HAEMOPHILIA CARE AT REFERENCE CENTRES: REVENUE REQUIREMENTS

Background

Haemophilia is the generic term given to a group of inherited haemorrhagic disorders characterised by a deficiency of one of the twelve factors needed for the clotting of blood. Haemophilia A (Factor VIII deficiency), haemophilia B (Factor IX deficiency) and von Willebrand's disease (also Factor VIII deficiency) constitute 95% of patients. Patients with these disorders number about 7,000 in the UK. The more severely affected patients suffer frequent episodes of bleeding mainly as a result of injury not only of an obvious nature but also that due to the normal wear and tear of every day life. External bleeding is infrequent, the main problem being internal bleeding into muscles and joints. In severe cases such bleeding may occur two to three times a week, is extremely painful and if inadequately treated leads to damaged joints with contractures and eventual painful crippling. More serious bleeding may occur in vital organs and the commonest cause of death in haemophilia is from intracranial bleeding.

Treatment

Until 15 years ago the life span of haemophiliacs averaged about 25 painful and distressing years. At that time methods became available for extracting clotting factors from blood plasma and concentrates of Factor VIII and Factor IX became available. These take the form of freeze-dried white powders which are dissolved in water and injected in small volume by syringe into a vein. A prototype concentrate of Factor VIII called cryoprecipitate is less generally useful because it

is of variable potency, of larger volume and must be stored in a liquid state in a deep freeze. With the development of factor concentrates factory-prepared from large pool normal plasma it became possible to teach patients (or their parents) to inject the Factor VIII into a vein themselves at home (or work) and so abort most of the bleeds. As a result the life of most haemophiliacs has been revolutionised and their expected life span is now approaching 70 years of relatively normal existance, with it is to be hoped, reasonably normal joints. However, this result has only been achieved with the development of a system of comprehensive haemophilia care undertaken in a nationwide system of Haemophilia Centres.

Risks of Treatment

1. Resistance. About 10% of patients become resistant to treatment Although blood products to overcome this to a certain extent are available, they are very expensive and these patients are developing chronic joint disabilities and are at increased risk of death.
2. Viruses. All blood products are known to be contaminated with viruses.

(a) Hepatitis. In the past the major worry has related to hepatitis viruses. Symptomless carriers of the viruses exist in the general population and they may thus contaminate donated blood. Although tests for one of these viruses (hepatitis B) are used to screen blood donors it is only to be expected that an occasional donation will escape this net. In addition there are at least two other hepatitis viruses (Non A, non B) for which there are no tests. Factor VIII (and IX) concentrates for technical reasons are prepared from plasma pools i.e. mixtures of donated plasma (the fluid part

7c

of blood) from over 5,000 donations. All preparations of Factor VIII and IX even from British 'voluntary' plasma are therefore known to be contaminated with hepatitis viruses. For these reasons it has always been necessary to handle these blood products with great care in hospital and home. At large haemophilia centres at which patients and their relatives are instructed, dedicated nursing staff have been appointed to supervise tuition and the administration of blood products.

(b) AIDS. The advent of the acquired immunodeficiency syndrome (AIDS) has highlighted the importance of centralised control of haemophilia therapy. This is also a virus disease spread by infected blood products. Because of its serious nature the emergence of this disease has re-emphasised the necessity to review facilities for haemophilia treatment. Evidence is accruing that a high proportion (over 50%) of severe haemophiliacs in the UK have been infected with the AIDS virus (HTLVIII) and may have become 'healthy' carriers. It is not expected however that most of them will develop the disease known as AIDS but it may be possible for them to pass on the virus from their blood.

Heat-treated Factor VIII concentrate is now available but it has proved difficult to sterilise it and still retain therapeutic effectiveness. The AIDS virus seems to be sensitive to heat but the first generation of heat-treated concentrates can still transmit the hepatitis viruses. The effectiveness of first generation heat-treated Factor VIII concentrates with regard to the AIDS virus seems to be reasonable but has not been extensively tested in clinical practice and they are certainly not sterile.

General Management

Although much publicity has been given to the problems of blood product treatment the management of haemophilia is not just a matter of injecting Factor VIII or Factor IX and the services of an experienced care team are required.

Physiotherapy

Many patients particularly those over the age of 20 years have developed chronic joint changes with consequent progressive arthritis. In the absence of cheap, safe replacement therapy analogous for instance to insulin for diabetes which could be administered on a regular basis many younger haemophiliacs develop target joints in which arthritis develops. In order to prevent these and to delay deterioration of joints in older people skilled experienced physiotherapy is needed.

Orthopaedic Surgery

In order to correct contractures and improve joint function surgical corrective or preventive measures are often needed particularly in older patients.

Dental Surgery

For obvious reasons dental care is vital and at most large Haemophilia Centres regular Haemophilia Dental Clinics are held. The AIDS problem is posing special problems in this area.

Haemophilia Nurse

An experienced nurse usually a Sister is an essential member of the Haemophilia Centre staff. She co-ordinates treatment, controls and records blood products used, teaches patients (or relatives the technique of intravenous injection, undertakes home visits and collects treatment data and statistics. She is the central point of reference

7e

for the Haemophilia Centre with regard to patients and relatives.

Social Worker

Most employers and teachers have only the vaguest ideas of the nature of haemophilia and patients have many problems with education and employment. A haemophiliac in a family affects all members and generates a disproportionate amount of emotional problems which are being greatly increased by the AIDS crisis. Housing, transport and attendance form some of the social problems aggravated by these disorders. A dedicated social worker is an essential member of the haemophilia team.

Laboratories

The diagnosis and follow-up of patients requires skilled laboratory technical and scientific staff in order to undertake the complex measurements needed to control treatment. Some patients present especially difficult diagnostic problems which can only be solved by laboratory detective work which is often beyond the skill and experience of routine laboratories. Even the day to day assays require constant experience if accuracy and precision are to be maintained.

Genetic Aspects

Although the broad aspects of inheritance patterns of these conditions are known there are many exceptions to the rules. In addition the advice to be given in individual families may vary considerably with the degree of severity of the condition. In most centres therefore genetic counselling is best undertaken by the Haemophilia Physician in conjunction with the nurse and social worker and if needed calling upon a formal geneticist for statistical advice

7F

and for logistic support for amniocentesis or chorionic biopsy. Determination of carrier status and prenatal diagnosis by phenotype clearly involve complex laboratory coagulations tests and some larger Haemophilia Centres have set up facilities to undertake genotype assignment (gene probing).

Haemophilia Physician

The doctor in clinical charge of haemophilic patients is usually a Consultant Haematologist but especially in some of the larger centres for historical reasons, he/she is sometimes a specialised Physician or in one large centre, a Paediatrician. The actual career route is less important than the need to have experienced all aspects of Haemophilia care including general medicine and at the laboratory bench. It is advantageous that the haemophilia consultant looks after the haemophilic problems of children and adults thus giving continuity of knowledge over an extended time-scale.

From the above account it is apparent that adequate care of haemophilia involves a multidisciplinary team. As will be enlarged below, these disorders are uncommon therefore in order that members of a team receive adequate experience and incentive centralised management is essential.

Clerical Staff

The large volume of treatment and clinical data and the need to follow-up patients regularly has increased the need for clerical assistance. Each large Haemophilia Centre requires dedicated secretarial staff.

79

THE ORGANISATION OF HAEMOPHILIA TREATMENT IN THE U.K.

The Patients

A total of 7187 patients with inherited haemorrhagic disorders were registered in the U.K. by 1984. Of these 2799 were treated in 1983. These include 2118 with haemophilia A and 311 with von Willebrand's disease i.e. 2429 treated with Factor VIII concentrate and 370 with haemophilia B treated with Factor IX concentrate.

Some of the balance of the patients are of course treated in other years and all may develop acute or chronic physical problems or need social, psychological, genetic or other types of advice. All need to be followed up on a regular basis.

The special needs of haemophilic patients were recognised by the Health Departments, and certain hospitals at which numbers of patients were already being managed were recognised as Haemophilia Centres and their functions described in HC(76)4 which is attached as appendix 1. At that time the main function of Haemophilia Centres was conceived as relating to the diagnosis and registration of patients and to the specific treatment of episodes of bleeding by administration of blood products. However it was recognised that intravenous infusion of Factor concentrates could conveniently be administered to patients at their local hospitals and in order to keep these within the system such hospitals, perhaps only dealing with these restricted aspects of one or two patients, were designated as Associate Haemophilia Centres. By the same token it was recognised that the specialised functional and advisory functions were more appropriately located at 7 larger centres, which were termed Haemophilia Reference Centres, and which were

7h

situated across the country mainly on an ad hoc geographical basis and by virtue of service already developed by the experience and energy of individual Haemophilic doctors. The geographical areas served by the Centres were duly designated and several crossed regional boundaries to subserve in effect a supraregional function.

The functions of these Centres included the following:

1. To provide a diagnostic reference service both clinical and laboratory on a 24 hour basis.
2. To provide a 24 hour clinical and therapeutic service.
   (a) For patients within reasonable geographical location.
   (b) A clinical reference service for patients domiciled more distantly.
3. To provide and supervise the home treatment program and to maintain a documented stocks of specialised therapeutic concentrates (in association with local hospital Pharmacies or other appropriate agencies).
4. To provide expert diagnostic facilities for genetic diagnosis and specialised counselling and a general advisory serice to families.
5. To provide and support the necessary back-up facilities in
   Dental surgery
   Orthopaedic surgery
   Physiotherapy
   Social Work
   General surgery.
6. To maintain records, data on blood product usage batch numbers of products used etc to permit donor tracing.

7. To provide regular follow-up facilities for all patients.

Later two centres in Scotland, Glasgow Royal Infirmary and Edinburgh Royal Infirmary and one in Northern Ireland at Royal Victoria Infirmary, Belfast, obtained recognition as Haemophilia Reference Centres by their respective Health Departments.

Development of Haemophilic Organisation since 1976

When the HC(76)4 was promulgated there were 53 Haemophilia or Associated Centres. Since then additional Centres or Associate Centres have been recognised so that now there are a total of 109 Centres (Reference Centres, Centres and Associate Centres). This increase has resulted from changing patterns of treatment:

(a) There has been a natural desire on the part of Districts in which large centres are situated to demur about costs of materials. Haemophilia physicians have therefore been conditioned not to resist some decentralisation of haemophilia care as a line of least resistance.

(b) The appointment of more Consultant Haematologists to District General Hospitals has accelerated this process.

(c) The Haemophilia Society and individual patients welcomed decentralisation as this made replacement therapy available locally.

Thus the introduction of home treatment coincided with other pressures for decentralisation and an increase in the number of designated Haemophilia Centres. However, it has gradually become apparent that decentralisation has gone too far:-

(a) Some so called Haemophilia Centres deal with very few e.g. less than 10 patients. Staff therefore cannot obtain on-going experience that justifies the term "Centre".

7j

(b) The advent of home treatment has increased the need for out-patient surveillance and documentation of therapy as well as the need for support staff at the larger centres and Reference Centres e.g. nursing, social work, physiotherapy, clerical, etc.

(c) The advent of the AIDS crisis has highlighted the fact that the care of the relatively small overall number of haemophiliacs should be concentrated where the necessary expertise exists or can be gathered. Haemophilia is therefore one condition which requires more rather than less centralisation.

The Need for Central Funding

From the foregoing it is clear that for the adequate management specific treatment, safe investigation and documentation of haemophilia it is necessary that the Centre staff deals with a sufficient number of patients to maintain their expertise and interest. Haemophiliacs are more or less scattered throughout the country and although some aspects of treatment of those in isolated areas will necessarily be devolved locally, nevertheless it is still important that their treatment data and clinical progress is documented at a large Centre or a Reference Centre.

1. Laboratory Investigation. A high proportion of treated haemophiliacs (over 50%) are positive for HTLVIII antibody and a further number will no doubt be found to be positive for antigen when tests become available. All regularly treated haemophiliacs and their blood should thus be regarded as potentially infective.

The Advisory Committee on Dangerous Pathogens has published interim guideline for laboratory testing of samples from AIDS, AIDS-

7K

related and HTLVIII positive patients. These recommendations indicate that the laboratory tests needed for the rational therapy of severe bleeds or for monitoring surgery in haemophilia will be carried out in the safest and most cost effective manner in larger centres e.g. Reference Centres. Additional facilities will be needed at these Centre for safe testing of infective samples.

2. Treatment Materials. There is evidence that heat-treatment of Factor VIII concentrates inactivates the HTLVIII virus. Although it can be argued that HTLVIII positive patients could be treated with unheated concentrates the risks of superinfection with HTLVIII have not been elucidated. Furthermore it seems unreasonable for the ACDP to lay down stringent criteria for handling potentially infected samples in the laboratory whilst at the same time allowing clinical staff to be exposed to unheated and hence potentially infected concentrated. Domestic exposure to such concentrates would be even more undesirable. Thus, although theoretical objections may be raised concerning the effect of heat on plasma proteins, the practicality of the situation dictates that these be prescribed. Not only is this true of Factor VIII concentrates but also of Factor IX for the treatment of haemophilia B and resistant haemophilia A.

3. Staff. The functions of a Haemophilia Reference Centre are outlined above. At present staff costs are borne by the Districts with variable Regional allocations.

76

The type of staff required for haemophilia management is outlined above. An average Haemophilia Reference Centre treating 135 patients annually and offering support to Haemophilia Centres in geographical proximity requires:-

A nursing Sister (w.t.)
Assistant nurse (p.t.)
Secretary (w.t.)
Clinical Assistant (p.t.)
Social Worker (p.t.)
Chief MLSO (p.t.)
2 MLSO's (w.t.)
Scientist (Whitley A) (w.t.)
Consultant Director (p.t.)
Physiotherapist, Dental Surgeon etc., (p.t.)

It should be noted that most Haeophilia Reference Centres also undertake routine services in Haematology or Medicine (or Paediatrics) for non-haemophilic patients thus accounting for instance for the part-time designation of the Consultant, Chief MLSO etc. The above requirements are those needed solely for the management of haemophiliacs. The AIDS crisis has also highlighted the need for adequate supportive counselling at Reference Centres.

4. Total Revenue Requirements. These are set out in detail in Appendix 2. but must be considered to be estimates. More exact figures would require professional assessment.

For a Reference Centre treating 135 patients annually costs are summarised below. Until now Factor IX concentrate has been obtained entirely from NHS sources but during 1985-1986 it is likely that commercial heat-treated Factor IX will need to be purchased until NHS heat-treated Factor IX concentrate becomes available. Thus requirements for 1985-1986 and 1986-1987 are set out separately for a Reference Centre dealing with 135 patients per annum.

7m

(a) 1985-1986

	With Heated Concentrates	For comparison with unheated Concentrates
	£	£
Concentrate	360,000*	180,000
Staff	90,000	90,000
In-patients	72,000	72,000
	522,000	342,000

= £3866 per patient p.a.

* Includes heated Factor VIII and IX

(b) 1866-1987 (at 1985 costs)

	£	
Concentrate	267,000*	180,000
Staff	90,000	90,000
In-patients	72,000	72,000
	429,000	342,000

= £3240 per patient p.a.

* Includes only heated Factor VIII. Factor IX from BPL.

(c) 1987 on (if BPL Factory and plasma supply comes on line)

	£	
Concentrate	0	(note: Regional costs for plasma)
Staff	90,000	
In-patients	72,000	
	160,000	(at 1985 costs)

plus costs of plasma and requirements of Regional Blood Transfusion Centres.

The number of patients who reside outside District boundaries varies from Region to Region but probably averages 75%. Therefore Districts will have to bear the excess cost of 75% of £522,000 i.e. £390,000 (including heated Factor IX) for a medium sized Reference Centre in 1985. Thus although the overall cost per treated patient is very much less than that of some other services

(e.g. chronic renal dialysis), a disproportionately high proportion is borne by Districts. It should be noted that figures have been worked out on the basis of an average Reference Centre and may be higher in some larger Centres (e.g. Oxford and the Royal Free Hospital).

It must also be noted that the additional costs consequent upon the use of heated concentrates as illustrated above is not only for the purpose of patient management but also represents a Public Health measure to limit the spread of HTLVIII in the community. Thus to this extent districts are already providing additional subsidy to Regions.

Regional or Supraregional?

In some areas of the country e.g. South Wales, North East, the geographic area covered by the Haemophilia Reference Centre closely approximates to the Regional boundaries. From this point of view it could be argued that support for Haemophilia Services should be met from Regional allocations. In other parts of the country the Reference Centre catchment area crosses Regional boundaries and could functionally be described as Supra-Regional. However, since these geographic areas in either case were related to expertise and facilities available it seem equitable to define a common means of funding. In the light of present developments with regards to AIDS the Haemophilia Reference Centre directors strongly recommend that centralisation of haemophilia services be strengthened. The minimum staff and therapeutic requirements for 135 patients are set out above and the establishment and funding

of Reference Centres should be increased to meet these. The constraints imposed by the AIDS emergency have been quite unexpected and have not been accounted for in District or Regional budgets. It is therefore clear that the increased requirement for strengthening the safety and efficiency of haemophilia care will need to be met by central funding. Whether this will be met by designating Reference Centres as subserving a supraregional function or by increased central funding to Regions specifically for this purpose will depend upon local circumstances. The object of this document is to put forward the general case for increased central funding for haemophilia care and to attempt to quantify this in terms of cost per patient.

Throughout this document, also, consideration has been given only to Revenue requirements of Haemophilia Reference Centres serving about 135 patients. Additional capital costs needed to bring individual Reference Centres up to minimum standards where needed and the costs of meeting the additional Revenue requirements of larger centres will depend upon local circumstances. These and the costs of meeting the other local requirements of the AIDS crisis and all the recommendations of the ACDP have therefore not been addressed.