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Royal Cornwall Hospitals NHS Trust

Primary Haemostatic Disorders - Haemophilia and Related Conditions - Clinical Guideline

V3.0

May 2022

1. Aim/Purpose of this Guideline

1.1. The Royal Cornwall Hospital Haemophilia Centre at Truro is a designated treatment centre for the care and management of patients with inherited bleeding disorders. This document outlines the basis of the acute and long-term care and management of these patients, in accordance with current recommendations and the National Service Specification for Haemophilia and Related Conditions (NHS England 2013).

1.2. This version supersedes any previous versions of this document.

1.3. Data including patient name, details of bleeding disorder and treatment recommendations are held on a local excel spreadsheet which patients are verbally consented.

1.4. Data is also held on the National Haemophilia Database which also holds details of treatment used. Patients are given an information leaflet and asked to verbally consent to this.

Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation

The Trust has a duty under the Data Protection Act 2018 and General Data Protection Regulations 2016/679 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed, and documented. We cannot rely on opt out, it must be opt in.

Data Protection Act 2018 and General Data Protection Regulations 2016/679 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the Data Protection Act 2018 and General Data Protection Regulations 2016/679 please see the Information Use Framework Policy or contact the Information Governance Team

Royal Cornwall Hospital Trust rch-tr.infogov@nhs.net

2. The Guidance

2.1. **Symptoms and the Investigation of Primary Haemostatic Disorders**

- Bruising
- Joint bleeds
- Muco-cutaneous bleeding
- Muscle bleeds
- Unexplained surgical bleeding

2.1.1. **Investigation**

2.1.1.1. **Level 1- Basic Screen**

A “coagulation screen” of the platelet count, PT and APTT are basic initial tests.

2.1.1.2. **Level 2- and in liaison with a Consultant Haematologist**

In patients with a history suspicious of primary bleeding diathesis, Von Willebrand’s disease is most commonly identified, and screening tests should be:

- Platelet count and morphology
- Blood group
- PT and APTT
- Factor VIII & Von Willebrand Screen

To be received in laboratory within 4 hours

(NB paediatric minimum sample for PT, APTT, FVIII complex is 2mls in paediatric tubes).

Consider platelet function tests in patients with a significant history (20ml sample) **to be received in laboratory within 60 minutes.**

Ensure that requests for coagulation tests other than PT and APTT are discussed with laboratory staff before sampling the patient. Some tests require special setup in the laboratory.

2.1.1.3. **Level 3**

In patients with prolonged prothrombin time or APTT not otherwise explained, specific factor assays will be done with inhibitor studies. Patients with a normal coagulation screen but abnormal bleeding should undergo platelet function tests and nucleotide assays, as indicated, arranged with the laboratory.

Platelet Function tests require liaison with the laboratory before sampling the patient.

2.1.1.4. **Level 4**

Where a specific diagnosis is indicated, supplementary tests may be required e.g., Von Willebrand’s disease: RIPA, collagen binding assay, multimeric analysis Haemophilia: genetic analysis.

2.1.2. **Clinical classification of bleeding disorders.**

2.1.2.1. Summary for Haemophilia A & Haemophilia B

Phenotype	Factor Level IU/dl	Clinical Bleeding (typically of the joints)
Mild	>5	Infrequent usually resulting from trauma.
Moderate	1 – 5	Infrequent, occasionally spontaneous.
Severe	<1	Frequent and spontaneous

2.1.2.2. Von Willebrand's disease

This is different to haemophilia as the severity depends on quantitative and, or qualitative reductions in von Willebrand factor multimers. Bleeding is more commonly mucocutaneous.

Type	Von Willebrand factor multimers	disease severity	management
1	quantitative reduction	mild	usually desmopressin
2	subtyped e.g. 2a, 2b, 2bN by quantitative and qualitative reduction	mild	usually factor (derived from human plasma)
3	severe reduction of all multimers	severe	Factor (derived from human plasma)

2.1.2.3. Factor XI deficiency

This is relatively rare. Patients rarely bleed unless the factor level is <15 iu/dl and this is usually muco-cutaneous (ENT or GU).

2.1.2.4. Factor XII deficiency

Usually recognised as the cause for a prolonged APTT in otherwise healthy patients. Bleeding is most unusual and specific therapy is not necessary.

2.1.2.5. Rare deficiencies

Other single coagulation factor deficiencies eg factors II, V, VII, X, XI and XIII.

2.1.2.6. Patient registration

2.1.2.7. Departmental excel spreadsheet database

All patients registered with the RCH-T Haemophilia Centre are recorded on a password protected excel spreadsheet (see section 8) with their diagnosis and treatment of choice. This database is also held in the transfusion Section of the Laboratory and issued to relevant clinical areas.

2.1.2.8. Hospital records

The patient's PAS & Oceano record will state 'Ref Haemostasis Guidance'

	Within working hours	**Outside working hours**
Adults	Contact Haemostasis Nurse and attend the Department	07833057447
Children*	Contact Haemostasis Nurse and attend Paed Obs	01872 253468

2.1.2.9. Red UKHCDO Bleeding Disorder Cards

All patients are issued these cards from the Haematology Department, detailing the nature of their disorder, their Haemophilia Centre and contact number. Patients should carry the card with them and show to attending clinical staff in the event of bleeding, or other challenges. If the patient is responsive to specific therapy such as desmopressin this will be marked on the card.

2.1.2.10. United Kingdom Haemophilia Centres Doctor's Organisation Database

All patients should be registered after explanation of this national database with the patients, or parental, verbal consent, via secure website. An information sheet is available.

2.2. **Treatment Recommendations**

2.2.1. On-Call

2.2.1.1. All registered patients who may be bleeding may self-refer and have 24-hour access to emergency care as follows:

*Child is defined as aged up to 16th birthday or 16-17year olds under paediatric follow up

2.2.1.2. Patients with non-bleeding problems will be sent in by the usual means The On-Call Consultant Haematologist should routinely be informed of a patient's attendance, either with or without specific bleeding problems.

2.2.2. Acute Management of Bleeding.

- This is dependent on the nature of the bleed, the deficiency, and its severity.
- Frequent attenders will have a Care Management Plan in place which is available to read on Maxims
- Treatment should be administered promptly, and patients should never be discharged without treatment unless in consultation with the on-call haematology consultant.

2.2.3. Investigations

2.2.3.1. If a severe bleed, check the full blood count and take a citrate (coagulation) sample for "save plasma". For a known Factor deficiency do not wait for results before treating.

2.2.3.2. Group and screen if indicated, e.g., Haematemesis.

2.2.3.3. There is nothing to be gained by repeating a patient's APTT, or baseline factor level, as this will be prolonged as per usual.

2.2.4. Treatments of Choice

2.2.4.1. Haemophilia A (Factor VIII(8) Deficiency).

Level of Severity	Treatment
Mild	Usually desmopressin
Moderate	Usually factor VIII concentrate
Severe	Always factor VIII concentrate
Head injury	Factor concentrate, desmopressin is contra-indicated

2.2.4.2. Haemophilia B (Factor IX (9) Deficiency)

These patients do not respond to desmopressin and require specific concentrate therapy.

2.2.4.3. Haemophilia A & B management outline:
The following are considered emergencies in the context of Haemophilia Care:

- Ileo-**Psoas Bleed** – presents as hip pain and the patient will be unable to extend hip. Requires urgent treatment with factor to 100iu/dl and urgent CT or MRI scan and discuss with Consultant Haematologist

- **Head & Neck bleed**

- **Any bleed which results in the patient becoming haemodynamically unstable**

Treatment recommendations are based on World Federation of Haemophilia Treatment Guidelines (3rd ed 2020) and the following is broad guidance only:

Condition/bleed site	**Requisite post-treatment factor level IU/dl for haemostasis**	**Additional Management**
Minor spontaneous bleeding or joint bleed	40-60	Consider admission for bed rest or review following day
Severe bleeding, e.g., muscle, joint or profuse haematuria	40 - 60	Admit for bed rest
Significant Head injury	80-100	**Urgent CT.** BD therapy*, or by infusion - consider factor levels.
Major surgery	80-100	BD therapy*, or by infusion - consider factor levels.

*OD in haemophilia B

2.2.4.4. Von Willebrand's disease

Most patients have mild type 1 disease and have an excellent response to desmopressin.

Desmopressin is best avoided in the treatment of significant head injury. Type 2 patients have a variable response to desmopressin, whilst this is ineffective in type 3 disease, when factor concentrate is required for control of haemorrhage.

2.2.4.5. Rare factor deficiencies

These may require factor concentrate, as below, or for milder bleeding tranexamic acid may be appropriate, as advised by the on-call haematology consultant.

2.2.4.6. Factor Concentrate Dosage see also Appendix 3

The dosage is roughly calculated using a series of formulae based on known factor half-life and kinetics

When bleeding is severe post-infusion levels may be taken to ensure adequate treatment, thereafter repeat levels are at defined intervals.

2.2.4.7. Haemophilia A (factor VIII deficiency)

Recombinant Factor VIII (eg**, Advate, ,NovoEight and Elocta**)

Dose either as target IU/kg, as per Appendix 3, or by target rise in IU/dl when *the dose = patient's weight x (target IU/dl - baseline factor level) x 0.5*

2.2.4.8. Haemophilia B (factor XI deficiency)

Recombinant Factor IX **Benefix** or **Idelvion**
Dose either as target IU/kg, or by target rise rise in IU/dl when *the dose = patient's weight x (target IU/dl - baseline factor level)*

2.2.4.9. Von Willebrand's Disease

Intermediate human derived purity Factor VIII Concentrate eg **Wilate**.

the dose = patient's weight x (target IU/dl - baseline factor level) x 0.5

2.2.4.10. Other deficiencies for which concentrates are available

Factor XI deficiency

Fresh frozen plasma (FFP) 15-20 ml/kg or **BPL Factor XI Concentrate**

the dose = patient's weight x (target IU/dl - baseline factor level) x 0.5

NB The post infusion level should be checked

The total dose of concentrate should not exceed 30 U/kg and peak factor XI 100 IU/dl.

Otherwise, there is a significant risk of thrombosis

2.2.4.11. Desmopressin acetate (OCTIM 15microgrammes/ml ampoule).

Different preparations are available – for subcutaneous use please order from pharmacy by brand name. Out of hours stock is available from the fridge in MAU, ED & Lowen Ward

This synthetic analogue of anti-diuretic hormone will boost factor VIII and von Willebrand factor levels 2 to 4-fold by promoting endothelial cell release.

It is given once daily and often the effect wanes after the first one or two injections.

As it activates the fibrinolytic pathways, tranexamic acid will be given in conjunction with desmopressin.

Due to its anti-diuretic effect, patients may be at risk of water intoxication with hyponatraemia and at worst convulsions and coma.

Therefore patients **should be water-restricted, drinking only to quench their thirst** (eg adults use maximum 2 litres or for children 2/3rd of usual maintenance), for the following 24 hours and with repeated administration check U&E, weight and urine output daily. It is (generally) **contra-indicated** in children under two years of age.

It may be administered by the SC, IV or intra-nasal routes

Patients will usually have undergone a trial of desmopressin to determine whether this is suitable therapy as reported on the database and their red Bleeding Disorder card.

Dose = 0.3 micrograms/kg either undiluted SC, or IV in 50-100 ml saline over 20 minutes. Subcutaneous and intravenous are equally efficacious.

Tranexamic acid – orally: 25 mg/kg tds for 7 days (adults typically 1 g tds)

I.V: 10mg/kg tds

Mouth wash: cf dental surgery section.

N.B. Tranexamic acid should be used with caution in patients with haematuria, pregnancy or those with a thrombotic history.

There is also an intra-nasal preparation of desmopressin - usual adult dose 300 micrograms, ie two actuations (sprays) every 12 hours under medical supervision.. This must be sprayed and not sniffed as this reduces absorption. The activity is equivalent to about 60% of the IV/SC preparation.

2.2.5. **Primary Platelet Disorders**

In either qualitative or qualitative platelet disorders, transfusion of platelets may be required, although these are generally used sparingly as patients may develop antibodies. On occasions some patients may respond to desmopressin. Management should be discussed with the consultant.

2.2.6. Supportive care

Rest, bed rest where appropriate.

A cold compress will often give good analgesia.

Appropriate analgesia starting with Paracetamol and/or Dihydrocodeine but avoiding Aspirin and non-steroidal anti-inflammatory drugs. The COX-2 NSAID's do not have an anti-platelet effect and may be suitable, or alternatively COX-2 selective NSAID's.

2.2.7. Physiotherapy

Once an acute joint or muscle bleed has settled then aggressive physiotherapy is necessary to ensure return of full mobility and maintain power around the joint which is essential to its stability in protecting the joint from progressive arthritis.

2.2.8. Prophylactic Therapy

- This is used as either primary or secondary therapy to prevent bleeding
- The aim is to maintain the trough factor level to prevent spontaneous bleeds and joint destruction.
- It generally commences in childhood, around one to two years of age and is generally continued into adulthood.
- It may also be given in established patients with increasingly troublesome target joints usually for a set period of time, and also in the post-operative period
- Sporadic prophylaxis with either desmopressin or concentrate may also be used in milder patients before an activity which would normally result in haemorrhage.

2.2.9. Home and community care

Wherever appropriate, the care of patients with haemophilia and their families should be delivered in the home setting which will minimise absence from school and work and help patients to live more effectively with their lifelong bleeding disorder

Patients and their families will be educated as to the importance of keeping formal records of all treatments and episodes of bleeding, to enable them to provide the Haemophilia Centre with essential outcome data; the keeping of appropriate records in the home setting will be monitored by the Haemophilia Centre (cf section 7)

2.2.10. **Inhibitors**

Between 10 and 15% of patients with severe haemophilia A will acquire allo- antibodies to infused factor concentrate resulting in loss of efficacy of treatment. If this is suspected it can be confirmed by specific assay. Management is initially with increased doses of factor concentrate, bypassing agents such as FEIBA 50-100 IU/kg, or recombinant activated factor VII (r-FVIIa) 270 mcg/kg.

Emicizumab is a new monoclonal antibody which bridges the activation of Factor IX to Factor Xu without the need for FactorVIII are now licensed and approved for use by NHSE in liaison with a Comprehensive Care Centre – usually Bristol.

Given the potential considerable cost of treatment if Factor VIII inhibitor treatment is required, it is necessary to inform the Trust/Commissioners of new patients with Factor VIII inhibitors.

2.2.11. **Acquired Haemophilia**

Rarely, acquired haemophilia may be seen, usually in the elderly population, due to Factor VIII autoantibodies. The bleeding pattern is closer to that of Von Willebrand's Disease rather than congenital haemophilia.

Diagnosis should be suspected when there is no history of bleeding but APTT is unexpectedly prolonged and does not correct with mixing studies, and the FVIII level is low with an inhibitory antibody. Liaise with Consultant Haematologist. Guidelines for the management of Acquired Haemophilia are frequently updated by UKHCDO

Initial management should be to achieve Haemostasis: Either:

activated prothrombin complex concentrate ie (Baxter Healthcare) FEIBA 50- 100/kg max 200u/kg/day),

or

(Novo Nordisk) r-FVIIa eg one to three doses of 90 mcg/kg every 3 hrs or 270mcg/kg stat.

Immunosuppression:

First line: Prednisolone 1mg/kg/d and/or cyclophosphamide eg 50-100mg/d **Second line:** High dose immunoglobulin 2g/kg over 2-5 days

If there is no response within 6-8 weeks, second line therapies may be considered. These include Rituximab, and Cyclosporin A, multiple immunosuppressive agents (eg Azathioprine) and modified Malmo or Bonn regimens.

As with inhibitors in congenital patients it is advisable to inform the Trust/Commissioners of new patients

2.3. Clinical Review

Adult patients are generally reviewed in the Wednesday Haemostasis Clinic to determine patterns of bleeding, revise therapy schedules and assess complications such as arthritis or hepatitis C. Where necessary, multidisciplinary referrals are made.

Dependent on the disease severity review should be offered:

- Mild disease – every 1 year (this can be by telephone review)
- Moderate/Severe disease– every 6 months

2.3.1. Arthropathy/physiotherapy

Patients who experience joint bleeds and or have chronic arthropathy need assessment for the range of treatments by physiotherapists who are responsible for monitoring joint function and improving joints and muscles on a long-term basis. Physiotherapy may be required acutely. Joint routine review will be:

All patients with significant arthropathy – 6 monthly reviews

All other patients with severe haemophilia, or minor arthropathy- annual review

Orthopaedics- review as indicated

Haemophilia Joint Health Scores (HJHS) should be recorded at these reviews.

2.3.2. Children

The care of severely affected children and young people needs to be influenced by their changing physical and emotional development and as needed requires he regular input of specialist paediatric services.

Wednesday afternoon (quarterly with Dr Mullett) review as above, to include 6 monthly joint clinic with Paediatric Haematologists from Bristol Children's Hospital.

2.3.3. Standard follow-up investigations for patients with bleeding disorders

Full blood count, LFT's, specific factor if deficiency known.

Investigations for patients receiving regular factor therapy

As above plus coagulation for specific deficiency and inhibitor screen (state time and dose of last treatment on request form).

2.4. Special circumstances

2.4.1. Surgery

General and dental surgery must always b planned with the Haemostasis Team who will issue suitable pro-forma (Appendix 6).

Patients will be managed as detailed on the pro-forma.

Where appropriate further treatment is determined by levels taken in the post- operative period, thereafter daily.

Regular clinical assessment of haemostasis is crucial.

Patients at risk of viral transmission will be identified on the pro-forma.

2.4.2. Dental surgery

The necessity for the intensity of supportive therapy is largely consequent on the requirement for regional anesthesia. Evidence shows that tranexamic acid mouthwash is highly concentrated in the gums.

2.4.3. Dental extraction

Usually, it will be undertaken in the Oral Surgery Department.

Where possible this should be undertaken by local infiltration and, or intra-ligamental anesthesia,

When a mandibular block is required, overnight observation in hospital may be necessary:

Usually, desmopressin/factor treatment is as outlined for general surgery, Oral Tranexamic acid (5%) mouth wash is used and possible tranexamic acid-soaked surgical gauze.

2.4.4. Restorative therapy

Often may be undertaken by the patient's general dentist.

Simple local infiltration and, or intraligamental anaesthesia can be managed with oral tranexamic 25 mg/kg tds for 7 days (adults typically 1 g tds)

2.4.5. Hepatitis

The routine requirements for vaccination against Hepatitis A and B is no longer routinely recommended for patients with inherited bleeding disorders unless they have additional risk factors.

2.5. New patients

Those new patients with National Haemophilia Database (NHD) registerable diagnosis, should be given an NHD information sheet and asked for their verbal consent to be entered on the central NHD database.

All patients with NS registerable diagnosis should be entered on the Departmental excel database (section 8), at the time of diagnosis.

2.6. Treatment records

Patients, or their parents, should record of home infused factor usage and bleeding episodes, to enable collation of outcome data for the purposes of on-going care, audit and submissions to Commissioners.

This may be done either with either a Haemtrack handwritten paper record or preferably by Internet based systems (www.haemtrack.nhs.uk).

RCH-T Centre haemostasis patients' database.

This Excel spreadsheet lists current patients, their diagnosis and treatment of choice. The database is accessible on the Haematology Oncology server at g:/haemophilia/haemostasis patients MMYY.doc (current version).

Electronic copies are updated quarterly and circulated to:

All haematology consultants,

Dr A Mullett, Consultant Paediatrician

Dr A Clark Consultant Haematologist (Bristol Childrens Hospital) Haemostasis Clinical Nurse Specialist

Unit managers of Haematology clinic, Lowen, Polkerris, Sennen and AMU

Unit managers of the Accident and Emergency Departments at RCH and WCH Coagulation and Transfusion laboratory seniors

The Haemophilia Team and Data Manager should undertake data collection and collation

2.7. Carrier detection, genetic counselling, and antenatal diagnosis

2.7.1. Haemophilia carriers

Carriers of haemophilia may have low levels of factor VIII or factor IX and similar clinical problems to patients with mild haemophilia. These patients may also have particular problems with menorrhagia and bleeding at childbirth Factor VIII or IX assays should be recorded for all carriers of haemophilia.

Those who are identified as haemophilia carriers with or without low factor VIII or IX levels should be formally registered with NHD. Those with low Factor VIII and IX levels should be reviewed in the same manner as patients with mild haemophilia.

2.7.2. Identification of the haemophilia gene and carrier

Genetic counselling should be available before, during and after the process of haemophilia genetic analysis.

A pedigree study should be carried out for each family, to identify obligate carriers, possible carriers and non-carriers. Genetic analysis should be undertaken to establish carriership for female members of the family where there is a patient with haemophilia

Following a diagnosis of carriership, there should be specialised genetic counselling and education, so that carriers can understand the transmission of haemophilia within their own family

All patients with haemophilia should, with written consent, have genetic variation detection carried out

Identification of potential female carriers is essential, and a robust system must be in place to ensure they are offered testing at an appropriate age/time.

2.7.3. The carrier for Severe or Moderate Haemophilia and pregnancy

- Pregnancy is a potentially serious undertaking in haemophilia as both the mother and infant are at increased risk of bleeding
- Formal education about the transmission of haemophilia within the family should be given before starting a pregnancy, if at all possible
- There should be access to an expert fetal medicine unit for discussion of antenatal diagnosis and pre-implantation diagnosis
- A documented care plan for the delivery of any male infant should be established
- There must at all stages of the pregnancy be close collaboration between the obstetric team and the Haemophilia Centre
- Post-natal confirmation of the diagnosis should be carried out as soon as possible

3. Monitoring compliance and effectiveness

Information Category	Detail of process and methodology for monitoring compliance
Element to be monitored	Adherence to the Standard Contract for Haemophilia Service Specification (NHS England 2013) via quarterly reporting to the Specialised Services Quality Dashboard
Lead	Haemostasis MDT
Tool	Specialised Services Quality Dashboard
Frequency	Quarterly
Reporting arrangements	The reports will be discussed at each monthly MDT. Any changes identified in practice will be recommended.
Acting on recommendations and Lead(s)	Haemostasis MDT
Change in practice and lessons to be shared	Required changes to practice will be identified and actioned as necessary at each haemostasis MDT A lead member of the team will be identified to take each change forward where appropriate. Lessons will be shared with all the relevant stakeholders.

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Inclusion & Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Information Category	Detailed Information
Document Title:	Primary Haemostatic Disorders - Haemophilia and Related Conditions - Clinical Guideline V3.0
This document replaces (exact title of previous version):	Guidance for the Management of Primary Haemostatic disorders (Haemophilia and Related Conditions) V2.0
Date Issued/Approved:	May 2022
Date Valid From:	May 2022
Date Valid To:	May 2025
Directorate / Department responsible (author/owner):	Dr A Forbes, Consultant Haematologist & Haemophilia Director
Contact details:	01872 252524
Brief summary of contents:	Guidance for the care and management of patients with Primary Haemostatic Disorders at RCHT
Suggested Keywords:	Factor 8, Factor VIII, Factor 9, Factor IX Haemostasis, Haemophilia, von willebrand disease, bleeding
Target Audience:	RCHT: Yes CFT: No KCCG: No
Executive Director responsible for Policy:	Medical director
Approval route for consultation and ratification:	Haemostasis MDT
General Manager confirming approval processes:	Ian McGowan
Name of Governance Lead confirming approval by specialty and care group management meetings:	Suzanne Atkinson
Links to key external standards:	Standard Contract for Haemophilia Service

Information Category	Detailed Information
	Specification (NHS England 2013) Guidelines for the Management of Haemophilia (World Federation of Haemophilia 2020)
Related Documents:	See reference list
Training Need Identified?	No
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet & Intranet
Document Library Folder/Sub Folder:	Clinical / Haematology

Version Control Table

Date	Version Number	Summary of Changes	Changes Made by
Jan 2012	V1.0	Initial Issue, in new Trust Format	Dr MD Creagh Haemophilia Director
April 2015	V1.2	Updated standards in line with new national contracts. Updated guidance in line with recent publications. Rewritten to fit Trust Clinical Guideline format	Dr MD Creagh, Haemophilia Director Sarah Johns Haemostasis CNS
June 2018	V2.0	Updated standards in line with new national contracts. Updated guidance in line with recent clinical advances	Sarah Johns Haemostasis CNS Dr MD Creagh Haemophilia Director
May 2022	V3.0	• Updated with new international guidance. • Updated product list and availability • Updated internal and external contact details for Haemostasis Team	Sarah Johns

Appendix 2. Equality Impact Assessment

Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity & Inclusion Team rcht.inclusion@nhs.net

Information Category	Detailed Information
Name of the strategy / policy / proposal / service function to be assessed:	Primary Haemostatic Disorders - Haemophilia and Related Conditions - Clinical Guideline V3.0
Directorate and service area:	General Surgery and Cancer Haematology
Is this a new or existing Policy?	Existing
Name of individual completing EIA (Should be completed by an individual with a good understanding of the Service/Policy):	Sarah Johns
Contact details:	01872 252524

Information Category	Detailed Information
1. **Policy Aim - Who is the Policy aimed at?** (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed)	Guidelines for Care & Management of Patients with Primary Haemostatic Disorders at RCHT
2. **Policy Objectives**	To ensure safe and effective 24 hour care for patients with Primary Haemostatic Disorders at RCHT
3. **Policy Intended Outcomes**	Safe and effective delivery of care
4. **How will you measure each outcome?**	Audit of care delivery

Information Category	Detailed Information
5. Who is intended to benefit from the policy?	Patients with Haemostatic Disorders who require routine and emergency care at RCHT
6a. Who did you consult with? (Please select Yes or No for each category)	• Workforce: Yes • Patients/ visitors: Yes • Local groups/ system partners: No • External organisations: No • Other: No
6b. Please list the individuals/groups who have been consulted about this policy.	**Please record specific names of individuals/ groups:** Haemostasis MDT
6c. What was the outcome of the consultation?	No action required - Approved
6d. Have you used any of the following to assist your assessment?	None

7. The Impact

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

Protected Characteristic	(Yes or No)	Rationale
Age	No	
Sex (male or female)	No	
Gender reassignment (Transgender, non-binary, gender fluid etc.)	No	
Race	No	

Protected Characteristic	(Yes or No)	Rationale
Disability (e.g. physical or cognitive impairment, mental health, long term conditions etc.)	No	
Religion or belief	No	
Marriage and civil partnership	No	
Pregnancy and maternity	No	
Sexual orientation (e.g. gay, straight, bisexual, lesbian etc.)	No	

A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment: Dr M D Creagh, Sarah Johns and Human Rights, Equality & Inclusion Lead

If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:
Section 2. Full Equality Analysis

Appendix 3. Synopsis of the acute management of patients with haemophilia and related conditions

On Presentation: Assess the site and extent of the bleed, the national standard is assessed within 30 minutes of presentation

Investigations

- It is unnecessary to repeat the APTT or Factor level
- For a severe bleed check the full blood count and a citrated sample for “save plasma”.
- Group and screen if clinically indicated.
- Management is dependent on the nature of the bleed, the deficiency and its severity, as documented in the patient’s red Bleeding Disorder card
- *Routinely* confirm the management and need for further therapy with the on-call Consultant Haematologist

Treat promptly

Determine additional measures e.g. rest or admission

NB *The On call Consultant Haematologist should routinely be informed* of a patient’s attendance with a bleeding problem and they should never be discharged without treatment unless in consultation with the on-call haematology consultant,

Appropriate treatment- (as directed by Consultant Haematologist)

Coagulation Factors should be ordered from Blood Bank on a Transfusion Request Form.

Desmopressin (ordered as OCTIM) should be ordered from pharmacy by it’s brand name, out of hours held in the fridges on MAU, ED & Lowen

Haemophilia A -

Severity	**Baseline factor Level**	**Treatment**
Mild	>5	Usually desmopressin
Moderate	1 – 5	Usually factor concentrate.
Severe	<1 iu/dl	Always factor concentrate

Haemophilia B

These patients do not respond to desmopressin and require specific FIX concentrate therapy

Von Willebrand's disease

Most patients have mild type 1 disease and have an excellent response to desmopressin, Desmopressin should be avoided in the treatment of significant head injury.

Type 2 patients have a variable response to desmopressin, and is ineffective in the severe type 3 disease, for these patients factor concentrate is required for control of haemorrhage.

Factor concentrate, administration and dosage

Recombinant (genetically) manufactured, or a plasma derived specific product.

Re-constitute with the accompanying diluent as per the manufacturer's recommendations. infuse intra-venously, as per manufacturer's instructions.

Diagnosis	**Appropriate choice of product** Consult excel spreadsheet for individual patients
Haemophilia A (factor VIII deficiency)	Recombinant Factor VIII
Haemophilia B (factor IX deficiency)	Recombinant Factor IX
Von Willebrand's Disease	Plasma derived Factor VIII
other deficiences, e.g. FXI,	as per consultant direction

General treatment outline – as per World Federation of Hemophilia (WFH) Guidelines (2012)

Condition/bleed site	Requisite post-treatment factor level for haemostasis
Minor spontaneous bleeding or joint bleed	40-60
Severe bleeding, e.g., muscle or profuse haematuria	40-60
Major surgery or significant **head injury***	80-100

Desmopressin (acetate) – OCTIM 15microgrammes/ml synthetic analogue of anti-diuretic hormone

Boosts factor VIII and von Willebrand factor levels 2 to 4-fold, give either IV (in 100mls 0.9% Sodium Chloride), or subcutaneously once (or twice daily), activates the fibrinolytic pathways so give tranexamic acid in conjunction.

Best avoided in significant head injury, due to ADH effect, patients should be water-restricted, to quench their thirst for the following 24 hours.

Desmopressin dose = 0.3 micrograms/kg either undiluted SC or IV in 50-100 ml saline over 20 minutes

Tranexamic acid – orally: 25 mg/kg tds for 7 days (adults typically 1 g tds) I.V: 10mg/kg tds

N.B. Should not be used in patients with haematuria, pregnancy or those with a thrombotic history.

Additional management:

In the case of severe trauma or surgery further factor may be administered by bolus or infusion

May require admission for bed rest +/- further therapy at direction of Consultant Haematologist.

Appendix 4. RCH guidance: Congenital bleeding disorders - management of pregnancy and the newborn.

All patients with haemophilia A & B to have genealogy completed

Offer counselling and phenotypic/genetic diagnosis to potential carriers Offer follow up for carriers and partners considering pregnancies

Confirmation of suspected family history and counselling

At booking, refer known or possible carriers to Haematology Dept for: Confirmation of family bleeding disorder

Counseling regarding

the diagnosis and its implications antenatal diagnosis

Establish the risk for an affected fetus

As indicated arrange phenotypic/genetic diagnosis by cordocentesis or CVS sexing (20 weeks) by USS of known or potential carriers

Determination of maternal risk of bleeding:

Factor levels at 32-36 weeks of gestation

Peri-partum management plan, covering possible use of desmopressin, or as necessary (recombinant) factor concentrate, if difficult labour, borderline levels, or unexpected bleeding.

Plan for delivery:

Delivery of a possible affected case should be at RCH, unless otherwise agreed Delivery route should be on the basis of obstetric indications

But avoid ventouse, instrumental delivery and fetal scalp monitoring

Management of neonate):

For severe and moderate only: Obtain **urgent** 5ml cord (sky blue citrated) or 1ml venous blood (blue paediatric bottle) sample for coagulation screen/ specific factor analysis Inform Consultant Haematologist of birth

Avoid IM injections Give oral vitamin K

In an affected neonate:

If traumatic delivery, consider specific factor concentrate Consider routine USS to exclude ICH at day 3.

Consider early hepatitis B vaccination (by SC route)

Blood tests by heel prick sampling should be taken with great care (pressure for 3 minutes)

Arrange follow up in joint Paediatric Haemostasis Clinic

Obstetric Management Plan for Patients with Inherited Bleeding Disorders

Name:		***DOB:***	
Address:		***CR No:***	
		NNHS No:	
EDD:			
Haematology Consultant:			
Obstetrician:			
Diagnosis:			
Pre pregnancy blood results:			
Third trimester blood results (date):			
Pre pregnancy weight (kg):			
Previous Medical History:			

This patient will need to be admitted as soon as labour begins, aim should be for an atraumatic birth but must be guided by obstetric indication.

Plan for delivery		
On admission:	*Inform Consultant Obstetrician* *Inform On call Consultant Haematologist* *Check bloods as indicated:*	*YES / NO* *YES / NO* *YES / NO*
Initial treatment once labour is established:	•	
Monitoring:	•	
Post-Partum:	• .	

Anaesthetic plan

General Care of mothers with a bleeding disorder:

- Plan for delivery at Delivery Suite, RCH Truro
- Where delivery is planned (IOL or CS) plan for a Monday or Tuesday
- Avoid prolonged 1st or 2nd stage labour (allow adequate time e.g within guidance)
- Avoid Ventouse , can do gentle forceps as this may be safer than fully dilated lscs
- FSE can be used , but only one application and if would benefit clinical situation
- Avoid FBS

Care of the Neonate

Risk to the neonate:	
During delivery:	
Post delivery:	
Additional Information:	

Copies to:

- Patient – to be held in maternity notes
- Consultant Obstetrician
- Haemophilia Director
- Consultant Paediatrician
- Obstetric Anaesthetist
- Delivery Suite
- Blood Transfusion Laboratory
- Coagulation Laboratory

References:

Management of Inherited Bleeding Disorders in Pregnancy (RCOG & UKHCDO - April 2017)

Appendix 5. Vaccinations and injections In Children with bleeding disorders

Children with Haemophilia, Von Willebrand's disease and other bleeding disorders can get painful muscle bleeds (haematomas) if given intramuscular injections. Alternative routes are preferred- Deep subcutaneous injection for most vaccinations

Oral vitamin K following birth

Vitamin K deficiency may occur in the first few months of life and can lead to serious bleeding (Haemorrhagic disease of the newborn). Babies in the UK are offered Vitamin K to prevent this, usually by intramuscular injection. If given orally several doses are needed because it is not so well absorbed into the body compared to intramuscular injection. Doses are given:

Following birth

Second dose at 4-7 days

Third dose at 1 month and each subsequent month if exclusively breast-fed. (Third and subsequent doses not required if on formula milk or weaned)

Vaccinations

Routine childhood vaccinations should be given by the subcutaneous route, except BCG, which is given intradermally. MMR vaccination should be given deep subcutaneous injection. These vaccinations can be done at the usual recommended ages and can be done in the GP surgery or school.

Intradermal injection for BCG

Appendix 6. List of additional documents, pro-formas and templates:

The following guidance and pro-formas are available on the Haematology Oncology server (under k:/protocols and specific diseases/haemostasis/)

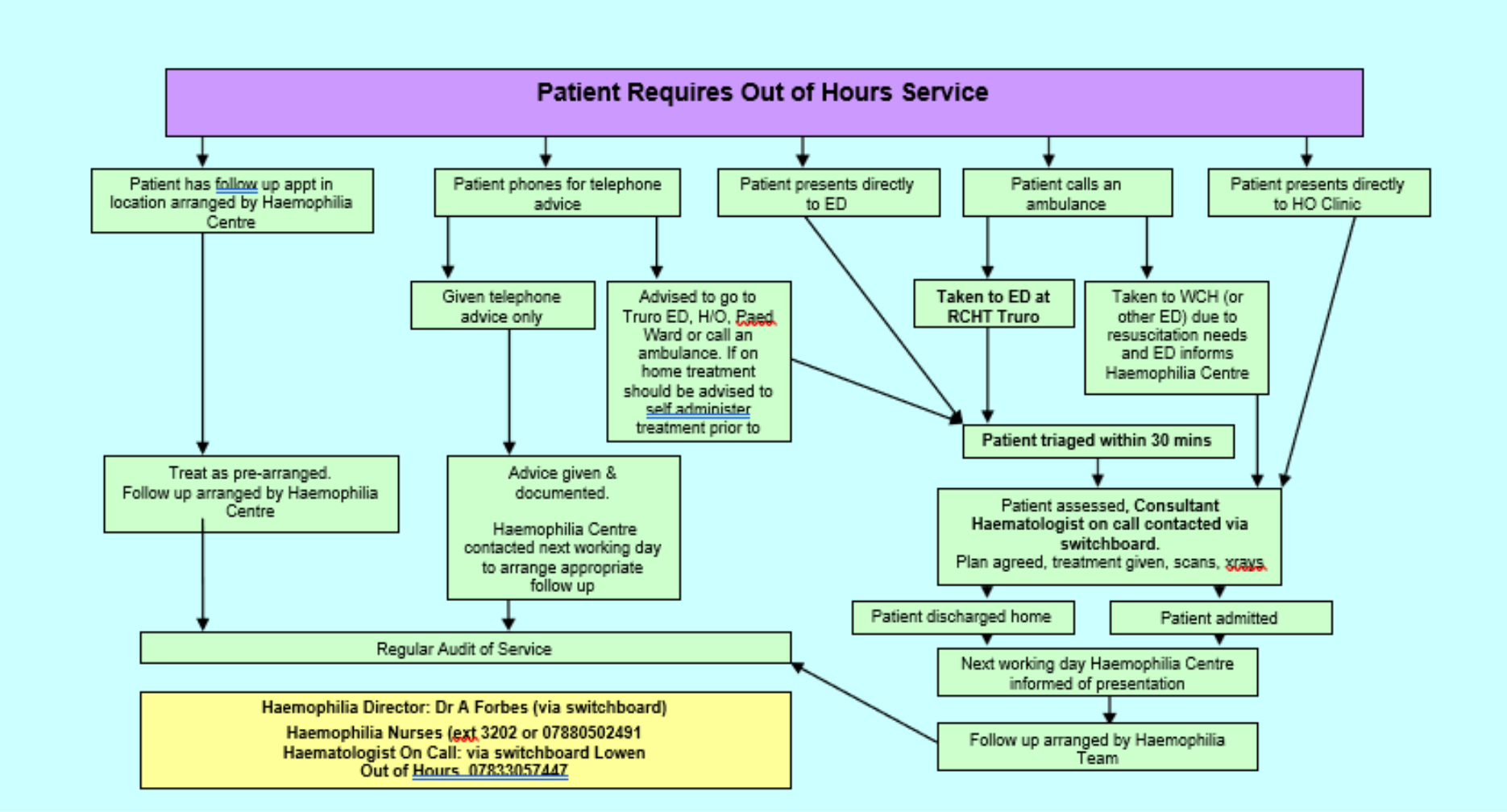
Management of primary disorders of haemostasis Protocol for factor concentrate management in surgery Protocol for use of desmopressin management in surgery

Surgery in patients with low risk of bleeding

Desmopressin and Tranexamic acid patient information

Clinical guideline for the prescribing and administration of continuous infusion of clotting factor concentrates

Appendix 7. RCHT Pathway for Out of Hours Assessment Treatment and Follow Up of Patients With Primary Haemostatic



Appendix 8. Availability of Coagulation Factor Concentrates

Whilst preferable not to change product for a patient on regular treatment*, where treatment is necessary (usually for a holidaymaker) it is acceptable to substitute the patient's usual product for one held in stock at RCHT.

*Many visitors with a severe bleeding phenotype will carry their own emergency (initial) supply of factor

Type of Product	**Indication for use**	**Products held in stock at RCHT**	**Brand names of other products**
Recombinant Factor VIII	Moderate & Severe Haemophilia A	NovoEight (NovoNordisk) Advate (Baxter) Elocta (Sobi) EHL Esperoct (Novonordisk)EHL	Helixate (CSL Behring) Refacto AF (Pfizer
Plasma Derived Factor VIII (intermediate purity)	Moderate & Severe Haemophilia A Type 2 & 3 von Willebrand Disease which is unresponsive to desmopressin or where desmopressin is contraindicated	Wilate (Octapharma) Voncento (CSL) (2:1 ration vw:f8)	Alphanate (Grifols)
Recombinant Factor IX	All types of Haemophilia B	Benefix (Wyeth) Idelvion (CSL) EHL	Alprolix (Sobi) EHL
Plasma Derived Factor IX	All types of Haemophilia B	Not held in stock	Mononine (CSL Behring) Replinine VF (BPL) Alphanine (Grifols) Haemonine (Biotest UK)
Recombinant Von Willebrand Factor	VWD unresponsive to desmopressin and those naïve to previous plasm products. NB care must taken to maintain adequate FVIII level	Veyvondi – by special order only	None
Bypassing Agents	All inhibitor patients	FEIBA (pd) (Baxter) NovoSeven (recombinant) (NovoNordisk)	NA

Activated Prothrombin Complex Concentrates (APCC's)		Beriplex (CSL Behring)	Octaplex (Octapharma)

Appendix 9. References and links

These guidelines are drawn together with reference to published guidance from the UK Haemophilia Centre Doctors' Organisation (UKHCDO).
http://www.ukhcdo.org/UKHCDOguidelines.htm

Emergency and out of hours care for patients with bleeding disorders –
Standards of care for assessment and treatment.(2010) UKHCDO website

Guideline on the selection and use of therapeutic products to treat haemophilia and other hereditary bleeding disorders. A United Kingdom Haemophilia Center Doctors' Organisation (UKHCDO) guideline approved by the British Committee for Standards in Haematology Haemophilia, 14, 671-684

The diagnosis and management of von Willebrands Disease: a UKHCDO guideline approved by the BCSH (BJH 2014)doi10.111/bjh13064http://www.blackwellpublishing.com

Guideline for the Diagnosis and Management of the Rare Coagulation Disorders Haemophilia, Volume 19, Issue 3, pages e191–e192, May 2013

Guidance on the dental management of patients with haemophilia and congenital bleeding disorders British Dental Journal, 215:497-504, 2013

Diagnosis and treatment of factor VIII and IX inhibitors in congenital haemophilia: (4th edition) Br J Haematol, 160:153-170, 2013

Diagnosis and management of acquired coagulation inhibitors: a guideline from UKHCDO Br J Haematol, 162:758-773, 2013

Recombinant Factor VIIa concentrate versus plasma derived concentrates for the treatment of acute bleeding episodes in people with Haemophilia A and inhibitors. Hind D, Lloyd-Jones M, Makris M, Paisley S. (Cochrane Review). In: The Cochrane Library, Issue 3, 2004. Chichester, UK: John Wiley & Sons, Ltd.

Guidelines on the diagnosis, management and prevention of hepatitis in haemophilia (Haemophilia (2001), **7**, 339-345) http://www.blackwellpublishing.com

Neonatal haemostasis and thrombosis - British Committee for Standards in Haematlogy 2002

The Haemophilia Society offers support and patient information at
http://www.haemophilia.org.uk

Appendix 10. Members of the Haemostasis Team

Consultant Haematologist & Haemophilia Director	Dr A Forbes	01872 252501
Consultant Haematologists	Dr M Furtado	
	Dr R Witherall	
	Dr D Tucker	
	Dr B Pottinger	
	Dr E Parkins	

Nurses

Advanced Nurse Practitioner	Sarah Johns	01872 253202 07880502491
Clinical Nurse Specialist	Davina Hocking	Rcht.haemostasisnurses@nhs.net
Nurse Specialist	Jenny Green	

Paediatrics

Consultant Paediatrician	Dr A Mullett

Obstetrics

Consultant Obstetrician	Dr S Haynes

Physiotherapy

Physiotherapist	Sophie Hendriksz

Laboratory

Lead Coagulation BMS	Claire Errington
Coagulation BMS	Megan George
Lead Transfusion BMS	Ian Sullivan
Transfusion BMS	Sam Passmore
Transfusion BMS	Georgina Morley

Bristol Comprehensive Care Centre

Haemophilia Consultants	Dr A Clark	0117 342 1872
	Dr A Knott	
Paediatric Nurse ANP	Anna Farrell	