

10 MUSCULOSKELETAL COMPLICATIONS

Adolfo Llinás¹ | Pradeep M. Poonnoose² | Nicholas J. Goddard³ | Greig Blamey⁴ | Abdelaziz Al Sharif⁵ | Piet de Kleijn⁶ | Gaetan Duport⁷ | Richa Mohan⁸ | Gianluigi Pasta⁹ | Glenn F. Pierce¹⁰ | Alok Srivastava¹¹

¹ Fundacion Santa Fe de Bogota and Universidad de los Andes, Bogota, Columbia

² Department of Orthopaedics, Christian Medical College, Vellore, India

³ Department of Trauma and Orthopaedics, Royal Free Hospital, London, UK

⁴ Adult Bleeding Disorders Clinic, Winnipeg Health Sciences Centre, Winnipeg, Canada

⁵ Amman, Jordan

⁶ Van Creveldklinik, University Medical Center Utrecht, Utrecht, the Netherlands

⁷ Lyon, France

⁸ Empowering Minds Society for Research and Development, New Delhi, India

⁹ Orthopedic and Traumatology Department, Fondazione IRCCS Policlinico San Matteo di Pavia, Pavia, Italy

¹⁰ World Federation of Hemophilia, Montreal, QC, Canada

¹¹ Department of Haematology, Christian Medical College, Vellore, India

All statements identified as recommendations are consensus based, as denoted by **CB**.

10.1 | Introduction

- Hemophilia is characterized by acute bleeds, over 80% of which occur in specific joints (most commonly the ankle, knee, and elbow joints, and frequently the hip, shoulder, and wrist joints) and in particular muscles (iliopsoas and gastrocnemius).^{1,2} Spontaneous bleeding may occur depending on the severity of the disease (see Chapter 2: Comprehensive Care of Hemophilia – Table 2-1), or breakthrough bleeding may occur depending on the prophylactic treatment approach.
- In children with severe hemophilia, the first joint and muscle bleeds typically occur when they begin to crawl and walk, usually between 1 and 2 years of age, but sometimes in later toddler years.³
- Recurrent joint bleeds cause progressive joint damage as a result of blood accumulation in the joint cavity and synovial inflammation. This leads to complications such as chronic synovitis and hemophilic arthropathy.^{1,2} For discussion and recommendations on joint bleeds, see Chapter 7: Treatment of Specific Hemorrhages and Table 7-2.
- Inadequate treatment of intramuscular bleeds can lead to muscle contractures, especially in bi-articular muscles (e.g., calf and psoas muscles), often within the first decades of life.^{1,2} Other more serious complications such as compartment syndrome and pseudotumours may also

develop. (See “Clotting factor replacement therapy” and 10.5 Pseudotumours, below.)

- Prophylaxis to prevent bleeding episodes is considered the standard of care to the extent that resources permit.⁴
- Successful treatment to achieve complete functional recovery generally requires a combination of clotting factor concentrate (CFC) replacement therapy or other hemostatic coverage (e.g., bypassing agents for patients with inhibitors) and physical therapy.

Patient/caregiver education

- Patient education on musculoskeletal issues in hemophilia is critical and should encompass joint and muscle health, recognition and treatment of musculoskeletal bleeds, pain management, musculoskeletal complications, and the importance of physical therapy and rehabilitation. A multidisciplinary approach to addressing the bleed and its consequences is essential.⁵ (See Chapter 2: Comprehensive Care of Hemophilia.)

10.2 | Synovitis

- Following acute hemarthrosis, the synovium becomes inflamed, hyperemic, and friable. This acute synovitis can take several weeks to resolve.^{2,6,7}
- Failure to manage acute synovitis results in recurrent hemarthroses and subclinical bleeds^{1,2}; the synovium becomes chronically inflamed and hypertrophic, and the joint becomes prone to further bleeding. A vicious cycle

of bleeding, loss of joint motion, and inflammation can ensue which ultimately leads to irreversible cartilage^{7,8} and bone damage and impaired joint function.⁶

- If this process exceeds 3 months, it is defined as chronic synovitis.
- Regular assessments are required until the joint and synovial condition are fully rehabilitated, and there is no evidence of residual blood and/or associated synovitis.⁹ Physical examination for joint changes (e.g., in joint circumference, muscle strength, joint effusion, joint angle, pain according to a visual analogue scale) should be conducted at all routine follow-ups. (See Chapter 11: Outcome Assessment.). However, in many cases, the synovium never returns to its original state.
- Given that clinical signs do not always adequately represent the actual situation, ultrasound evaluation is advised.^{9,10} Magnetic resonance imaging (MRI), while currently the gold standard for imaging, is expensive technology, time-consuming, and is not feasible for very young children.⁶

RECOMMENDATION 10.2.1:

- **For people with hemophilia, the WFH recommends regular physical assessment of the synovial condition after every bleed, preferably using suitable imaging techniques such as ultrasound (when feasible) until the situation is controlled, as clinical assessment alone is inadequate to detect early synovitis. **CE****

Treatment of chronic synovitis

- The goal of chronic synovitis treatment is to suppress synovial activation and reduce inflammation to preserve joint integrity and function.^{11,12}
- Nonoperative options include prophylaxis for 6-8 weeks (for those not on regular prophylaxis), physical therapy, and selective COX-2 inhibitors to reduce inflammation.^{13,14}

RECOMMENDATION 10.2.2:

- **For patients with hemophilia who have chronic synovitis and no access to regular prophylaxis, the WFH recommends nonsurgical treatment, including short-term prophylaxis for 6-8 weeks to control bleeding; physical therapy to improve muscle strength and joint function; and selective COX-2 inhibitors to reduce pain and inflammation.**
- **REMARK: Physical therapy with individualized goals and exercises based on the patient's functional level should start slowly with increasing progression of weight-bearing activities.**

- **REMARK: For patients with acute pain and recurrent bleeding, bracing may stabilize the affected joint and limit motion, but caution is advised as prolonged immobilization leads to muscle weakness, so isometric exercises even within bracing are advised.**
- **REMARK: If unresponsive to nonsurgical interventions, treatment should be escalated to treat the synovitis directly, by the treatment intervention of the local expert. **CE****

RECOMMENDATION 10.2.3:

- **For patients with hemophilia who have chronic synovitis (characterized only by minimal pain and loss of range of motion) the WFH recommends consultation with an experienced musculoskeletal specialist in a hemophilia treatment centre. **CE****

Physical therapy for synovitis

- Physical therapy^{15,16} under the direction of a hemophilia treatment centre is advised throughout the entire rehabilitation trajectory, with progressive exercises to build up to full weight bearing and complete functional recovery. This may include daily exercises to improve muscle strength and restore joint range of motion.¹⁷
- Functional training may commence based on practical goals for each individual.¹⁸
- Bracing may be appropriate to stabilize the affected joint and limit movement in order to prevent recurrent bleeding and synovial impingement during movement.¹⁹ (See Chapter 7: Treatment of Specific Hemorrhages – Joint hemorrhage – Physical therapy and rehabilitation.)
- In chronic cases that no longer respond to nonoperative measures, synovectomy/synoviorthesis may be indicated.

Synovectomy/synoviorthesis

- Synovectomy should be considered if chronic synovitis persists with frequent recurrent bleeding not controlled by other means.
- The procedure can be performed in several ways: chemical or radioisotope intra-articular injection (synoviorthesis); arthroscopic synovectomy; or open surgical synovectomy.^{20,21}
- Nonsurgical synovectomy should always be the first procedure of choice for all patients.
- Radiosynovectomy is indicated for synovitis (confirmed clinically or by point-of-care ultrasound) causing 2 or more bleeds in a particular joint over the last 6 months despite adequate treatment.⁹

- Radioisotope synovectomy using a pure beta emitter (phosphorus-32, yttrium-90, rhenium-186, or rhenium-188) is highly effective, has few side effects, and can be accomplished in a single outpatient procedure.^{9,22-30}
- Choice and dose of radioisotope depend on the joint to be injected, the condition of its synovium, and available radioisotopes.
- Prophylaxis should be administered prior to radiosynovectomy; one dose of CFC is usually sufficient for a single injection of the radioisotope.
- Where possible, simultaneous administration of intra-articular steroids is recommended.³¹
- The joint should then be rested for at least 24-48 hours^{31,32} in a splint or other immobilization device, after which rehabilitation can commence.
- Rehabilitation after radiosynovectomy is less intensive than after surgical synovectomy, but it is still required to help patients regain strength, proprioception, and functional use of the joint.¹⁵ An individualized rehabilitation program for at least 3 weeks may be appropriate.²⁶ Intensive exercise and weight bearing should be avoided immediately following radiosynovectomy.³³
- The aim of treatment is to reduce synovitis and the frequency of bleeds, thereby indirectly reducing pain. It has no effect on articular degeneration. With the improvement in pain and the reduction of bleeds, the patient may regain function through appropriate rehabilitation. Pain reduction typically occurs 1-3 weeks postinjection.^{31,32}
- The minimum interval between repeated treatments in the same joint is 6 months.³¹
- If radioisotopes are not available, chemical synoviorthesis with either rifampicin or oxytetracycline chlorhydrate may be considered. Chemical synoviorthesis may be painful, and the sclerosant injection should be combined with an intra-articular local anesthetic to minimize pain, supplemented by oral analgesics (a combination of acetaminophen/paracetamol and an opioid) as required.³⁴⁻³⁶
- Frequent injections may be required; typically, 5-6 weekly injections are needed until the synovitis is controlled.³⁴⁻³⁶
- **REMARK: Choice of isotope depends on the joint being injected and isotope availability.**
- **REMARK: The joint should be immobilized for at least 24 hours, followed by progressive rehabilitation for restoration of strength and function.**
- **REMARK: When radioisotopes are not available, chemical synoviorthesis with either rifampicin or oxytetracycline chlorhydrate (once weekly injection for 5-6 weeks) is an alternative, accompanied by one dose of CFC per treatment, a local anesthetic, and oral analgesics. **CB****
- In cases where chronic synovitis is resistant to treatment with radiosynovectomy, selective embolization of the blood vessels that supply the synovium may be performed. This procedure is to be performed only in specialized medical imaging centres.³⁷
- Surgical synovectomy may be considered when other less invasive procedures have failed or when an additional procedure is required that must be performed through arthroscopy³⁸ such as removal of a tibial anterior osteophyte of the ankle.
- Arthroscopic synovectomy is suggested over open synovectomy.³⁹
- If surgical synovectomy (either open or arthroscopic) is necessary, ensure longer prophylaxis coverage with CFCs or other appropriate hemostatic agents sufficient for the procedure and postoperative rehabilitation. The procedure must be performed by an experienced team at a dedicated hemophilia treatment centre.

RECOMMENDATION 10.2.5:

- **For patients with hemophilia who have chronic synovitis that no longer responds to nonoperative interventions, the WFH recommends surgical synovectomy (preferably arthroscopic, not open) only by an experienced team in a hemophilia treatment centre. **CB****
- See also Chapter 7: Treatment of Specific Hemorrhages – Table 7-2; Chapter 8: Inhibitors to Clotting Factor – Hemophilia A/Hemophilia B – Surgery and invasive procedures; and Chapter 9: Specific Management Issues – Surgery and invasive procedures.

RECOMMENDATION 10.2.4:

- **For patients with hemophilia who have unresolved chronic synovitis, the WFH recommends nonsurgical synovectomy as a first-line treatment option using radioisotope synovectomy with a pure beta emitter (phosphorus-32, yttrium-90, rhenium-186, or rhenium-188). One dose of CFC per dose of isotope should be used.**

10.3 | Hemophilic arthropathy

- Hemophilic arthropathy can result from a single bleed or recurrent bleeds. It generally evolves gradually from

hemarthrosis to chronic synovitis and extended erosions of the articular surface, culminating in the final stage of joint destruction, chronic hemophilic arthropathy,⁴⁰ which often manifests during the second decade of life, particularly if prophylactic therapy is unavailable or inadequate.

- Muscle bleeds can result in joint deformity and contracture, particularly with bleeds within the psoas muscle or gastrocnemius. Fixed flexion contractures result in loss of motion and significant functional impairment and thus need to be prevented.
- As the arthropathy worsens, range of motion and swelling of the joint often subside due to progressive fibrosis of the synovium and capsule. As the joint becomes ankylosed (stiffened), pain may diminish or disappear.
- The appropriate radiographic technique for assessing chronic hemophilic arthropathy depends on the stage of progression.
- MRI is useful to assess early arthropathy and will show early soft tissue and osteochondral changes.⁴¹⁻⁴³
- Ultrasound imaging is useful for assessing soft tissue and peripheral cartilage pathology in early hemophilic arthropathy.⁴⁴
- Plain radiographs are insensitive to early change and are used to assess late arthropathic changes.^{45,46}
- See Chapter 11: Outcome Assessment.

Treatment of chronic hemophilic arthropathy

- The goals of treatment are to reduce the incidence of hemarthroses, improve joint function, relieve pain, and help the patient continue or resume normal activities of daily living.
- Treatment options for chronic hemophilic arthropathy depend on many factors including:
 - the stage of the condition;
 - the patient's symptoms;
 - the patient's age;
 - the impacts on the patient's lifestyle and functional abilities;
 - the resources available.
- Pain should be controlled with appropriate analgesics.
- See Chapter 2: Comprehensive Care of Hemophilia – Pain management.

Physical therapy for hemophilic arthropathy

- Physical therapy aimed at preserving muscle strength and functional ability is an essential component of treatment of chronic hemophilic arthropathy.
- The intensity of physical therapy should be increased gradually and adapted according to prophylaxis coverage;

physical therapy should be less intense in patients with limited access to CFC replacement.

- In settings with limited resources and factor availability, physical therapy without factor coverage may be performed if the treatment is coordinated by an experienced multidisciplinary team with musculoskeletal expertise.⁴⁷
- Intermittent prophylaxis coverage may be necessary if breakthrough bleeding occurs as a result of physical therapy.¹⁶ Other modes of therapy such as exercise therapy, manual therapy, electrotherapy, and hydrotherapy have been used to complement physical therapy.⁴⁸

RECOMMENDATION 10.3.1:

- **For the prevention and treatment of chronic hemophilic arthropathy in people with hemophilia, the WFH recommends a combination of regular replacement therapy to reduce frequency of bleeding and physical therapy aimed at preserving muscle strength and functional ability. Physical therapy may be done with or without factor coverage, depending on availability and the patient's response to therapy. **CB****
- Other conservative management techniques include:
 - serial casting to correct deformities⁴⁹;
 - traction devices;
 - bracing and orthotics to support painful and unstable joints¹⁹;
 - walking aids or mobility aids to decrease stress on weight-bearing joints;
 - adaptations to the home, school, or work environment to allow participation in community activities and employment, and to facilitate activities of daily living.⁵⁰

RECOMMENDATION 10.3.2:

- **For the prevention and treatment of the sequelae of joint arthropathy in people with hemophilia, the WFH recommends nonsurgical measures such as bracing, orthotics, mobility aids, and serial casting and traction devices to aid in the correction of flexion contractures. This may be done with or without factor coverage. **CB****

Surgical interventions

- If nonsurgical measures fail to provide satisfactory pain relief and improved function, surgical intervention may be necessary.
- Surgical procedures, depending on the specific condition, may include:
 - synovectomy and joint debridement, if required³⁸;

- arthroscopy to release intra-articular adhesions and correct impingement, especially in the ankle or elbow joint⁵¹;
 - extra-articular soft tissue release to treat contractures⁵²;
 - osteotomy to correct angular deformity;
 - external fixators to assist in deformity correction⁵³;
 - prosthetic joint replacement (knee, hip, shoulder, elbow, or ankle)⁵⁴;
 - radial head excision for select patients with radiocapitellar arthropathy⁵⁵;
 - arthrodesis for painful ankle joint arthropathy.
- Adequate resources, including prophylaxis (e.g., sufficient supply of CFCs) and postoperative rehabilitation, must be available to support and increase the likelihood of success of any surgical procedure.⁵⁶⁻⁵⁸

RECOMMENDATION 10.3.3:

- **For patients with hemophilia with chronic hemophilic arthropathy for whom nonsurgical measures have failed to provide satisfactory pain relief and improved function, the WFH recommends consultation with an orthopedic specialist on surgical intervention options which may include:**
 - synovectomy and joint debridement;
 - arthroscopy to release intra-articular adhesions and correct impingement;
 - extra-articular soft tissue release to treat contractures;
 - osteotomy to correct angular deformity;
 - arthrodesis (of the ankle);
 - joint replacement in end-stage arthritis.
- **REMARK: Adequate resources including a sufficient supply of CFCs or other appropriate hemostatic agents (e.g., bypassing agents for patients with inhibitors) and postoperative rehabilitation services must be available to increase the likelihood of success for any surgical procedure. **CB****
- See also Chapter 7: Treatment of Specific Hemorrhages – Joint hemorrhage and Table 7-2; Chapter 8: Inhibitors to Clotting Factor – Hemophilia A/Hemophilia B – Surgery and invasive procedures; and Chapter 9: Specific Management Issues – Surgery and invasive procedures.

10.4 | Muscle hemorrhage

- Bleeds may occur in any muscle of the body, often as a result of injury or a sudden stretch.
- A muscle bleed is defined as an episode of bleeding into a muscle, determined clinically and/or by imaging studies. It is generally associated with pain and/or swelling and functional impairment, e.g., a limp associated with a calf bleed.⁵⁹
- Early identification and proper management of muscle bleeds are important to prevent permanent contracture, re-bleeding, and possible later formation of pseudotumours.⁶⁰
- Symptoms of a muscle bleed include:
 - discomfort in the muscle and maintenance of the limb in a position of comfort;
 - severe pain if the muscle is actively contracted or stretched;
 - tension and tenderness upon palpation; and
 - swelling.
- Sites of muscle bleeding that are associated with neurovascular compromise, such as the deep flexor muscle groups of the limbs, require immediate management to prevent permanent damage and loss of function. These groups include:
 - the iliopsoas muscle (risk of femoral nerve palsy);
 - the superficial and deep posterior compartments of the lower leg (risk of posterior tibial and deep peroneal nerve injury); and
 - the flexor group of forearm muscles (risk of Volkmann's ischemic contracture).
- Bleeding can also occur in more superficial muscles such as the biceps, hamstrings, quadriceps, and gluteal muscles.
- There is emerging evidence that suggests musculoskeletal ultrasound (MSKUS) may be useful in differentiating between muscle bleeds and other regional pain syndromes.^{61,62} Nonetheless, if a patient or clinician suspects a muscle bleed or has difficulty assessing whether a bleed is in progress, hemostatic treatment is advised immediately before performing confirmatory investigations or awaiting such results.

Clotting factor replacement therapy

- An untreated muscle bleed can result in compartment syndrome (a deep muscle bleed within a closed space) with secondary neurovascular and tendon damage and muscle contracture and necrosis. In addition, an injured muscle that is not properly rehabilitated can exert secondary effects on the adjacent joints.⁶³

- The best practice to achieve the best outcomes is to treat muscle bleeds with CFC immediately, ideally when the patient recognizes the first signs of discomfort or right after trauma, to raise the patient's factor level to stop the bleed. Factor replacement therapy should continue until bleeding symptoms and signs resolve, generally for 5-7 days or longer, if symptoms indicate recurrent bleeding or worsening neurovascular symptoms.⁶⁴⁻⁶⁶ (See Chapter 7: Treatment of Specific Hemorrhages – Table 7-2.)
- Repeat infusions are often required, particularly if there is a potential risk of compartment syndrome and/or if extensive rehabilitation is required.^{2,67}
- See Chapter 8: Inhibitors to Clotting Factor for the management of bleeds in patients with inhibitors.

RECOMMENDATION 10.4.1:

- **All hemophilia patients with muscle bleeds should be given clotting factor replacement therapy immediately and, where applicable, be observed for neurovascular complications associated with the bleed. **CB****

Clinical monitoring and management

- It is important to monitor the patient continuously for possible compartment syndrome. Symptoms of possible compartment syndrome include increasing pain, loss of sensation, loss of function, and poor blood supply in the distal area. If in doubt, measure the compartment pressure.
- Pain should be assessed frequently and regularly, as it is an indirect measure of compartment pressure.
- Acute muscle bleeds may require escalating the analgesia protocol to obtain relief. (See Chapter 2: Comprehensive Care of Hemophilia – Pain management.)
- In addition to factor replacement therapy or other appropriate hemostatic therapy, clinicians may apply the following measures as adjunctive management of acute muscle bleeds:
 - Rest the injured muscle.
 - Where possible, elevate the affected area; this may help to reduce the associated swelling.⁶⁸
 - If appropriate, splint the affected limb in a position of comfort and adjust to a position of function as pain subsides.
 - Apply ice/cold packs around the muscle for 15-20 minutes every 4-6 hours for pain relief. Do not apply the ice directly on the skin.
- See also “Physical therapy and rehabilitation for muscle bleeds” below.

RECOMMENDATION 10.4.2:

- **For all hemophilia patients with muscle bleeds, the WFH recommends detailed clinical assessment, grading, and monitoring of pain according to the WHO pain scale, as muscle bleed pain may be an early indicator of reversible neurovascular and tissue damage.**
- **REMARK: While many pain assessment scales exist, use of the WHO pain scale is preferred because it is a simple and universal tool that permits uniform measurement of pain in people with hemophilia and generates comparable population-level outcome data important to advancing hemophilia treatment and research. **CB****

Compartment syndrome

- Neurovascular compromise is a musculoskeletal emergency and requires direct, continuous observation and monitoring of the need for fasciotomy. Prophylaxis should be administered to raise and maintain factor levels for 5-7 days or longer as symptoms indicate, along with physical therapy and rehabilitation to restore baseline muscle function.⁶⁹⁻⁷¹ (See Chapter 7: Treatment of Specific Hemorrhages – Table 7-2.)
- If compartment syndrome is suspected on clinical grounds, measure the compartment pressure. If confirmed, fasciotomy should be performed within 12 hours of onset of the compartment syndrome.⁷²⁻⁷⁴ Late fasciotomy has a very high incidence of complications and is contraindicated.⁷⁵
- Earlier fasciotomy is associated with improved patient outcomes, including decreased muscle and nerve injury. Once a motor nerve deficit has occurred, patients rarely recover fully after fasciotomy.
- In patients with hemophilia, if there is uncertainty regarding the adequacy of hemostatic response, as may occur in patients with high-responding inhibitors, a longer observation period may be warranted to possibly avoid fasciotomy and the risk of uncontrolled bleeding after the procedure. However, any delay in performing fasciotomy once compartment syndrome is established may lead to suboptimal outcomes in muscle recovery and subsequent loss of function.⁷⁶

RECOMMENDATION 10.4.3:

- **In hemophilia patients with muscle bleeds with evidence of compartment syndrome and neurovascular compromise, a fasciotomy is required within 12 hours from the time of onset of symptoms before irreversible damage sets in due to tissue necrosis. **CB****

Physical therapy and rehabilitation for muscle bleeds

- Physical therapy should begin as soon as pain subsides and should be progressed gradually to restore full muscle length, strength, and function.^{15,73} Supervised physical therapy and rehabilitation directed by a physical therapist experienced in hemophilia management should be initiated:
 - Ensure appropriate prophylaxis coverage during physical therapy and rehabilitation. In settings with limited resources and factor availability, physical therapy without factor coverage may be performed during the rehabilitation period if the treatment is coordinated by an experienced multidisciplinary team with musculoskeletal expertise.⁴⁷
 - Use serial casting or splinting as required to correct any contracture.
 - Use supportive bracing if there has been nerve damage.
 - Regularly evaluate the patient for pain during physical therapy, which may suggest re-bleeding.⁷⁷

Iliopsoas hemorrhage

- Iliopsoas hemorrhages can potentially lead to musculoskeletal damage; therefore, early and effective factor replacement therapy or other appropriate hemostatic therapies are essential to minimize and prevent the related complications.⁶⁵
- An iliopsoas hemorrhage has a particular presentation that can sometimes be misleading.⁶⁸ Signs may include pain in the lower abdomen, groin, and/or lower back, with inability to straighten or stand up from a seated position; and pain on extension, but not on rotation, of the hip joint.⁶⁴ The symptoms of iliopsoas hemorrhage may mimic those of acute appendicitis, including a positive Blumberg's sign (rebound tenderness).⁹ It can also be mistaken for a hip joint bleed.
- There may be paresthesia in the medial aspect of the thigh or other signs of femoral nerve compression, such as loss of the patellar tendon reflex, quadriceps weakness, and ultimately muscle wasting.⁹
- Patients with an iliopsoas bleed may need to be hospitalized for observation and pain control.
- Strict bed rest may be indicated. Ambulation with crutches should be avoided as muscle contractions may exacerbate pain and bleeding.⁶⁴⁻⁶⁶
- It is useful to confirm the diagnosis and monitor patient recovery using imaging studies (ultrasound, CT scan,⁵⁹ or MRI⁷⁸).⁶⁴⁻⁶⁶

- Physical activity should be restricted until pain resolves and hip extension improves. A carefully supervised program of physical therapy is essential to restore complete hip extension and full activity and function, and prevent re-bleeding.⁶⁴⁻⁶⁶
- If residual neuromuscular deficits persist, further orthotic support may be necessary, particularly to prevent flexion of the knee due to quadriceps weakness.
- See also Chapter 7: Treatment of Specific Hemorrhages – Table 7-2, and Chapter 8: Inhibitors to Clotting Factor.

10.5 | Pseudotumours

- A pseudotumour is a potentially limb and life-threatening condition unique to hemophilia.
- It develops as a result of inadequately treated soft tissue bleeds, usually in muscle adjacent to bone, which can be secondarily involved.
- If untreated, a pseudotumour can become massive, causing pressure on the adjacent neurovascular structures and possibly resulting in pathologic fractures.
- A fistula can develop through the overlying skin.
- Pseudotumours may be assessed and serially followed up using ultrasound imaging.
- A more detailed and accurate evaluation of a pseudotumour can be obtained with a CT scan and MRI.

RECOMMENDATION 10.5.1:

- **For hemophilia patients with soft tissue bleeding and signs of a possible pseudotumour, the WFH recommends clinical assessment and radiological confirmation using X-ray, ultrasound, and magnetic resonance imaging, as appropriate.**
- **REMARK: While ultrasound is useful for serial assessment of a soft tissue pseudotumour, MRI provides more detailed information prior to surgical intervention.**
- **REMARK: A CT scan or CT angiogram may be indicated, especially for a large pseudotumour and/or pre-operative planning. **CB****
- Management of a pseudotumour depends on its site, size, growth rate, and effect on adjoining structures. Options include factor replacement therapy and monitoring, aspiration, radiation, surgical excision, and surgical ablation.
- For small early pseudotumours, a short course (6-8 weeks) of factor replacement therapy can be attempted, and the pseudotumour can be monitored using serial ultrasound screening. If the pseudotumour is shown to be shrinking,

continue factor replacement therapy in combination with repeat ultrasound evaluation for 4-6 months.^{79,80} (See Chapter 7: Treatment of Specific Hemorrhages – Table 7-2.)

RECOMMENDATION 10.5.2:

- **For patients with hemophilia who have developed small early pseudotumours (prior to acquiring a pseudocapsule) and have no access to regular prophylaxis, the WFH recommends a short course (6-8 weeks) of clotting factor replacement therapy with possible continuation of therapy if serial ultrasound evaluations indicate that the pseudotumour is shrinking, with repeat evaluation after 4-6 months. **CB****
- The management of pseudotumours is complex and associated with a high rate of potential complications. Therapeutic alternatives include embolization, radiation, percutaneous management, surgical removal, and filling of the dead cavity.⁹
- Aspiration of the pseudotumour followed by injections of fibrin sealant, arterial embolization, or radiotherapy may heal some smaller lesions.^{81,82}
- Surgical excision may be necessary for large pseudotumours. Removal of the pseudotumour with the pseudocapsule—rather than evacuation of the hematoma—is required.
- Surgical resection of large abdominal/pelvic pseudotumours, which present a special challenge in the surgical management of hemophilia, must only be performed by a surgical team with experience in hemophilia. Preoperative embolization has been found to be useful in excision of these large tumours.

RECOMMENDATION 10.5.3:

- **For patients with hemophilia who have developed large pseudotumours, the WFH recommends surgical excision of the pseudotumour with the pseudocapsule, performed only by a surgical team with experience in hemophilia, in a hemophilia treatment centre wherever possible, followed by close monitoring and long-term prophylaxis to prevent recurrence of bleeding.**
- **REMARK: Fluctuations in factor levels during the first postoperative year may increase the likelihood of bleed recurrence. Therefore, close monitoring and optimal correction of factor levels are of paramount importance. **CB****
- See also Chapter 7: Treatment of Specific Hemorrhages – Table 7-2; Chapter 8: Inhibitors to Clotting Factor – Hemophilia A/ Hemophilia B – Surgery and invasive

procedures; and Chapter 9: Specific Management Issues – Surgery and invasive procedures.

10.6 | Fractures

- Fractures are not frequent in patients with hemophilia despite a high incidence of osteopenia and osteoporosis, possibly due to lower levels of ambulation and intensity of activities.⁸³
- However, a patient with hemophilic arthropathy may be at risk for fractures around a joint with significant loss of motion and in bones that are osteoporotic.
- Treatment of a fracture requires immediate factor replacement therapy.⁸³⁻⁸⁵ Ideally, patients should be on continuous prophylaxis (e.g., high doses of CFC) and factor levels of at least 50 IU/ dL should be maintained for at least a week.^{11,83-85} Subsequently, lower levels may be maintained for 10-14 days while the fracture becomes stabilized and to prevent soft tissue bleeding. (See Chapter 7: Treatment of Specific Hemorrhages – Table 7-2.)

RECOMMENDATION 10.6.1:

- **For people with hemophilia who incur fractures, the WFH recommends immediate treatment with clotting factor concentrates or other hemostatic agents, and continued treatment to maintain sufficiently high factor levels for bleed control for a week or longer, depending on the likelihood of bleeding due to fracture site or stability. Subsequently, lower factor levels may be maintained for 10-14 days to prevent soft tissue bleeding while the fracture becomes stabilized. Clinical monitoring is paramount due to the risk of compartment syndrome. **CB****
- The management plan should be devised for the specific fracture and include appropriate prophylaxis coverage if surgical procedures are necessary.
- Avoid full circumferential plaster and split casts if possible, especially in the early stages; splints are preferred.⁸³ Monitoring, especially of forearm fractures, is mandatory in order to avoid complications such as compartment syndrome.
- Consider external fixators for open/infected fractures.⁸⁶
- Avoid prolonged immobilization if possible as it can lead to significant limitation of range of motion in the adjacent joints.^{83,84}
- Arrange for physical therapy as soon as the fracture is stabilized to restore range of motion, muscle strength, and function.³³

RECOMMENDATION 10.6.2:

- For people with hemophilia who incur fractures, the WFH recommends splints over full casts to avoid compartment syndrome (especially in the early stages), and external fixators for open or infected fractures. **CE**

RECOMMENDATION 10.6.3:

- For people with hemophilia who incur fractures, the WFH recommends avoiding prolonged immobilization and advises supervised physical therapy and rehabilitation as soon as the fracture is stabilized to restore range of motion, muscle strength, and function. **CE**
- See also Chapter 7: Treatment of Specific Hemorrhages – Table 7-2; Chapter 8: Inhibitors to Clotting Factor – Hemophilia A/ Hemophilia B – Surgery and invasive procedures; and Chapter 9: Specific Management Issues – Surgery and invasive procedures.

10.7 | Orthopedic surgery in hemophilia

- For patients with hemophilia undergoing orthopedic surgery, best results are achieved in dedicated hemophilia centres where skillful multidisciplinary teams are prepared to manage these patients using tailored approaches.^{5,11}
- Multiple-site elective surgery with simultaneous or staggered procedures may simultaneously allow for a more expedient recovery of gait and overall function, as well as for judicious use of factor replacement therapy⁸⁷ or other hemostatic agents. (See Chapter 7: Treatment of Specific Hemorrhages – Table 7-2.)
- Use of local coagulation enhancers may be appropriate. Wound infiltration with local anesthetic agents (lignocaine/lidocaine and/or bupivacaine) with an adrenaline and fibrin sealant/spray is useful to control oozing when operating in extensive surgical fields.^{56,88,89}
- Postoperative care in patients with hemophilia requires, in addition to factor replacement therapy (continuous infusion preferred) or other prophylaxis, close monitoring of pain, and often higher doses of analgesics in the immediate postoperative period.⁵⁶
- Good communication with the postoperative rehabilitation team is essential.³³ Knowledge of the details of the surgery performed and intra-operative joint status will facilitate planning of an appropriate rehabilitation program.
- As part of comprehensive care, both pre- and postoperative physical therapy is needed to achieve optimal functional outcome.³³

RECOMMENDATION 10.7.1:

- For patients with hemophilia requiring orthopedic surgery, especially in cases where oozing is present at closure as well as dead space or cavities, the WFH suggests the use of local coagulation enhancers and wound infiltration with local anesthetic agents (lignocaine/lidocaine and/or bupivacaine) with an adrenaline and fibrin sealant or spray to control blood oozing when operating in extensive surgical fields. **CE**

RECOMMENDATION 10.7.2

- For patients with hemophilia requiring orthopedic surgery, the WFH recommends factor replacement therapy and close pain control and monitoring, with higher doses of analgesics in the immediate postoperative period. **CE**

RECOMMENDATION 10.7.3:

- For patients with hemophilia in the postoperative period following orthopedic surgery, the WFH recommends gradual rehabilitation by a physical therapist experienced in hemophilia management. **CE**
- See also Chapter 7: Treatment of Specific Hemorrhages – Table 7-2; Chapter 8: Inhibitors to Clotting Factor – Hemophilia A/ Hemophilia B – Surgery and invasive procedures; and Chapter 9: Specific Management Issues – Surgery and invasive procedures.

10.8 | Joint replacement

- Joint replacement is indicated in cases of established hemophilic arthropathy with associated pain and functional impairment not responsive to nonsurgical or other surgical treatments.
- Joint replacement should be performed only in recognized hemophilia treatment centres with experienced orthopedic surgeons and appropriate hematological and laboratory support.
- Such centres will have a multidisciplinary team including a nurse, social worker, and physical therapist familiar with the requirements of hemophilia patients undergoing arthroplasty.⁹⁰

Hemostasis during the perioperative period

- Meticulous hemostasis is critical for the success of the surgical procedure. The specific plasma factor levels needed during different phases of surgery are described in Chapter

7: Treatment of Specific Hemorrhages – Table 7-2. Some centres use continuous infusion of factor replacement therapy, particularly during the first 72 hours, which more consistently maintains a protective factor trough level.⁹¹

- The use of perioperative antifibrinolytics and fibrin sealants has been shown to reduce blood loss. However, there is no consensus on the duration of postoperative treatment.⁹²
- There is usually no need for deep vein thrombosis prophylaxis in those undergoing arthroplasty under factor coverage unless very high plasma levels are maintained during the postoperative period.⁹³ (For venous thromboembolism and thromboprophylaxis considerations for surgery, see Chapter 9: Specific Management Issues – Surgery and invasive procedures.)

Surgical considerations


- In the knee, there is often an anteroposterior/medio-lateral mismatch, which should be anticipated. Occasionally, a custom implant may be required. Significant angular deformity, patellar subluxation, and posterior subluxation of the tibia are often encountered, all of which may require extensive soft tissue release.
- Bilateral simultaneous knee replacement has been recommended in some instances, and consideration should be given to undertaking additional procedures if indicated.⁸⁷
- The principles of knee replacement are the same as in the general population. Most often, posterior-stabilized implants or implants with stems and augments for associated bony defects are used.
- Antibiotic-loaded cement should be used in all cases where cement fixation is performed.
- Wound closure should be meticulous.
- There is no consensus on the use of drains.
- There is no consensus on the best type of fixation for hip replacement.⁹⁴

Postoperative physical therapy

- Physical therapy should be started as soon as possible, ideally on the day of the surgery. Therapy sessions need to focus on regaining body functions such as range of motion and muscle strength before increasing functional training and endurance.
- To prevent the formation of joint adhesions, early mobilization and dedicated work on regaining motion are critical.⁹⁵ During this phase, attention to delayed wound and tissue healing and risks for re-bleeds is also required. Functional rehabilitation should be the goal, but only when all possible body functions are restored.

- Physical therapists at the hemophilia treatment centre are generally the best resource for devising a safe and comprehensive outpatient program. Alternatively, the hemophilia physical therapist can contact a physical therapist in the patient's community to arrange for postoperative care.⁵⁷

RECOMMENDATION 10.8.1:

- **For patients with hemophilia, the WFH recommends joint replacement only in cases of established hemophilic arthropathy that is not responsive to nonsurgical or other surgical treatments, and that is accompanied by associated pain, functional impairment, and loss of participation in activities of daily living.**
- **REMARK: Perioperatively, tranexamic acid and fibrin sealants may be used to reduce blood loss.**
- **REMARK: Physical therapy should ideally start on the day of surgery with early mobilization and appropriately progressive exercises to regain motion and muscle strength.** 

Complications and long-term considerations

- Patients with hemophilia tend to have less favourable knee functional scores and more postoperative complications following knee replacement, compared to the general population. This is mainly due to complicating factors and multijoint involvement.⁹⁶⁻⁹⁸
- Knee surgery should not be delayed for too long, as preoperative flexion deformity has a significant effect on postoperative outcome. Knees with flexion deformity of more than 25 degrees have a higher risk of a poor outcome and of developing postoperative flexion deformities.⁹⁹
- Historically, infection rates following arthroplasty in hemophilia patients were higher than those seen in the general population. However, these infection rates have decreased over the past decade. Today, they are reported to be almost the same as in the general population.⁵⁴
- Patients with hemophilia are at a higher risk of contracting a delayed secondary infection.¹⁰⁰
- Patients with HIV or HCV infection may have a higher risk for prosthetic joint infection.
- The long-term survival of joint replacement implants may be the same as in the general population, depending on the level of expertise of the hemophilia care team, the type of implant used, and the severity of musculoskeletal disease of the joint.^{54,101}
- See also Chapter 8: Inhibitors to Clotting Factor – Hemophilia A/ Hemophilia B – Surgery and invasive procedures, and Chapter 9: Specific Management Issues – Surgery and invasive procedures.

10.9 | Psychosocial impacts of musculoskeletal complications

- Despite great strides in hemophilia care in recent years, people with hemophilia continue to face psychosocial challenges with hemophilia-related musculoskeletal complications. In particular, this affects those who grew up prior to prophylaxis and those who do not have access to prophylaxis.¹⁰²
- A study of people with moderate and severe hemophilia found that those with more significant arthropathy experienced a lower quality of life, especially in the physical domain.¹⁰³
- Psychosocial limitations from hemophilic arthropathy may be compounded by¹⁰⁴:
 - gait changes;
 - multiple joints being affected;
 - chronic pain.
- The psychosocial impacts of these compounding factors may result in¹⁰⁴:
 - lost time from school or work;
 - limitations in sports participation;
 - decreased socialization and/or increased isolation;
 - negative self-perceptions related to body image, masculinity, and/or self-esteem;
 - lack of a sense of normalcy;
 - limited physical flexibility with sexual positioning;
 - challenges in personal relationships;
 - role loss and/or role changes;
 - increase in fatigue;
 - negative coping behaviours.
- In people with hemophilia, disability from joint disease frequently occurs at an earlier age than in the general population and may impair their ability to perform reliably in the workplace. This may cause individuals to retire earlier than planned, result in unwanted role loss or shifts in all aspects of life, and negatively impact finances.¹⁰⁴
- Psychosocial interventions should be tailored to meet the specific circumstances and needs of each individual, including their physical, emotional, social, educational, and cultural needs.¹⁰⁵
- Individual psychosocial intervention strategies may be aimed at helping individuals adapt to pain and functional impairment¹⁰⁵ and develop coping strategies such as:
 - identifying/recognizing stressors and strengths;
 - prioritizing concerns (i.e., setting goals and priorities and developing strategies to address issues one by one);
 - examining options;

- seeking information;
- strengthening support systems;
- communicating effectively;
- reframing the situation;
- using distraction techniques;
- using coping self-statements.¹⁰⁶
- Psychosocial intervention strengthens patient resilience by fostering self- and health efficacy, cognitive flexibility, hardiness, optimism, and self-advocacy.
- Peer mentoring and group learning opportunities help foster support, reduce isolation, enhance receptivity to information, and strengthen resilience.¹⁰⁷

RECOMMENDATION 10.9.1:

- **For patients with hemophilia who have chronic musculoskeletal pain or functional limitations, the WFH recommends psychosocial interventions tailored to meet the specific needs of each individual based on their physical, emotional, social, educational, and cultural circumstances. **CB****

RECOMMENDATION 10.9.2:

- **For patients with hemophilia who have chronic musculoskeletal pain or functional limitations, the WFH recommends specific individualized psychosocial assessments and intervention strategies aimed at achieving better quality of life, including psychosocial counselling, educational and employment counselling, and financial planning. **CB****

RECOMMENDATION 10.9.3:

- **For patients with hemophilia who have chronic musculoskeletal pain or functional limitations, the WFH recommends the promotion of support networks, peer mentoring, and group educational opportunities to support their ability to cope with musculoskeletal complications, reduce social isolation, and strengthen resilience. **CB****

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.