IN CONFIDENCE

0008

REPORT on two cases of reaction to EDINBURGH FACTOR VIII CONCENTRATE

Patient (1) [redacted] ([redacted])

Factor VIII Concentrate (2 bottles of batch 89) given about 11.30 a.m. on 3.9.75. Patient well after infusion and left G.R.I. by ambulance. About 30 minutes after infusion finished, patient began to feel generally unwell, "hot and cold", shivery and shaking. Shaking and muscular twitching became uncontrollable - brought back to G.R.I.

At time of arrival was pale, sweating, still feeling unwell, pulse rate was 120/minute. B.P. satisfactory at 120/80. Still shivering +++. Slight erythematous rash on back of neck. Given Hydrocortisone 100 mgs. I.V. stat, and Piriton 10 mgs. I.V., and gradually settled over next 15-20 minutes. Tachycardia settled. No further symptoms. Kept in G.R.I. for about 2 hours, by which time was completely settled - discharged home, no further effects.

This patient has previously complained of tiredness, headache and rash after Edinburgh Factor VIII Concentrate.

Patient (2) [redacted] ([redacted])
[redacted]

Patient was in-patient in Ward 3, and receiving Factor VIII therapy post nasal polypectomy.

Factor VIII Concentrate (4 bottles of Batch 90) given at 4.10 p.m., infusion finished at 4.30 p.m. At about 5 p.m. patient began to feel generally unwell, shivery and muscles began to twitch. Patient immediately went to bed. When seen at this time, was sweating and muscles twitching uncontrollably (? Rigor) - temperature normal when checked. Pulse 115/minute B.P. 110/70. Given Hydrocortisone 100 mgs I.V. and Piriton 10 mgs. I.V., with considerable improvement. Condition markedly improved in 10-15 minutes, and about 1 hour later settled completely.

NOTE:

In both of these cases Factor VIII was given following 10 mgs. Piriton I.V., prior to infusion, and Concentrate infusion was given in each case over 20-30 minutes.

0009

REQUIREMENTS FOR FACTOR VIII

PART 1. DEMAND

1. The proformae sent by Haemophilia Directors after the last meeting of the Haemophilia Centre and Regional Transfusion Directors have been analysed and the information (for 1974) is presented as a series of Tables.

2. Table 1 shows the number of haemophilia patients (418) registered at the various centres. As will be noted later, the Law centre issues cryoprecipitate direct to a number of hospitals in the West, but even though treated locally, these patients are registered at the parent haemophilia centre and so included in the table. There will almost certainly be a number of additional patients unrecognised as such, in particular Aberdeen considers that the number of haemophilia patients in the Orkneys and Shetlands is almost certainly under-estimated.

3. Table II indicates treatment patterns under the headings "on demand" (spontaneous bleeding episodes) "Emergency" (surgical and dental procedures), "casual" (visitors registered elsewhere) and "von Willibrand's disease".

The figures are those from haemophilia centres: a number of hospitals obtain cryoprecipitate direct from the RTC for convenience; in the West of Scotland 86% of issues were to the Royal Infirmary and the Queen Mother's Hospital, these are included in the table. The remaining 14% was issued to eight other hospitals and one G.P. (in Mull). Some of these issues were small, for example 12 units in the year, and it was not thought profitable to obtain detailed information concerning each of these issues. Two of the more major users (Western Infirmary, Glasgow and Ballochmyle Hospital) were approached; the general treatment patterns conform to those in recognised haemophilia centres, from a severe case requiring treatment every 2-3 days with 10 units of cryoprecipitate (increased to 18 in 1975), to mild cases requiring 6 units on one to two occasions a year.

There are considerable differences in the proportion of haemophilia patients requiring on demand treatment as shown in Table III. In compiling this table the Glasgow figures of those treated (Table II and IV) have been increased by 14% to give an approximation of the additional patients treated in hospitals other than the two designated centres and receiving this percentage of the total issues of cryoprecipitate from Law. 34% of the total haemophilia population required on demand treatment (48% of child and 30% of adult sufferers), but far fewer, with the exception of adult patients in Dundee, required treatment in Glasgow than in other centres.

13% of the haemophilia population required emergency treatment (31% of child and 9% of adult patients) and similarly the proportion of adults was considerably less in Glasgow and Dundee than in other centres (for example 2.7 adult haemophilia patients required emergency treatment in Glasgow compared with 21% in Edinburgh).

All the casual requirements were for spontaneous bleeding episodes, whereas most of the cases of von Willibrand's disease required treatment for operative procedures such as dental extraction.

There is also a wide variation, not brought out in the tables, in individual patient requirements; in Aberdeen, for example, the average number of treatment events is 15 per year for adults, but the range is from 2-70; in Inverness with 16 registered haemophilia patients, two patients require almost weekly therapy and together account for some 66% of the cryoprecipitate used.

4. Tables IV-VI record the requirements of cryoprecipitate for the various treatment patterns. The figures refer to cryoprecipitate in donation units, not in terms of Factor VIII, as centres variously estimate yields of Factor VIII per donation as 50-75, or even 80, units. Table VII shows requirements in terms of

Factor VIII units in this light.

To Table IV can be added a further estimated 300 treatment events for patients not treated in designated centres, in a range of 6-10 donations per treatment, using a total of 2703 donations (recorded as "miscellaneous" under Glasgow in Table VI).

The average amount of cryoprecipitate used per treatment of a spontaneous bleeding episode (Table IV) is fairly constant between centres with the exception of the adult treatment centre in Glasgow which adopts a regime of treatment continued over a number of days. As experience is gained with concentrated factor, a more precise estimate of requirements will be possible. This can never be absolute in terms of Factor VIII units as, though vials are put up in "250" unit amounts, final freeze-drying may affect the final activity and one vial of a batch does not necessarily reflect the activity of all the vials. It is hoped that the variation can be kept to 200-300 units per vial.

The variations in the amount of cryoprecipitate required for emergency treatment (Table V) are to be expected as much depends on the type of emergency, varying from major surgical procedures (one child in Aberdeen requiring nearly 500 donations) to dental extractions covered by some 10 donations.

5. Table VII indicates the activity of donations at two yield levels 50 and 75 Factor VIII units per cryoprecipitate donation. To the final amounts (1446000 or 2169000 units) should be added 104000 representing the 260 vials of concentrated factor (at that time issued as 400 units per vial) used in 1974 (Table IX).

The average yearly requirements per haemophilia patient registered was 4000-6000 units of Factor VIII, depending on the estimated yield from cryoprecipitate.

These, however, are the figures for 1974. Comparison of the issues of cryoprecipitate in the six months ending 30 June 1974 and the same period in 1975 (Table IX) shows an overall increase of 50%; issues in July-September 1975 were 10% greater than in the preceding quarter. If this trend is continued in the last quarter of this year the average requirements for registered haemophilia patients in 1975 will be 6600-10000 units of Factor VIII, the latter figure being the estimate arrived at in the paper discussed at the last meeting (i.e. 4 million units of Factor VIII per year for Scotland).

The upward trend in requirements of Factor VIII since the introduction of cryoprecipitate in 1970 has not yet flattened out, whether future requirements will exceed an average of 10000 units per registered patient per year will depend very much on experience gained with the more sharply defined activity of the concentrated factor.

6. Table VIII consolidates the Haemophilia Directors' forecasts of those who would benefit by home treatment. Fourteen children and 51 adults, in both cases some 16% of registered patients, are judged suitable, with the proviso that there are probably a number of haemophilia sufferers unrecognised in remoter areas such as the Northern Isles, for whom home therapy would be indicated.

PART 2. SUPPLY

7. The issues of cryoprecipitate in donation units and of Factor VIII concentrates at six monthly intervals ending 30 June 1974, 31 December 1974 and 30 June 1975 are recorded in Table IX.

There are discrepancies between demand and supply figures, but the main point to note from this table is the upward trend in requirements for cryoprecipitate discussed in paragraph 5.

8. Issues of concentrated Factor VIII listed in SNBTS letter of 22 August 1975 were based on the consolidated use of cryoprecipitate for 1974 recorded in Table VI.

These issues were not achieved in full due to late arrival of labels and a ten day halt in issues after the reactions reported in Glasgow.

The issues from 1 September - 30 October 1975 were:

14-11-75.

Centre	15 ml doses		100 ml doses
Glasgow	502	629	
Edinburgh	348	415	
Dundee	20	40	
Aberdeen	40	80	
Inverness	84	168	15

9. The issues are provisional and can be modified if necessary. Only small reserves are available at the PFC for unforeseen emergencies.

10. Regional Transfusion Directors have been requested to reduce cryoprecipitate production and increase fresh frozen plasma supplies to the PFC when regional reserve stocks are built up.

1 - 14/11

A D E G I

40 20 67 126 ~~84~~