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Self-Sufficiency

SNBTS Self-Sufficiency Programme

These notes have been produced primarily to facilitate discussion with regard to the future SNBTS planning of the availability of factor VIII and IX concentrates within the Scottish Health Service.

1980

For BTS Subcommittee & SHHD

FACTOR VIII CONCENTRATES

Whilst it is recognised that many problems have yet to be solved with regard to the optimal management of haemophilia A patients and thus the requirements of factor VIII concentrates, the time is opportune to reconsider the SNBTS facility to meet genuine clinical needs.

The aim of the SNBTS is to eliminate the necessity for the purchase of factor VIII concentrates from commercial concerns and, in discharging this duty, close collaboration with Haemophilia Centre Directors is both welcomed and anticipated.

TRENDS AND PRESENT SUPPLY/DEMAND POSITION

(Year ending 31st March, 1980)

1.01 Total Fresh Plasma processed for Factor VIII Concentrates (Kg)

(Details in Appendix 1 (a))

1975	1976	1977	1978	1979	1980
10,323	14,363	16,295	19,581	20,553	25,059

1.02 Total Cryoppt. Issued from Regional Centres (Donations)

(Details in Appendix 1 (b))

1975	1976	1977	1978	1979	1980
35,048	39,736	28,018	31,151	35,199	30,273

1.03 Total PFC Issues of Intermediate VIII (i.u. x 10^6)

(Details in Appendix 1 (c))

1975	1976	1977	1978	1979	1980
0.11	0.79	1.33	1.55	1.66	1.99

1.04 Commercial Purchases of Factor VIII

Satisfactory figures are only available for 1979 and 1980. These are as follows:-

1979 .. .. .. 850,000 i.u.

1980 .. .. .. 1,000,000 i.u.

(Until 1980 commercial purchases were made exclusively in the West of Scotland. 1981 figures will show that other Regions are now purchasing commercial factor VIII.).

1.05/....

1.05 Summary (i.u. x 10^6)

	1975	1976	1977	1978	1979	1980
Cryoppt.*	3.50	3.97	2.80	3.15	3.52	3.02
P.F.C.	0.11	0.79	1.33	1.55	1.66	1.99
Commercial	(0.05)	0.09	(0.5)	(0.7)	0.85	1.00
TOTAL	(3.66)	4.85	(4.63)	(5.4)	6.03	6.01

*Assumed each donation gives 100 i.u. of factor VIII.

Figures in brackets are 'guesstimates'.

FUTURE DEVELOPMENTS IN DEMAND

2.01 This is a particularly difficult problem at the present time, primarily because the practice of Home Therapy is still evolving, the appropriate method of managing patients with inhibitors is unresolved and the unequivocal evidence that haemophilia patients are living longer, thus increasing the overall population and becoming subject to similar disease processes of older age-groups in the non-haemophilia population which are amenable to surgical intervention.

2.02 Despite these difficulties efforts are now required which will enable the SNBTS to formulate long term plans which can, if necessary, be adjusted at a later date. In seeking to obtain comment and guidance the author would make the following comments, which are based on discussions with colleagues in various parts of the world (including the U.K.).

2.03 (i) Home Therapy for Severe Cases

Home Therapy now covers a wide variety of clinical approaches and dosage regimes. Some examples are given below:-

	Oxford	Newcastle	U.S.A.+	Lord Mayor Treloar	West Germany (Bonn)
Annual Requirement per patient (i.u.)	20,000	50,000	65,000	100,000	200,000
* Requirement per 10^6 total population per year (iu x 10^6)	0.7	1.75	2.3	3.5°	7.0

* Calculations assume 70 haemophilia patients/10^6 pop. and 50% are severe.

° Figure likely to be excessive for overall calculations because population is unusual (young school boys).

+ Discussion with Dr L. Aledort (New York).

(ii)/....

2.04 (ii) Mild and Moderate Haemophiliacs (without inhibitors) and Von Willebrand's Syndrome

Surveys over the years would indicate that this group is likely to be satisfactorily covered by 250,000 i.u./10^6 pop./yr.

2.05 (iii) Inhibitor Patients

This is a controversial area with regard to optimum therapy. Suggest most clinicians would favour (if available) high dose VIII, in preference to immunosuppression/plasmapheresis and animal VIII, for severe emergency situations.

Suggest 2 such patient episodes/10^6 total pop./yr. and would each need 250,000 i.u./episode: thus an additional 500,000 i.u. p.a.

2.06 (iv) Elective Surgery

Suggest: 50,000 i.u. per major operation
20,000 i.u. per minor operation
1,000 i.u. per dental treatment

Suggest, also, that for each 10^6 total pop./yr. there would be a requirement for 2 major and 2 minor operations and 20 dental procedures. Thus, in approximate terms, it would be advisable to provide an additional 150,000 i.u./10^6 total pop./yr. for this item.

2.07 (v) Increasing Age of Haemophilia Population

The improved life expectancy of haemophilia patients over the past 10 years is now self-evident and it can be assumed that very many more patients will live into middle and old age. Thus, the total population requiring ordinary factor VIII maintenance will increase. In addition will come a likely heightened demand for blood resources (in line with the non-haemophiliac community) due to the increasing incidence of surgery and/or support for diseases associated with an ageing population: cardiovascular disease; malignancy and orthopoedic (fractured neck of femur).

It is almost impossible to cover this area of expansion, because of the extreme paucity of data available to us. However, further studies are being done and, in the meantime, we might be well advised to consider an expansion factor of 100,000 i.u. per 10^6 pop. per annum for the next 10 years. This is likely to be a significant under-estimate.

SUMMARY/....

2.08 Summary

I believe it would be appropriate, for planning purposes, to accept the figures from Newcastle for the single largest contributor (Home Therapy).

It is probable that this figure has a sufficient margin of clinical flexibility to make it realistic for the next 10 years.

Based on this assumption the following Table can be drawn up:-

	VIII (i.u.)/10^6 total pop./yr.
Home Therapy	1.75
Moderate/mild etc. patients	0.25
Inhibitor Patients	0.50
Elective Surgery	0.15
Ageing of Population	0.10
Total	2.75 (Reaching 3.75 in 2007.)

Annual Increment of 40,000 i.u/year for 25 years.

P.F.C. FACTOR VIII YIELDS

3.01 Over the years there has been considerable controversy and misunderstanding with regard to the definition of fractionation yields. The figures given below are unambiguous: they refer to the number of i.u. of factor VIII (produced by P.F.C.) which will reach the bed-side per litre of fresh frozen plasma processed:-

1975	1976	1977	1978	1979	1980
193	195	148	165	190	250

3.02 P.F.C. staff have made considerable efforts, from mid 1978, to improve yields. This includes the development and introduction of a new system for thawing of fresh frozen plasma. Further improvements of existing equipment are anticipated: current data would suggest that an average figure of 300 i.u./litre will be achieved by mid 1981. Support for this conclusion can be found by comparing the figures below:-

	Fresh Plasma (Kg) to P.F.C. from Regions		Issue of VIII (x 10^6 iu) from P.F.C. to R.T.C.s	
	1979/80	1980/81	1979/80	1980/81
1st Quarter	5087	5176	0.45	0.82
2nd Quarter	4220	5626	0.53	0.92
3rd Quarter	4033	5369	0.57	1.13

3.03 Available evidence from various parts of the world indicates that yields from plasma pools of less than 1000 litres for an intermediate concentrate of 250 i.u./litre can be considered to be more than satisfactory.

REGIONAL CENTRE (CRYOPPT.) YIELDS

4.01 Evidence from recent surveys in the U.K. and U.S.A. (American Red Cross) would suggest that this type of product gives an average yield of at least 400 i.u./litre of plasma processed. There is good evidence to suggest newer approaches to the cryoprecipitation procedure will elevate this to in excess of 500 i.u./litre. (It is worth emphasising that these newer approaches have been introduced to P.F.C. and partly explain the recent improvements there. However, the further purification steps which are to be made and the demands of Good Manufacturing Practice give rise to the further losses.)

4.01 Recent preliminary studies in the SNBTS (West of Scotland) have confirmed that freeze-drying of cryoprecipitate results in a negligible loss and that current RTC yields are therefore likely to be maintained. The final product can be stored in a domestic refrigerator.

QUALITY OF FACTOR VIII CONCENTRATES

5.01 Although a somewhat over-simplification, currently available factor VIII concentrates can usefully be banded into 3 groups:-

	VIII/mg. protein (i.u.)	Max. Solubility i.u./ml.	Yield (i.u./litre)
Group I (Cryoppt.)	< 0.2	≯ 5	450
Group II (Intermediate)	0.2-0.5	5-20	250
Group III (High Purity)	> 0.5	> 20	180

5.02 The recent declaration by Her Majesty's Government that it is the intention, in the U.K., to develop its Blood Transfusion Services to such an extent that we are self-sufficient in blood and blood products makes it vitally important that all interested parties examine the question of the quality of factor VIII concentrates in some detail. In doing so it is the view of the author that it must be recognised that limitations on financial resources will certainly represent the single most important barrier which will prevent an early ideal solution for haemophilia A patients. Set against this, however, is the fact that the 'ideal solution' is not yet known and that these patients must inevitably, to some extent, share financial resources with others. Thus, without detracting from the urgent need for action, it should be recognised and accepted by all parties that compromises of some sort will be an essential pre-requisite for the foreseeable future. The parties concerned include the patients and relatives, the clinical teams responsible for their care, the Blood Transfusion Services (which include their Fractionation Centres) and the Medicines Inspectorate (the body concerned with establishing and policing codes of good manufacturing practice).

5.03 It is of interest to consider the future fresh plasma requirements for Scotland, based upon the proposed target of 2.75×10^6 i.u. VIII/10^6 pop./yr. and product options (yields).

	Litres of FFP per annum	Litres/10^6 pop./yr.
Group I only	32,000	6,000
Group II only	57,000*	11,000
Group III only	79,000*	15,000

(* Fractionation at these levels will almost certainly lead to significant excesses in albumin availability. Current annual donation input of SNBTS is approx. 280,000. 200 ml. of plasma from every donation would give approx. 56,000 litres of FFP.)

5.04/....

5.04 The existing annual donation input is high by international standards and with it comes a high red cell wastage (in excess of 35% - 70,000 donations p.a.). These high red cell wastage rates, coupled with increased future demands for fresh plasma, are leading the SNBTS to consider the desirability of developing a plasmapheresis programme for fresh plasma.

5.05 The figures provided in the sections above indicate that in order to meet the desired aim of self-sufficiency considerable compromise will be necessary with regard to the quality of products prepared. It is of interest to note that countries in which substantial fractionation facilities have already been developed have, nevertheless, opted to make freeze-dried cryoppt. the single major product for haemophiliacs (Switzerland, Finland, Netherlands, Belgium and France). (Moreover, in the U.S.A., a country in which the cost of VIII per i.u. is the lowest in the world, they still use approximately 45% of the VIII concentrate in the form of cryoppt. - on the grounds of cost to the patient - and one major organisation is now considering the desirability and feasibility of producing a freeze-dried product.)

5.06 These European countries use intermediate and high purity preparations only when indicated - many Home Therapy programmes are dominated by freeze-dried cryoppt. Detailed data (for 1980) is available from two countries:-

	Total Volume of Fresh Plasma Obtained (litres)/ 10^6 pop./yr.	% to F.D. Cryoppt.	% to A.H.F.
Belgium	11,000	80	20
Finland	7,000	85	15

SPECIFIC PROPOSALS FOR DISCUSSION

6.01 1. That a target for 2.75 x 10^6 i.u. of VIII/10^6 pop./yr. be considered as the one to which the SNBTS should aim for the next 5 years with an increment thereafter of 100,000 i.u. p.a.

6.02 2. That Freeze Dried Cryoppt. be produced, with a view to studying, on a multicentre basis, its role in Home Therapy, with specific emphasis on side effects, efficacy, practicability and cost.

6.03 3. That studies be considered and planned with a view to delineating the clinical role of intermediate VIII and a higher purity VIII.

6.04 4. That P.F.C. be encouraged to undertake studies to:

(a) Further improve the yield of intermediate VIII (which would include increased pool sizes).

(b)/....

(b) Develop a product of higher potency (per mg. total protein) than intermediate VIII.

FACTOR IX CONCENTRATES

SUPPLY AND DEMAND

7.01 Fortunately, because of the much smaller number of haemophilia B patients than A, the supply of these products is always more than adequate, with one exception, see below. P.F.C. issues to Regional Centres can be summarised as follows:-

	1975	1976	1977	1978	1979	1980
DEFIX (II, IX & X) ($x10^6$ iu of IX)	0.5	0.71	0.76	1.1	0.86	1.0
PPSB (II, VII, IX & X) (i.u. of IX)	27,000	57,000	105,000	130,000	70,000	44,000

PROBLEMS AND MATTERS OF INTEREST

8.01 1. Viral Hepatitis Transmission

Several reports have implied that the risks of transmitting agents likely to cause hepatitis is higher for factor IX than VIII concentrates. The evidence is not firm but may relate to differences in pool size (the former usually being larger). Nevertheless, continuing efforts are being made to improve matters and a stage has been reached at P.F.C. when clinical studies will soon be required (see below).

8.02 2. Thrombogenicity

Evidence has been accumulated from many parts of the world that some preparations of factor IX concentrate are thrombogenic in man - varying from local thrombosis to fatal disseminated intravascular coagulation. Patients at particularly high risk are those with liver disease. This latter feature is of particular importance because haemophilia B patients are a high risk group for hepatitis and the use of factor IX concentrates in the management of haemostatic failure associated with liver disease in general has increased in popularity over the last 10 years, as has their use in the acute reversal of oral anticoagulant therapy and in the neonate.

8.03/....

8.03 The SNBTS has been fortunate in this area: it has a research group particularly interested in the problem, which now has an international reputation, a range of products which appear to have an excellent record and two new products which seek to improve the position further (see below).

8.04 This problem is of more than academic interest to all clinical colleagues in Scotland because there is considerable pressure from the U.K. licensing authority to limit the use of factor IX concentrates to haemophilia B, on the grounds of safety and known efficacy. Indeed, it has been informally indicated to P.F.C. that PPSB will not get a licence on grounds that there is a satisfactory (? superior) alternative - DEFIX.

8.05 It is the view of the author, and others, that there is a need (though limited) for factor IX concentrates in the management of some non haemophilia B patients and that a minority of these will also require factor VII. It is accepted that PPSB is not an ideal product from a transfusion service point of view because it requires EDTA anticoagulant and thus the red cells, platelets and factor VIII are lost.

3. Partial Solutions

9.01 Two new products are currently at an advanced stage of development:

(a) Supernine:

Further purification of DEFIX has led to a product which we believe may be both safer with regard to virus transmission and thrombogenicity.

(b) Factor VII Concentrate:

This product, not quite as well advanced as Supernine, will be ideal for congenital VII deficient patients - none known in Scotland. It's primary use will be to administer separately to those non-haemophilia B patients who need VII in addition to II, IX and X.

SOME PROPOSALS/....

SOME PROPOSALS FOR DISCUSSION

10.01 1. Haemophilia Directors agree to initial clinical studies of Supernine which will lead to the issue of a product licence. Subject to agreement, Dr Cash (or deputy) and Mr Watt (or deputy) liaise with appropriate colleagues in order to establish clinical studies.

10.02 2. As (1) but for factor VII concentrate when available.

10.03 3. Establish systems for determining quantities of factor IX concentrates used in haemophilia B and non-B patients on an annual basis.

APPENDIX 1 (a)

SNBTS: FRESH PLASMA PROCUREMENT FOR FACTOR VIII PRODUCTION

		1975°		1976		1977		1978		1979		1980	
		Litres	Litres per 10^6 Pop	Litres	Litres per 10^6 Pop	Litres	Litres per 10^6 Pop	Litres	Litres per 10^6 Pop	Litres	Litres per 10^6 Pop	Litres	Litres per 10^6 Pop
ABERDEEN	Cryoppt.*	225*		158		192		257		220		449	
	To P.F.C.	3		43		129		654		1,188		1,831	
	TOTAL	228	459	201	404	321	646	911	1,833	1,308	2,632	2,280	4,588
DUNDEE	Cryoppt.	167		195		56		200		123		57	
	To P.F.C.	212		484		792		864		1,006		1,572	
	TOTAL	379	808	679	1,366	848	1,808	1,064	2,269	1,129	4,838	1,629	3,473
EDINBURGH	Cryoppt.	1,846		2,535		2,176		1,994		2,720		3,183	
	To P.F.C.	1,357		2,611		4,347		4,985		3,982		3,786	
	TOTAL	3,203	2,839	5,146	4,562	6,523	5,782	6,979	6,187	5,602	4,966	6,969	6,178
GLASGOW	Cryoppt.	4,454		5,112		3,047		3,765		3,678		2,785	
	To P.F.C.	819		1,457		4,163		5,573		7,322		9,574	
	TOTAL	5,373	1,878	6,569	2,296	7,210	2,520	9,338	3,264	11,000	3,845	12,359	4,320
INVERNESS	Cryoppt.	318		497		Nil		Nil		11		3	
	To P.F.C.	832		1,271		1,393		1,289		1,503		1,819	
	TOTAL	1,140	5,067	1,768	7,858	1,393	6,191	1,289	5,729	1,514	6,729	1,822	8,098
GRAND TOTALS		10,323	2,210	14,363	3,297	16,295	3,389	19,581	3,856	20,553	4,602	25,059	5,314

* Cryoppt. converted to litres by multiplying donations processed by 0.2

° Year ending 31st March

APPENDIX 1 (b)

SNBTS: REGIONAL CENTRE ISSUES OF CRYOPPT. (DONATIONS)

	1975°	1976	1977	1978	1979	1980
ABERDEEN	1,124	1,967	1,005	1,228	1,320	1,987
DUNDEE	833	1,049	192	922	603	343
EDINBURGH	9,232	11,112	9,970	11,069	13,329	15,375
GLASGOW	22,271	24,515	16,800	17,932	19,922	12,568
INVERNESS	1,588	1,093	51	Nil	25	Nil
TOTALS	35,048	39,736	28,018	31,151	35,199	30,273

° Yrs. ending 31st March

APPENDIX 1 (c)

P.F.C. ISSUES OF INTERMEDIATE VIII TO REGIONAL CENTRES

(i.u. x 10^6)

	1975	1976	1977	1978	1979	1980
ABERDEEN	0.009 (0.02)	0.05 (0.1)	0.1 (0.2)	0.09 (0.18)	0.12 (0.24)	0.10 (0.18)
DUNDEE	0.008 (0.02)	0.03 (0.1)	0.08 (0.2)	0.09 (0.2)	0.10 (0.22)	0.14 (0.32)
EDINBURGH	0.025 (0.02)	0.24 (0.2)	0.30 (0.25)	0.21 (0.18)	0.31 (0.26)	0.28 (0.23)
GLASGOW	0.05 (0.02)	0.37 (0.13)	0.65 (0.23)	0.9 (0.31)	0.95 (0.33)	1.33 (0.46)
INVERNESS	0.018 (0.08)	0.09 (0.4)	0.16 (0.7)	0.14 (0.64)	0.18 (0.8)	0.134 (0.61)
TOTALS	0.11 (0.02)	0.79 (0.15)	1.33 (0.25)	1.55 (0.30)	1.66 (0.32)	1.99 (0.38)

(Figures in brackets - VIII issues/10^6 pop.)

INFORMATION FROM DENMARK

In 1979 the Danish Health Authorities agreed to a target of 2×10^6 i.u. factor VIII/10^6 population/yr. Investigations are now in hand to revise this further. It is believed (but not yet approved by Health Authorities) that a more realistic figure will be 3×10^6 i.u./10^6 pop./yr..

BELGIUM FIGURES (1980)

1. Aiming for 12,000 litres of fresh plasma/10^6 pop./year.

2. Currently processing as follows:-

Product	Volume (L/10^6 pop.)	Stated Yield (i.u./L)	Return (i.u. x 10^6)
Freeze Dried Cryoppt.	9,600	500	4.8
A.H.F. (H.P.)	2,400	100	0.24
TOTAL	12,000		5.04

3. Current use of "NHS" Material in Belgium = 5.0×10^6 i.u./10^6 pop./yr.

AMERICAN SURVEY OF FACTOR VIII USAGE IN 1980

This survey has been carried out by Dr L. Aledort, Medical Director of the American Haemophilia Society and a practising Haemophilia Centre Director.

The figures represent current use by a group of American Haemophilia A patients who are managed in Comprehensive Care Clinics in which some form of prophylactic home therapy programme is practiced. Dr Aledort records that for the past 3 years this group's requirements has plateaued at the figure below:-

(a) Population Surveyed:

(i) 1,318 patients surveyed.

(ii) 66% were severe, 19% moderate and 15% mild.

(b) Annual Consumption of factor VIII (i.u.) per patient:

Severe	-	64,800
Moderate	-	34,862
Mild	-	12,689

(c) Calculations for Scotland:

Assuming 50% severe	-	5 x 35 x 64,800	=	11.3×10^6
25% moderate	-	5 x 17 x 34,862	=	2.9×10^6
25% mild	-	5 x 17 x 12,689	=	2.2×10^6
		Total		16.4 (3.2×10^6 i.u./ 10^6 pop./yr.)

PREDICTED EFFECT ON FACTOR VIII SUPPLIES OF IMPROVED SURVIVAL OF HAEMOPHILIA A PATIENTS IN SCOTLAND

(a) Assumptions:

(i) There will be 150 new (additional) patients born in Scotland in the next 25 years and 50% will be severe. [i.e. 1 pt/yr/1m pop.]

(ii) Only the 70+ years will 'drop off'.

1 in - 25 = 25 new patients

(b) New Requirements:

(a) Routine Support of New Patients (0 - 24 years)

(i)	75 severe x 50,000 i.u.	=	3.75
(ii)	75 mild/moderate x 7,000 i.u.	=	0.53
(iii)	Elect. Surg. 150 x 2,000 i.u.	=	0.30
(iv)	Support for those with Inhibitors 150 x 7,000 i.u.	=	1.05

(b) Excess for Non-Haemophilia

Surgery (new patients and age shift)	=	0.15
Total	=	4.78 p.a. 25 yrs

(c) Annual Increase over Scotland over 25 years would be 200,000 i.u. p.a. (4.78/25).

* i.u./10^6 pop. 40,000 i.u.

(c.f. me originally calculated at 100,000).

DEFINITION OF OPERATION GROUPS

Operation Group	Description
'Cardiac'	Operations affecting myocardium
	Closed valvotomy
	Open valvotomy
	Heart valve replacement
	Other valvuloplasty
	Operations on septum within heart cavity
	Operations on heart walls, N.E.C.
	Other operations on open heart
'Lung/Bronchus'	Incision or puncture of lung
	Excision and destruction of lesion of lung
	Lobectomy
	Pneumonectomy
	Operations upon bronchus, N.E.C.
	Excision and destruction of bronchus or lesion
	Other operations on lung
'Hernias'	Relief of strangulated inguinal hernia
	Repair of inguinal hernia, N.E.C.
	Operation on femoral hernia
	Abdominal operation on diaphragmatic hernia
	Secondary repair of hernia, N.E.C.
	Operation on abdominal hernia, N.E.C.
'Gastric'	Incision of stomach
	Pyloromyotomy
	Gastrectomy, total or radical
	Partial gastrectomy
	Excision of lesion of stomach
	Gastrostomy
	Gastro-enterostomy
	Repair of stomach
	Closure of abnormal opening in stomach
	Plastic operation on stomach
	Vagotomy, N.E.C.
	Vagotomy with gastro-enterostomy
	Vagotomy with other gastric operation
	Other operations on stomach
	Repair of perforated duodenal ulcer
'Colon'	Colectomy and resection, N.O.S.
	Complete colectomy
	Colostomy, primary
	Enterostomy modifications, N.E.C.
	Colon by-pass
	Mobilisation of bowel
	Excision of lesion of large intestine
	Resection of bowel for interposition

Operation Group	Description
'Haemorrhoids'	Injection of haemorrhoids Ligature of haemorrhoids Destruction of haemorrhoids Haemorrhoidectomy Removal of tags Other operations on haemorrhoids
'Gall Bladder etc.'	Incision of bile duct Removal of calculus from bile ducts Drainage of bile duct Anastomosis of bile ducts Cholangiography Other operations on bile ducts Incision of gall bladder Removal of stones from gall bladder Cholecystectomy Anastomosis of gall bladder to jejunum Other anastomosis of gall bladder Repair of gall bladder Other operation on gall bladder
'Prostate'	Prostatectomy, suprapubic Prostatectomy, retropubic Prostatectomy, perineal Prostatectomy, per-urethral Prostatectomy, N.E.C. Radical prostatectomy Destruction of lesion of prostate Other operations on prostate
'Orthopoedic'	Total hip replacement Other arthroplasty of hip Excision of internal structure of knee Reduction with internal fixation of hip, thigh, upper end of femur
'Varicose Veins'	Ligation or division of vein, N.E.C. Operation on varicose veins, N.E.C.
'All Others'	All other operations including minor procedures but excluding:- Injection for general action Operations with ill-defined site Non-operative procedures Anaesthetic procedures Diagnostic radiography and radiotherapy

NUMBER OF SURGICAL PROCEDURES/ 10^6 MALE POP./YEAR
IN SCOTLAND (24 MONTHS 1978 - 1979)

Procedure	Age Group			
	0 - 24 (1,030,700)	25 - 49 (791,450)	50 - 69 (508,700)	70+ (161,000)
Cardiac	63	236	524	43
Lung/Bronchus	12	66	504	211
Hernias	1,632	1,795	5,321	6,238
Gastric	396	1,270	1,733	2,132
Colon	59	198	1.028	2,222
Haemorrhoids	33	716	811	518
Gall Bladder etc.	23	493	1,435	1,822
Prostate	3	69	3,187	12,415
Orthopoedic	558	1,393	1,835	4,146
Varicose Veins	78	1,023	1,223	168
Total/10^6 Male pop./yr.	2,857	7,259	15,868	29,915

Figures in ( ) are populations in each age group in 1978/79.

NUMBER OF MAJOR SURGICAL PROCEDURES ON MALE PATIENTS, BUT UNRELATED TO HAEMOPHILIA, EXPECTED PER YEAR IN SCOTLAND*

Procedure°	Age Group			
	0 - 24	25 - 49	50 - 69	70+
Cardiac	65	187	267	7
Lung/Bronchus	13	52	257	34
Hernias	1,683	1,421	2,707	1,005
Gastric	409	1,056	882	344
Colon	61	157	523	358
Haemorrhoids	35	567	413	84
Gall Bladder etc.	24	391	730	294
Prostate	3	55	1,621	2,000
Orthopaedic	576	1,103	934	668
Varicose Veins	80	810	622	27
All Others	34,950	24,456	21,314	10,190

* Figures are derived from NORMAL MALE population in Scotland analysed over a 24 month period.

° See Separate Sheet.

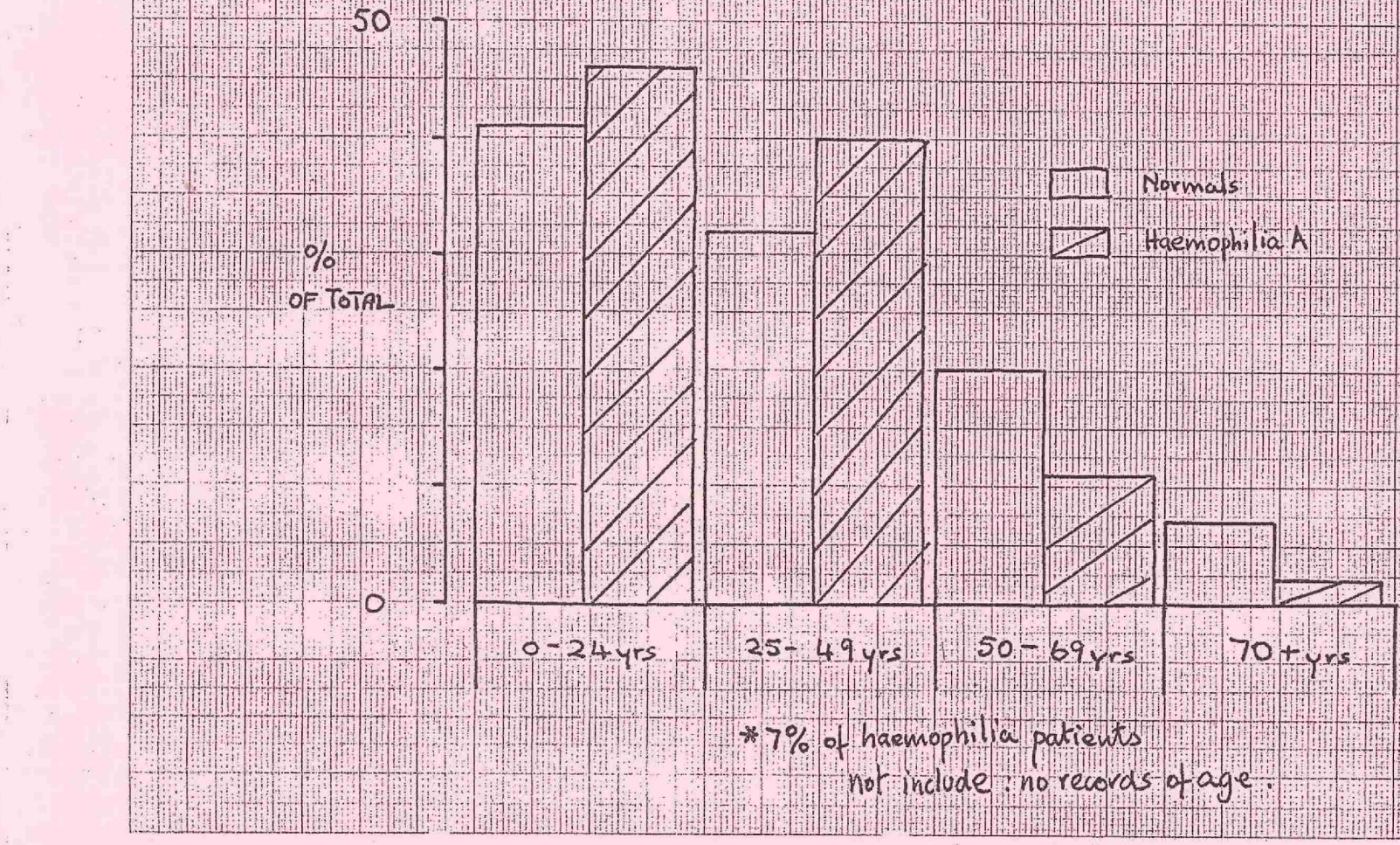
APPROXIMATE TOTAL NUMBER OF NON HAEMOPHILIA RELATED SURGICAL PROCEDURES PER YEAR FOR HAEMOPHILIA POPULATION IN SCOTLAND

Age	YEAR	
	1981	2006
0 - 24	0.4 (137)	0.4 (137)
25 - 49	0.9 (121)	1.0 (137)
50 - 69	0.5 (32)	1.9 (121)
70+	0.2 (6)	1.0 (32)
Total factor VIII at 50,000 i.u. per operation	100,000 (2 x 50,000)	215,000 (4.3 x 50,000)

(Figures in brackets for 1981 are existing age group populations. * Note 25 patients not included because Oxford Register has no information on age).

2.0 — 4.3
= 1
2.5

AGE MATCHED POPULATION DISTRIBUTION OF HAEMOPHILIA A PATIENTS* AND NORMAL MALES IN SCOTLAND (1980)



*7% of haemophilia patients not include: no records of age.