

## ANNUAL RETURNS for 1993

The attached tables and graphs contain the information available from the UK Haemophilia Centre Directors Annual Returns. Returns were requested from 107 Centres and returns have been received from 102 Centres. Seventeen Centres sent in discrepant or incomplete data and still have some queries outstanding. As requested at the AGM held on 07.10.91, we have compiled a list showing the dates the returns were received from Centres, the Centres whose returns are incomplete and the Centres who have not yet sent in their returns (Appendix A). One Centre reported that no patients with coagulation defects were treated by them during 1993.

By 31.12.93 there were 5,406 patients with haemophilia A known to Haemophilia Centres (Table 1). This is an increase of 54 compared with the previous year. Thirty-seven per cent of these patients were severely affected with factor VIII levels <2% average normal. The incidence of antibodies to factor VIII remains as approximately 5% of all haemophilic patients (Table 2) although 15 new cases were detected during the year and are being investigated by Dr. Brian Colvin and Dr. Charles Hay on behalf of the Adverse Events Working Party.

The total number of patients with Christmas disease now stands at 1,098 (Table 3) which is 17 more than in the previous year. Thirty-two per cent of the patients are severely affected. The number of patients with antibodies to factor IX has increased as two new cases were detected in 1993 (Table 2).

The number of patients reported as suffering from von Willebrands disease has risen to 3,503 (Table 4) which is 374 more than in 1992. Forty-eight have factor VIII:c levels <2% of average normal and of these 26 required treatment in 1993 and 12 were on home therapy. Forty-six per cent of all von Willebrands patients treated had factor VIII:c levels greater than 30% of normal. Five patients with von Willebrands disease had antibodies to factor VIII (Table 2).

### **Treatment of patients**

Of the 5,406 haemophiliacs registered 2,263 (42%) received replacement therapy in 1993 (Table 5) and 1,443 (Table 1) were receiving home therapy. The total amount of factor VIII used at Haemophilia Centres in 1993 was 140M units, an increase of 3M units over the amount used in the previous year. Patients with haemophilia A received 135M units, 3.3M units more than in 1992 (table 5 and Fig. 1). Patients with von Willebrands disease used 4.8M units (Table 5) compared with 5M units in 1992. The total amount of BPL/PFC factor VIII used decreased by 4.2M and the amount of other factor VIII concentrates rose by 7.4M compared with 1992. Fig. 2 shows the various brands of factor VIII used in 1993 as a proportion of the total amount used.

A total of 6.7M units of human factor VIII was used to treat 82 haemophilia A patients who had factor VIII antibodies (Table 6). In addition 429,000 units of porcine factor VIII, 1.7M units of BPL/PFC factor IX, 10,000 units of other factor IX, 6.5M units of FEIBA and 99,000 units of Autoplex were used.

With regard to factor IX, the total amount of factor IX used has increased since 1992 by 2.8M units to 23.8M units. There has been a decrease of 507,000 units in the amount of BPL/PFC Factor IX used to treat haemophilia B patients and an increase of 3.3M units in other brands of factor IX used to treat haemophilia B patients (Table 7 and Fig. 2). 1.3M units of BPL/PFC factor IX and 17,000 units of other brands of factor IX were used to treat haemophilia A patients who had factor VIII antibodies. Fig. 3 shows the various brands of factor IX used in 1993 as a proportion of the total amount used.

Table 8 gives an analysis of the causes of death in the 110 patients with haemophilia A, 6 with Christmas disease and 10 with von Willebrands patients who died in 1993. AIDS was the commonest cause of death - 59 (47%), with cerebral haemorrhage and liver disease - 12 (10%) joint second. There were nine cancer deaths (including one case of hepatoma), and seven patients died from ischaemic heart disease and six from pneumonia (not PCP). The cause of the death of ten patients was not known at their Haemophilia Centres. Further details regarding the cause of death in patients diagnosed as having AIDS are given in Table 9, from which it will be seen that respiratory diseases were the most common cause - 12 (20%). Clinical information/autopsy details were not given for 25 patients. Table 10 shows the HIV status of the patients known to have died in 1993.

Table 11 shows the number of patients with rare blood coagulation defects known to Haemophilia Centre Directors, the number treated in 1993 and the number on home treatment. Platelet defects form the largest group registered (439), followed by Factor XI deficiency (383) and Factor XII deficiency (343).

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Table 1

Haemophilia A patients known at Haemophilia Centres in 1993, showing the number of patients treated during 1993, with the severity of the coagulation defect and age. Patients known to have died before 01.01.93 have been excluded.

Age (Years)	Number of Patients Factor VIII Level (%)														
	<2% a.n.			2-10% a.n.			>10% a.n.			Not Known			Total		
	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993
<5	134	123	33	100	60	8	65	29	3	2	1	0	301	213	44
5-9	183	162	127	111	84	28	83	26	3	1	0	0	378	272	158
10-14	177	148	132	105	59	36	102	29	6	3	1	0	387	237	174
15-19	131	113	100	117	72	29	101	23	6	10	0	0	359	208	135
20-29	419	311	283	273	101	45	269	57	8	16	0	0	977	469	336
30-39	409	301	251	294	95	34	265	29	3	26	0	0	994	425	288
40-49	268	171	134	236	72	19	193	30	3	21	0	0	718	273	156
50-59	141	107	79	157	45	15	155	19	3	12	0	0	465	171	97
60-69	62	40	29	112	35	9	150	33	3	6	0	0	330	108	41
70+	36	19	7	86	22	3	113	28	0	11	0	0	246	69	10
N/K	21	1	0	13	0	0	9	0	0	208	13	4	251	14	4
<b>TOTAL</b>	<b>1981</b>	<b>1496</b>	<b>1175</b>	<b>1604</b>	<b>645</b>	<b>226</b>	<b>1505</b>	<b>303</b>	<b>38</b>	<b>316</b>	<b>15</b>	<b>4</b>	<b>5406</b>	<b>2459</b>	<b>1443</b>

Table 2

The number of patients known to Haemophilia Centre Directors on 31.12.93 and the occurrence of Factor VIII and Factor IX antibodies. Patients known to have died before 31.12.93 have been excluded.

	Haemophilia A	Haemophilia B	von Willebrands
Cumulative total number of patients known at Centres	5296	1092	3493
Cumulative total number of patients with factor VIII or IX antibodies	277	9	5
% with factor VIII or IX antibodies	5.2	0.82	0.14

Table 3

Haemophilia B patients known at Haemophilia Centres in 1993, showing the number of patients treated during 1993, with the severity of the coagulation defect and age. Patients known to have died before 01.01.93 have been excluded.

Age (Years)	Number of Patients Factor IX Level (%)														
	<2% a.n.			2-10% a.n.			>10% a.n.			Not Known			Total		
	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993
<5	25	21	7	18	11	1	7	1	0	0	0	0	50	33	8
5-9	35	25	15	30	15	4	20	6	0	2	0	0	87	46	19
10-14	30	21	18	35	26	10	24	5	1	1	0	0	90	52	29
15-19	27	23	20	40	23	9	28	4	1	2	0	0	97	50	30
20-29	64	49	46	75	34	18	40	3	0	8	0	0	187	86	64
30-39	66	46	39	70	28	8	46	10	2	4	0	0	186	84	49
40-49	55	38	30	57	18	4	38	11	0	3	0	0	153	67	34
50-59	18	15	10	27	12	6	32	6	0	4	1	0	81	34	16
60-69	17	14	10	28	11	4	15	5	1	0	0	0	60	30	15
70+	8	4	2	25	6	2	16	3	0	3	1	0	52	14	4
N/K	3	0	0	3	1	0	4	1	0	45	5	1	55	7	1
<b>TOTAL</b>	<b>348</b>	<b>256</b>	<b>197</b>	<b>408</b>	<b>185</b>	<b>66</b>	<b>270</b>	<b>55</b>	<b>5</b>	<b>72</b>	<b>7</b>	<b>1</b>	<b>1098</b>	<b>503</b>	<b>269</b>

Table 4

von Willebrands disease patients known at Haemophilia Centres in 1993, showing the number of patients treated in 1993, with the Factor VIIIc level and age in 1993. Patients known to have died before 01.01.93 have been excluded.

Age (Years)	Factor VIIIc Level											
	<2% a.n.			2-14% a.n.			15-29% a.n.			>30% a.n.		
	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993	In Reg	Trtd 1993	On HT 1993
<5	1	1	0	19	12	3	25	6	0	72	15	0
5-9	6	4	1	28	12	2	35	10	1	139	25	0
10-14	4	3	1	21	10	1	49	10	3	159	23	1
15-19	2	2	1	22	5	1	45	7	0	176	15	1
20-29	11	4	3	74	23	4	104	12	0	465	50	2
30-39	9	2	1	70	19	7	136	22	1	407	34	2
40-49	9	4	4	57	12	3	128	20	1	332	36	2
50-59	2	3	1	35	8	0	78	8	2	186	14	0
60-69	2	1	0	24	8	1	42	6	0	103	9	0
70+	2	2	0	18	1	0	53	5	1	118	10	0
N/K	0	0	0	2	0	0	9	0	0	22	3	0
TOTAL	48	26	12	370	110	22	704	106	9	2179	234	8
										202	38	0
										3503	514	51

Table 5

## Factor VIII units used by Haemophilia Centres in 1993

Type of Patient	Total number * of patients treated	Plasma	Cryo.	BPL/PFC F.VIII conc.	Other F.VIII conc.	Total F.VIII Units
Haemophilia A **	2263	-	-	86,809,000	48,226,000	135,035,000
Carriers of Haem. A	35	-	-	357,000	64,000	421,000
von Willebrands ***	322	3,000	16,000	2,985,000	1,809,000	4,813,000
Acquired Haem. A ****	19	-	-	29,000	29,000	58,000
Acquired von Willebrands *****	6	-	-	43,000	96,000	139,000
TOTAL	2645	3,000	16,000	90,223,000	50,224,000	140,466,000
% TOTAL	-	0.00	0.01	64.23	35.76	-

\* Adjusted for duplicates and excluding patients who did not receive blood products

\*\* Including materials used for treatment of Haemophilia A patients with factor VIII antibodies  
(See Table 6)

\*\*\* von Willebrands disease patients also received 470,000 units of vWF

\*\*\*\* Acquired Haemophilia A patients also received the following materials:

Porcine F.VIII:	449,000 units
FEIBA:	359,000 FEIBA units
R VIIa:	624 mg.
Autoplex:	6,000 units

\*\*\*\*\* Acquired von Willebrands disease patients also received 13,000 units of vWF

Table 6

Materials used by Haemophilia Centres in 1993 to treat 82 Haemophilia A patients who had F.VIII antibodies.  
In addition, 8 other patients were treated but received no blood products.

Material	Factor VIII units		
	Used at Hospital	Supplied for HT	Total F.VIII units
Plasma	-	-	-
Cryoprecipitate	-	-	-
BPL/PPL F.VIII conc.	2,640,000	3,100,000	5,740,000
Other Human F.VIII conc.	357,000	553,000	910,000
Total Human F.VIII conc.	2,997,000	3,653,000	6,650,000
Porcine F.VIII	349,000	80,000	429,000
Other Materials:			
	Units	Units	Units
FEIBA	3,293,000	3,184,000	6,477,000
AUTOPLEX	99,000	-	99,000
BPL/PFC F.IX conc.	953,000	735,000	1,688,000
Other F.IX conc.	4,000	6,000	10,000

These patients also received 6151.6 mg. of RVIIa

Table 7

## Factor IX Units used by Haemophilia Centres in 1993

Type of Patient	Total number of Patients *	Plasma	BPL/PFC IX	Other IX	Total Units
Haemophilia B **	498	-	14,516,000	7,682,000	22,198,000
Carriers of Haemophilia B	21	-	56,000	238,000	294,000
Haem. A patients with F.VIII antibodies	16	-	1,284,000	17,000	1,301,000
Acquired Haemophilia B	1	-	6,000	-	6,000
TOTAL	536	-	15,862,000	7,937,000	23,799,000
% TOTAL	-	-	-	-	-

\* Adjusted for duplicates and excluding patients who did not receive blood products

\*\* Including 6 Haemophilia B patients with Factor IX antibodies

In addition 1 Haemophilia B patient with F.IX antibodies received 182,000 units of FEIBA

Table 8

Causes of death of 110 Haemophilia A, 6 Haemophilia B and 10 von Willebrand's disease patients in 1993, showing severity of coagulation defect and age at death.

Cause of death	F.VIII /IX level %	Age at Death (years) and Number of Deaths *									
		<5	5-9	10-19	20-29	30-39	40-49	50-59	60-69	70+	TOTAL
AIDS **	<2	-	-	2	12	17	7	9	2	-	
	2-10	-	-	2	3	1	1	1	-	1	59(2)
	>10	-	-	-	-	1	-	-	-	-	
Cerebral haemorrhage/ Stroke	<2	2	-	1	-	1	1	1	1	1	
	2-10	-	-	-	-	-	-	1	-	-	12
	>10	1	-	-	-	1	-	-	-	1	
Ischaemic heart disease	<2	-	-	-	1	-	1	-	-	1	
	2-10	-	-	-	-	-	-	-	1	-	7
	>10	-	-	-	-	-	-	1	1	1	
Cancer	<2	-	-	-	-	-	-	3(1)	-	-	
	2-10	-	-	-	-	-	-	-	-	1	9(1)
	>10	-	-	-	-	-	-	2	-	2	
	n/k	-	-	-	-	-	-	-	-	1	
Liver disease	<2	-	-	-	1	5	1	3	-	-	
	2-10	-	-	-	-	-	-	-	1	-	12
	>10	-	-	-	-	-	-	-	1	-	

/ cont.

Table 8 (continued)

Cause of death	F.VIII /IX level %	Age at Death (years) and Number of Deaths *									
		<5	5-9	10-19	20-29	30-39	40-49	50-59	60-69	70+	TOTAL
Pneumonia (Not PCP)	<2	-	-	-	1	1(1)	1	-	-	1	6(1)
	2-10	-	-	-	-	-	-	-	-	1	
	>10	-	-	-	-	-	-	1	-	-	
Massive haematemesis	<2	-	-	-	-	-	1	-	-	-	1
Renal failure	<2	-	-	-	1	-	-	-	-	-	1
Epileptic fit	2-10	-	-	-	-	1	-	-	-	-	2
	>10	-	-	1	-	-	-	-	-	-	
Post-operative sepsis and renal failure	<2	-	-	-	-	-	1	-	-	-	1
Peritonitis	<2	-	-	-	-	1	-	-	-	-	1
Lymphoma (not AIDS)	<2	-	-	-	1	1	-	-	-	-	2
Accident - Head injury - RTA	<2	-	-	-	-	-	-	-	1	-	3
	2-10	-	-	1	-	-	-	-	-	-	
	n/k	1	-	-	-	-	-	-	-	-	
Not known	<2	-	-	-	-	-	2	-	-	-	10
	2-10	-	-	-	-	-	1	1	2	2	
	>10	-	-	-	-	-	-	-	-	2	
TOTAL		4	-	7	20(3)	30	17	22	11	15	126(4)

/ cont.

Table 8 (continued)

\* Figs. in brackets() = Number of patients who had F.VIII antibodies

\*\* See Table 9 for further details.

There were also 13 other deaths during 1993:

2 Acquired Haemophilia A	1 Myocardial infarct 1 Chest infection
2 Congenital Fibrinogen deficiency	2 Cerebral haemorrhage
4 Factor XI (PTA) deficiency	1 Liver failure/ lymphoma 1 Massive G.I. bleeding 1 Chronic myeloid leukaemia 1 Details not known at Centre
1 Factor XII (Hageman) defect	1 Details not known at Centre
2 Platelet defect	1 Adrenoleukodystrophy 1 Brain tumour
1 Haemophilia A carrier	1 Myocardial infarct
1 wife of HIV- haemophiliac	AIDS

Table 9

## Cause of death during 1993 in patients diagnosed as having AIDS

Clinical Information/Autopsy Details  
PatientsNumber ofRespiratory Diseases

PCP	2	}	13
PCP / septicaemia	1		
Pneumonia / bronchopneumonia	6		
Mycobacterial pneumonia	1		
Pneumonia / septicaemia	2		
Pulmonary aspergillosis	1		

Cerebral infections

HIV-related encephalopathy	1	}	7
Cryptococcal meningitis	2		
Cerebral lymphoma	3		
Cerebral toxoplasmosis	1		

Other infections

MAI	4	}	7
Septicaemia	3		

Other conditions

AIDS wasting syndrome	1	}	7
HIV-related lymphoma	1		
G.I. bleeding	1		
Intracranial haemorrhage	2		
Subdural haematoma	1		
Hepatitis C / chronic wasting	1		

No details	25
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TOTAL	59
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Table 10

HIV status of Haemophilia A, Haemophilia B and von Willebrands disease patients known to have died during 1993

Cause of Death	Number of Patients			
	HIV Status			Total
	Positive	Negative	Not Known	
AIDS	58	-	1	59
Cerebral haemorrhage/stroke	5	4	3	12
Ischaemic heart disease	2	4	1	7
Cancer	1	4	4	9
Liver disease	8	4	-	12
Pneumonia (not PCP)	3	2	1	6
Renal failure	1	-	-	1
Post-operative sepsis and renal failure	1	-	-	1
Peritonitis	1	-	-	1
Lymphoma (not AIDS)	2	-	-	2
Epileptic fit	-	1	1	2
Massive haematemesis	-	1	-	1
Accident	2	-	1	3
Not known	3	3	4	10
TOTAL	87	23	16	126

Table 11

Number of Patients with rare congenital blood coagulation defects known to UK Haemophilia Centres, showing the number treated with blood products during 1993 and the number on home treatment.

Coagulation defect	Number of Patients		
	In Register in 1993	Treated in 1993	On HT in 1993
Congenital Fibrinogen Deficiency	62	11	2
Congenital Prothrombin Deficiency	11	-	-
Factor V Deficiency	37	7	-
Factor VII Deficiency	122	15	1
Factor X Deficiency	71	19	4
Factor XI (PTA) Deficiency	383	33	-
Factor XII (Hageman) Deficiency	343	2	-
Factor XIII (FSF) Deficiency	25	16	-
Combined XI + XII Deficiency	3	-	-
Combined II + VII + X Deficiency	4	-	-
Combined V + VIII Deficiency	18	6	-
Combined XI + VIII Deficiency	6	-	-
Combined VIII + IX Deficiency	1	-	-
Other combined defects	1	-	-
Antithrombin III Defect	80	3	-
Platelet Defects	439	32	-
Fletcher Factor	8	-	-
<b>TOTAL</b>	<b>1614</b>	<b>144</b>	<b>7</b>

FIG.1

FACTOR VIII UNITS USED BY U.K. HAEMOPHILIA CENTRE DIRECTORS IN 1981-93  
TO TREAT HAEMOPHILIA A PATIENTS

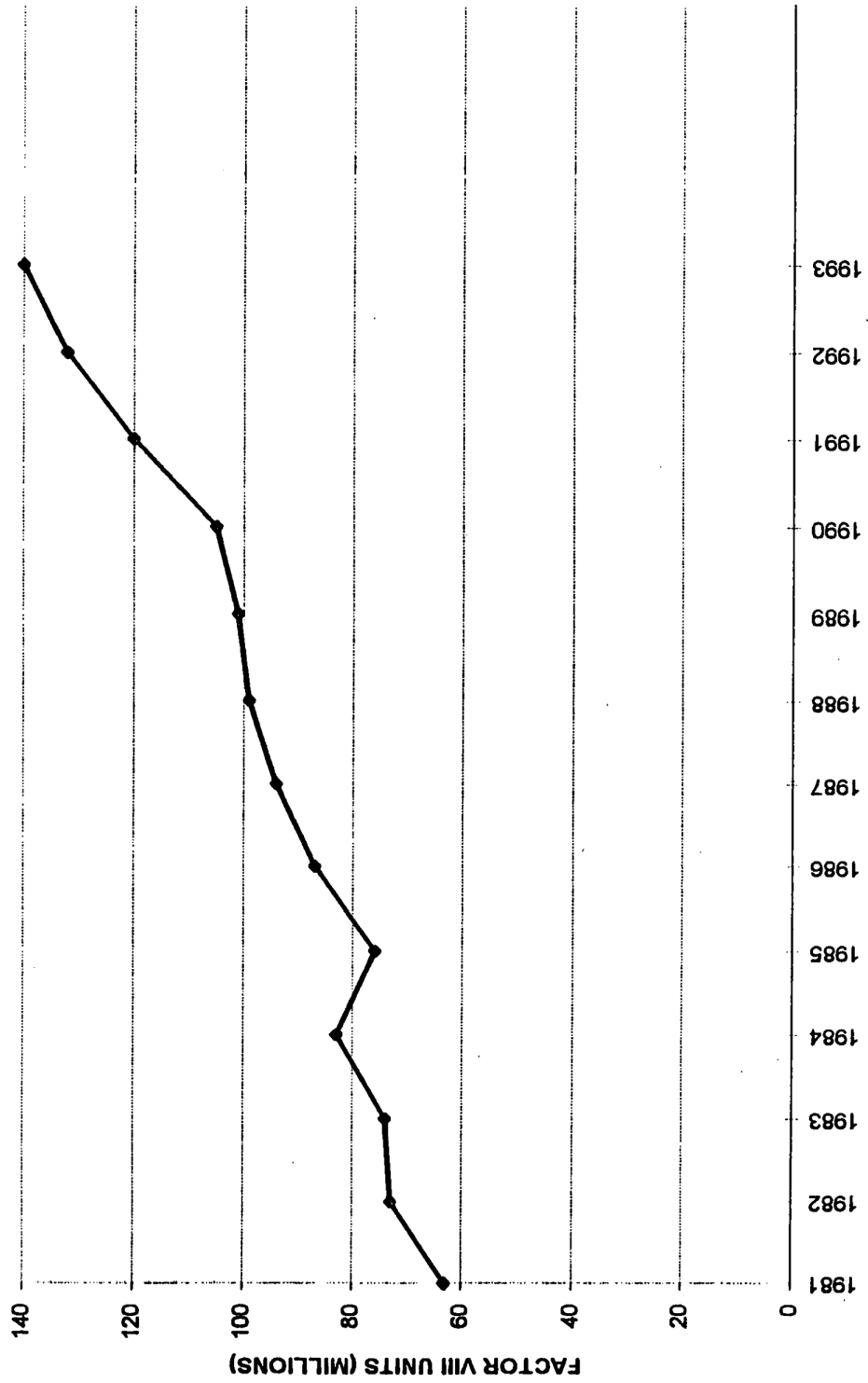
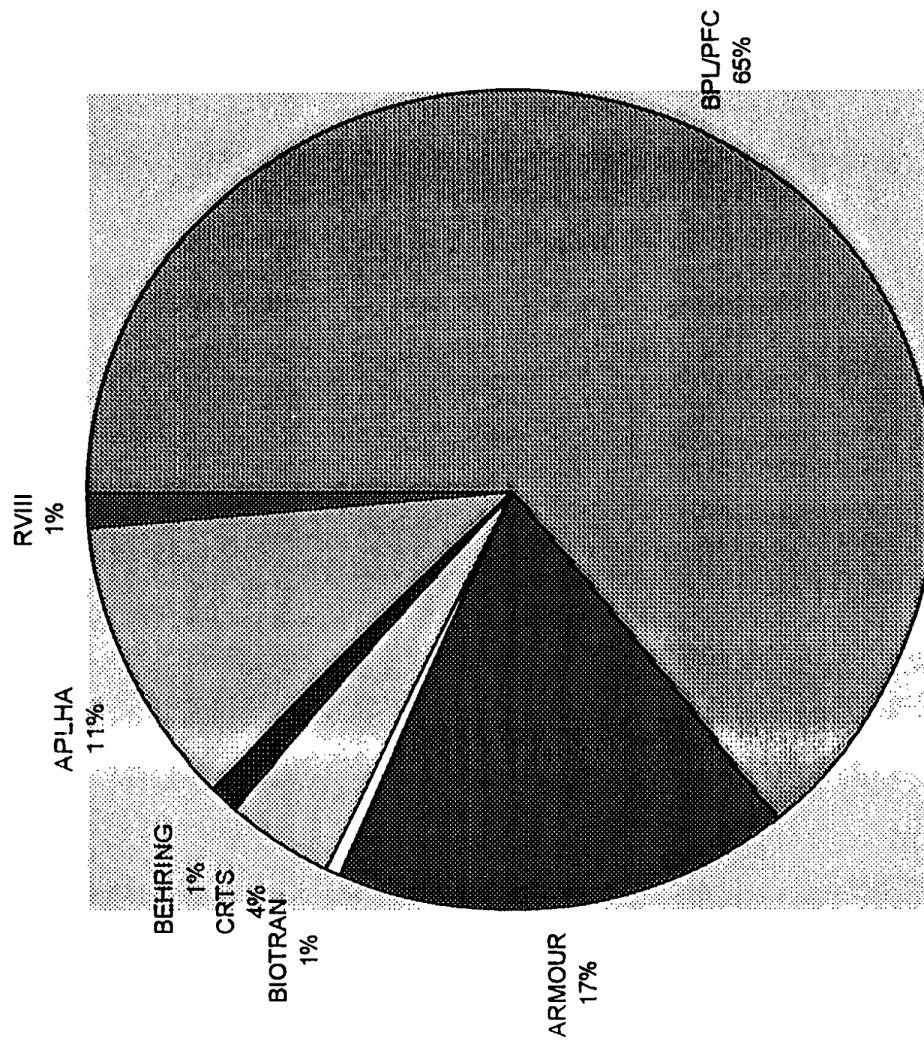


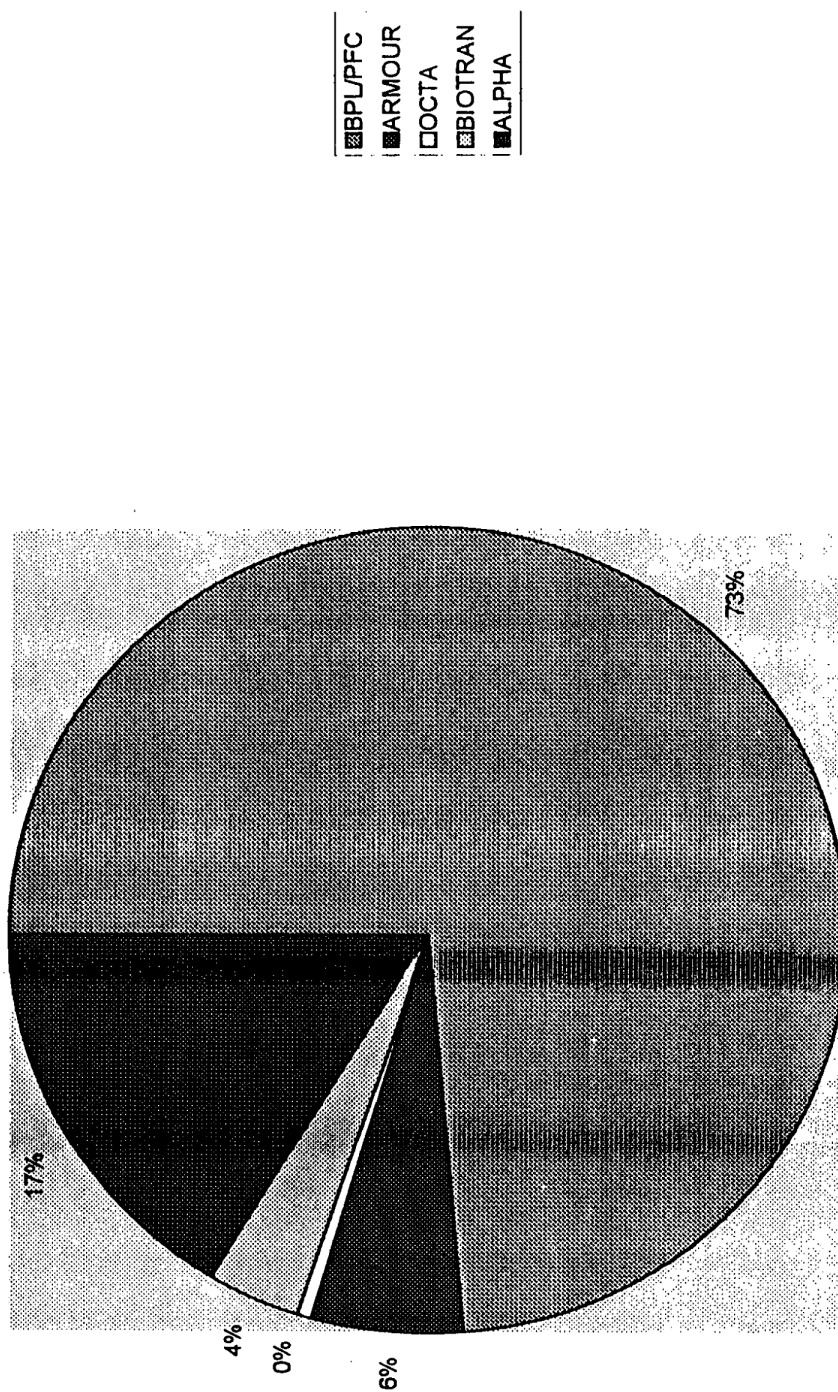
FIG.2  
 FACTOR VIII CONCENTRATES USED BY U.K. HAEMOPHILIA CENTRES IN 1993



- BPL/PFC
- ARMOUR
- BIOTRAN
- CRTS
- BEHRING
- APLHA
- RVIII

FIG.3

FACTOR IX CONCENTRATES USED BY U.K. HAEMOPHILIA CENTRES IN 1993



Date Complete Annual Returns Received from Centres

<u>Date Received</u>	<u>Centre</u>
08.03.94	Hastings
09.03.94	Newport
15.03.94	Alton Brighton
16.03.94	G.O.S. Lewisham
17.03.94	Chatham Redhill
22.03.94	Blackburn
23.03.94	Hull Chertsey
24.03.94	Staffordshire Thornton Heath Bedford
25.03.94	York
28.03.94	Bath Worthing Colchester
29.03.94	Southend
30.03.94	Salisbury Shrewsbury/Telford
06.04.94	Swansea
08.04.94	Hillingdon
14.04.94	Maidstone
15.04.94	Kettering Lincoln Margate
16.04.94	Lancaster

**Date Received****Centre**

20.04.94	Chelsea and Westminster
22.04.94	Bournemouth/Poole
25.04.94	Torquay Chichester
26.04.94	Eastbourne
28.04.94	Oxford
29.04.94	Huddersfield
03.05.94	Wolverhampton
09.05.94	Camberley
10.05.94	Exeter
12.05.94	Pembury Carshalton
18.05.94	Norwich
19.05.94	Barnstaple
20.05.94	Portsmouth
27.05.94	Truro Liverpool (Children's)
01.06.94	Stevenage Newcastle            } Carlisle               } combined Middlesbrough       } returns Sunderland           } Whitehaven           }
05.06.94	Glasgow (Children's)
06.06.94	Luton Ipswich
07.06.94	Taunton/Yeovil
14.06.94	Hereford Bangor
16.06.94	Birmingham (Children's) Bradford

Date ReceivedCentre

20.06.94	Worcester The Royal London Hospital
23.06.94	Northampton
04.07.94	Manchester (Children's)
12.07.94	Derby
14.07.94	Charing Cross
15.07.94	Birmingham (Adults) Leicester Kingston-upon-Thames
18.07.94	Hammersmith
22.07.94	Manchester (Adults)
29.07.94	Inverness
01.08.94	Sheffield (Children's)
02.08.94	Leeds
03.08.94	Milton Keynes
07.08.94	Harrogate
09.08.94	Dorchester Plymouth Roehampton
11.08.94	Southampton
15.08.94	UCH/Middlesex Hospital
06.09.94	Liverpool (Adults) Aberdeen
12.09.94	Dundee
13.09.94	The Royal Free Hospital
22.09.94	Belfast

**Incomplete**

**Data received included in report but data incomplete/queries outstanding**

St. Thomas'  
Glasgow Royal Infirmary  
Bristol  
Coventry  
Sheffield (Adults)  
Nottingham  
St. Mary's Hospital  
Cambridge  
Harrow  
Chelmsford  
Peterborough  
St George's Hospital  
King's College Hospital  
Cardiff  
Edinburgh  
Carlisle  
Slough

**No returns**

Harlow  
Winchester  
Guy's Hospital (now amalgamated with  
St. Thomas')  
Ashford  
Epsom