

FILE UNDER  
CONCENTRATE

NEWCASTLE AHA (T)  
Recd - 8 DEC 1979

& DO NOT LET NEWCASTLE HAEMOPHILIA CENTRE

PJ TAKE AWAY

21/10/76

Treatment of Haemophilia

Report to the Newcastle Area Health Authority (Teaching) on the use of anti-haemophilic globulin within the Northern Regional Haemophilia Service.

## 1. Available blood products

Haemophilic bleeding can only be controlled by the intravenous injection of anti-haemophilic globulin (A.H.G. or Factor VIII). Although AHG is present in animal as well as human blood, treatment with animal products is unfortunately antigenic and therefore reserved for critical care situations. Human blood products containing AHG at present available for treatment are

- a. Fresh frozen plasma (F.F.P.)
- b. Cryoprecipitate (Cryo)
- c. AHG Concentrate

FFP only provides a small dosage of AHG in an unacceptably high volume of plasma and is only rarely used for control of minor haemorrhage in adults.

Although, with expert preparation, cryo, is a good vehicle for AHG, in comparison concentrate has the following advantages:

- known dosage
- smaller volume
- easier preparation
- syringe injection
- lower incidence immediate side effects
- easier storage (4°C as opposed to deep freeze)
- longer shelf life
- use for home therapy, travel and work away from home.

The major disadvantage of concentrate is a higher incidence of hepatitis.

## 2. Availability of blood products

Cryo is made by the Blood Transfusion Service (BTS) from blood collected from Regional donors.

AHG concentrate can only be made from large, multidonor "pools" of plasma which, because Factor VIII activity has a short half-life, must be deep frozen within 18 - 24 hours of collection. The process of manufacture is called fractionation. During fractionation blood components other than AHG are produced for clinical use.

There are three fractionation plants in the UK. AHG produced in Oxford is all used for Oxford patients. That produced at Elstree is available to any Haemophilia Centre but is in very short supply. A new plant in Edinburgh will be commissioned in the near future - at present very little AHG concentrate may be obtained from this Scottish source.

Production of the British AHG product is directly linked to the volume of fresh plasma supplied for fractionation. Until sufficient plasma is forthcoming from Regional Centres the fractionation plants cannot produce enough concentrate. On present estimates only two thirds of the target



figure for concentrate needed to treat Britains 3,000 severe haemophiliacs will be met by 1977. A further difficulty is that when plasma is used for AHB concentrate production cryoprecipitate cannot be produced; there is therefore likely to be a time lag during the changeover from cryoprecipitate to concentrate production. In this period demands for commercial AHB may increase to cover treatment needs.

Shortfall of supply to meet the clinical demand is at present made up by importing commercial AHB concentrate. Three firms have DHSS import licences. The products are 'Hemofil', 'Kryobulin' and 'Profilate'.

### 3. The position in the Northern Region

With the reorganisation of the UK Haemophilia Centre network (new DHSS memorandum for circulation in the near future) the RVI becomes a Reference Centre for the Northern Region, with associate centres at Sunderland, Middlesbrough, Darlington, Carlisle and Whitehaven. Newcastle therefore has a prime responsibility for the management of all patients with hereditary bleeding disorders in the Region. In practice haemophiliacs receive immediate care at their local centres, or, in a few cases, at District General Hospitals known to the Centre network. The Newcastle Centre Director is contracted to the RHA with consultant responsibility throughout the Region, rather than to one hospital or one group of hospitals.

Because of the rarity of haemophilia and the expense of optimum treatment the consultants concerned with haemophilia in the Newcastle Region have agreed that all surgery, management of complications, and control of the home therapy programme should be the responsibility of the Newcastle Centre. This means that Newcastle carries a disproportionate financial burden in comparison with other areas.

#### Patients concerned and where they live

Of the 180 haemophiliacs known to us, 91 are severely affected (Factor VIII less than 1%). Distribution by AHA is:

Northumberland	9
Cumbria	12
Durham	10
Cleveland	27
Newcastle	10
Gateshead	6
North Tyneside	2
South Tyneside	7
Sunderland	8
	<hr/>
	91

In general, clinical and therapeutic problems requiring intensive management and a high financial cost are found in this group of patients.

#### AHB use in the Region

Figures for 1973 and 1974 are:

1973	<u>Cryoprecipitate</u>	Newcastle	538,230, VIII Units
		Region	351,610, VIII Units
	<u>PPF</u>	Total	100,000 VIII Units (estimate)
	<u>Concentrate</u>	Total	<u>132,500</u> VIII Units
TOTAL VIII UNITS (1973) = <u>1,122,340</u>			
APPROX. NO VIII UNITS/SEVERE HAEMOPHILIAC = <u>12,500</u>			

1974	<u>Cryoprecipitate</u>	Newcastle Region	587,230, VIII Units 379,260, VIII Units
	<u>FFP</u>	Total	80,000, VIII Units
	<u>Concentrate</u>	Total	432,240, VIII Units
Total VIII Units (1974)			= 1,478,730

APPROX NO VIII UNITS/SEVERE HAEMOPHILIAC = 16,430

To date (end November 1975) 895,330 VIII Units of commercial concentrate have been bought for use in 1975.

#### 4. Comparison with other figures

Estimated for use VIII units/patient/year from various sources:

UK Centre Directors	1975	12,000*
MRC Working Party	1974	15,000 - 20,000
Scotland	1975	18,000
USA	1973	20,000

\* this is 1974 - 75 average use and is low because most Centres had not started home therapy programmes.

The Northern Region figures are therefore in keeping with expert estimates for both the UK and the USA.

#### 5. Home therapy

Because home therapy (HT) can only be run successfully on concentrate the introduction of the Newcastle HT programme in 1973 (when the commercial concentrates were first licenced by the DHSS) is responsible for the larger proportion of the extra finance required to run the Centre.

Figures are:

##### Newcastle

November 1975

Home therapy: patients from Northern Region

No: Haem A on HT	November 1975	=	42
" " B " " " "	" " " "	=	1

Taking 38 Haem A patients who have remained in Northern Region throughout programme (i.e. with known VIII consumption/unit time:

Time on HT (months)	Mean	=	14
	Range	=	1 - 25
Consumption AHG/month(vials)	Mean	=	5.91
	Range	=	1.1 - 15.5
Mean no. FVIII units/vial throughout programme		=	265
Mean no. FVIII units/patient/cal month		=	1566.3
Mean no. FVIII units/patient/year		=	<u>18,796</u>
At 12 p/unit (HemoFil) cost/patient/year		=	<u>£2,256</u>



Multiplying the mean number of units/patients/year for HT by 38 gives 714,248 VIII units /year.

Approximately 180,000 of commercial concentrate have been bought in the past year 9895,330 - 714,248) to make up the deficit in BTS supplied VIII products for in-patient use.

#### 6. Estimates for 1976/77

The appended graph shows the almost parallel rise in patients on HT and commercial concentrate use. This rise can be expected to increase until all suitable patients are on HT. At present 10 patients are on the waiting list for training. Once all initial waiting list training is complete the HT programme should settle at about 60 patients, requiring 1,127,760 units/year. At present cost of 12p/unit this would mean a financial outlay of £135,331/annum. Taking into account the in-patient deficit (£21,600/annum) a grand total of £156,931 is the estimate for 1976/77.

#### Ways in which this total may be altered in practice

- i With all suitable severe haemophiliacs on HT we might expect a decrease in the amount of AHG concentrate required for in-patient use. However, the greatest short term demand for concentrate occurs when a haemophiliac with antibodies to Factor VIII experiences a life threatening bleed. Although there have been a number of interesting developments in the treatment of these bleeds we are concerned about potentially harmful side effects, and prefer to manage our antibody patients, at least initially, with massive doses of AHG. To date this policy has been effective. However it does account for two periods of increased demand shown on the graph (April - June 1974 + April - June 1975). With the expected increase in British AHG concentrate production we are placing a bid for regular supply of NHS concentrate with Elstree in an attempt to eventually obtain enough free product to cover in-patient demand. We cannot foresee any possibility of running the HT programme on NHS concentrate in the near future, but, once again, our need will be made clear to the appropriate authorities.
- ii All surgical procedures are at present performed under cryoprecipitate cover in Newcastle. To date 40 operations (including dental extractions) have been performed in 1975. With the NHS changeover from cryo to concentrate we may have to cover some surgery with commercial concentrate for a period. This is at present indeterminate.

#### 7. Conclusions

- A. On present estimates we expect a financial commitment of around £156,000 a year by 1977. This figure is calculated on the present DHSS price of 12p/unit for commercial AHG concentrate. It could be lowered if NHS concentrate becomes available in sufficient volume to cover in-patient prescriptions. It is unlikely that NHS concentrate will be available for home therapy by 1977. The figures do not take account of future inflation.
- B. As the majority of severely affected haemophilic patients live outside the boundaries of the Newcastle Area Health Authority (Teaching) it would seem appropriate that the financial commitment involved be sought either from the Northern Regional Health Authority or from the various Area Health Authorities by proportion. (The Regional responsibility of the Newcastle Centre is already recognised by both the NRHA and the DHSS).
- C. The finance involved in the present care of haemophiliacs is only shown in this report in terms of the drug bill. Savings in ambulance and hospital

time, and in long term savings to patients and their families through the home therapy programme have not been taken into account.

The Staff of the Newcastle Centre wish to thank the AHA(T) for Newcastle and the Northern RHA for their support and financial help in the past two years.

GRO-C

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November 1975

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