


A NATIONAL SERVICE
SPECIFICATION
FOR HAEMOPHILIA
AND OTHER INHERITED
BLEEDING DISORDERS





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Foreword

I welcome this update of the service specification for patients with inherited bleeding disorders, the first version of which was published in 2001.

The updated specification reinforces the need for adequate and assured resourcing for maintaining services so essential for the provision of comprehensive care for haemophilia and other patients involved. Since the first version of the specification recombinant factor VIII and IX concentrates have been made available for all the United Kingdom haemophilia patients.

The continuing potential risk of transmitting infective agents associated with plasma-derived concentrates is recognised in the emphasis placed in this publication on the importance of ongoing financial support to guarantee patients recombinant factor concentrates.

Over recent years there have been marked advances in the genetic diagnosis of inherited bleeding disorders and it is good to see detailed coverage here of the requirements for establishing genetic services for patients with inherited bleeding disorders and their families across the UK. This too is most helpful.



The Rt Hon Lord Morris of Manchester AO QSO

February 2006

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Contacts for further information

The Haemophilia Alliance

E-mail: alliance@haemophilia.org.uk

Website: www.haemophiliaalliance.org.uk

Margaret Unwin

Chief Executive

The Haemophilia Society

First Floor, Petersham House

57a Hatton Garden London EC1N 8JG

Telephone no: 020 7831 1020

E-mail: margaret@haemophilia.org.uk

Dr Jonathan Wilde

Centre Director

West Midlands Adult Comprehensive Care Haemophilia Centre

University Hospital Birmingham NHS Foundation Trust

Edgbaston Birmingham B15 2TH

Telephone no: 0121 627 2353

E-mail: jonathan.wilde@uhb.nhs.uk

Christine Harrington

Nurse Consultant

RCN Haemophilia Nurses Association

Katherine Dormandy Haemophilia Centre

Royal Free Hospital London

Telephone no: 020 7830 2068

E-mail: christine.harrington@rfh.nthames.nhs.uk

Executive summary

- This specification documents the recommended models of care for patients with haemophilia and other inherited bleeding disorders and updates the inaugural version published in 2001.
- It reiterates that haemophilia is a complex disorder and effective management requires the provision of a comprehensive care programme delivered by a multidisciplinary team.
- Haemophilia is a life long potentially debilitating condition. The delivery of haemophilia care is expensive. However, modern treatment is remarkably effective. A child born with haemophilia today can look forward to an excellent quality of life, free of joint damage and a normal life expectancy.
- The specification endorses the requirement of close liaison between Comprehensive Care Centres and Haemophilia Centres and also between these treatment centres and health care commissioners. The importance of involvement of the patient in the health care process is stressed.
- Since the first specification genetic services for patients with hereditary bleeding disorders have continued to develop and it is important that resources are identified to support this expansion.

Introduction

This is the second version of the National Service Specification for Haemophilia and Other Inherited Bleeding Disorders and replaces the initial version that was published in 2001.

The specification has been formulated by the Haemophilia Alliance, a United Kingdom wide partnership between patients with inherited bleeding disorders and health care professionals involved in the delivery of haemophilia care.

The main aim of the specification is to inform those with responsibility for commissioning haemophilia services of the recommended standards of care that should be available for all patients with inherited bleeding disorders. There is an ongoing need to standardise high quality haemophilia treatment across the UK.

I Background

- 1.1 Inherited bleeding disorders are rare and complex conditions. There are two main forms of haemophilia. The most common is haemophilia A (deficiency of coagulation factor FVIII) with a prevalence of between 1:5,000 and 1:10,000 males. Haemophilia B (deficiency of coagulation factor IX) is less common with a prevalence of between 1:35,000 and 1:50,000 males. The disorder von Willebrand Disease (deficiency of the coagulation protein von Willebrand factor) is a more common but generally milder bleeding disorder affecting both males and females with a prevalence of at least 1:1,000. Other inherited bleeding disorders are clinically important - these include deficiencies of other clotting factors (e.g. factor V, factor X, factor XI) and disorders of platelets.
- 1.2 Effective management of patients with inherited bleeding disorders is complex and involves the provision of comprehensive care by a team of health care professionals with diverse skills.
- 1.3 Haemophilia affects the whole of the family, both medically and psychosocially. Furthermore, women who are carriers of haemophilia may also have low factor levels and therefore can often have significant clinical problems themselves. For these reasons, comprehensive care is provided for the family as a whole.
- 1.4 During the 1970s and early 1980s the majority of regularly treated patients with haemophilia were infected with either HIV and/or hepatitis B and C. There are continuing concerns about the theoretical transmission of other agents, including variant CJD. Infectious agent transmission has led to profound medical and psychosocial problems and makes the delivery of clinical care a particularly sensitive and important issue for all patients and their families.

- 1.5 Although the delivery of haemophilia care is expensive the lives of patients and their families can be transformed by high quality care. Effective prophylaxis and treatment in childhood prevents joint damage and the need for orthopaedic intervention later in life. A child born today with haemophilia is likely to have a normal life expectancy.

2 Target patient group

- 2.1 There are around 20,000 people in the UK registered at haemophilia centres with inherited bleeding disorders. This specification is aimed at the following patient groups:
- Haemophilia A
 - Haemophilia B
 - Female haemophilia carriers
 - Von Willebrand Disease
 - Other inherited coagulation factor deficiencies
 - Inherited platelet disorders.
- 2.2 Patients with haemophilia may be classified as severe, moderate or mild depending on their baseline factor VIII or IX level. The normal range for FVIII and FIX is 50-150iu/dl.

Patients with **severe** haemophilia:

- have levels of FVIII / IX less than 1iu/dl
- regularly experience episodes of spontaneous joint, muscle and soft tissue bleeding
- require treatment with coagulation factor concentrates on a regular basis to treat bleeds when they occur or as prophylaxis to prevent bleeds and protect joints from progressive damage leading to arthritis
- require regular clinical and laboratory review as part of a comprehensive care programme
- may have significant joint and muscle damage as a consequence of previous bleeds.

Patients with **moderate** haemophilia:

- have levels of FVIII / IX between 1 and 5iu/dl
- may experience episodes of significant bleeding which require treatment with coagulation factor concentrates
- may also have significant joint and muscle problems as a consequence of previous bleeds.

Patients with **mild** haemophilia:

- have levels of FVIII / IX greater than 5iu/dl
- tend to bleed infrequently and usually as a consequence of trauma or surgical procedures

- rarely require therapy with coagulation factor concentrates generally require less intensive follow up than patients with severe haemophilia
- may experience episodes of acute bleeding following trauma or during dental or surgical procedures.

2.3 Von Willebrand disease

- Von Willebrand disease is the most common of the inherited bleeding disorders and affects both males and females.
- There are a number of different subtypes of von Willebrand disease. Whilst many patients have only mild clinical problems a relatively small number are severely affected. Many of the severely affected patients experience medical and psychosocial problems similar to patients with severe haemophilia and should be managed as part of a comprehensive care programme.
- In contrast to haemophilia the major bleeding problems in von Willebrand disease are mucocutaneous in nature. Patients experience nose and gum bleeding and prolonged bleeding in association with trauma, dental extractions and surgery.
- Many female patients with von Willebrand disease have menorrhagia and may bleed excessively after childbirth. These patients should have access to appropriate obstetric and gynaecological services.
- A relatively small number of patients with von Willebrand disease were infected with HIV and viral hepatitis. These patients will require access to the same services as haemophilia patients with viral infections.
- The delivery of care to patients with von Willebrand disease at local level must be determined through discussions with the Regional Haemophilia Network (see below) and will depend upon clinical circumstances and the degree of expertise available in the Haemophilia Centre.

2.4 Other Inherited Coagulation defects

- Hereditary deficiencies of other coagulation factors include fibrinogen, prothrombin, factors V, VII, X, XI and XIII. Due to their pattern of inheritance these disorders affect males and females equally.
- Severely affected patients with these rare deficiencies should be offered the same comprehensive care programme as patients with severe haemophilia.
- The delivery of care to patients with rare coagulation disorders at local level must be determined by discussions through the Regional Haemophilia Network and will depend upon clinical circumstances and the degree of expertise available in the Haemophilia Centre.

2.5 Inherited platelet disorders

- The majority of inherited platelet disorders are associated with a mild bleeding tendency. The disorders that are associated with a severe bleeding tendency such as Glanzmann's thrombasthenia and Bernard-Soulier syndrome are rare.
- Severely affected patients with inherited platelet disorders should be offered the same comprehensive care programme as patients with severe haemophilia.

- The delivery of care to patients with inherited platelet disorders at local level must be determined by discussions through the Regional Haemophilia Network and will depend upon clinical circumstances and the degree of expertise available in the Haemophilia Centre.
- 2.6 Commissioners, in conjunction with Haemophilia Centres and UKHCDO, should maintain an accurate profile of patients with the above disorders within their catchment area.

3 Methodology

3.1 Multidisciplinary input

This service specification has been written by members of the Haemophilia Alliance, a health care professional / patient partnership established to further the aims and objectives of the haemophilia community.

Members of the Haemophilia Alliance are:

- The UK Haemophilia Centre Doctors Organisation (UKHCDO)
- The UK Haemophilia Society
- The UK RCN Haemophilia Nurses Association (UK RCN HNA)
- The Haemophilia Chartered Physiotherapists Association (HCPA)
- The Clinical Scientists Group
- The Institute of Biomedical Science.

In addition, an advisory patient group was established to contribute and respond to each draft of the specification. The final draft was then widely distributed throughout the haemophilia community as well as to commissioners of haemophilia care and the Departments of Health for England, Scotland, Wales and Northern Ireland. The specification was then modified accordingly, following feedback comments.

3.2 Literature searches

Wherever possible, recommendations in the specification are related to formal levels of published evidence (appendix 2).

3.3 Literature searches

Literature searches of Medline were carried out to identify any existing service specifications or protocols related to the delivery of haemophilia care. The following key words were used:

- haemophilia
- inherited bleeding disorders
- service specification
- service framework.

4 Service objectives

- To respond to the complexity and rarity of haemophilia and other inherited bleeding disorders by establishing appropriate multi-disciplinary health care systems.
- To deliver care in a way that aims to minimise the pain, incapacity and physical disability that may be characteristic of haemophilia and related conditions.
- To ensure that the care of patients with hereditary bleeding disorders is as safe as possible, conforms to national clinical guidelines and is monitored by objective external clinical audit.
- To be responsive to the life long medical and psychosocial needs of patients with hereditary bleeding disorders and their families.
- To promote an holistic approach to patient care, ensuring that all patients have access to a wide range of specialist multi-disciplinary services.
- To provide an environment in which patients are able to make informed decisions about treatment and are enabled to become independent throughout their lifetime, thereby minimising disruption to education and work.
- To promote the delivery of care within the patient's own community, wherever possible.

5 Service standards and delivery

5.1 All patients with inherited bleeding disorders should have access to a comprehensive care programme. This may be provided by a Comprehensive Care Centre or a Haemophilia Centre, or a combination of the two, depending upon local expertise.

5.2 **Patient choice**

Haemophilia is a life long disorder and the relationship between carers and patients and their families is central to successful care. Whilst it is important to respect patient choice all patients should be encouraged to register with their local haemophilia centre. This will ensure that the patient is known to the centre in the event of an emergency presentation requiring specialist management.

5.3 **Types of haemophilia**

It is essential that all patients with haemophilia and other inherited bleeding disorders are registered and treated at designated treatment centres (appendix 2). Two levels of treatment centre are recognised in Health Service Guideline HSG(93)30:

- Comprehensive Care Centres
- Haemophilia Centres.

5.4 **Comprehensive Care Centres**

A Comprehensive Care Haemophilia Centre (CCC) carries out the following functions and activities:

- co-ordination of the delivery of haemophilia services – both in hospital and in the community including liaison with affiliated Haemophilia Centres
- a 24 hour advisory and response service for patients, families, hospital doctors, general and dental practitioners and affiliated Haemophilia Centre health care professionals
- delivery of a comprehensive care programme for paediatric and / or adult patients with haemophilia and related conditions
- provision of coagulation factor concentrates both for hospital treatment and home therapy programmes including prophylactic therapy and home delivery of factor concentrate where appropriate
- home treatment training programmes including home and school visits where appropriate
- counselling for patients and their families including family support groups
- social work support and welfare advice
- physiotherapy
- general and specialist surgery
- an interventional and restorative dental service
- rheumatological and orthopaedic review service with provision of surgery where appropriate
- a specialised obstetric and gynaecological service for the management of haemophilia carriers and women with von Willebrand Disease and other hereditary bleeding disorders
- specialised services for patients with HIV and viral hepatitis
- a diagnostic and reference laboratory service providing a full repertoire of tests enabling the diagnosis and monitoring of inherited disorders of haemostasis
- a 24 hour laboratory service for clotting factor assays and inhibitor screens
- genetic counselling and diagnosis in conjunction with specialist genetic laboratories
- participation in clinical trials and research and development
- participation in clinical and laboratory audit and in their hospital's clinical governance programme
- participation in the national UKHCDO & HNA triennial CCC audit programme
- participation in educational programmes for medical and nursing staff, biomedical scientists and related health care staff
- provision of educational programmes for patients and their families concerning all aspects of haemophilia care.

5.5 Haemophilia centres

Expertise in Haemophilia Centres (HCs) varies widely. Some centres offer the majority of services that are provided by a CCC. At a minimum, a Haemophilia Centre must be able to provide the following:

- a 24 hour emergency treatment service for patients with haemophilia and other inherited bleeding disorders
- provision of home treatment programmes
- provision of appropriate clinical advice to patients and families
- provision of adequate supplies of factor concentrate for hospital and home treatment
- a 24 hour diagnostic and monitoring laboratory service for the more common inherited bleeding disorders either on site or by arrangement with their local CCC
- participation in clinical and laboratory audit and in their Trust's clinical governance programme.

5.6 The delivery of comprehensive care

The cornerstone of the treatment of haemophilia is comprehensive care delivered by a multi-disciplinary and specialised team on a 24 hour basis. In practice this involves a core team consisting of the following personnel:

Haemophilia centre medical staff who carry out routine and emergency treatment and follow up clinical reviews.

Haemophilia nursing staff who co-ordinate much of the day to day treatment, co-ordinate supplies of coagulation factor concentrates and are responsible for education of patients and their families including training for home treatment programmes.

Haemophilia centre physiotherapist who offers a range of acute treatments for patients with active bleeds and is responsible for monitoring joint function and improving joints and muscles on a long term basis.

Haemophilia Data Manager who collates clinical and financial data relating to Centre activity.

Haemophilia social worker who provides advice on welfare benefits as well as providing psychosocial support.

Haemophilia centre laboratory staff who provide a diagnostic and factor replacement monitoring service.

A network of other clinical and specialised services, including multidisciplinary clinics held in conjunction with the haemophilia team, will also be involved in the delivery of comprehensive care. These include the following:

- **Rheumatology and orthopaedics** – patients with severe haemophilia benefit from regular assessment by a specialist orthopaedic surgeon or rheumatologist at least once a year depending on clinical circumstances. These clinics will monitor joint and muscle problems and identify the need for surgical intervention.

- **Surgery** – surgery in patients with haemophilia and related disorders is complex. It is recommended that these procedures should be performed at a Centre with expertise and that provides a comprehensive care programme.
- **Dental care** – the dental care of patients with haemophilia can be complex and it is recommended that interventional procedures, especially extractions, are performed in hospital dental departments in close liaison with haemophilia centres.
To optimise dental care it is recommended that haemophilia patients have access to restorative dental services within their hospital dental department.
- **Specialised services for HIV** – prior to the introduction of virucidal treatment of concentrates in 1985 more than 1,200 patients with bleeding disorders in the UK were infected with HIV. Around 360 of these patients are still living and continue to require specialised HIV care for their medical and psychosocial problems.
- **Specialised services for hepatitis** – Around 5,000 patients with haemophilia and other inherited bleeding disorders were infected with hepatitis B and / or C from treatment prior to the introduction of donor screening and virucidal treatment of concentrates. Many of these patients have progressive liver disease requiring specialist medical and psychosocial care. Patients co-infected with HIV and hepatitis B or C especially require specialist care.
- **Paediatrics** – the care of children and young people needs to take into account their physical and emotional development. Care must be provided in a paediatric setting by or in association with staff trained in the care of children.
- **Obstetrics and Gynaecology** – there are important management issues surrounding the antenatal care of a mother who is a haemophilia carrier; and the delivery of a child who has haemophilia. Gynaecological expertise is frequently required for carriers of haemophilia, women with von Willebrand disease and women with other inherited bleeding disorders.
- **Counselling services and clinical psychology** – patients with haemophilia and their family members often have complex psychological issues requiring specialist counselling or clinical psychology input.
- **Genetics** – all people with haemophilia and related disorders should have access to specialised genetic services for inheritance counselling and mutational analysis to enable confirmation of diagnosis, determination of carrier status and antenatal fetal testing.

5.7 Establishment of regional haemophilia networks

All patients with inherited bleeding disorders should have access to a comprehensive care programme. This may be provided by a Comprehensive Care Centre or a Haemophilia Centre, or a combination of the two, depending upon local expertise.

It is considered essential that a system of local or regional haemophilia networks is in operation with the specific responsibility of establishing and monitoring appropriate standards of care for patients with haemophilia and related disorders. The constitution of each haemophilia network should be multi-disciplinary and as well as a CCC Director might include, a Haemophilia Centre Nurse, a patient representative and a commissioning representative. Every haemophilia centre within each region should have a representative on the network. Networks should carry out the following functions:

- ensure that all patients with haemophilia and other inherited bleeding disorders have access to a comprehensive care programme, as appropriate
- ensure implementation of the national service specification
- assume responsibility for the quality of the haemophilia service within the region, including regular clinical audit and assessment of models of service delivery.
- discuss and react to any issues emanating from audit of haemophilia centres, in consultation with UKHCDO, UK RCN HNA and The Haemophilia Society.
- define appropriate relationships between the regional CCC(s) and HCs
- co-ordinate strategic planning of haemophilia services
- maintain dialogue with service users.

5.7.1 All HCs must establish a formal relationship with one or more nominated CCCs. Many smaller HCs play a critical role in providing effective emergency care at a local level for patients with hereditary bleeding disorders. However patients may need to attend the CCC for more comprehensive elements of care. It is recognised that there are a number of HCs that, although not meeting all the criteria for comprehensive care status, are able to offer a standard of care similar to that offered by CCCs. The level of collaboration will therefore depend upon the degree of expertise available in the HC and will be agreed by the regional haemophilia network.

5.7.2 HCs and CCCs that enter into shared patient care arrangements must ensure that all patients with severe and moderate hereditary bleeding disorders have a comprehensive care review performed at least six monthly. Review arrangements for patients with mild haemophilia should be determined between the HC and CCC in liaison with the regional haemophilia network. Complex bleeding problems and cover for surgical procedures must be discussed with the CCC.

5.7.3 All patients reviewed at the CCC under a shared care arrangement should have a letter written following review that includes the following information:

- current clinical problems
- updated summary of joint damage
- current treatment regimen and any changes since last review
- management plan
- date of next review.

6 Quality standards

All haemophilia treatment centres must comply with the following national standards:

Data collection

- All centres must maintain up to date registers of patients under their care
- All centres must submit data to the UKHCDO central data base.

Clinical

- Wherever possible, all patients must be managed according to current guidelines produced by the UKHCDO
- Nursing and physiotherapy standards must comply with current guidelines produced by UK RCN HNA and HCPA.

Laboratory

- All laboratories will possess full accreditation through Clinical Pathology Accreditation (CPA) UK Ltd
- All laboratories will participate in an accredited National External Quality Assurance Scheme in haemostasis. Trial performance must be available for formal inspection by commissioning authorities and external auditors. Persistent poor performance must be addressed and rectified as a matter of priority.

Audit

- CCCs should continue to be audited as part of the UKHCDO and UK RCN HNA triennial audit scheme using the standardised audit tool proforma. The audit team should include a patient / parent representative where possible
- Responsibility for audit of Haemophilia Centres within any one region is the responsibility of the Regional Haemophilia Network, working in collaboration with those centres and with UKHCDO, UK RCN HNA and The Haemophilia Society
- Results of CCC and HC audits should be open and made readily available to relevant stakeholders.

7 Treatment recommendations

7.1 Facilities

- Patients should be treated at all times in hospitals that are CCCs or HCs.
- There should be dedicated disabled car parking spaces for patients / parents in the vicinity of the haemophilia centre.
- There should be appropriate disabled access throughout the haemophilia treatment area.

- The clinical treatment of patients with haemophilia should take place in a dedicated clinical area that should be comfortable, quiet and appropriately equipped. These areas must have a facility to allow confidential interviews between staff and patients particularly those with HIV and hepatitis virus infections.

7.2 On-call arrangements

- Patients with haemophilia and other inherited bleeding disorders are often not treated appropriately if they present to accident and emergency departments, especially out of hours.
- A policy covering the attendance arrangements for patients presenting out of hours which is made clear to both patients and junior medical staff covering haematology should be in place. It is especially important that patients are informed of whom they should contact in the event of an emergency.
- Accident and emergency departments should have a protocol in place for the management of patients presenting directly to them. In particular this should contain the arrangements for contacting on-call haemophilia unit staff especially if the nearest centre is at another hospital.
- There should be an experienced senior haematologist on call at all times who should have an appropriate level of training and experience in the management of bleeding disorders.
- Junior medical staff responsible for the care of haemophilia out of hours should receive formal education about haemophilia and its treatment as part of their induction programme when they join the unit.
- A written protocol for the management of patients with haemophilia and related disorders must be issued to junior medical staff.
- Local ambulance controls must be instructed to take patients with haemophilia and related conditions to the nearest Haemophilia Treatment Centre unless the patient's condition is such that accident and emergency unit care is essential.
- There must be appropriate laboratory arrangements in place for the out of hours monitoring of patients with haemophilia and related disorders.
- The exact way in which on-call arrangements are delivered to acceptable standards will need to be determined at local level depending upon staff levels and facilities. HCs may decide to establish shared on call arrangements with their local CCC.

7.3 Treatment of children

The care of children with haemophilia and other inherited bleeding disorders can be complex and should only be carried out by clinical staff who are experienced in the management of children with inherited bleeding disorders. The care of such children should be carried out in conjunction with general support from local clinical paediatric services.

The treatment of children should follow the guidance of the Department of Health National Service Framework for Children, Young People and Maternity Services, 2004.

- Facilities and staffing should be appropriate to the needs of children and adolescents with inherited bleeding disorders. In centres treating both children and adults there should be a separate designated area for the care of children.
- Children with haemophilia and other inherited bleeding disorders should have 24 hour access to a paediatric ward or alternative facility for the acute treatment of bleeding episodes.
- There should be appropriate levels of dedicated paediatric support available at all times.
- Haemophilia centre staff caring for children with haemophilia will be responsible for implementing home therapy programmes, prophylactic treatment and community care for them and their families.
- Transfer from paediatric to adult care is a particularly sensitive time for the teenager with a hereditary bleeding disorder particularly if the adult centre is at a different hospital. There should therefore be seamless and sensitive transition to adult care at an appropriate age

7.4 Prophylaxis

- Prophylaxis is defined as the regular administration of factor VIII or FIX concentrates (2-3 times a week) to patients with haemophilia to prevent acute episodes of bleeding into joints and muscles. The rationale behind the use of prophylaxis is the observation that children with moderate haemophilia (base line FVIII/FIX above 1iu/dl) only occasionally experience spontaneous bleeding episodes and do not tend to develop joint damage. Therefore the aim of prophylaxis in severe haemophilia is to maintain the basal FVIII/FIX level above 1iu/dl. Prophylactic administration of factor concentrate is also used to prevent bleeds in patients with other severe inherited bleeding disorders e.g. severe von Willebrand disease and FXIII deficiency.
- Prophylaxis is beneficial for children with haemophilia as it minimises disruption to the patient and the family that can result from frequent bleeding episodes.
- Whilst there is a paucity of randomised clinical trials (see Cochrane review reference 1) a series of case studies and widespread clinical experience throughout Europe indicate that effective prophylactic therapy can prevent long term damage to muscles and joints (references 2,3).
- An effective prophylactic dose is the minimum dose required to prevent spontaneous breakthrough bleeding. This will vary between patients. The exact dose may need to be determined by formal recovery and half life studies in which the decay of injected FVIII / FIX is monitored.
- The decision to introduce prophylaxis must be made on an individual basis taking into account the patient's and family's circumstances. Prophylaxis should be introduced at the onset of significant joint bleeding.
- Prophylactic therapy is administered in the home setting. The Haemophilia Centre will provide appropriate clinical and psychosocial support in liaison with community based services.

- Prophylactic therapy is a major undertaking for the parents of a child with haemophilia and should only be embarked upon once they have agreed to accept full responsibility for the treatment and are competent in factor administration.
- The duration of prophylaxis beyond childhood will depend upon individual circumstances. Following consultation with their treaters some patients may decide to continue into adulthood.
- Periods of prophylaxis may be advised in adult patients who develop frequent bleeds into a particular joint (a target joint). This will stabilise the joint and prevent the progression of joint damage. Some adult patients have frequent bleeding episodes and benefit from periods of prophylaxis to enable them to maintain independent mobility and continuing employment.

7.5 Home and community care

- Wherever appropriate the care of patients with haemophilia should be delivered in the home setting which will minimise hospital attendance and absence from school and work, enabling them to live as normal a life as possible.
- Community care can be optimised by the appointment of a specific liaison nurse, with responsibility for community care.
- Haemophilia Centres will liaise with patients and their families with regard to home therapy issues and will record the usage of coagulation factor concentrates.
- Haemophilia centres will liaise closely with primary health care providers to optimise care within the community.
- Wherever possible coagulation factor concentrates should be delivered directly to the patient's home saving them the inconvenience of attending the centre for treatment supplies.
- Patients and their families will be instructed as to the importance of recording all bleeding and treatment episodes so as to provide the Haemophilia Centre with essential outcome data. Concordance with this will be closely monitored by the Centre.

7.6 Outpatient review

- All registered patients should be offered a regular clinical and multi-disciplinary review (where appropriate) and records kept of non-attendance.
- At a minimum patients with severe / moderate haemophilia should be seen six monthly and those with mild haemophilia annually.
- Patients with frequent bleeding episodes, coagulation factor inhibitors, complications of bleeding episodes such as symptomatic arthropathies and those with chronic viral infections acquired from previous coagulation factor concentrate treatment may require more frequent review.
- Patients with haemophilia on regular coagulation factor treatment should be screened regularly for an inhibitor.
- All patients with inherited bleeding disorders are at increased likelihood of requiring blood transfusion and should therefore be vaccinated against hepatitis A and B if not already immune.

7.7 Patient education and support

- Hereditary bleeding disorders have a significant impact on the patient and family leading not only to physical disability but also to problems with schooling, employment and relationships.
- Appropriate mechanisms should be in place for the psychosocial support of the patient and the family particularly regarding provision of social welfare and counselling services. This may require joint commissioning with social services.
- The establishment of support groups at a local level is recommended and can be facilitated by the Haemophilia Society.

7.8 Patient participation

- Patients and their carers should be encouraged to be active participants in and assume appropriate responsibility for their delivery of care.
- Effective haemophilia care can be optimised by the establishment of a close dialogue between the Haemophilia Centre and patients.
- It is recommended that local patient groups are established which liaise closely with the Haemophilia Centre and act as a sounding board for developments in care. The establishment of such groups can be facilitated by the Haemophilia Society.
- Patients should be involved in Haemophilia Centre Audit schemes and should be given access to the results of these.

7.9 Use of coagulation factor concentrates

- All patients with hereditary bleeding disorders should be treated in accordance with the recommendations of the UKHCDO (references 4,5).
- Due to the potential for transmission of transfusion associated infectious agents in plasma derived products, recombinant coagulation factor concentrates are the treatment of choice for patients with inherited bleeding disorders, in accordance with UKHCDO recommendations (reference 4).
- In the absence of suitable recombinant preparations, patients with severe von Willebrand disease and those with rare hereditary clotting factor deficiencies (deficiencies of FV, FX, FXI etc.) will require treatment with plasma derived virucidally treated coagulation factors for the foreseeable future in accordance with UKHCDO recommendations (reference 4).

7.10 Inhibitors

- Around 30% of patients with severe haemophilia A develop an antibody against factor VIII following administration of factor VIII concentrate. This is known as an inhibitor. The care of patients with inhibitors is time consuming, costly and expensive. In approximately half of these patients the inhibitor is transient and eventually disappears. In patients with a persistent inhibitor levels remain either low (<5 inhibitor units) or can reach much higher levels. Bleeding episodes in patients with inhibitors are more difficult to treat and so there is significant morbidity and mortality associated with inhibitor development. Low level inhibitor patients can be successfully treated with high doses of FVIII. However, patients with high inhibitor

levels do not respond to FVIII concentrate and require treatment with alternative 'by-pass' haemostatic agents FEIBA or recombinant activated FVII (rFVIIa). Inhibitor development in haemophilia B is far less common occurring in around 3% of patients.

- The management of patients with inhibitors is complex and should only be carried out in centres with appropriate clinical and laboratory resource and experience in the use of 'by-pass' haemostatic agents.
- Acute episodes of bleeding in patients with inhibitors should be treated according to published UKHCDO recommendations (reference 6).
- Every confirmed new inhibitor should be reported as an adverse event to the UKHCDO, the concentrate manufacturer and the Committee for Safety of Medicines (CSM).
- The care of patients with low level inhibitors should be co-ordinated with a Comprehensive Care Centre.
- The care of patients with high inhibitor levels should be supervised by a Comprehensive Care Centre. The extent to which these patients can be managed at a local Haemophilia Centre must be determined through discussion within the regional haemophilia network.
- The clinical care of inhibitor patients is very expensive primarily due to the cost of the haemostatic agents used to treat them. Furthermore inhibitor development and bleeding episodes in inhibitor patients is wholly unpredictable. For these reasons commissioners are advised to consider participating in financial risk reduction strategies in association with other commissioning agencies.

7.11 Immune tolerance

- Immune tolerance is a treatment strategy aimed at eradicating inhibitors. It involves the administration of high doses of factor VIII or IX over an extended period in the expectation that the immune system will no longer recognise the factor as being a foreign protein and stop antibody formation.
- Eradication of the inhibitor has substantial cost saving implications as the patient can recommence treatment with factor VIII / IX concentrates (reference 7).
- Immune tolerance programmes should follow the recommendations of the UKHCDO (reference 6).
- Successful eradication of an inhibitor can lead to a significant improvement in quality of life and life expectancy.
- It is generally agreed that patients with a newly diagnosed inhibitor – particularly children - are more likely to benefit from immune tolerance if this is initiated soon after the development of the inhibitor. Immune tolerance is less likely to be successful when the inhibitor is long established and of high titre.
- The management of patients on immune tolerance programmes is complex and should only be carried out in centres with appropriate experience and expertise.
- Immune tolerance programmes are very expensive and should be discussed fully with commissioners prior to commencement and agreement reached as to the proposed treatment regimen and costs. Commissioners may find it useful to seek expert independent advice before agreeing to fund an immune tolerance programme.

- Scientific information concerning the outcome of immune tolerance programmes is limited and it is strongly recommended that patients being considered for immune tolerance are entered into appropriate clinical trials which have results reported to relevant national and international inhibitor databases.

7.12 **Treatment of acquired infections**

- The transmission of viral infections (HIV, hepatitis B and C) that occurred as a result of treatment with contaminated coagulation factor concentrates prior to the late 1980s has had a profound effect on the haemophilia community.
- Patients and families affected by HIV and hepatitis infection experience particularly complex medical and psychosocial needs.
- Nearly all patients with HIV have been co-infected with hepatitis B and / or C. HIV can accelerate the course of hepatitis virus associated chronic liver disease and infection with hepatitis C may worsen the outcome of HIV infection.
- It is essential that patients with HIV infection are reviewed regularly by an HIV specialist and that treatment strategies are in accordance with national published guidelines (reference 8).
- It is essential that patients with viral hepatitis are reviewed regularly by a hepatitis specialist and that treatment strategies are in accordance with published guidelines, in particular the National Institute for Clinical Excellence (NICE) guidelines on the treatment of hepatitis C. (references,9,10,11).
- It is essential that patients with HIV and hepatitis infection - and their families - have appropriate access to psychological and social welfare support services: these should be provided by statutory and voluntary sector agencies.

7.13 **Acquired haemophilia and acquired von Willebrand's disease**

- Acquired haemophilia and acquired von Willebrand's disease are severe and often life threatening bleeding disorders which occur due to the development of inhibitor antibodies to factor VIII and von Willebrand factor. They usually occur spontaneously but are sometimes associated with auto-immune conditions, pregnancy and malignancy. They are rare conditions and affects both males and females.
- The management of patients with acquired haemophilia and acquired von Willebrand's disease is particularly complex, time consuming and expensive and should preferably be carried out in CCCs. Bleeding episodes are managed with the expensive 'by-pass' haemostatic agents FEIBA or rFVIIa.
- The treatment of acquired haemophilia should follow UKHCDO guidelines (reference 6).
- All new cases of acquired haemophilia and acquired von Willebrand's disease should be notified to commissioners at the earliest opportunity.

7.14 **Adverse events**

- Any adverse events that occur in association with the administration of coagulation factor concentrates, e.g. allergic reactions and inhibitor development, should be reported through the existing orange card scheme of the UKHCDO and the yellow card scheme of the CSM.

7.15 **Clinical trials**

- Haemophilia Centres participating in coagulation factor concentrate trials must inform commissioners of this, the number of patients involved and the intended duration of the trial.

8 Genetic Services (reference 12)

8.1 **Carriers of haemophilia and women with inherited bleeding disorders**

- Carriers of haemophilia may have low levels of factor VIII or factor IX and if this is the case may have clinical problems similar to patients with mild haemophilia. Similar problems may occur in women with other inherited bleeding disorders.
- In these groups bleeding may occur after trauma or invasive procedures. Child birth and menorrhagia may require specialist treatment. Carriers of haemophilia with low coagulation factor levels and women with inherited bleeding disorders should have access to appropriate obstetric and gynaecology services.
- All carriers or potential carriers of haemophilia should have their factor VIII or factor IX level measured before an invasive procedure and in young children when venous access is adequate. Those with low levels should be registered with a haemophilia centre and followed up regularly.
- Potential carriers of haemophilia should be offered genetic counselling and testing to confirm their status when they are old enough to understand the issues involved and give informed consent.
- A relatively small number of carriers of haemophilia and women with inherited bleeding disorders were infected with HIV and / or hepatitis B or C. These patients require access to the same range of services as described for virally infected patients with haemophilia.

8.2 **Genetic information and genetic counselling**

- It is recommended that the diagnosis, coagulation factor level and mutation within a family should be definitively confirmed, wherever possible.
- Haemophilia centres should maintain a genetic register of families with inherited bleeding disorders. This should include a regularly updated pedigree so that potential carriers can be identified, families can be offered appropriate services and to ensure that genetic counselling is accurate.
- Each family should have a genetic file separate from the main notes and each individual should have a section of this file that can be kept confidential.
- Families and individuals affected with inherited bleeding disorders should have access to information about clinical phenotype, therapeutic options and genetic information relevant to their diagnosis.
- Families should also have access to genetic counselling delivered by an individual trained in genetic counselling and knowledgeable about inherited bleeding disorders. Access to genetic counselling may be required before, during and after genetic testing and when considering reproductive choices.

- The option for genetic counselling separate from the haemophilia centre and by non-haemophilia centre staff should be available.
- Individuals should receive written confirmation of the information they have been given at clinic appointments.

8.3 **Laboratory genetic testing**

- All Haemophilia centres should have a formal relationship with a genetic laboratory so that all patients and families have access to genetic testing.
- Laboratories undertaking genetic tests for inherited bleeding disorders should be part of the UKHCDO Haemophilia Genetics Laboratory Network, comply with standards and practices agreed by that group and participate in external audit.
- Written, informed consent should be taken by the requesting clinician before genetic tests are performed. This should include specific consent for genetic tests and storage of genetic material. Specific permission to share relevant results with other professionals or family members to improve accuracy of genetic counselling for other family members should be recorded.
- All patients with haemophilia should be offered mutation analysis.
- Tests to allow carrier status to be established at an appropriate age should be available to all potentially affected female members of families with haemophilia.
- Individuals should receive written confirmation of laboratory test results given at clinic visits.

8.4 **Laboratory genetic testing**

- Pregnancy is a potentially serious undertaking for women who have, or are carriers of, an inherited bleeding disorder as both mother and infant are at increased risk of bleeding.
- It is recommended that education about the transmission of the inherited bleeding disorder in the family and relevant genetic tests are undertaken before pregnancy, if possible. Mutation analysis in the relevant parent should be undertaken prior to pregnancy if there is any possibility that prenatal diagnosis may be requested.
- There should be access to an expert in fetal medicine for discussion of antenatal and pre-implantation diagnosis.
- Counselling related to antenatal diagnosis should be performed by fetal medicine staff and haemophilia centre staff. Appropriate support should be available throughout the process.
- For antenatal diagnosis, procedures and communication between haemophilia centre, fetal medicine department, laboratories and GP should be formalized in a written protocol.
- Obstetric management of women with inherited bleeding disorders, and known or potential carriers of haemophilia, should be carried out in (or in close association with) haemophilia centres that have expertise in the area. At all stages of pregnancy there must be close collaboration between the obstetric and haemophilia teams.

- Appropriate haemostatic agents for both mother and infant should be immediately available.
- A documented care plan for the delivery and aftercare of any infant at risk of having a bleeding disorder should be established.
- Postnatal confirmation of the diagnosis should be carried out as soon as possible.

9 Record keeping and data collection

Accurate recording of clinical information is essential for the effective delivery of haemophilia care. Financial arrangements and data handling can be complex and it is strongly recommended that commissioners provide haemophilia treatment centres with the financial and human resource to facilitate the collation of information required.

- All haemophilia centres must maintain accurate medical records
- All haemophilia centres must maintain a patient register with a clear indication of those patients who are on regular treatment and those who attend for regular review
- All haemophilia centres must report any treatment related adverse events to UKHCDO, the regional network and where appropriate to the Committee for Safety of Medicines
- All haemophilia centres must issue patients with medical cards giving details of their inherited coagulation disorder and preferred treatment option
- All data must comply with the Data Protection Act of 1998, including the new Medical Information Act, with informed consent being obtained from patients for their clinical details to be held on a central register
- All haemophilia centres must submit annual returns to the centralised data base of the UKHCDO and to their commissioning authorities
- All haemophilia centres will respond to requests for patient data from the UKHCDO and its working parties
- All haemophilia centres must have a system in place for the monitoring of factor usage by patients on home treatment programmes
- All haemophilia centres must acquire and install a data system that is able to communicate electronically with the national haemophilia data system, thereby enabling real time capture of information, including patient registration details and coagulation factor usage.

10 Outcomes

- 10.1 All centres delivering haemophilia care must collect detailed information concerning the outcome of treatment.
- 10.2 As part of their home therapy package patients and parents must agree to provide the treatment and outcome data that is requested by the Haemophilia Centre.
- 10.3 Haemophilia Treatment Centres must agree the outcome data to be collected with their commissioners. It is recommended that at the very least the following data must be recorded:
- Total units of coagulation factor concentrate used by each patient per year
 - Total number of treatments received by each patient per year
 - Amount of coagulation factor concentrate given for prophylaxis and for on demand / emergency therapy
 - Number of breakthrough bleeds on prophylactic regimens
 - Total number of inpatient days due to bleeds
 - Surgical procedures performed, including units of coagulation factor concentrates used
 - Days missed from school due to bleeds
 - Days missed from work due to bleeds
 - Status report on joint and muscle damage by both clinical and where appropriate radiological assessment.
- 10.4 An annual report should be produced by Haemophilia Treatment Centres for their commissioning authority. Outcome data should form the main part of this report which should also include information on the other activities on the Centre such as audit, teaching and research.

11 Service Agreements

- 11.1 Commissioners must maintain an accurate profile of patients with inherited bleeding disorders who reside within their catchment area.
- 11.2 Commissioners must maintain appropriate contractual arrangements with CCCs and HCs which must reflect the specific levels of care required for the three patient categories of severe, moderate and mild haemophilia.
- 11.3 The components of the haemophilia service contractual agreement which should be kept separate:

- A component for the clinical delivery of comprehensive care
- A component for the use of coagulation factor concentrates
- Consideration should be given to a separate contract for patients with inhibitors, whose care is particularly costly, complex and unpredictable
- Funding of laboratory genetic services.

11.4 The occurrence of bleeding episodes in patients with haemophilia is unpredictable. The contractual problems that may result as a consequence of high levels of coagulation factor consumption can be minimised by maintaining regular dialogue between commissioners and providers.

In particular, service providers must notify commissioners at the earliest opportunity of the occurrence of any of the following:

- New cases of severe haemophilia or other severe bleeding disorders
- Unanticipated heavy usage of coagulation factor concentrates
- Development of new coagulation factor inhibitors
- Scheduling of major surgical procedures
- Introduction of new treatment strategies
- Scheduling of immune tolerance programmes.

Regular meetings should be convened between CCCs, commissioners and regional haemophilia networks to monitor contract activity and to discuss care development issues.

Because of the unpredictable and costly nature of haemophilia care commissioning authorities may wish to participate in risk sharing arrangements with other commissioning authorities.

12 Date of issue

2006

13 Recommended Review Date

13.1 It is recommended that this specification is reviewed every three years.

Appendix I

References

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Appendix 2

Designated centres for haemophilia treatment as at Feb 2006

Comprehensive care centres

Belfast (Royal Belfast Hospital for Sick Children and Belfast City Hospital)

Birmingham (Princess of Wales Children's Hospital)

Birmingham (University Hospital Birmingham)

Cambridge (Addenbrooke's Hospital)

Canterbury (Kent and Canterbury Hospital)

Cardiff (University Hospital of Wales)

Edinburgh (Royal Hospital for Sick Children and Royal Infirmary of Edinburgh)

Glasgow (Royal Hospital for Sick Children and Glasgow Royal Infirmary)

Hampshire (North Hampshire Hospital Basingstoke and Southampton General Hospital)

Leeds (St James' University Hospital)

Leicester (Leicester Royal Infirmary)

Liverpool (Alder Hey Children's Hospital and Royal Liverpool University Hospital)

London: Great Ormond Street Hospital for Sick Children

The Royal Free Hospital

The Royal London Hospital

St Thomas' Hospital

Manchester (Royal Manchester Children's Hospital)

Manchester (Manchester Royal Infirmary)

Newcastle (Royal Victoria Infirmary)

Nottingham (University Hospital Queen's Medical Centre)

Oxford (Churchill Hospital)

Sheffield (Sheffield Children's Hospital and Royal Hallamshire Hospital)

Haemophilia Centres

England

Barnstaple (North Devon District Hospital)	Medway (All Saints Hospital Chatham)
Bath (Royal United Hospital)	Milton Keynes (Milton Keynes Hospital)
Bedford (Bedford General Hospital)	Middlesborough (Middlesborough General Hospital)
Blackburn (Blackburn Royal Infirmary)	Northampton (Northampton General Hospital)
Bournemouth / Poole (Royal Bournemouth Hospital)	Norwich (Norfolk and Norwich Hospital)
Bradford (Bradford Royal Infirmary)	Peterborough (Peterborough District Hospital)
Brighton (Royal Sussex County Hospital)	Plymouth (Derriford Hospital)
Bristol (Adults - Bristol Oncology Centre, Children – Royal Hospital for Sick Children)	Portsmouth (St Mary's General Hospital)
Camberley (Frimley Park Hospital)	Salisbury (Salisbury District Hospital)
Carshalton (St Helier Hospital)	Shrewsbury (Royal Shrewsbury Hospital)
Chertsey (St Peter's Hospital)	Southend (Southend Hospital)
Chichester (St Richard's Hospital)	Stoke-on Trent (North Staffordshire Hospital)
Colchester (Colchester District General Hospital)	Sunderland (Sunderland District General Hospital)
Coventry (Walsgrave Hospital)	Taunton Hospital (Taunton and Somerset Hospital)
Derby (Derbyshire Royal Infirmary)	Thornton Heath (Mayday Hospital)
Dorchester (West Dorset Hospital)	Torbay (Torbay Hospital)
Eastbourne (Eastbourne District General Hospital)	Tunbridge Wells (Pembury Hospital)
Exeter (Royal Devon and Exeter Hospital)	Truro (Royal Cornwall Hospital)
Great Yarmouth (James Paget Hospital)	Whitehaven (West Cumberland Hospital)
Hastings (Conquest Hospital)	Wolverhampton (New Cross Hospital)
Hereford (Hereford County Hospital)	Worcester (Worcester Royal Infirmary)
Hillingdon (Hillingdon Hospital)	Worthing (Worthing Hospital)
Huddersfield (Huddersfield Royal Infirmary)	York (York District Hospital)
Hull (Hull Royal Infirmary)	
Ipswich (The Ipswich Hospital)	
Kettering (Kettering General Hospital)	
Kingston upon Thames (Kingston Hospital)	
Lancaster (Royal Lancaster Infirmary)	
Lincoln (Lincoln County Hospital)	
London: Hammersmith Hospital	
Lewisham Hospital	
St Georges Hospital	
Luton (Luton and Dunstable Hospital)	

Scotland

Aberdeen (Aberdeen Royal Infirmary)
Dundee (Ninewells Hospital)
Inverness (Raigmore Hospital)

Wales

Bangor (Ysbyty Gwynedd)
Newport (Royal Gwent Hospital)
Swansea (Singleton Hospital)

