

Appendix A

Annual Returns from Haemophilia Centres

Since 1969, the U.K. Haemophilia Centre Directors have supplied data for annual collation and analysis in Oxford and 4 reports have been published in the Medical Press on their behalf (Biggs, 1974; Biggs and Spooner, 1977a and b; Biggs and Spooner, 1978). By mid-January 1978, all Haemophilia Centres had sent in their 1976 Annual Returns and a report on this data was presented to the Reference Centre Directors. Following discussion, the Reference Centre Directors decided that a detailed Annual Report should not be published in the Medical Press each year but that a report should be submitted for publication at 3-5 year intervals. It was therefore agreed that the next report on behalf of all U.K. Haemophilia Centre Directors should be submitted for publication during 1979 and should cover the 3 years 1976-78. In the meantime, the Annual Statistics would be given to all the Directors as soon as they were available.

The attached tables and graphs summarise the information which is at present available from the 1976 and 1977 Annual Returns. We are still waiting for the 1977 Annual Returns from a few Centres. It will be seen from Figs. 1-4 that the upward trend in the amount of materials required to treat Haemophilia A and Haemophilia B patients is continuing. Tables 1-14 give the data for 1976 received from 84 Centres and Tables 15-20 summarise the data which is at present available from the 1977 Annual Returns.

To enable us to prepare the 3-year report for publication next year, we hope Directors will be able to let us have their 1978 Annual Returns by the end of June 1979. A set of forms regarding the 1978 Annual Returns will be sent to all Directors in January; these forms will not be substantially different from the 1977 Annual Returns forms.

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18th October, 1978.

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Table 1

Haemophilia A

Number of patients treated:* 1,886

Materials received by these patients:

| | F.VIII units | % of all human blood products |
|----------------------------|--------------|-------------------------------|
| Plasma | 15,480 | 0.05 |
| Cryo | 15,716,710 | 46.61 |
| NHS Concs. | 6,915,323 | 20.51 |
| Commercial Concs. (Human) | 11,064,802 | 32.82 |
| Other Human Concs. | 3,807 | 0.01 |
| Total human blood products | 33,716,122 | 100.00 |
| Animal F.VIII Concs. | 341,190 | |
| Total all materials | 34,057,312 | |

Average per patient of human blood products = 17,877 units F.VIII

" " " including animal blood products = 18,058 units
F.VIII

* adjusted for duplicates

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Table 2

Haemophilia A patients known at Haemophilia Centres on 31.12.76, showing the severity of the defect, the number of patients treated during 1976 and the proportion of patients on home treatment.

| Basic F.VIII Level % | Haemophilia A Patients known at Centres on 31.12.76* | | Haemophilia A Patients treated during 1976 | | | | | |
|-------------------------|--|---------|--|--------------------|--|----------------------------|--|------------------|
| | | | All Patients | | | Patients on Home Treatment | | |
| | Number | % total | Number | % total treated | % total known in severity Group | Number | % total treated in severity Group | % total on HT |
| <2 | 1,787 | 52.76 | 1,221 | 64.74 | 68.33 | 418 | 34.23 | 93.51 |
| 2 - 10 | 799 | 23.59 | 434 | 23.01 | 54.32 | 28 | 6.45 | 6.27 |
| >10 | 539 | 15.91 | 163 | 8.64 | 30.24 | 1 | 0.61 | 0.22 |
| Unknown | 262 | 7.74 | 68 | 3.61 | 25.95 | - | - | - |
| TOTAL | 3,387 | 100 | 1,886 | 100 | 55.68 | 447 | 23.70 | 100 |

* excluding those known to have died prior to 1976.

Table 3

Haemophilia A patients known at Haemophilia Centres on 31.12.76, showing the age distribution, the number of patients treated during 1976 and the proportion of patients on home treatment.

| Age on 31.12.76 (Years) | Haemophilia A Patients known at Centres on 31.12.76* | | Haemophilia A patients treated in 1976 | | | | | |
|----------------------------|--|---------|--|--------------------|-------------------------------------|----------------------------|---------------------------------------|------------------|
| | | | All Patients | | | Patients on Home Treatment | | |
| | Number | % total | Number | % total treated | % total known in Age Group | Number | % total treated in Age Group | % total on HT |
| <5 | 171 | 5.05 | 106 | 5.62 | 61.99 | 6 | 5.66 | 1.34 |
| 5 - 9 | 319 | 9.42 | 219 | 11.61 | 68.65 | 39 | 17.81 | 8.73 |
| 10 - 19 | 838 | 24.74 | 545 | 28.90 | 65.04 | 179 | 32.84 | 40.05 |
| 20 - 29 | 663 | 19.58 | 417 | 22.11 | 62.90 | 122 | 29.26 | 27.29 |
| 30 - 39 | 436 | 12.87 | 266 | 14.10 | 61.01 | 59 | 22.18 | 13.20 |
| 40 - 49 | 297 | 8.77 | 144 | 7.64 | 48.48 | 27 | 18.75 | 6.04 |
| 50 - 59 | 213 | 6.29 | 104 | 5.51 | 48.83 | 11 | 10.58 | 2.46 |
| 60 - 69 | 138 | 4.07 | 39 | 2.07 | 28.26 | 3 | 7.69 | 0.67 |
| 70+ | 58 | 1.71 | 14 | 0.74 | 24.14 | 1 | 7.14 | 0.22 |
| Unknown | 254 | 7.50 | 32 | 1.70 | 12.60 | - | - | - |
| TOTAL | 3,387 | 100 | 1,886 | 100 | 55.68 | 447 | 23.70 | 100 |

* excluding those known to have died prior to 1976.

Table 4

Haemophilia B (Christmas Disease)

Number of patients treated: 296*

Materials received by these patients:-

| | F. IX Units | % of all Materials |
|-------------------|-------------|--------------------|
| Plasma | 17,680 | 0.31 |
| NHS Concs. | 5,532,654 | 99.48 |
| Commercial Concs. | 11,500 | 0.21 |
| TOTAL | 5,561,834 | 100 |

Average per patient = 18,790 units F. IX.

* Adjusted for duplicates.

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Table 5

Christmas Disease (Haemophilia B) patients known at Haemophilia Centres on 31.12.76, showing the severity of the defect, the number of patients treated during 1976 and the proportion of patients on home treatment

| Basic F.IX Level % | Haemophilia B Patients known at Centres on 31.12.76* | | Haemophilia B Patients treated during 1976 | | | | | |
|-----------------------|--|---------|--|--------------------|--|----------------------------|--|------------------|
| | | | All Patients | | | Patients on Home Treatment | | |
| | Number | % total | Number | % total treated | % total known in severity group | Number | % total treated in severity group | % total on HT |
| <2 | 225 | 39.27 | 162 | 54.73 | 72.00 | 49 | 30.25 | 81.67 |
| 2 - 10 | 169 | 29.49 | 87 | 29.39 | 51.48 | 11 | 12.64 | 18.33 |
| >10 | 95 | 16.58 | 34 | 11.49 | 35.79 | - | - | - |
| Unknown | 84 | 14.66 | 13 | 4.39 | 15.48 | - | - | - |
| TOTAL | 573 | 100 | 296 | 100 | 51.66 | 60 | 20.27 | 100 |

* excluding those known to have died prior to 1976.

Table 6

Christmas Disease (Haemophilia B) patients known at Haemophilia Centres on 31.12.76, showing the age distribution, the number of patients treated during 1976 and the proportion of patients on home treatment.

| Age on 31.12.76 (Years) | Haemophilia B Patients known at Centres on 31.12.76* | | Haemophilia B Patients treated during 1976 | | | | | |
|----------------------------|--|---------|--|--------------------|-------------------------------------|----------------------------|---------------------------------------|------------------|
| | | | All Patients | | | Patients on Home Treatment | | |
| | Number | % total | Number | % total treated | % total known in age group | Number | % total treated in age group | % total on HT |
| <5 | 33 | 5.76 | 23 | 7.77 | 69.70 | 1 | 4.35 | 1.67 |
| 5 - 9 | 61 | 10.65 | 37 | 12.50 | 60.66 | 8 | 21.62 | 13.33 |
| 10 - 19 | 141 | 24.61 | 78 | 26.35 | 55.32 | 16 | 20.51 | 26.67 |
| 20 - 29 | 109 | 19.02 | 62 | 20.95 | 56.88 | 15 | 24.19 | 25.00 |
| 30 - 39 | 60 | 10.47 | 35 | 11.82 | 58.33 | 11 | 31.43 | 18.33 |
| 40 - 49 | 49 | 8.55 | 20 | 6.76 | 40.82 | 4 | 20.00 | 6.66 |
| 50 - 59 | 29 | 5.06 | 15 | 5.07 | 51.72 | 1 | 6.67 | 1.67 |
| 60 - 69 | 25 | 4.36 | 8 | 2.70 | 32.00 | 2 | 25.00 | 3.33 |
| 70+ | 17 | 2.97 | 5 | 1.69 | 29.41 | 1 | 20.00 | 1.67 |
| Unknown | 49 | 8.55 | 13 | 4.39 | 26.53 | 1 | 7.69 | 1.67 |
| TOTAL | 573 | 100 | 296 | 100 | 51.66 | 60 | 20.27 | 100 |

* excluding patients known to have died prior to 1976

Table 7

Carriers of Haemophilia A

Total number of patients treated: 19

Materials received by these patients:-

| | F.VIII Units | % Total all Materials |
|-------------------|--------------|-----------------------|
| Cryo | 16,105 | 28.13 |
| NHS Concs. | 36,340 | 63.48 |
| Commercial Concs. | 4,800 | 8.39 |
| TOTAL | 57,245 | 100.00 |

Average per patient = 3,013 units of F.VIII

Table 8

Carriers of Haemophilia B (Christmas Disease)

Total number of patients treated: 5*

Materials used to treat these patients:-

| | F.IX Units | % Total all Materials |
|------------|------------|-----------------------|
| Plasma | 1,600 | 25.40 |
| NHS Concs. | 4,700 | 74.60 |
| TOTAL | 6,300 | 100.00 |

Average per patient = 1,260 units F.IX

* Plus 2 patients who received no blood products.

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Table 9

Basic Factor VIII or Factor IX Levels of Carriers of Haemophilia A or Haemophilia B (Christmas disease) treated with blood products during 1976.

| Basic Coagulation Factor level % | Patients treated during 1976 | | | |
|-------------------------------------|------------------------------|--------------------|---------------------------|--------------------|
| | Carriers of Haemophilia A | | Carriers of Haemophilia B | |
| | Number | % total treated | Number | % total treated |
| <10 | 2 | 10.53 | 1 | 20.00 |
| 10 - 19 | 1 | 5.26 | 1 | 20.00 |
| 20 - 29 | 8 | 42.11 | - | - |
| 30 - 39 | 4 | 21.05 | 1 | 20.00 |
| 40 - 49 | 1 | 5.26 | - | - |
| 50 - 59 | 1 | 5.26 | - | - |
| ≥60 | - | - | 1 | 20.00 |
| Unknown | 2 | 10.53 | 1 | 20.00 |
| TOTAL | 19 | 100.00 | 5 | 100.00 |

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Table 10

Von Willebrand's disease

Total number of patients treated: 186*

Materials used to treat these patients:-

| | F.VIII Units | % Total all Materials |
|-------------------|--------------|--------------------------|
| Plasma | 9,040 | 1.14 |
| Cryo | 674,045 | 84.63 |
| NHS Concs. | 41,025 | 5.15 |
| Commercial Concs. | 72,358 | 9.08 |
| TOTAL | 796,468 | 100.00 |

Average per patient = 4,282 units F.VIII

* adjusted for duplicates.

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Table 11

Blood Coagulation Factor VIII Levels of von Willebrand's disease patients treated with blood products during 1976

| Factor VIII Level % | Patients treated in 1976 | |
|------------------------|--------------------------|--------------------|
| | Number | % total treated |
| <10 | 36 | 19.35 |
| 10 - 19 | 29 | 15.59 |
| 20 - 29 | 38 | 20.43 |
| 30 - 39 | 32 | 17.20 |
| 40 - 49 | 19 | 10.22 |
| 50 - 59 | 12 | 6.45 |
| >60 | 6 | 3.23 |
| Unknown | 14 | 7.53 |
| TOTAL | 186 | 100.00 |

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Table 12

Cases of Jaundice (Hepatitis)

Haemophilia A

| <u>Treatment Year</u> | <u>No Haemophiliacs treated</u> | <u>Incidence of Jaundice</u> | <u>% patients who developed Jaundice</u> |
|---------------------------|-------------------------------------|----------------------------------|--|
| 1976 | 1,886 | 56 (61) | 2.97 (3.24) |

() the number in brackets indicates the total including patients who were asymptomatic.

Carriers of Haemophilia A:

1 of the 19 patients treated during 1976 (5.26%) was reported to have developed hepatitis.

Haemophilia B (Christmas disease):

5 of the 296 patients treated during 1976 (1.69%) were reported as having developed hepatitis.

Carriers of Haemophilia B:

None of the 5 patients treated during 1976 were reported as having developed hepatitis.

Von Willebrand's disease:

5 of the 186 patients treated during 1976 (2.69%) were reported as having developed hepatitis.

The detailed analysis and report on the hepatitis cases will be made by the Hepatitis Working Party.

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Table 13

The occurrence of anti-factor VIII or anti-factor IX antibodies

Eighteen new cases of anti-factor VIII antibodies were detected in haemophilia A patients during 1976 and three haemophiliacs with long-standing antibodies were reported in the Annual Returns for the first time in 1976. No new cases of anti-factor IX antibodies in haemophilia B (Christmas disease) patients have been reported. The incidence of anti-factor VIII or anti-factor IX antibodies in haemophilia A or B patients known at Haemophilia Centres on 31.12.76 was as follows:-

| | Haemophilia A | Haemophilia B |
|--|---------------|---------------|
| Cumulative total number of patients known at Centres | 3,387* | 573* |
| Cumulative total number with anti-factor VIII or IX antibodies | 195* | 5* |
| % with anti-factor VIII or IX antibodies | 5.76 | 0.37 |

* excluding patients known to have died prior to 1976.

Ninety-seven (49.74%) of the haemophilia A patients with anti-factor VIII antibodies and 3 (60%) of the haemophilia B patients with anti-factor IX antibodies were treated at Haemophilia Centres during 1976. Details of the treatment received by these patients is being studied by the Working Party on the Treatment of Patients with Factor VIII Antibodies.

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Table 14
Deaths reported in 1976 Annual Returns

| Cause of Death | Number of Patients | |
|---------------------------------------|--------------------|---------------|
| | Haemophilia A | Haemophilia B |
| Cerebral haemorrhage | 3 | 1 |
| G.I. haemorrhage | 1 | - |
| Intrapulmonary haemorrhage | 1 | - |
| Accident | 2 | - |
| Coronary occlusion due to atheroma | - | 1 |
| Post-tonsillectomy* | - | 1 |
| Not known | 2 | 1 |
| TOTAL | 9 | 4 |

- * Prior to tonsillectomy the patient was not known to have a coagulation defect. Christmas disease (20% P. IX) was diagnosed post-operatively.

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Table 15
Treatment of Haemophilia A Patients in 1977

The total amount of human blood products (factor VIII Units) used by 96 Haemophilia Centres to treat 1,975 patients, showing the proportion of material used for home treatment and for patients having factor VIII antibodies. Data from 4 Centres whose returns are at present incomplete have been excluded from this table.

| Reason Used | Factor VIII Units | % Total |
|---|-------------------|---------|
| Hospital treatment: | | |
| Patients with no factor VIII antibodies | 28,051,887 | 68.15 |
| Patients with factor VIII antibodies* | 1,979,727 | 4.80 |
| Home treatment: | | |
| Patients with no factor VIII antibodies | 10,923,649 | 26.54 |
| Patients with factor VIII antibodies | 209,453 | 0.51 |
| TOTAL | 41,164,716 | 100.00 |

*These patients also received the following materials:-

| | |
|----------------------|---------------|
| NHS Factor IX | 265,160 Units |
| Commercial Factor IX | 10,000 " |
| Animal Factor VIII | 16,000 " |
| FEIBA | 2,471,838 " |
| PROPLEX | 138,170 " |

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Table 16

Factor VIII Units Used in 1977

The total amount of material used by 100 Haemophilia
Centres to treat Factor VIII deficient patients

| Diagnosis | Number of Patients | Factor VIII Units | Average per patient | % Total |
|---------------------|-----------------------|----------------------|------------------------|---------|
| Haemophilia A | 2,084 | 46,222,746 | 22,180 | 95 |
| Von Willebrand's | 254 | 2,159,541 | 8,502 | 4 |
| Carriers of Haem. A | 39 | 51,318 | 1,318 | 1 |
| TOTAL | 2,377 | 48,433,605 | 20,376 | 100 |

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Table 17

Treatment of Haemophilia B (Christmas Disease)
Patients in 1977

The total amount of blood products (factor IX Units) used by Haemophilia Centres to treat Christmas Disease patients. Data from 4 Centres whose returns are at present incomplete have been excluded from this table

| Reason Used | Factor IX Units | % Total |
|---------------------------------------|-----------------|---------|
| Hospital Treatment: | | |
| Patients with no Factor IX antibodies | 5,261,319 | 76.4 |
| Patients with Factor IX antibodies | 37,202 | 0.54 |
| Home Treatment | 1,566,460 | 22.82 |
| TOTAL | 6,864,981 | 100.00 |

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Table 1^B

Factor IX Units Used in 1977

The total amount of material used by Centres to treat patients with congenital coagulation defects

| Diagnosis | Number of Patients | Factor IX Units | Average per patient | % Total |
|--------------------------------|--------------------|-----------------|---------------------|---------|
| Haemophilia B | 321 | 7,891,016 | 24,583 | 96.13 |
| Carriers of Haem. B | 9 | 42,330 | 4,703 | 0.52 |
| Haem. A with F.VIII antibodies | 11* | 275,160 | 25,145 | 3.35 |
| TOTAL | 341 | 8,208,506 | 24,072 | 100.00 |

*Data to be clarified. Patients not treated exclusively with Factor IX.

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Table 19

The number of patients known to Haemophilia Centre Directors on 31.12.77 and the occurrence of factor VIII and factor IX antibodies

| | Haemophilia A | Haemophilia B |
|---|---------------|---------------|
| Cumulative total number of patients known at Centres | 3,699* | 650* |
| Cumulative total number with factor VIII or IX antibodies | 208* | 6* |
| % with factor VIII or IX antibodies | 5.62 | 0.92 |

* excluding patients known to have died prior to 1977

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Table 20

The incidence of hepatitis in patients treated during 1977

| Diagnosis | Number of patients treated | Number of cases of Jaundice reported* | % jaundiced |
|--------------------------|----------------------------|---------------------------------------|-------------|
| Haemophilia A | 2,084 | 49 (54) | 2.35 |
| Haemophilia A Carriers | 39 | 1 | 2.56 |
| Haemophilia B | 321 | 7 | 2.18 |
| Haemophilia B Carriers | 9 | Nil | Nil |
| Von Willebrand's Disease | 254 | 3 | 1.18 |
| TOTAL | 2,707 | 50 (65) | 2.22 |

* The figures in brackets are the total number when asymptomatic cases are included.

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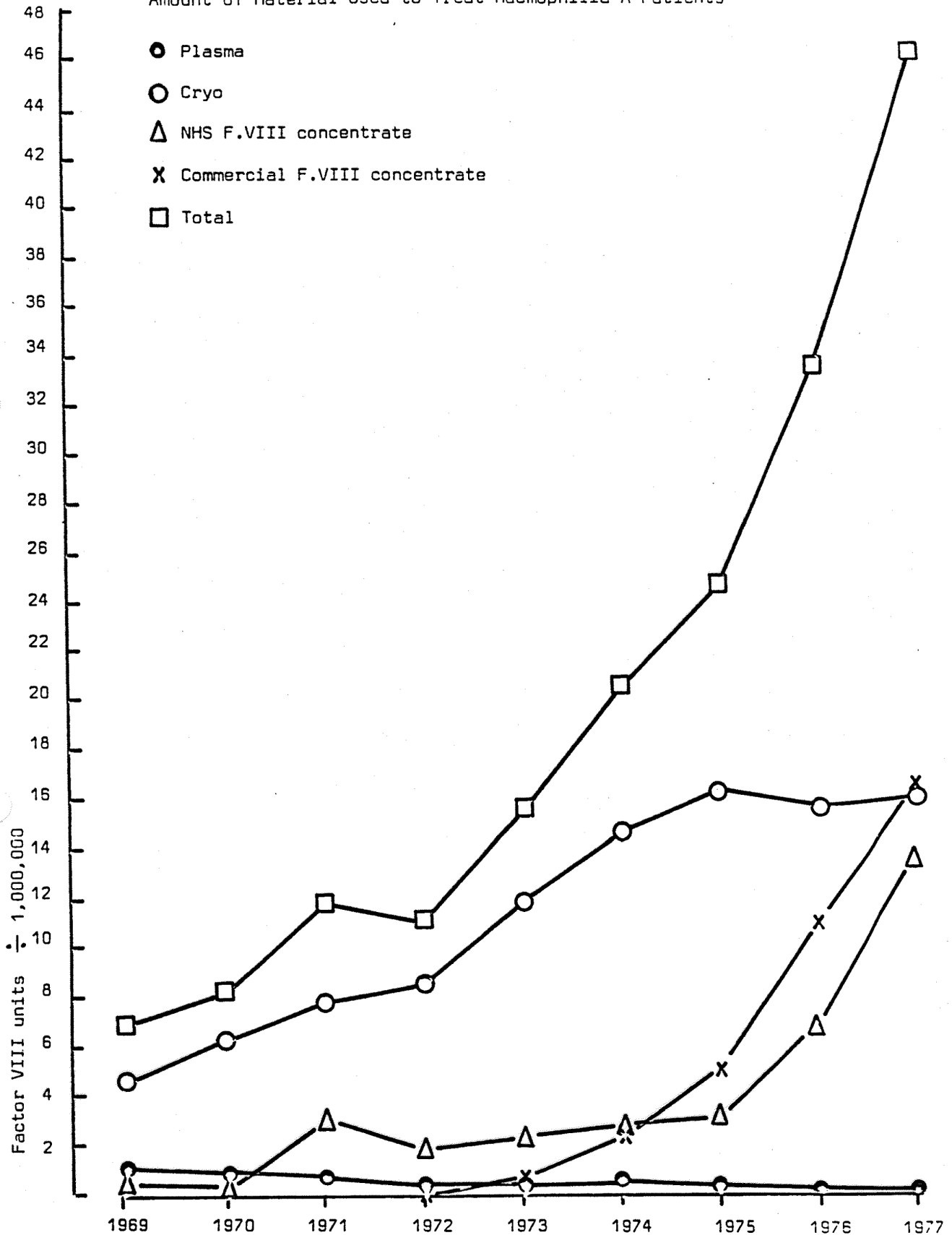
References

- Biggs, R. (1974) Jaundice and antibodies directed against factors VIII and IX in patients treated for haemophilia or Christmas disease in the United Kingdom. British Journal of Haematology, 26, 313.
- Biggs, R. and Spooner, R. (1977a) Haemophilia treatment in the United Kingdom from 1969 to 1974. British Journal of Haematology, 35, 487.
- Biggs, R. and Spooner, R.J.D. (1977b) Haemophilia Centre Directors' Annual Statistics for 1975. British Journal of Haematology, 36, 447.
- Biggs, R. and Spooner, R.J.D. (1978) National Survey of haemophilia and Christmas disease patients in the United Kingdom. Lancet i, 1143.

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Fig. 1

Amount of Material Used to Treat Haemophilia A Patients



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Fig. 2

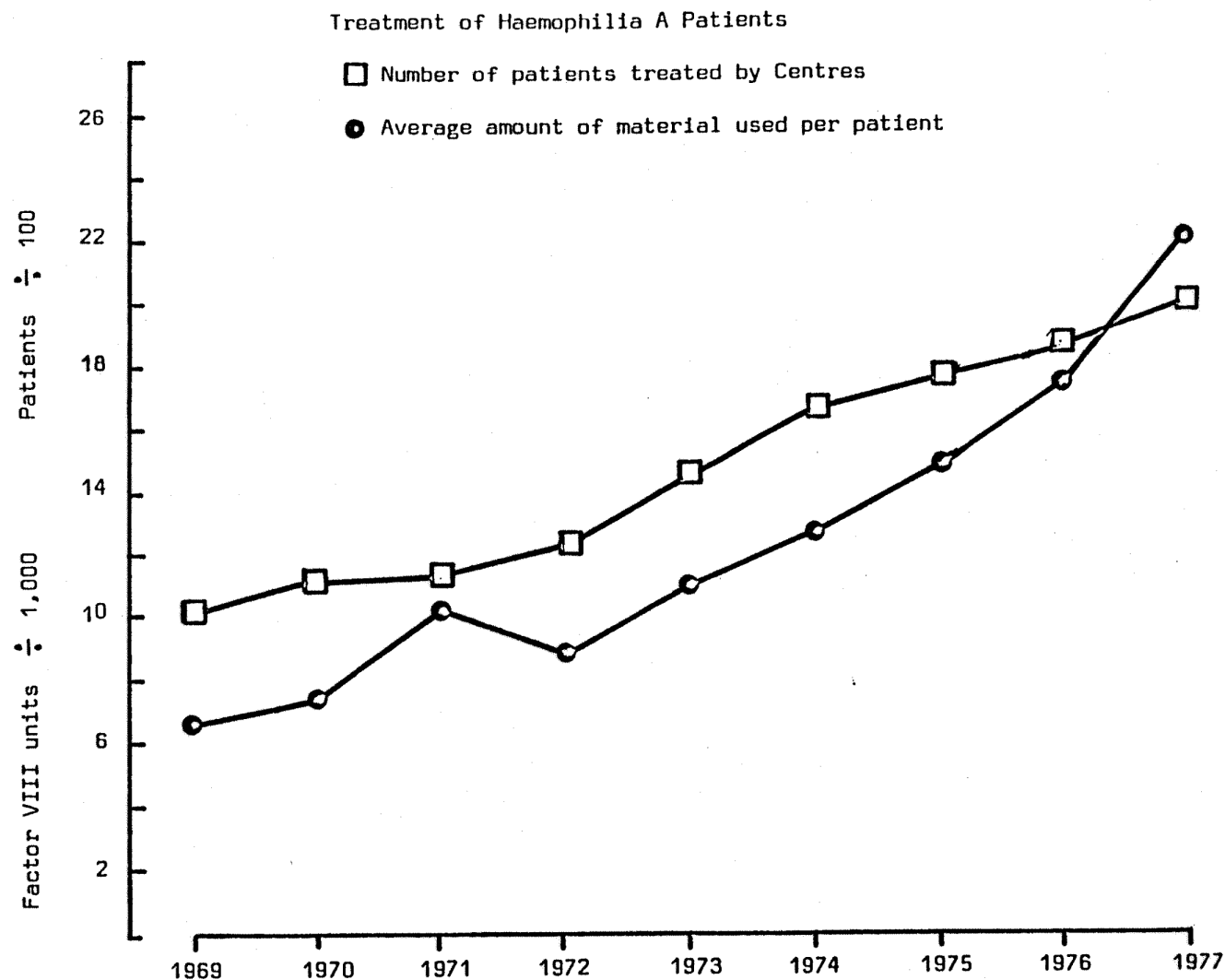
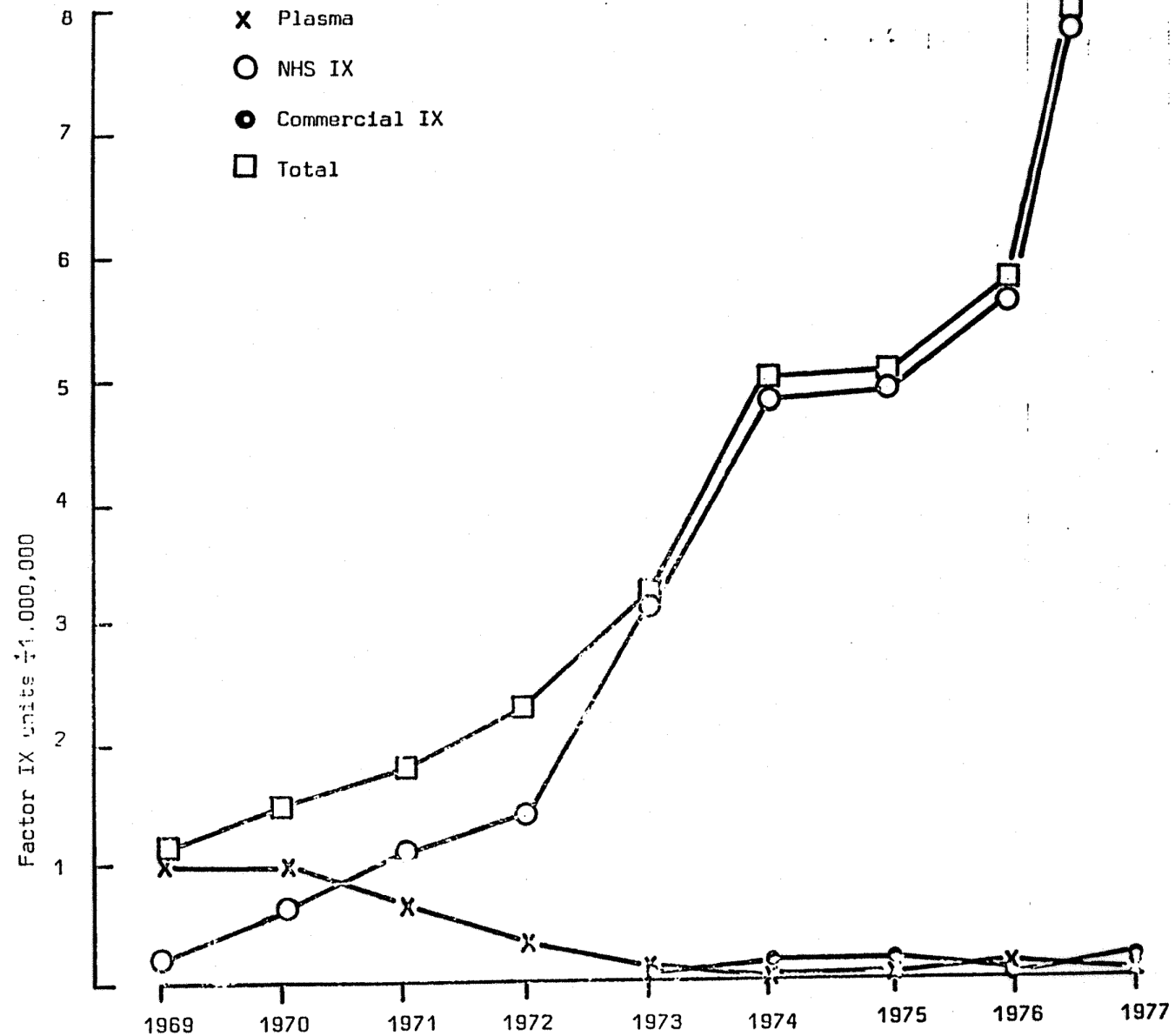


Fig. 3

Amount of material used to treat Christmas Disease Patients



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Fig. 4

Treatment of Christmas Disease Patients

