HAEMOPHILIA CENTRE AND HAEMOSTASIS UNIT

ROYAL FREE HAMPSTEAD NHS TRUST

An analysis of treatment for patients with inherited coagulation disorders

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Overview of the increasing costs of treatment for patients with congenital coagulation disorders at the Royal Free Hospital

Background

'The haemophilic condition'

The haemophilic population in the United Kingdom comprises a group of patients whose medical management is both complex and costly. Some of the complexity arises due to the rarity of the condition, its lifelong nature, its variable severity, and the fact that patients do not appear "ill" in the accepted sense of the term. It may not always be understood that the lack of prompt, appropriate treatment may lead to prolonged hospitalisation and the misuse or even on occasion the wastage of expensive blood products.

Health Service Guidelines - NHS Management Executive HSG(93)30

The Royal Free Hospital haemophilia centre is the largest centre in the UK with almost 1700 patients registered with inherited bleeding disorders. (Fig 1) It can be seen that there has been both an increase in the numbers of patients registered and those treated during the years 1980-94. (Figures 1-4)

The practice is unique in containing such a large number of patients with factor XI deficiency. (Figure 2) It is particularly significant that the proportion of UK patients treated at the Royal Free has increased from 6% in 1976 to almost 13% in 1994. (Figure 6)

Haemophilia A, factor VIII deficiency, is the commonest haemophilia and therefore the use of factor VIII reflects the increasing practice. In 1994, 14 million units were used compared to < 2 million units in 1976. (Figure 7)

In the UK there has been an increase in usage of factor VIII from 35 million units in 1976 to 140 million units in 1994.

However, the usage of FVIII at the Royal Free as a percentage of that used in the UK has been relatively constant - around 9%. (Figure 9).

It is interesting that although we treat 14% of the patients in the UK, we use 9% of the factor VIII consumed in the UK. (Figure 10)

Treatment for von Willebrand's Disease

A significant change in treatment has occurred for von Willebrand's disease. Factor VIII concentrate containing von Willebrand factor did not become available until 1992. It can be seen that the annual usage of 2.5 million units of FVIII for this condition in 1994 accounted for 18% of all FVIII used at the Royal Free (Figure 11)

Children and Prophylaxis

Children have been treated with prophylaxis during the last two years to prevent bleeds occurring and resultant joint damage. Figure 12 shows the annual factor VIII used during 1994-95. This represents 2 million units of treatment. At present our children are treated with intermediate purity 8Y (BPL) which costs 17p per unit. As haemophilia treaters we believe children under 10 years should be treated with recombinant factor VIII at a cost of 40p per unit, which would prevent viral transmission. Thus a switch to recombinant factor VIII would result in an increase in cost of approximately £460,000.

Hometreatment for Adults

Figures 13 and 14 show the range of treatment for adults. Some have been on prophylaxis since their teenage years - others treat on demand. The patient who used 500,000 during 1994-5 has severe von Willebrand's Disease, HIV and HCV infection. In January 1994 he had a tonsillectomy because he was thought to have a lymphoma secondary to HIV. He bled extensively at operation and continued to bleed for six months post-operatively.

Operations

Traditionally when a patient with haemophilia goes to theatre, factor VIII is given in bolus. The patient is treated to 100%, monitored and maintained to at least 50% for 10 days post-operatively. This uses more factor VIII and results in peaks and troughs (Figure 15). It is clearly much safer to use constant infusion (Figure 16) when the level of factor VIII is maintained at 100%. This is a new treatment and at present only one factor VIII concentrate has been shown to be stable over time ie 'monoclate' (Armour). In this particular operation, the constant infusion used 109,000 units, a saving of 41,000 units over the bolus management.

HIV Infection

50% of our patients infected with HIV 1979-85 have now died, but over 60 remain alive. We expect a steady death rate over the next decade and we know that in the year prior to death, the clotting factor consumption increases by 50%.

HCV Infection

We have identified 242 patients who were infected with HCV during 1965-85 (over 100 of whom have both HIV and HCV).

We know that 10% have progressed to liver failure over 20 years from infection.

When patients progress to liver failure they require other clotting factors (VII, FVIII and IX) because the liver normally makes all clotting factors.

Acquired Haemophilia

This unpredictable condition is difficult to treat and often requires Porcine factor VIII (£1 per unit).

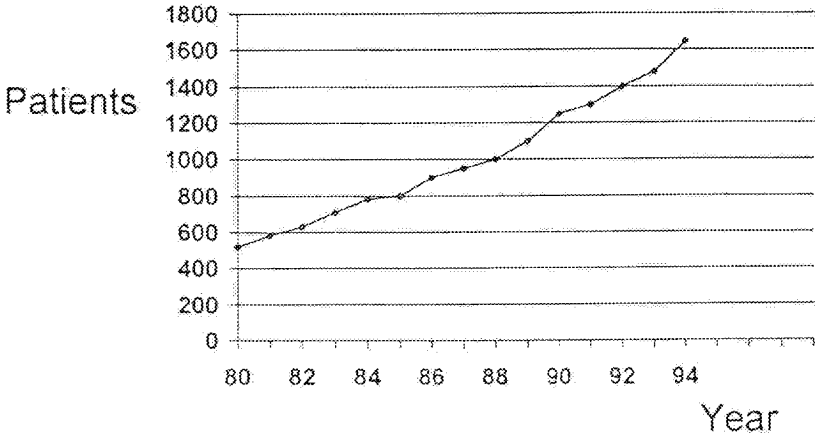
The most recent patient developed this inhibitor post-natally. She has been treated with approximately £150,000 concentrate over a two-month period.

'Free' Clotting Factor Concentrate

This is shown in the table. This treatment is provided in the context of therapeutic trials, reflecting our international status as a training centre of the World Federation of Haemophilia.

1.

Annual returns: haemophilic patients registered at the Royal Free



2.

Royal Free Haemophilia Centre

Diagnosis distribution 18 November 1994

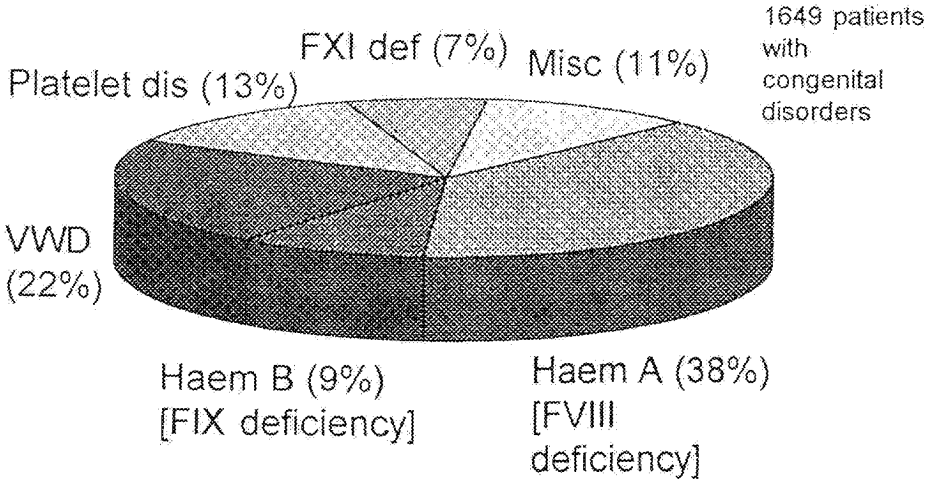


Fig 1: *Annual returns - haemophilic patients registered at the Royal Free*

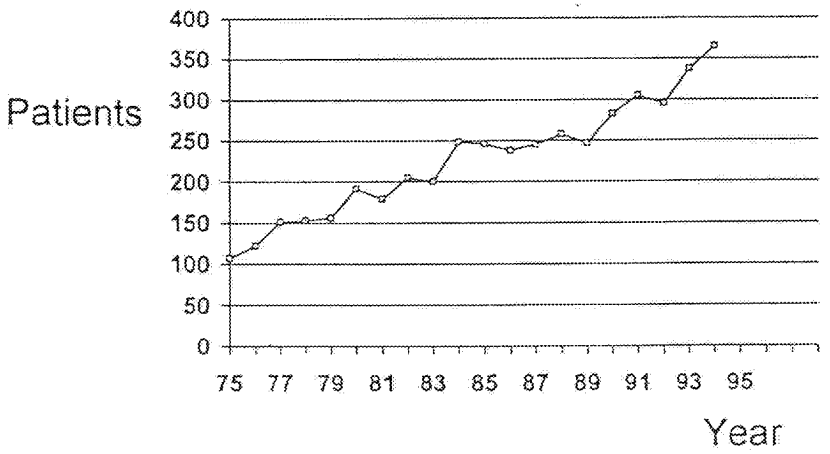
This shows the increasing number of patients registered on our data base 1980 - 1994. All these patients have life-long, inherited bleeding disorders.

Fig 2: *Royal Free Haemophilia Centre - Diagnosis Distribution*
18 November 1994

This shows the distribution of the various clotting factor deficiencies and inherited bleeding disorders.

Factor XI deficiency is very common in Jewish patients and our 115 registered patients represent one third of the UK population.

Annual returns: haemophilic patients treated at the Royal Free: 1975 - 1994



Annual returns: haemophilic patients registered and treated at the Royal Free

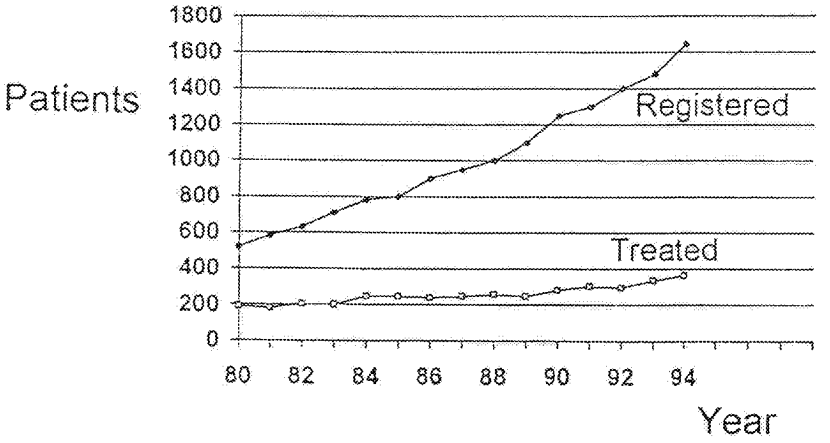


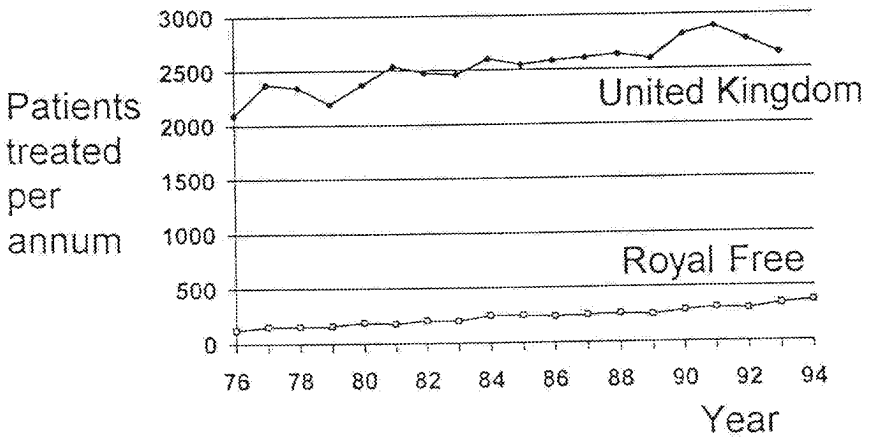
Fig 3: *Annual returns - haemophilic patients treated at the Royal Free: 1975 - 1994*

This shows the increasing number of patients who have received treatment with the clotting factor concentrates VII, VIII, IX and XI during the years 1975 - 1995.

Fig 4: *Annual returns: haemophilic patients registered and treated at the Royal Free*

It can be seen that as our database of registered inherited bleeding disorders increases over the years 1980 - 94, an increasing number of patients receive treatment with clotting factor concentrate.

Annual returns: haemophilic patients treated



Annual returns: Royal Free haemophilic patients as percentage of UK treated

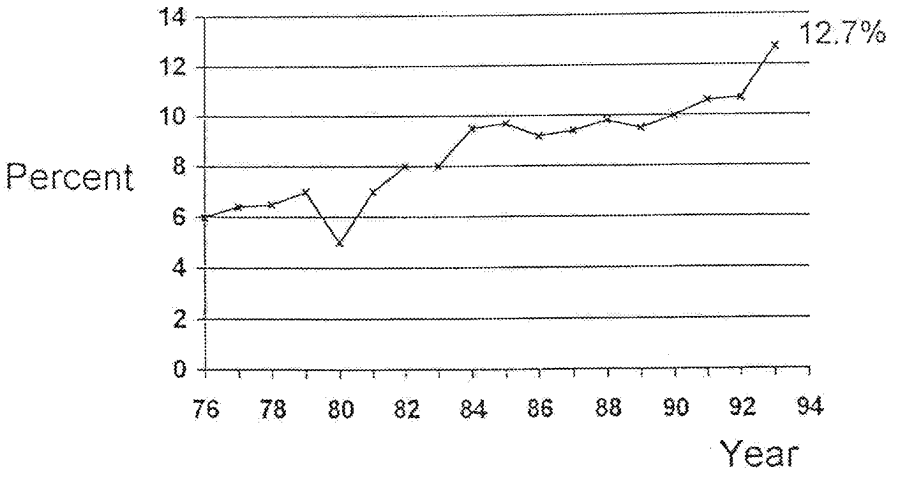


Fig 5: *Annual returns: haemophilic patients treated*

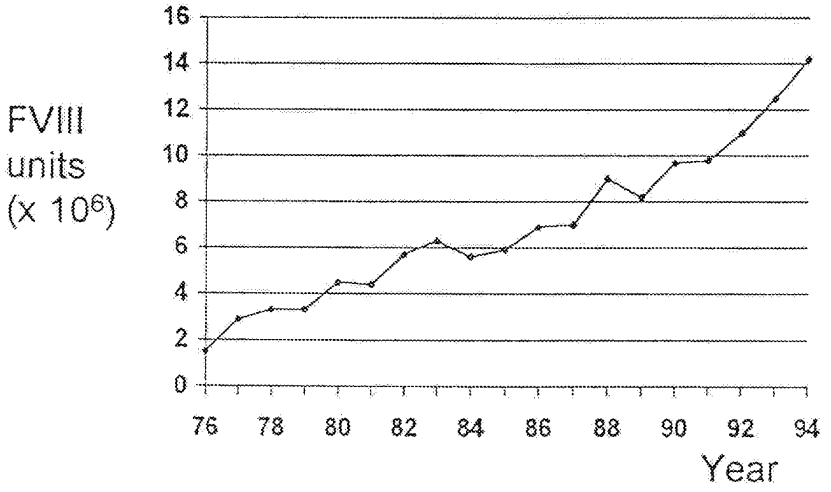
In the UK all information about patients treated with haemophilia has been established on a central database at Oxford since 1976.

This figure compares our patients treated with those treated in the UK during the years 1976- 94.

Fig 6: *Annual Returns: Royal Free haemophilic patients as percentage of UK treated*

It can be seen that the Royal Free treated 12.7% of patients treated in the UK in 1994 compared with 6% in 1976.

Royal Free: annual FVIII consumption



Annual returns: FVIII consumption

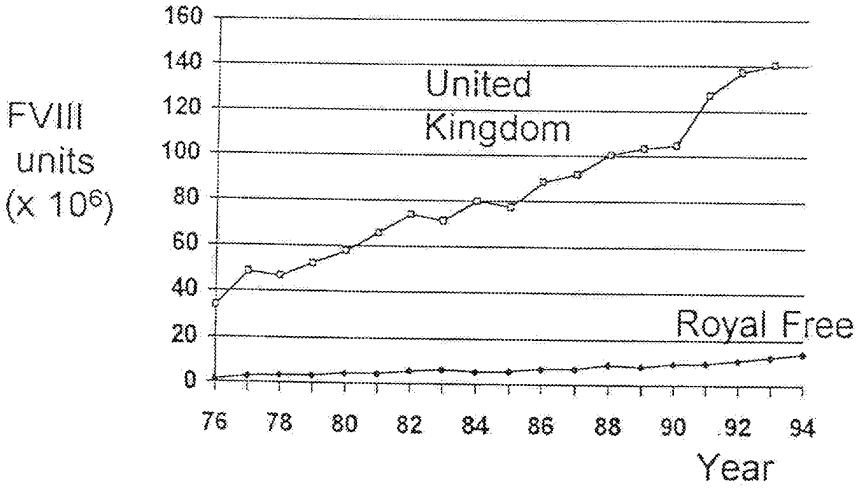


Fig 7: *Royal Free: Annual FVIII Consumption*

This shows the increasing use of factor VIII concentrate for the years 1976 - 94.

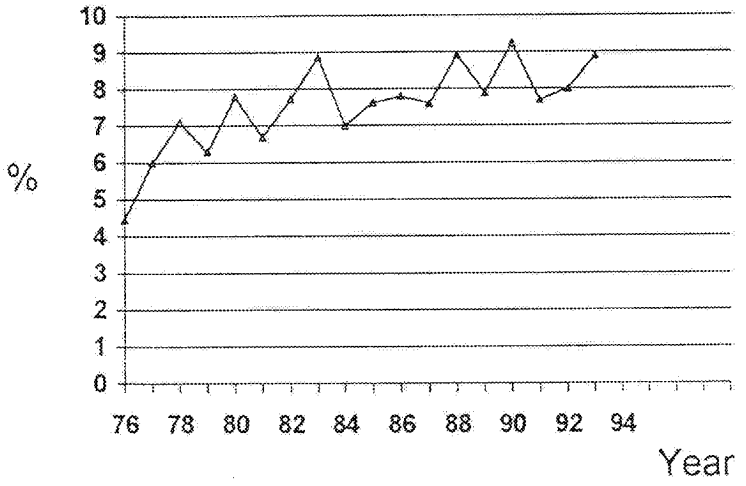
There was a 'flattening' of the curve during the years 1982 - 85. This was the peak of the AIDS epidemic and many patients stopped using treatment and risked bleeding. Non-emergency surgery also reduced.

Figure 8: *Annual returns: FVIII consumption*

This compares the Royal Free Consumption of factor VIII with that in the UK.

9

Annual returns: RFH FVIII consumption as % of UK consumption



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Annual returns: RFH FVIII consumption as % of UK consumption

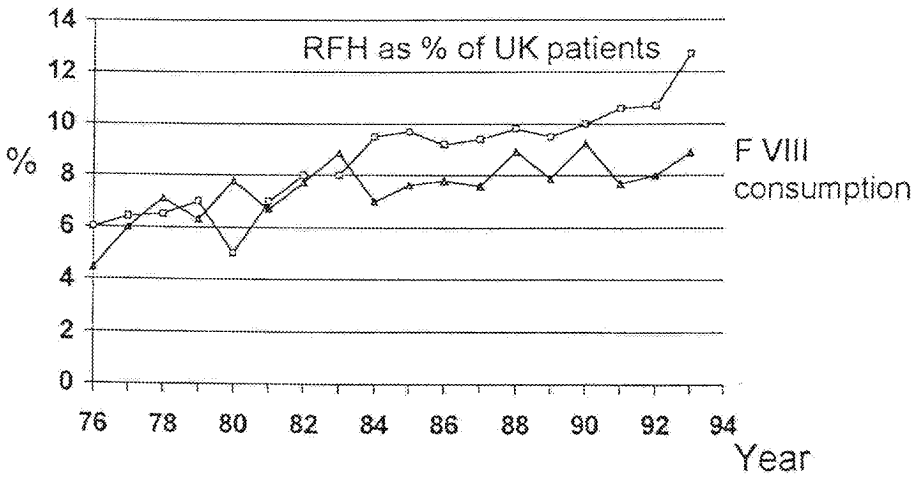


Figure 9: *Annual returns: Royal Free Hospital FVIII consumption as % of UK consumption*

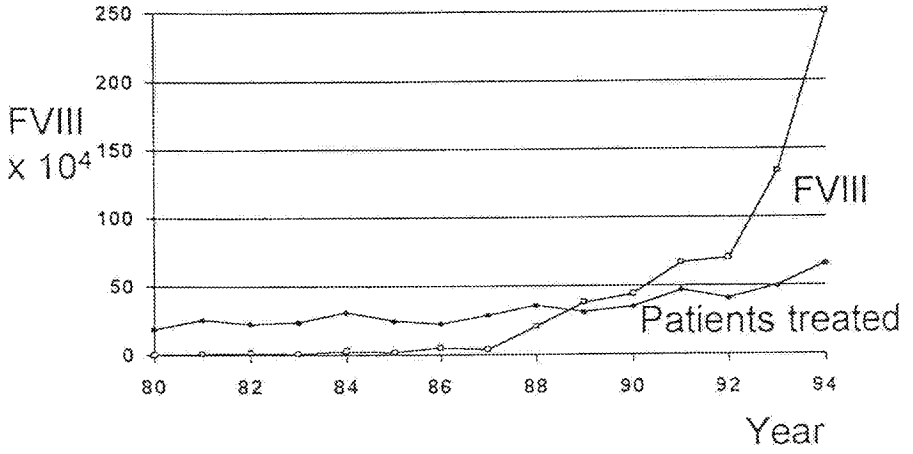
It can be seen that there has been almost a constant proportion of FVIII used at the Royal Free compared to the UK.

Figure 10: *Annual returns: Royal Free Hospital FVIII consumption as % of UK consumption*

Whereas the proportion of UK patients treated at the Royal Free has increased during the years 1976 - 94, the factor VIII consumption has increased to a lesser extent.

11

Annual use of FVIII for Von Willebrand's disease



12

Annual FVIII use by 27 children using prophylactic treatment: 1994-5

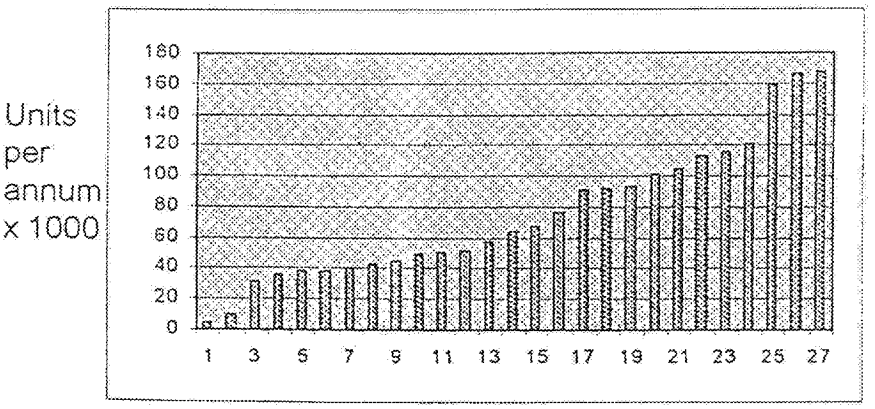


Figure 11 *Annual use of factor VIII for von Willebrand's Disease*

Factor VIII concentrate rich in von Willebrand factor was not available until 1992.

It can be seen that treatment for von Willebrand's Disease (2.5 m units) now represents 18% of factor VIII used at the Royal Free.

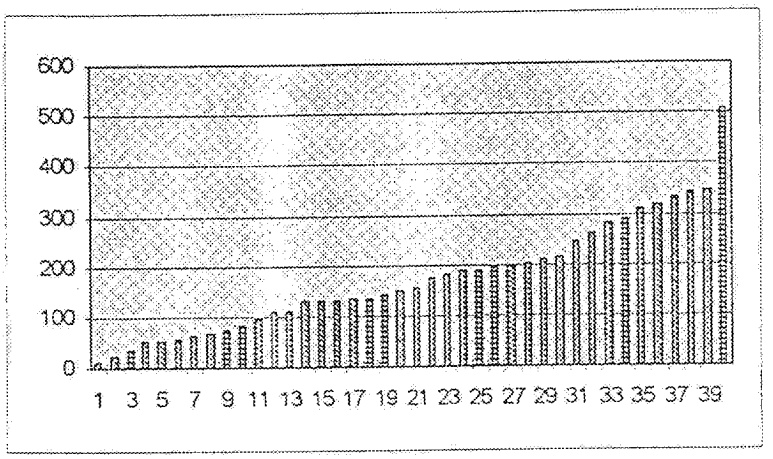
Figure 12: *Annual FVIII used by 27 children using prophylactic treatment 1994 - 95.*

Children are treated with prophylaxis to prevent bleeds occurring.

The range of treatment represents the range of weight of the children.

13

Annual FVIII use by 40 adults using prophylactic treatment : 1994-5



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Annual FVIII use by 65 adults using on-demand treatment: 1994-5

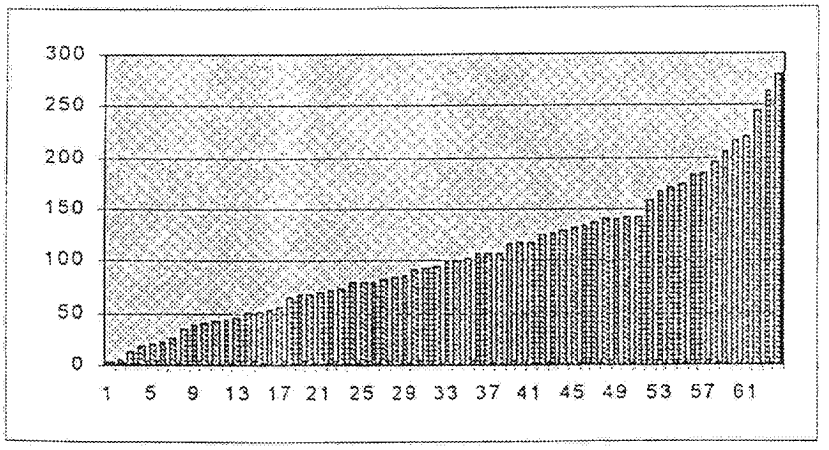


Fig 13: *Annual factor VIII use by 40 adults using prophylactic treatment 1994 - 95.*

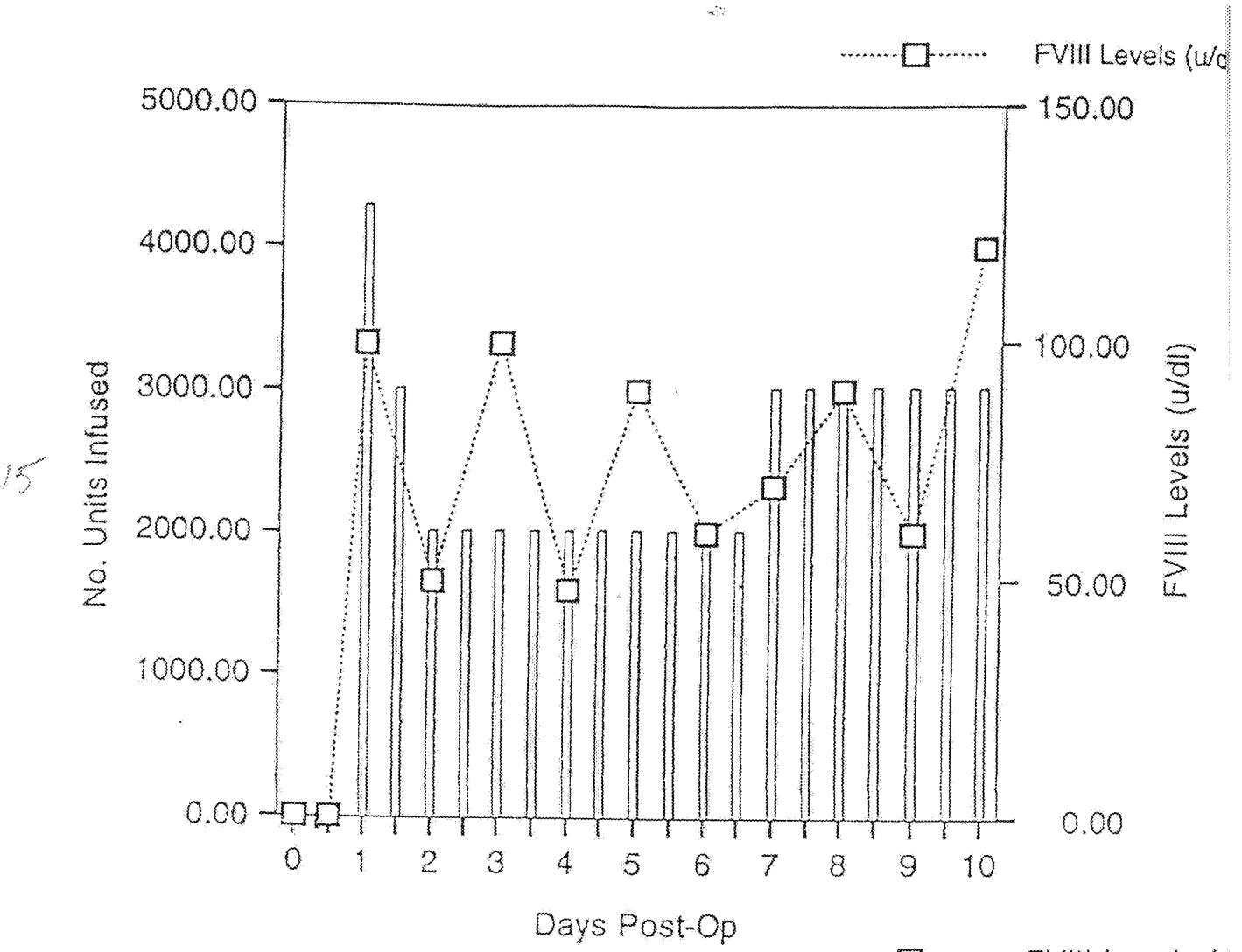
The patient using > 500,000 is a patient with von Willebrand's Disease and HIV infection who had a tonsillectomy in January 1994. He continued to bleed in the retrophyrynx for many months post-surgery.

Fig 14: *Annual FVIII use by 65 adults using on-demand treatment 1994 - 5.*

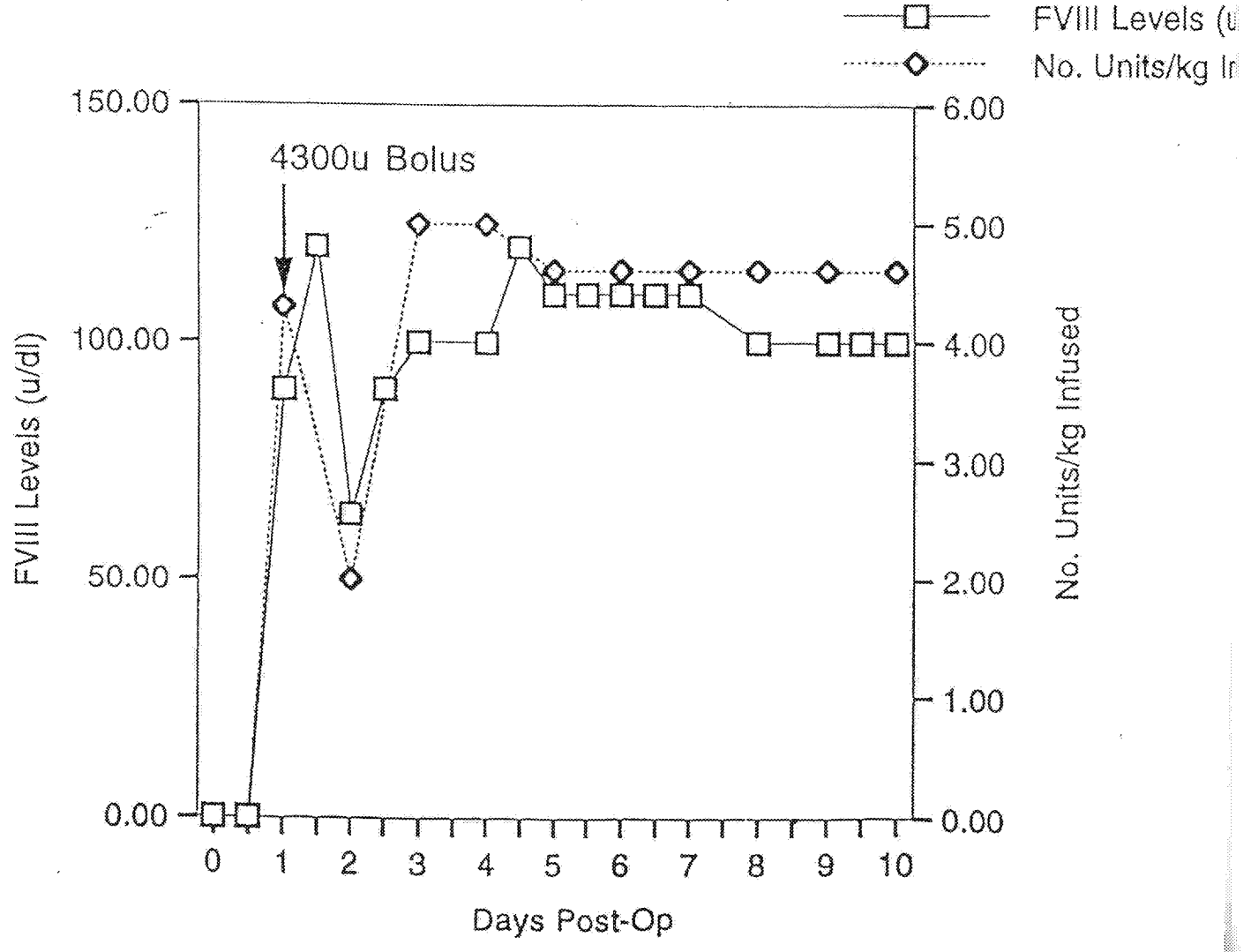
The treatment for an acute bleed is 35 u/kg.

On average, patients have 30 bleeds per year.

The weight of patients is variable - some with HIV infection weigh as little as 35 kg, others are > 100 kg.


FVIII Levels (u/d
5000.00
4000.00
3000.00
2000.00
1000.00
0.00
No. Units Infused
150.00
100.00
50.00
0.00
FVIII Levels (u/dl)
0 1 2 3 4 5 6 7 8 9 10
Days Post-Op

15


FVIII Levels (u
No. Units/kg In
150.00
100.00
50.00
0.00
FVIII Levels (u/dl)
4300u Bolus
6.00
5.00
4.00
3.00
2.00
1.00
0.00
No. Units/kg Infused
0 1 2 3 4 5 6 7 8 9 10
Days Post-Op

16

Fig 15: *Factor VIII levels post-operatively showing peaks and troughs secondary to bolus infusion.*

Fig 16: *Factor VIII level post-operatively showing constant level FVIII 100 u/dl using constant infusion*

Clotting factor concentrate obtained 'free'

in the context of therapeutic trials

		U	£
1988 - 1994	'Kogenate recombinant FVIII (60p)	1,059,887	(635,932)
1991 - 1992	'Monoclate' high purity FVIII (24p)	312,515	(75,003)
1992 - 1993	9MC BPL high purity FIX (27p)	172,565	(46,592)
1993 - 1994	'Replenate' high purity FVIII (35p)	2,000,000	(700,000)
1995 - ongoing	Pharmacia - recombinant FVIII (60p)	16,465	(9,879)
1995 - ongoing	FEIBA - activated FIX (60p)	24,000	(14,400)
1995 - ongoing	Genetics Institute - recombinant FIX	149,250	(89,550)
		Total	£1,572,000