987	562,520 i.u.	141,000 i.u.

APPENDIX I(c)

NHS HUMAN FACTOR VIII CONC EDN DISTRIBUTED FROM
HAEMOPHILIA CENTRE 165, RAIGMORE HOSPITAL from 1983 to 1987

HAEMOPHILIA A (Severe)

	HIV Negative	HIV Positive	TOTAL
1983	317,763		317,763
1984	337,070		337,070
1985	275,360	83,880	359,240
1986	215,960	87,490	303,450
1987	284,160	85,570	369,730

HAEMOPHILIA A

1986	1 bag Cryoprecipate	

HAEMOPHILIA B (mild)

1983		600
1984		Nil
1985		2,400
1986		2,700
1987		1,800