Physiotherapy Information Pack

Haemophilia

Produced by the Haemophilia Chartered Physiotherapists Association
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1. **Background**

Haemophilia describes a group of inherited bleeding disorders in which there is a lifelong defect in the clotting mechanism of the blood. The most common conditions are Haemophilia A (deficiency of factor VIII) and Haemophilia B (deficiency of factor XI). Haemophilia A occurs in approximately one of 5000 live male births and is 5-6 times more common than haemophilia B. Haemophilia A and B are clinically similar and can only be distinguished by assays of factor VIII and IX activity. Haemophilia is an X-linked recessive condition and therefore only males are affected.

The severity of the condition is related to the percentage of clotting factor in the blood.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Percentage of normal clotting factor levels</th>
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<tr>
<td>Severe</td>
<td>&lt;1%</td>
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<tr>
<td>Moderate</td>
<td>1-5%</td>
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<tr>
<td>Mild</td>
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For physiotherapists the severity of the patient’s bleeding disorder is probably the most important thing to establish on initial assessment.

Patients with severe haemophilia can experience bleeding episodes with minimal or no trauma. For patients with moderate and mild haemophilia joint or muscle bleeds usually occur due to a specific event such as trauma or surgery. Although bleeding can occur at almost any site, intra-articular bleeding is the most common manifestation, accounting for about 80% of all bleeds, and the ankles, knees and elbows are most frequently affected. Muscle bleeds account for a further 10%.

Currently, there is no cure for haemophilia and treatment focuses on the regular provision of the missing coagulation factor to control or prevent bleeding.

**Treatment of Haemophilia**

Intravenous replacement of the deficient clotting factor is used to treat and prevent bleeding episodes in patients with haemophilia. Currently recombinant factor concentrates, that have been genetically engineered, are the treatment of choice.

Treatment can be given “on-demand” or as prophylaxis.

**On Demand** treatment is used to treat bleeds promptly when they arise, aiming to stop the bleed and prevent re-bleeding. Patients with severe haemophilia usually have a stock of factor at home that they can access quickly when needed. Other patients will have to travel to their nearest hospital/treatment centre for a factor rise.
**Prophylaxis** is used for many patients with severe haemophilia and involves a regular infusion of the deficient coagulation factor. The aim of prophylaxis is to prevent bleeding episodes by maintaining factor levels above 1% at all times. In patients with factor VIII deficiency this is usually achieved with 3 infusions per week, compared with only 2 per week for factor IX due to the longer plasma half-life of factor IX. Prophylaxis commences as early as 2 years of age and can continue into adulthood.

PWH who have been on prophylaxis for life, should experience very few joint bleeds and therefore have very little joint damage. Older patients who did not have access to this type of treatment before the 1980’s will almost certainly have bleeding related joint damage as described below.

**Inhibitors**

The most significant treatment –related complication is the development of antibodies, known as inhibitors, against the administered clotting factor. The patients’ immune system recognizes the infused factor as a foreign material and mounts an immune response against it. This makes the use of standard FVIII/IX ineffective and necessitates the use of a “bypassing agent” such as activated prothrombin concentrates (FEIBA) or recombinant factor VIIa (Novo7). These are less effective than standard factor replacement and have a much shorter half-life of about 1.5 hours. They are also more expensive.

Inhibitors develop in about 25-30% of patients with severe haemophilia and are more commonly seen in FVIII deficiency than FIX.

In young patients with persistent inhibitors immune tolerance regimens may be used to eradicate the inhibitor. Regular (usually daily) infusions of high doses of factor are administered in an attempt to eradicate further inhibitor production. Timing of physiotherapy intervention around the administration of factor treatment is even more crucial with these patients.

**Viruses:**

In the 1970’s and 1980’s a large number of haemophiliacs worldwide were infected with viruses such as HIV and Hepatitis B and C. This was a result of the use of clotting factor derived from contaminated human plasma.

**Signs and symptoms of a bleed**

Following an acute bleed the joint is usually presents warm, swollen and held in an open-pack position of ease. Usually all joint movements are painful. Contraction of the muscles around the joint also increases pain.
The patient may not recall any precipitating event to trigger the joint bleed, but careful questioning regarding their recent activity may point to a cause the patient had not noticed at the time.

Prompt factor replacement to stop the bleeding is the essential first step in the management of a joint bleed. This acute episode of haemarthrosis usually is resolved in about 1 week, the blood being progressively removed from the joint space by the synovial membrane. It can take up to 2-4 weeks or longer before full recovery of the joint to baseline strength and flexibility.

**Joint damage**

Haemophilia is characterized by intra-articular bleeds mainly affecting the ankles, knees and elbows. Bleeding into the joint initiates a cycle of synovial inflammation and cartilage destruction. Over the long-term, this cycle causes irreversible damage to the joint leading to haemophilic arthropathy. This can affect multiple joints causing joint stiffness, pain and functional deficits. Haemophilic arthropathy exhibits 2 main features – chronic synovitis and blood-induced cartilage damage.

**Chronic synovitis**
The synovial membrane is responsible for the removal of blood from the joint space. Following a large bleed, or several bleeds in close succession, the large volume of blood triggers an inflammatory response in the synovial cells. The membrane becomes thickened, friable, and more vascular and is susceptible to more frequent bleeding episodes. This vicious cycle of bleed – synovial inflammation – re-bleed is known as Chronic Synovitis. The joint will generally appear swollen and may be warm but may not necessarily be painful. The inflamed synovium releases tissue-destructive inflammatory mediators such as enzymes and cytokines, which damage the articular cartilage. Ultimately the synovial tissue becomes fibrotic.

As the presence of synovitis causes ongoing cartilage damage, it is important that it is recognized early and treatment started as soon as possible. Initially regular prophylaxis is used, aiming to break the bleed – synovitis – bleed cycle. If this is ineffective, a synovectomy may be indicated.

Synovitis also causes hypertrophy of the epiphyseal plates, resulting in various deformities such as leg length discrepancies and angular deformities.

**Blood induced cartilage damage**
In addition to this synovitis driven damage, it is now known that the presence of blood in a joint has a directly harmful effect on articular cartilage. It is recognized that the iron which is released from the breakdown of red blood cells affects normal cartilage turnover and results in a net loss of proteoglycans from the extra-cellular matrix. This effect has been shown to last at least 10 weeks and
possibly much longer. Therefore, even one joint bleed can be sufficient to initiate a process of degeneration within the articular cartilage resulting in long term joint damage.

Additionally, there is evidence that younger cartilage is more susceptible to blood-induced damage, therefore young children are at particular risk of joint damage from haemarthrosis. It is also known that impaired cartilage is at least as susceptible to blood-induced joint damage as healthy cartilage. Thus prevention and proper treatment of joint bleeding is important in joints already affected by bleeding related damage.

Importantly, degenerative changes become more noticeable when haemarthroses are combined with loading of the affected joint. This suggests that restriction in joint loading directly after a joint bleed is advisable. Keeping the patient non weight-bearing with elbow crutches for knee or ankle bleeds or the use of a sling for an upper limb bleed is advisable.

This combination of synovial-mediated inflammation and cartilage-mediated degeneration results in joint damage and eventually Haemophilic Arthropathy. The associated signs and symptoms may be similar to other arthritic conditions, including pain, loss of ROM, muscle imbalance, impaired proprioception and poor biomechanics.

The Ankle:
The ankle is often the first joint to be affected by joint bleeds and therefore by the 2\textsuperscript{nd} decade evidence of joint damage may be seen. The most common deformities associated with ankle arthropathy are:

- Fixed plantarflexion, usually because of anterior osteophytes
- Valgus hindfoot, due to medial distal tibial overgrowth
- Planovalgus foot – because of talar flattening and subtalar involvement

The Knee:
Degenerative changes in the knees may be influenced by altered foot/ankle biomechanics. Common abnormalities include:

- Fixed flexion deformity
- Varus or valgus angular deformity
- Loss of flexion range

The Elbow:
Is commonly affected by joint bleeds/damage, three main patterns of joint damage seen are:

- Radio-ulnar involvement with enlargement of the radial head and resultant limitation of pronation/supination
- Medial joint involvement affecting the humero-ulnar joint with resultant limitation of flexion/extension
Global arthritis with generalised degenerative changes and loss of ROM in all directions.

End stage arthritis often necessitates orthopaedic surgery such as total knee replacement, ankle arthrodesis, joint debridement, arthroscopy, synovectomy etc

2. Process of rehabilitation from bleed to end of rehabilitation

Initial assessment

If a bleed is suspected, no active movements should be done until haemostasis is achieved. Once active bleeding has stopped, a normal assessment can be done to distinguish between joint and soft tissue bleeds, static and dynamic structures.

Stages of Rehabilitation

1. Haemostasis
2. Controlling pain
3. Restoring range of movement
4. Re-establishing neuromuscular control
5. Developing strength and power
6. Preparing for sport-specific activity

The acute inflammatory phase:

- (3 – 5 days) incorporates stage 1 and 2. PRICE advice should be implemented with special consideration in haemophilia to a few points;

If a joint bleed is diagnosed in a weight bearing joint, protective weight bearing strategies should be employed for around 2 weeks, to protect the vulnerable, inflamed, overactive cartilage after that normal sub acute rehabilitation should be resumed.

If a soft tissue bleed is diagnosed, the normal tissue healing phases should be adhered to once bleeding has stopped, namely: acute inflammatory phase – 3 – 5 days. Repair phase - 3 days to 4-6 weeks. Remodeling phase: 3-6 weeks, up to 6 months.

Other protective strategies to consider are walking aids, weight bearing status, splinting, taping, orthoses, supports, braces, and in rare cases such as hip flexor bleeds, bed rest may be indicated. In children consider the use of a pushchair.
If a muscle bleed is suspected, the therapist should be vigilant for the signs and symptoms of compartment syndrome and caution with compressive strategies such as tubigrip is advised as this can further increase the compartment pressure. If a bleed is present in a closed fascial compartment, nerves and tissue can become compromised and tissue death can ensue. This is an emergency situation requiring close monitoring and potential surgical release.

Protection with walking aids can be challenging if chronic joint problems exist in the upper limb and atypical strategies may need to be considered.

Pain relief may be required however it must be remembered that standard non steroidal anti inflammatory medications affect the clotting chain and are not appropriate.

**The Repair Phase:**

- (3 days to 4-6 weeks) incorporates stages 3 – 4 and early stage 5.

  During this phase the aim is a graded return to full function. Therapeutic interventions should be timed as closely as possible to factor replacement therapy.

  In haemophilia (particularly relevant for hip flexor bleeds), the newly formed clot is particularly vulnerable to re-bleed at the 8 day point, and this should be taken in to consideration when progressing exercises.

**Stage 3 - Restoring range of movement:** Consider the following: Passive range of movement (physiological or accessory) Active assisted range of movement, active range of movement, passive stretch, dynamic stretch, Maitland mobilisations, muscle energy techniques and from 4 weeks onwards myofascial release techniques (with caution and factor replacement.) Hydrotherapy can also be good at this stage.

**Stage 4 - Neuromuscular control:** When 75% of pre-bleed range is restored. Includes early functional strengthening, isometrics, continued range of movement exercises, proprioceptive exercise, PNF patterning, core stability and control work.

**The Remodelling phase:**

- (4 weeks up to 6 months) incorporates stages 5 and 6.

This is the phase in Haemophilia with a high attrition rate. Patients may need explanation to maintain motivation. At this point possible biomechanical issues
contributing to initial injury may need addressing. Collagen realignment into functional patterns occurs during this phase and full rehab is important to prevent future injury.

Stage 5 - Strength and power: Begin this phase in earnest when approximately 75% of strength is achieved. And should include more advanced proprioceptive work, PNF patterning, isotonic strengthening (concentric and then eccentric) including open chain strengthening and increasing load.

Stage 6 - Sport specific activity: Begin when 90% return to normal. This may not be appropriate where chronic joint arthropathy is present. Include isokinetics with multiple speeds at lower loads, agility drills and in some cases plyometrics.
3. PRICE

The initial management of a bleed alongside the support of increased factor replacement as advised by the medical team is taken from the management principles of an acute sports injury. PRICE is generally accepted practice in the acute management of an injury or bleed but like most physical therapies there is wide variation in practice but below is the general consensus on current practice.

The ‘PRICE’ acute bleed management strategy should be a key point to educate the patient, patient’s family and others involved in their care, for example the school.

Protection – protect the bleed from undue stress to minimise disruption to healing
With splint, bandage, sling, crutches. Duration dictated by pain and haemostasis

Rest – decreases the metabolic demands, avoids any stress which may disrupt the fragile fibrin bonds and avoids increasing the blood flow to the area. With either complete rest of activities or advice on activities to avoid. Resting in a splint also helps with pain relief from relaxing and resting muscle spasm.

Ice – Used primarily to help decrease pain, and to lesser extent to limit tissue damage- (decreases temperature of tissues, decreases metabolic demands, vasoconstriction of the small vessels to limit bleeding, and helps swelling). Wrap crushed ice in a damp towel, a cold gel pack or CryoCuff® as appropriate for the area, for 10-12 mins, every 1-2 hours, for the first 24 – 72 hours.

Compression – Can help reduce swelling and provide comfort as appropriate.

Elevation – This can help reduce swelling, where practical try and elevate the affected joint or muscle above the level of the heart.

In the non-acute setting and when educating others about acute management ‘P’ can be substituted and thought about in a few different ways…

Protection – wearing the correct protective clothing / equipment for the activity.
Prevention –taken steps to minimize injuries occurring (e.g. warming up)
Preparation – knowing where treatment / ice packs are
Prophylaxis – thinking about timing activities with higher risks and prophylaxis.

Paediatrics a few handy hints to be aware of…

- As we know repeated joint bleeds if suffered whilst they are younger will likely lead to haemophilia arthropathy in later life but it also important to be aware that the repeated bleeds mean that the epiphysis is exposed to increased blood supply and can lead to a leg length difference or angular deformity.
• You may be asked on the appropriate sports that should be done at school or have you any information for the PE teachers. There are some good resources for schools and about sport on [www.factorfitness.co.uk](http://www.factorfitness.co.uk).
4. **Orthopaedic Management and Surgery**

**HAEMOPHILIC ARTHROPATHY**

Most characteristic radiographic findings:
- Subchondral cysts
- Osteoporosis
- Enlarged epiphyseal plate
- Irregular subchondral surfaces
- Narrowing of the joint space
- Gross incongruency of articulating bones surfaces
- Joint deformity.

In the final stages of joint disease fibrous or osseous ankylosis will take place.

Note that there is a lack of correlation with pain and level of joint radiographic findings – many patients will present with severe joint destruction over many years with little or no pain.

Surgical intervention is usually symptomatic and will depend on the degree of pain and functional impairment e.g. joint replacement.

But in some cases such as children and young people, other surgical interventions may be considered first:

- Resection of radial head and partial synovectomy to improve elbow pronation/supination.
- Knee joint debridement to delay a TKR
- Osteotomies around knee or ankle for varus/valgus mal-alignments
- Curettage and bone filling with cancellous bone
- Fibrin seal of some large subchondral cysts.
- Surgical excision of large anterior osteophytes of ankle.

**Knee Joint**

The operation is a standard resurfacing TKR with adequate surgical synovectomy.

However, it must be appreciated that the surgery itself is not always straightforward, given high incidence of joint deformity and soft tissue contractures.

**Of special note:** Post operatively these patients often require higher doses of opiates for longer periods than patients undergoing TKR for OA. The reason for this remains unclear.
**Elbow Joint**

The elbow is the 2\textsuperscript{nd} most common site for arthropathy in haemophilia.

Destructive changes here occur insidiously as it is not a classical weight bearing joint, and early limitations of flexion and extension seldom interfere with overall function.

The actual incidence of joint replacement is low, and there have been few reports published concerning total elbow replacement. Radial head excision and occasionally arthroscopic debridement may take place. Release and relocation of the ulnar nerve may be considered in those with severe neural symptoms secondary to joint arthropathy.

**Ankle Joint**

With repeated bleeds, it becomes more vulnerable, ultimately becoming a target joint, with relentless deterioration of function and comfort in the hindfoot.

In patient with synovitis and recurrent haemarthroses, and with congruent joint surfaces, synovectomy (surgical but now more commonly radioactive) may decrease pain and prevent recurrent bleeding. In more advanced cases, joint debridement and excision of osteophytes can restore some joint motion, especially Dorsiflexion. But unfortunately improvements are usually only short lived and surgery is usually needed within 5 years.

In patients with severe pain and end stage arthropathy, who have failed conservative treatment, an ankle arthrodesis may be indicated. Surgery is intended to produce a more comfortable hindfoot unit with, better ambulation and a reduced bleeding tendency.

There are relatively few reports of this in literature but experience is that procedure is well tolerated and can generally be assured provided care is taken with the final position of the talus and hindfoot.

**TOTAL HIP REPLACEMENT**

Haemophilic arthropathy of hip is relatively rare (4% patients). In medium to long term, the results with THR remain poor. Complications with this are those associated with the non complicated THR. Deep infection remains most significant and serious complication. Estimated infection rate with the haemophiliac is 3 times the expected norm and 33% incidence of aseptic loosening. Its Been proposed that this could be related to co-existing knee and ankle movement, resulting in stiff legged gait, so subjecting the hip to additional stress, which with the passage of time can loosen the prosthesis.
**INTRAMUSCULAR BLEEDS AND PSEUDOTUMOURS**

In majority of cases bleeds in muscle are caused by trauma, usually direct, and the pathology becomes quite evident due to the swelling, pain, local warmth and frequently a bruise.

The vast majority resolve spontaneously with no deficit. But it is important to examine patient carefully to ensure that there is no danger to vascular elements or neural compromise.

It is paramount to ensure that complete reabsorption occurs so as to avoid the risk of pseudotumour.

In Haemophilia, HIV+ status is strongly related to septic arthritis. This provides a clinical marker for immunodepression. It is important to remember that a swollen painful joint, mimicking a haemarthrosis could be septic arthritis especially if factor treatment fails to relieve symptoms.

Muscle haematomas can occur at any part of the body, and common sites include iliopsoas, flexor compartment of forearm, quads and biceps. The iliopsoas bleed is rarer in patients although it is one of the most dangerous, being limb and life threatening. A haematoma here can mimic appendicitis and care must be taken. Femoral nerve palsy may be present as an area of reduced sensation in the anterior aspect of the thigh. Attempts to extend the hip cause the patient pain and forces them into hyperlordosis of the lumbar spine. Need further investigations to clinically differentiate between this and an intra-articular hemorrhage of the hip. Imaging is vital – MRI +/- CT can be used, as can USS. Iliopsoas bleeds take a long time to improve and flexion contracture of hip may persist for weeks. Secondary haemorrhages are common and hence prophylactic treatment is advised.

Forearm and shin muscles are enclosed in a tight fascial compartment and small bleeds can cause a large rise in pressure in the space.

Treatment may be of conservative nature wherein haemostasis is established, the limb is elevated, analgesia provided, and as swelling decrease there will be a decrease in pain and an increase in function. If the pressure is very high then decompression is vital. Expectations for recovery time in Haemophilia patients should be based on the known healing times in normal muscle injury – hence why it is important to ascertain as soon as possible the mechanism of injury.

Pseudotumours are basically encapsulated haematomas and may take months to decrease in size, usually with an altered regimen of prophylaxis.
PHYSIOTHERAPY INTERVENTION FOLLOWING ORTHOPAEDIC SURGERY IN HAEMOPHILIA

Physiotherapy following elective surgery is largely dictated by the postoperative protocols of the Orthopaedic consultant.

One of the most important considerations is that both orthopaedic surgery and subsequent Physiotherapy is essentially the same for a person with Haemophilia as for a normal individual, provided sufficient levels of the missing factor are maintained throughout the course of treatment.

Factor treatment should be provided for physiotherapy, if the patient is not on prophylaxis, as well as during the in-patient period. This will mean liaising with the Haemophilia nursing team about times of treatment and co-incident physio input following factor treatment.

There are several factors unique to the haemophilia patient presenting for surgery:
- Age of the patient
- Multiple joint involvement
- Loss of joint ROM – in some patients it is pain relief rather than joint range that is the aim of the surgery.
- Possible pre-morbid soft tissue contracture.

PREOPERATIVE ASSESSMENT:

- ROM
- Muscle strength
- Joint circumference
- Mobility and use of walking aids
- Pain
- Extent of any other joint involvement
- ADL’s
- Functional assessment – e.g., Health assessment Questionnaire, HAL

The dangers of immobilisation following a bleed, injury or surgery are well known, and therefore Physiotherapy should commence as soon as possible. It is recommended to liaise with the Haemophilia team looking after the patient, for additional information and specialist knowledge before getting the patient up.

AIMS OF PHYSIOTHERAPY:

- Reduce swelling
- Recover full muscle strength
- Increase RoM – if applicable
- Minimise risk of short tissue adhesions and shortening
- Re-educate gait
- Maximise Function

**PROCEDURES AND PHYSIO INTERVENTION**

**SYNOVECTOMY:**
- May be surgical (open or arthroscopic) or radioactive.
- Some advocate early physio intervention immediately, whilst others recommend starting a few days post op.
- May use CPM for the knee
- The joint in question should be immobilized for 24hrs with a suitable sling or support. In the lower limb bed rest is also encouraged for the first 24 hours.
- Intensive Physio input may is required following synovectomy of knee because of tendency to lose ROM post procedure.

**TENDON LENGTHENING:**
- Relieves a fixed deformity without losing muscle function.
- Hams for knee and Tendo-achilles for ankle most common.

Post op limb is immobilised in splint to maintain new length but without adequate active control the contracture will recur.

Intensive physio is vital to maintain muscle length, improve strength, re-educate gait and minimise scar tissue formation.

**OSTEOTOMY:**
- To correct deformity with avoiding intra-articular surgery.
- Good for young patients.
- Correction of deformity allows more normal load distribution and relieving mechanical stress
- Knee and ankle most common joint joints.
- Physio focuses on re-establishing and maintaining range achieved with surgery.
- Any extension gained passively is soon lost if there is no active control.
- The CPM is used but must only be for short periods of 2-3 hours.
- Once stitches removed, can begin hydro, with land sessions to ensure ROM maintained.

**TOTAL JOINT REPLACEMENT:**
- Adequate pain relief is essential post operatively, but may be difficult to achieve.
- Large doses of opiates are often required
- USE ICE AS NECESSARY
- Physio begins immediately post operatively and follows standard protocol
- Bear in mind that same level of ROM and mobility as normal is not necessarily expected at discharge.

**ARTHRODESIS:**
- One of oldest orthopaedic procedures available and one of most successful.
- Usually ankle joint
- Surgery usually leaves patient no worse off than pre-op in terms of ROM but has benefits of being pain free.
- Below knee plaster in situ for 3 months post op and the patient is NWB for the first 2 months,
- Physio involves gait re-education and exercises around hip and knee while in plaster.
- Once out of plaster, physio to begin to improve muscle strength and proprioception.

**FRACTURE MANAGEMENT:**
- #'s occur in Haemophilia population as in any other patient group, and may increase as care enables people with Haemophilia to lead more active lives.
- Management will be similar to normal population but should be carried out in conjunction with Haemophilia unit so that initial haemostasis can be achieved quickly and maintained.
- No greater incidence of excessive bleeding, non-union or compartment syndrome than from normal population.
- Int and Ext fixation are first choice of treatment.

**COMPARTMENT SYNDROME:**
- Unusual, and when do occur are the result of local intramuscular bleeding.
- Physio to reduce swelling and relieve pressure on the nerve where this is possible, once haemostasis is achieved.

**IN CONCLUSION:**
Generally in most cases with Orthopaedic involvement, treat as with any normal patient population, the only care is to **MAKE SURE THE PATIENT HAS RECEIVED THEIR HAEMOPHILIA TREATMENT BEFORE ANY PHYSIO INTERVENTION.**
ORTHOPAEDIC HAEMOPHILIA KEYPONTS!

- **Musculoskeletal history** – ‘target’ joint – therefore may need care when mobilising

- **Pre-op mobility** – check ankles and knees if any lower limb operation

- **Reason for op** – from patient, haemophilia team, Surgeon
  - Prognosis/ Outcome may differ from non haemophiliac

- **Pain levels** and management from previous surgery

- Are they able to use **mobility aids**?
  - Assess elbows and wrists for bony deformity/ range

- **NO PHYSIO WITHOUT ADEQUATE PAIN CONTROL AND FACTOR TREATMENT**
5. Other rare bleeding disorders

**Von Willebrand disease**

Von Willebrand Disease (vWD) is a common and usually mild blood clotting disorder. It is thought that as many as 1% of the population may have the condition.

Von Willebrand factor (vWF) is an important blood clotting protein. It works along with the platelets, enabling them to stick to the damaged blood vessels and also helps the clotting factor reactions which eventually form the clot. In vWD, there is either a shortage of vWF, or there is something wrong with its structure so it doesn’t work properly.

vWF is linked to FVIII in the circulation, protecting it from breakdown and in vWD there may be a reduced amount of FVIII as a result, but this is different from Haemophilia A.

**How does vWF work?**

vWF is synthesised in endothelial cells (blood vessel wall). It is released under stress and by some hormones and by doing so enables the receptor site for vWF on the platelets to lock onto the vWF and hence to the vessel wall. As these collect they help form the plug.

vWF is an inherited disorder and is not linked to the sex of the individual. Different members of the family can be affected more or less severely than others.

Although the severity of the disease can vary from person to person, in many cases it is mild. The common problems include easy bruising, nose bleeds and heavy periods.

**How is it treated?**

**Tranexamic acid:**
This slows down the body’s natural process of breaking down a clot and so helps stop the bleeding and promotes the healing process.

**DDAVP:**
Often used for more serious problems such as minor ops and dental extractions. DDAVP is a copy of one of our body chemicals. It raises the missing vWF and FVIII levels by releasing them from storage sites, and can produce a rise of 3-5 times the normal level for that individual. The elevation will persist for 12-24 hours. Side effects include red eyes, flushing, and headache and water retention.
Clotting factor concentrates:
In those with very low levels of missing factor or those needing surgery there is a necessity to replace the missing factors by giving appropriate blood product concentrates. These are plasma derived

**Factor V deficiency**
Not to be confused with Factor V Leiden (a thrombotic disorder).
Symptoms include nosebleeds, mouth bleeds, bruising, bleeding after trauma

**Factor VII deficiency**
Symptoms may include nose and mouth bleeds, bleeding after trauma. Spinal and intracranial bleeding is a significant risk especially during birth.

**Factor X Deficiency:**
Symptoms can include bruising, joint and muscle bleeds, nosebleeds, haematuria, bleeding after trauma, GI bleeding.
This is a very rare disorder.

**Factor XI deficiency:**
Used to be known as Haemophilia c (and sometimes is still referred to in this way). It is one of the more common rare bleeding disorders. Around 8% of people from Ashkenazi Jewish backgrounds have the disorder.
Symptoms can include bleeding after trauma, mouth bleeds.

**Platelet disorders:**
A platelet is a small cell that makes up part of your blood. When you are hurt or bleeding, platelets are stimulated to stick to the damaged blood vessel wall. Certain proteins on the surface of the platelet are needed to stimulate this action. When the platelet is activated there are granules inside which release proteins and other substances to help clotting. Many platelet disorders are caused when these don’t work properly. Disorders occur when the numbers are low or the platelets don’t function properly because of their size or shape.

**Bernard-Soulier syndrome:**
Rare disorder caused by a deficiency on the surface of the platelet which means platelets don’t clump together effectively to form clots. Blood tests show a prolonged bleeding time, a low platelet count, platelets appear larger than normal through microscope.

**Glanzmann’s Thrombasthenia:**
Glanzmann’s is caused by a deficiency of a protein on the surface of the platelet – meaning the platelet fails to form a plug at the injury site. Blood tests show normal platelet count but bleeding time is much longer than normal and the platelets do not stick together at all.
6. **Pain Management** (This is a copy of Fact sheet from *The Haemophilia Society*)

**Pain management in haemophilia**

Pain is a distressing symptom that can affect people with haemophilia in a number of ways. A bleed into a joint can cause acute, severe pain whereas the long-term effects of recurrent bleeds can lead to chronic and disabling symptoms. Whilst the best care for painful bleeding episodes in haemophilia is prompt factor replacement, effective pain relief during this period is also essential, both to control the symptoms in the short term and allow other treatments such as physiotherapy as appropriate. There are a bewildering number of different methods of pain relief available and these are best described in different groups:

**Simple analgesics (Pain killers)**

**Paracetamol** – This is a commonly used analgesic for mild pain but it can be beneficial in severe pain when used in combination with other drugs. One of the great advantages of paracetamol is that it is relatively free of side-effects, unless taken in overdose, although it should be used with caution in cases of severe liver damage. In this case it should be discussed with the person treating your liver disease. It is recommended not to take these analgesics with large quantities of alcohol.

Paracetamol is available as a tablet or suppository. In the United States and many other parts of the world paracetamol is known as ‘acetaminophen’.

**Non-steroidal anti-inflammatory drugs and aspirin** – These include ibuprofen, diclofenac and naproxen amongst many others. Despite their efficacy in joint and muscle pain, they are generally best avoided in bleeding disorders. This is mainly because they can cause inflammation and ulceration of the stomach as well as affecting the function of platelets, both of which may increase the risk of bleeding. There are some situations where their use could be considered but this should only be on the advice of the haemophilia centre. In these cases “COX2” specific agents such as celecoxib are preferred. ‘Third generation anti-inflammatories’ are now being introduced for short-term usage and being prescribed by some haemophilia centres.

**Opiate analgesics**

**Mild opiates** – These include codeine, dihydrocodeine and tramadol. These agents are effective for mild to moderate pain and their efficacy is enhanced by the addition of paracetamol.
**Powerful opiates** – Morphine is the most widely used strong opiate, while other agents include diamorphine, pethidine and fentanyl. The dose can be increased as necessary to control the pain.

**Route of administration**
- **Oral** – Codeine and morphine are commonly given as tablets. Morphine liquid (oramorph) is useful for “breakthrough” pain and has a more rapid onset and is suitable for “as required” use.
- **Intravenous** – such as diamorphine. The injected route has the benefit of rapid onset of action but requires the use of a vein which can become a painful problem in itself.
- **Patches** – fentanyl. These are more appropriate for chronic pain.
- **Intramuscular injections** should be avoided in those with a bleeding disorder.
- **Patient Controlled Analgesia (PCA)** allows patients to manage their own pain relief and is a favoured option after surgery. It is usually given through a vein and reduces the time from onset of pain to delivery of relief. The regimens used are designed to prevent any risk of overdose.

**Side-effects** – The most important side-effects caused by opiates are nausea, constipation, itching and drowsiness. The degree to which these side-effects cause problems varies greatly from person to person. Symptoms can usually be effectively controlled by the addition of other drugs or by using a different type of opiate. Patients are often concerned about the possibility of addiction but this is not a risk when used appropriately for the control of acute or chronic pain and is certainly not a reason to withhold these agents. Overdose of opiates is very rare when used in a controlled hospital setting, but when it occurs can be easily treated with a rapidly effective antidote called naloxone.

**Chronic pain**
Long-term pain can sometimes be very disabling and also difficult to control. All the above methods are suitable but other drugs such as gabapentin or amitriptyline can be used, usually under the supervision of a specialist “chronic pain team.” Most centres’ will refer patients to a pain clinic if required.

**Other methods for pain control**
The importance of good **physiotherapy** is now increasingly being recognised as an important adjunct for chronic problems in relieving joint stiffness and pain (and improving muscle strength and endurance), which in turn increases mobility. A specially trained haemophilia physiotherapist may implement hydrotherapy and/or a “user-friendly” home exercise programme, after a full needs assessment. Also they will show someone how to use a **TENS machine** correctly and efficiently, which will provide pain relief, while it is being used, for two to three hours (and sometimes even longer).
Relaxation techniques, hot and cold therapy and advice on how to manage pain during activities by pacing oneself or altering the way activities are done are also important factors in managing pain. The physiotherapist, along with the orthopaedic surgeon, will also be instrumental in making any decisions about whether joint replacements are recommended.

Social support from family and friends is also important, as a means of distraction and as a “sounding board” for anxieties. Although if depression becomes an issue, support from a counsellor or a psychologist may be available through your GP or haemophilia centre. Counselling or psychotherapy may also be able to resolve any addiction issues. Joining a support group or participating in a self-management course, such as those available through the Expert Patient Programme, may also be valuable. Sharing experiences with others can put group members’ problems into a better perspective and help them learn how to change their behaviour through changing how they think about their condition.

Other positive coping techniques are the use of activities/hobbies as a distraction (except when experiencing a bleed). This is especially true for those who are not working. Imagery can be used alongside relaxation techniques, especially if there are sleep problems. Complementary therapies, such as aromatherapy, reflexology, acupuncture and Chinese massage, can also be useful.

Summary
The basic rules of pain control with analgesics are to:
• Treat the underlying cause effectively and quickly.
• Give as much pain relief as required to control the symptoms – this can be approached by gradually increasing the strength of the analgesics used until relief of symptoms. This is the concept of the “analgesic ladder” with simple analgesics at the bottom and strong opiates at the top.
• Control side effects when they occur by using other drugs or by choosing a different painkiller.
• Do not worry about becoming dependent on the drugs, as this is not a problem when these agents are used appropriately.

Remember that pain management is not just about taking the right painkillers, but also about improving quality-of-life. With a modern, patient orientated and multidisciplinary approach to pain control, it should be possible to achieve rapid and prolonged relief of symptoms for all patients.
Haemophilia Internet Resources

www.kogenate.co.uk
www.factorfitness.co.uk
www.haemophiliacare.co.uk
www.haemophilia.org.au
www.haemophilia.org.uk
www.haemophiliaalliance.org.uk
www.hemophilia.org
www.thereforyou.com
www.haemophilialife.co.uk
www.nnhf.org
www.haemophilia-forum.org
www.haemophiliaalliance.org.uk
www.wfh.org

Link to World federation of haemophilia Exercise booklet by Kathy Mulder

Outcome measures
- Haemophilia Joint Health Score (version 2.1)
- Petrini Scale
- Colorado Half point Joint score (adults)
- HAL
- PedHal (Paediatric version)
- HaemoQol

Standardized assessments
- Movement Assessment Battery for Children (ABC) – 2 is a standardised test of motor competence. There are 3 age bands 3-6 years, 7-10 years and 11-16 years. The test comprises of three subsections - manual dexterity, aiming & catching, & balance
- Visual Motor Impairment (VMI) – to identify visual motor difficulties
- SDQ – a brief behavioural screening questionnaire for 3-16 year olds. It comprises of 25 statements, involving different attributes which can be divided into 5 subsections (Emotional Symptoms, Conduct Problems, Hyperactivity / Inattention, Peer Relationship Problems and Prosocial Behaviour) which can be completed by a parent, teacher or child.
References:

- Bohn RL, Schramm W, Bullinger M, van den Berg M, Blanchettes V. Outcome measures in Haemophilia: more than just factor levels. *Haemophilia* 2004, 10, (Suppl 1); 2-8
• Berntorp E. Joint outcomes in patients with haemophilia: the importance of adherence to preventive regimens. *Haemophilia* 2009, 15, 1219-1227
• Riley RR, Witkop M, Hellman E, Akins S. Assessment and management of pain in Haemophilia patients. *Haemophilia* 2011, 17, 830-845
Contact Details

Please see UKHCDO website for list of all centre contact details:
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Birmingham Adults Jeanette Batchelor
Bradford Kathryn Ellison
Bristol RI (Paeds) Hannah Harbridge
Bristol RI (Adults) Ann Thomas
Cambridge (Adults) Alison Law
Canterbury (Adults) David Stephensen
Cardiff (Adults) Fiona Hall
Edinburgh (Adults) Jenna Reid
Edinburgh (Paeds) Jenny Forsyth
Great Ormond St Melanie Bladen and Nicola Hubert
Hammersmith London Val Roffi
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Manchester (Paeds) Lindsay Schaefer
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Royal Free London (Adults) Paul McLaughlin
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