Clinical Guideline
MANAGEMENT OF BLEEDING EPISODES IN CHILDREN WITH HAEMOPHILIA AND OTHER HERITABLE BLEEDING DISORDERS

SETTING
Bristol Royal Hospital for Children

FOR STAFF
Clinical

PATIENTS
Children with inherited bleeding disorders

1. INTRODUCTION

Haemophilia

Haemophilies A and B are the congenital deficiencies of clotting Factors 8 and 9 (F8 and F9, sometimes FVIII and FIX) respectively. The typical clinical manifestations are spontaneous and trauma-related haemorrhages. Common sites for bleeds include joints (haemarthroses), soft-tissue and muscle, and mouth. Of particular concern are intra-cranial haemorrhages. The cornerstone of therapy is prompt recognition and early replacement therapy with recombinant factor concentrate.

All children with severe haemophilia - baseline levels < 1 iu/dl (0.01 iu/ml or 1%) - and some with moderate or mild haemophilia – baseline levels 1-5 iu/dl and >5 iu/dl respectively - receive prophylactic recombinant factor replacement from the age of around 1. This is given every 24-96h depending on the factor used and the child and dramatically reduces the incidence of bleeds though bleeds do still occur. These children have a home supply of factor concentrate, their families are able to treat independently, and they often will have a Portacath indwelling central venous catheter.

Inhibitor patients

Some patients develop antibodies that inactivate the infused F8 (common) or F9 (rare). These antibodies are termed inhibitors. Management of children with inhibitors can be very complicated and often factor concentrate is ineffective. All inhibitor patients must be discussed with the second on call consultant for Benign Paediatric Haematology; this would normally be prior to treatment unless there is clear instruction in a recent treatment plan as to what to do.
**Von Willebrand Disease**

Von Willebrand Disease is a bleeding disorder of variable severity. Treatments include DDAVP, tranexamic acid, and in severe cases or bleeds, plasma-derived, intermediate purity factor 8 concentrate (Wilate or Voncento in BRHC). Patients should have an active treatment plan on Medway.

Other clotting factor deficiencies are rare and their management is specialised. Please seek advice.

As treatment for inherited bleeding disorders is given more and more in the community, in the absence of the Paediatric Haemophilia Team, the haemophilia expert is likely to be the parent. In the past, significant errors in patient care have almost always followed clinicians dismissing concerns raised by parents. Please listen to parents and pay attention to any concerns raised.

2. **WHO TO CONTACT**

During normal working hours, 8am to 6pm, treatment should be coordinated by the Benign Haematology CNSs, Anna Farrell (x28721, mobile 07747004996), and Caroline Roberts (x28721, mobile 07920545620) or Ocean Unit 28145.

Between 6pm and 10.30pm, the first contact should be the Paediatric Haematology/Oncology Registrar. Children may need to be assessed by the ED team initially but all treatment decisions should be discussed with the Haem/Onc Registrar and/or second on-call Benign Paediatric Haematology Consultant (rota in CED and with Haem/Onc Registrar and Consultant on call) who should be informed of all attendances.

In the rare instance that a child with a bleeding disorder presents after 10.30pm, they should be assessed and have initial management in ED. Advice should be sought from the second on-call Benign Paediatric Haematology Consultant and treatment given without delay.

3. **NECESSARY INFORMATION AND WHERE TO GET IT**

To manage a child with an inherited bleeding disorder accurately, certain information is essential:

- Diagnosis
- Baseline factor levels
- Regular treatment (if any)
- Normal treatment centre

This information is available in a number of sites:

- Special patient information on Evolve
- Clinic letters (on CDS/Evolve)
- UKHCDO bleeding disorders card
- On treatment register – attached to factor concentrate fridge in Ocean Unit
- Parents and/or patient

Up-to-date treatment plans should be on Medway and Evolve and sometimes with the family – please refer to this if current.
4. **DIAGNOSIS AND IMAGING**

**Imaging is not usually informative or necessary.** In most cases, a bleeding episode is obvious. Joint and soft tissue bleeds are characterised by pain, swelling, and limitation of movement. Plain X-rays are not helpful unless there is a significant trauma history. Ultrasound can sometimes be useful in assessing bleeds but should not delay treatment. **If in doubt, for all patients other than those on emicizumab (Hemlibra),** treat as a bleed especially if the child is unable/unwilling to use a limb or weight-bear.

Head injuries and possible GI bleeds should always be taken seriously in a child with haemophilia. Any head injury significant enough to result in hospital attendance should normally be treated to 100 iu/dl (100%) especially if the child is symptomatic. A low threshold for CT scanning is appropriate.

5. **TREATMENT – WHAT TO GIVE**

Treatment options in haemophilia and inherited bleeding disorders are complicated and can be confusing to those not in the field. It is imperative that children receive the correct product – **if in doubt, ask.**

Haemophilia A without inhibitors is treated with a recombinant factor 8 (rF8) product. There are a number of different products in use in BRHC including, **Refacto, Advate, Novoeight** and the long-acting products **Elocta** and **Bax855** (mostly trial patients). In general, children on regular treatment have their own supply and parents are encouraged to treat before they come in or to bring their product with them. Trial patients should receive trial supply.

Milder (baseline F8 > 10iu/dl) cases of Haemophilia A can sometimes be managed with **DDAVP.**

Haemophilia B is treated with F9. Products in use in BRHC include **Benefix, Alprolix and Idelvion.**

**Inhibitor patients** with antibodies against F8 or F9 require special treatment as factor concentrate is ineffective. Please discuss management with Benign Paediatric Haematology Consultant.

Some inhibitor patients will be receiving immune tolerance therapy with large doses of factor concentrate – treating bleeds in this group of patients is complicated and needs to be discussed with the Benign Paediatric Haematology Consultant. Treatment may involve high doses of factor, recombinant FVIIa (Novoseven - typical dose 270 microgram/kg), or activated prothrombin complex (FEIBA 50-100iu/kg).

Other inhibitor patients will be receiving **Emicizumab (Hemlibra) prophylaxis.** This is a new drug that mimics F8 and near-normalises the clotting system – our best estimates are that Hemlibra results in the clotting system working at the equivalent level to when F8 levels are 20iu/dl. Children with F8 levels of 20iu/dl very rarely bleed. The drug appears to be very safe when used on its own but life-threatening complications have been reported with the concomitant use of FEIBA in patients receiving Emicizumab. **Do NOT give FEIBA to Emicizumab patients.** In contrast to other haemophilia patients, the risk/benefit balance is not in favour of treating. If in doubt, the diagnosis of a bleed should be questioned. If treatment is necessary, significant bleeding or trauma should be treated with **Novoseven** 45 microgram/kg 4 hourly initially. Mild/moderate bleeding can be treated with **Tranexamic Acid** alone.
No recombinant concentrates are available for treatment for von Willebrand’s disease. vWD is treated with intermediate purity factor 8 concentrate – in BRHC this is Wilate or Voncento - milder cases can be managed with DDAVP.

Glanzmann’s Thrombasthenia is a severe platelet function defect and typically presents with mucocutaneous bleeding e.g. epistaxis. Although tranexamic acid is useful and Novoseven can be helpful, definitive treatment is with platelet transfusion. Children should be given HLA-matched platelets (ordered from NBS) if time allows.

TRANEXAMIC ACID, an antifibrinolytic, is a useful drug in haemophilia and other bleeding disorders. In mild cases or mild trauma, it can be given on its own or it can be a useful adjunct to factor replacement. It should not be used if there is macroscopic haematuria – risk of clot retention.

6. TREATMENT – HOW MUCH TO GIVE AND HOW TO PRESCRIBE IT

Mild haemophilia A and vWD can sometimes be managed with DDAVP (DESMOPRESSIN):

Dose: 0.3 micrograms/Kg subcutaneously (or IV)
Contraindications: Type IIb vWD (usually)
                    Age <2 years old

If it is appropriate for the child to receive DDAVP, this will usually be documented in their notes or on the patient list in Ocean Unit. The DDAVP used to treat children with bleeding disorders is OCTIM (15 micrograms/ml) kept in the factor fridge in the treatment room in Ocean Unit. For IV use, dilute down to 4 micrograms/ml concentration (generally best to use subcut). Appropriate advice should be given about restricting fluid intake if DDAVP is given.

**Dosage of factor concentrate**

Factor concentrate dosage is calculated using the following formula:

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\text{Number of units of factor} = \frac{\text{Rise required (iu/dl or %) x Weight (Kg)}}{K}
\]

Rise required = (target level – baseline).
K is the constant for the factor. The K value for factor 8 products (haemophilia A and vWD) is 1.5. The K value for F9 products is 1.

Target factor levels should be 60 – 120 iu/dl (or 0.6 – 1.2 iu/ml) for significant bleeding. Practically this means giving 40-80 iu/kg for F8 (normally twice the normal prophylactic dose); 60-100 iu/kg for F9. Round up to the nearest whole vial size except in very small infants.

**Factor concentrate must be prescribed using the trade name of the product and not generic factor concentrate (e.g. Refacto AF, not recombinant Factor 8). Factor concentrate should not be issued or given if prescribed incorrectly.**

Tranexamic acid is given at a dose of 15 mg/kg IV TDS or 15-25 mg/kg PO TDS.

IV Tranexamic acid can be used topically - soak swabs in IV solution.
7. TREATMENT – WHERE TO GET IT

Factor concentrates and DDAVP are kept in the factor fridge in the treatment room within Ocean Unit. Only designated staff may remove factor concentrate from the fridge. This would normally be one of the Benign Haematology CNSs, Ocean Unit staff, a member of the Haematology/Oncology medical team, ED staff or overnight, a member of the site team. Anyone removing factor from the fridge is responsible for making sure that they know which factor is appropriate for the patient and that they have a valid prescription, i.e., specific product prescribed not generic prescription. Please ensure the child’s details and the factor batch number is recorded in the haemophilia folder in Ocean Unit.

The keys for the factor fridge are kept on Ocean Unit. Out of hours and at the weekend these keys are kept in the key safe in the Ocean Unit drugs room. A supply of the factor concentrates used regularly are kept on Ocean Unit but the main haemophilia factor fridges are in BHOC and if the factor concentrate prescribed is not on Ocean Unit it can be obtained from D703 in BHOC. Factor concentrates will not be issued from D703 without a valid prescription.

If Recombinant FVIIa (Novoseven) is required, please note that this is kept in Blood Bank and will need to be obtained via the transfusion laboratory. It will not be issued without a valid prescription and authorisation from a Paediatric Haematologist.

8. TREATMENT – HOW TO GIVE IT

Each factor concentrate comes with a reconstitution device. These vary slightly from product to product. Each box of will have information on how to reconstitute the factor concentrate. The factor concentrate should be reconstituted at room temperature – this can be achieved by warming the vials in tepid water for 5 minutes. Once reconstituted the factor concentrate should be used within one hour or discarded.

Factor concentrate should be administered via slow intravenous injection. This is usually via a butterfly needle; if there is a possibility that further doses of factor concentrate will be needed then a cannula should be sited. Some children have a Portacath in situ which should be used; if parents are competent in accessing these they should be encouraged to do this.

9. FURTHER POINTS

a) Discuss all patients with the second-on consultant for Benign Paediatric Haematology/Haemophilia.

b) Severe joint bleed or ileo-psoas bleed – consider admission for bed rest/analgesia.

c) Have a low threshold for CT scan & admitting head injuries for observation.

d) Consider tranexamic acid.

e) NSAIDs should only be used if adequate factor replacement has been given.

f) Any surgical procedure (including LP) needs to have adequate factor cover.

g) Ensure the Paediatric Haemophilia team is informed of all attendances.
### References


- **Guideline on the selection and use of therapeutic products to treat haemophilia and other hereditary bleeding disorders.** Keeling et al. for the United Kingdom Haemophilia Centre Doctors’ Organisation (UKHCDO). Haemophilia (2008), 14, 671–684


- **Guidelines for the management of acute joint bleeds and chronic synovitis in haemophilia.** Hanley et al for the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO). Haemophilia (2017) 1-10

### Related Documents and Pages
- Bleeding Disorders in The Children’s Emergency Department
- Safe Administration of Replacement Factor Concentrate

### Authorising Body
- QUAF

### Safety

### Queries and Contact

Any queries should be directed to: Anna Farrell/Caroline Roberts, Paediatric Haemophilia CNSs, on ext 28721 or 07747 004996/07920545620 or to Oliver Tunstall/Emma Phillips, Paediatric Haematology Consultants, via hospital switchboard.

Out of hours contact the on call Paediatric Haemophilia consultant.