IMPLEMENTATION OF THE WORKING PARTY REPORT ON TRENDS IN THE DEMAND FOR BLOOD PRODUCTS.

A discussion paper for the Select Committee on blood transfusion.

A working group met in January 1977 "to consider the likely trends in the demand for blood products over the next 5 - 10 years, taking into account the practicalities of supply". The Department was seeking broad estimates of likely requirements of each of the major blood components which would enable Health Departments, in conjunction with Health Authorities, to plan the development of blood transfusion services and to consider the financial and other resource implications.

Broad aims: These conformed with WHO in being able to achieve NHS self-sufficiency in therapeutic blood products and discontinue commercial purchase.

Recommendations: (taken from the Council of Europe study on 'The indications for the use of albumin, plasma protein solutions and plasma substitutes'.)

Albumin 200 g/1000 population
Factor VIII 1000 iu/1000 population.

It was agreed that plasma volume sufficient to meet albumin need would also provide sufficient source material for other products - factors VIII, IX, VII and I and for normal human immunoglobulin.

A low interim target for albumin of 100 g/1000 population was set by the Working Party.

Recommended Procedure:

(1) Increase in blood donation rate to 50/1000 population
(2) Use of plasma-reduced blood at 60% of total donations.

Based on this procedure, the 'Trends' group calculated the following: Combining 1 + 2 gave a plasma yield of 8 litres per 1000 population, i.e. sufficient to produce 200 g albumin per 1000 population.

8 litres/1000 population was equivalent to a factor VIII yield of 1300 iu /1000 population, i.e. more than sufficient to meet all needs. Thus to

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meet factor VIII requirement, of the 8 litres plasma per 1000 population needed to meet albumin targets, only 4 litres/1000 population would be as FFP to meet factor VIII targets.

Initial Assessment of 'Trends' calculations:

Assume population from which NHS is serviced to be 50 M i.e. population which NBTS serves and from a proportion of which it has access to potential donors.

(3) 50 donations/1000 population = 2.5 M/year total i.e. an increase of approximately 20% on present rate.

(4) 8 litres plasma/1000 population = 400,000 litres p.a.
This figure must be reconciled with various approaches.

(5) Plasma taken at 60% of 2.5 M donations p.a. gives $0.6 \times 2.5 \times 10^6 \times 0.2$ = 300,000 litres p.a. assuming the mean plasma reduction from each unit is 200 m

The values in 4 and 5 do not agree.
In fact, the volume in 4 comprises FFP and time expired plasma and from the 'Trends' report p.3 para 5b, it is evident that total plasma capture is not 60% of all donations but 80%. Thus $.8 \times 2.5 \times 10^6 \times V = 400,000$ where V = 0.2 litre.

From 'Trends' it is assumed that a mean volume of 200 ml is taken from 2M donations p.a. of which 60% is FFP in that 'Trends' propose use of 60% of blood as cell concentrates.

Therefore

(6) Total plasma = 400,000 litres
of which

(7) FFP = 300,000 litres (see 5)

YIELDS Albumin 22.5 g/litre.

(8) From 6, output = 9000 kg = 180 g/1000 population.
Factor VIII → 230 iu/litre FFP

(9) From 'Trends' rate 4 litres/1000 population at a yield of 230 iu/litre
200,000 x 230 = 46 M iu = 840 iu/1000 population.

(10) From 7 above
300,000 x 230 = 69 M iu = 1380 iu/1000 population.

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Comments on 'Trends' figures:

To achieve 200 g albumin/1000 population using 80% of 2.5 M donations p.a. would require a mean plasma reduction of 222 ml per donation.

There are several substantial criticisms of the 'Trends' paper. The contradictions and ambiguities are self-evident, as are the assumptions. There is no provision for a 'regional' plasma requirement as FFP or for plasma used within RTCs. Expectation of 80% collection of plasma from whole blood is too high as would be the mean volume of 222 ml per donation when 75% of the collection is FFP (the mean haematocrit of the residual concentrated red cells = 69.5%).

There is no provision for regional cryoprecipitate production which uses at present an equivalent FFP volume of 45,000 litres p.a. or 27% of the current annual plasma input to BPL.

The 'Trends' figures derived from a theoretical maximum of 80% plasma collection from 2.5 M donations p.a. taking 222 ml per donation represents an unreasonable level of service occupancy. However, if this is a maximum figure, it is reasonable to accept 70% occupancy as a realistic service commitment. Is this sufficient?

(ii) $.8 \times 2.5 \times 10^6 \times .222 \times 0.7 = 310{,}800$ litres p.a.

This total includes all plasma; it will generate 140 g albumin/1000 population and 1430 iu factor VIII/1000 population (71.5 M iu) if it is all FFP. Assuming the actual collection volume to be 200 ml/donation, it would require 1,554,000 donations or 62% of 2.5 M whole donations.

This level of output would be acceptable as an interim production target. If 310,800 litres plasma p.a. were available, there is little doubt that current albumin needs would be met, perhaps over a 5-year period while a more accurate assessment of future demand was made. If 50% of 2.5 M donations were available as FFP, then 57.4 M in factor VIII intermediate concentrate could be produced - sufficient to meet current demand.

CONCLUSION

The Trends document is of value in establishing the Department's

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intent to review the needs of NBTS and to seek self-sufficiency in therapeutic blood products in accordance with WHO.

Its shortcomings relate to the use of the Council of Europe document primarily in establishing albumin demand where parallels in European and UK use may not exist. Equally, a plasma collection programme must be designed around the transfusion practice within the organisation to which it relates. The suggested approach which follows takes NBTS practice and facilities into consideration and makes proposals on feasible modifications to NBTS practice which should enable plasma collection to be simplified. At every level, the role of the regional services and the central fractionation laboratories must remain integrated so that there is a scheduled combined programme with agreed targets and dates, established financial policy and support, accountability and executive management.

Current Output and Proposed Targets

NBTS take approximately 2M donations per annum whole blood.
Plasma supply to BPL (1978) was 164,770 litres total (41% of 2M donations @ 200 ml plasma per donation) of which less than half was FFP (16.8% of 2M donations).

Production from this material was 140,000 containers of PPF (2520 kg albumin = 50.4 g/1000 population) and 15 M iu factor VIII; (yields cannot be determined from these figures).

Conscious of the inadequacy of this output, the Stop-Gap programme was outlined and introduced in June 1978 aimed at running until 1982/83 by which time it was deemed essential that new production facilities would be near their commissioning date on the Elstree site.

Stop-Gap falls into two phases:

Plasma for PPF and albumin	140,682 -- 155,000 -- 195,000 litres p.a.
Plasma for factor VIII	62,500 -- 93,600 -- 124,800 litres p.a.

Integrated Stage II. Stop-Gap targets are:

PPF	230,000 x 18 g containers
Albumin	12,000 x 20 g containers
Factor VIII	28.75 M iu as 115,000 x 250 iu.

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The date to achieve Stop-Gap Phase II output is set as April 1981 and is dependent upon

(a) A limited scheduled rebuilding programme being rigidly adhered to

(b) Full staffing recruitment.

To accommodate Stop-Gap Phase II albumin production, plasma input needs to rise to 195,000 litres p.a. total equivalent to 975,000 donations = approximately 50% of the current annual donation rate. This exceeds current intake by about 10%.

Factor VIII production at Phase II requires 125,000 litres FFP p.a. equivalent to 625,000 donations or 31.3% of the annual blood donation rate. This is an increase of approximately twice the current input of FFP.

To facilitate the implementation of the Stop-Gap Phase II programme by mid-1981, several proposals and modifications to the blood collection system are listed:

(i) Development of NBTS RIA at BPL and associated laboratories.

(ii) Development of a single plasma pack for abolition of 5L plasma pooling.

(iii) Introduction of regional pro-rata blood product supply aimed at phased implementation of regional self-sufficiency in factor VIII and albumin.

(iv) Phasing out of regional cryoprecipitate production and supply of freeze-dried whole plasma in regions introduced to pro-rata provision of factor VIII and albumin (PPF).

(v) Provision of plasma for Stop-Gap within existing total supply of plasma by concentrating on increasing the proportion of plasma collection as FFP.

(vi) To aim for 50% of total blood donations set aside for FFP collection.

(vii) To introduce 'regionalised' fractionation of plasma, i.e. to keep a single region's plasma segregated for preparation of coagulation factors. This allows for assessment of yield on source plasma, combined quality control surveillance by RTC and BPL and epidemiological limitation on distribution of batches within regions of source material supply: reference HBV and non-A non-B hepatitis.

(viii) To provide basis for regional accountancy in blood products.

(ix) To co-ordinate automated data processing (Codabar) between BPL and RTCs.

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Phased Redevelopment of BPL 1983/84

Stop-Gap makes interim provision for an increase in current output while new process areas are developed and commissioned.

The redeveloped BPL aims for self-sufficiency in therapeutic blood products within NHS.

Phased Redevelopment of BPL

Capacity	Factor VIII	120M iu p.a.	
	Albumin	200g/1000 population	
Intermediate targets	Factor VIII	90M iu p.a.	1985/90
	Albumin	150g/1000 population	

Plasma requirement at intermediate production

FFP 375,000 litres p.a. at current yields.

Plasma supply FFP in single closed-system packs.

Rationale for determining factor VIII requirements

Current haemophiliac population (1977)

patients treated	2084
units used	46,222,746
units/patient	22,180

Total number of Haemophilia A patients 3699

			Total Treated	Home Treated
<2% factor VIII	1787)		1221	418
2-10% " "	799)	1976	434	28
>10% " "	539)		163	1
Total	3387)			

Assume basic populations of 2000 haemophilia sufferers in need of full home therapy at 35,000 iu/year

= 70 M iu's

extras = 20 M iu's

+ allowance for 10 year growth period

Plasma requirement = 375,000 litres at 250 iu/L.

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Albumin production:

150 g albumin per 1000 population

from 375,000 litres are derived 168 g/1000 population

= 468,750 containers PPF.

Outputs over present rates = 6 x increase for factor VIII rising to 7-8 x

3 x increase for albumin rising to 4 x

Derivation of Plasma

(A) from whole blood at a maximum FFP collection rate of 60% of all donations

Stop Gap Phase II No increase in current donation rate required

Phased redevelopment output

1983/4 Commission plant at 25,000 L FFP p.a.

= 57.5 M iu factor VIII

112.5 g albumin/1000 population

= 1.25 x 200 ml donations or 62.5% of current whole blood donation rate

New plant could be commissioned within existing donation rate if all regions reached a distribution of plasma reduced blood of 60% of the total donation rate.

At 50% use of plasma reduced blood, total donations would need to rise from 2 M p.a. to 2.5 M p.a. by 1983/84, an annual growth rate 5% from 1979/80.

To commission at 250,000 litres p.a., an initial stockpile of FFP at BPL would be needed to offset the acute rise in supply caused by operating increased plant capacity. The stockpile would depend on existence of increased cold room storage planned in Stop-Gap.

Phased redevelopment Interim output 1985/1990

90 M iu factor VIII

170 g albumin/1000 population

FFP input required = 375,000 L p.a.

Source of plasma (FFP)

From whole blood at 60% plasma reduced blood (200 ml/donation)

= 3,125,000 total donations

Growth required = 56% over 11 years

≏ 5% per annum

3,125,000 donations p.a. approximates to 63/1000 population which is not more than reasonable.

(B) From whole blood and plasmapheresis:

300,000 litres from whole blood

75,000 litres from plasmapheresis

= 2.5 M donations whole blood (60% FFP collection)

= 150,000 x 500 ml phereses.

(C) Plasmapheresis

Theoretical example in NET and NWT RHA's to collect 75,000 litres FFP:

take 4 centres

10 couches/centre

8 h working day — pheresis time 1 h/patient

5 day week — 52 week year

Maximum 500 ml pheresis = 83,200

at 70% occupancy: 83,200 x 0.7 = 58240,

i.e. approximately $^{1}/_{3}$ above stated requirement.

∴ Total centres needed = 12 i.e. approximately 1 per region.

N.B. 2 plasmapheresis centres per region by 1984 could produce

28 x 7280 litres = 203,840 litres FFP p.a.

This would leave 171,160 litres p.a. to be gained from whole blood and this could be achieved without additional donation over 2M p.a. Decisions rest on whether expansion should be in whole blood or in plasmapheresis and must take into consideration the need for red cells.

Economics See attached paper.

At the regional level, e.g. NET RTC with an annual donation rate of 140,000

60% of 140,000 = 84,000 ≡ 16,800 litres.

At current yields this would generate

Factor VIII (at 230 iu/L) 3.864 M iu
(at 250 iu/L) 4.20 M iu
equivalent to £0.4 M at 10p/unit

Albumin 21,000 containers p.a.
equivalent to £0.63 M at £30/unit
total = £1.03 M i.e. ⩾ 50% annual RTC budget. 39/5

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	BPL				RTC					
PROGRAMME	FORECAST DATES	OUTPUT TARGETS P.A.	RAW MATERIAL NEEDS Total plasma TE & FFP litres x 1000	RAW MATERIAL NEEDS FFP litres x 1000	WHOLE BLOOD DONATIONS x 10^6	PLASMA REDUCED BLOOD % TE/FFP	PLASMA REDUCED BLOOD % FFP	TOTAL PLASMA SAVED TE & FFP L x 1000	FFP from whole blood Lx1000	FFP by plasmapheresis L x 1000
Up to present	1978/79	Alb 2520 kg FVIII 15M iu	112	65	2	40	17	165	62.5	-
STOP-GAP	1979→1983									
PHASES I	1979/1980	Alb 3488 kg FVIII 21.5 M iu	155	93.5	2				93.6	-
II	April 1981	Alb 4380 kg FVIII 28.75 M iu	195	124.8	2	50	32	195	125	-
REDEVELOPMENT AT BPL										
At Commission	1983/84	Alb 5625 kg FVIII 57.5 M iu	250	250	2 or 2.5	60 50	60 50	250 250	250 250	- -
Interim	1985/90	Alb 7500 kg FVIII 90 M iu	375	375	3.125 or 2.5 or 2	60 60 45	60 60 45	375 300 170	375 300 170	- 75 200
Final Capacity	1990 →	Alb 10,000 kg FVIII 120 M iu	500	500	-	-	-	-	-	-

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