5 TREATMENT OF SPECIFIC HEMORRHAGES

1. Bleeding in patients with hemophilia can occur at different sites (see Table 1-2 and Table 1-3), each of which requires specific management.
2. As a general principle in case of large internal hemorrhage, hemoglobin should be checked and corrected while other measures are being planned. Measures of hemodynamic stability, such as pulse and blood pressure, should be monitored as indicated.

5.1 Joint hemorrhage (hemarthrosis)

1. A joint bleed is defined as an episode characterized by rapid loss of range of motion as compared with baseline that is associated with any combination of the following: pain or an unusual sensation in the joint, palpable swelling, and warmth of the skin over the joint [1].
2. The onset of bleeding in joints is frequently described by patients as a tingling sensation and tightness within the joint. This "aura" precedes the appearance of clinical signs.
3. The earliest clinical signs of a joint bleed are increased warmth over the area and discomfort with movement, particularly at the ends of range.
4. Later symptoms and signs include pain at rest, swelling, tenderness, and extreme loss of motion.
5. A re-bleed is defined as worsening of the condition either on treatment or within 72 hours after stopping treatment [1].
6. A target joint is a joint in which 3 or more spontaneous bleeds have occurred within a consecutive 6-month period.
7. Following a joint bleed, flexion is usually the most comfortable position, and any attempt to change this position causes more pain.
8. Secondary muscle spasm follows as the patient tries to prevent motion and the joint appears "frozen".
9. The goal of treatment of acute hemarthrosis is to stop the bleeding as soon as possible. This should ideally occur as soon as the patient recognizes the "aura", rather than after the onset of overt swelling and pain.
10. Evaluate the patient clinically. Usually, X-rays and ultrasound are not indicated.
11. **Administer the appropriate dose of factor concentrate to raise the patient's factor level suitably (refer to Tables 7-1 and 7-2). (Level 2) [2-5]**

12. The definitions listed in Table 5-1 are recommended for the assessment of response to treatment of an acute hemarthrosis [1].
13. **Instruct the patient to avoid weight-bearing, apply compression, and elevate the affected joint. (Level 3) [4]**
14. Consider immobilizing the joint with a splint until pain resolves.
15. Ice/cold packs may be applied around the joint for 15-20 minutes every four to six hours for pain relief, if found beneficial. Do not apply ice in direct contact with skin [39].
16. **If bleeding does not stop, a second infusion may be required. If so, repeat half the initial loading dose in 12 hours (hemophilia A) or 24 hours (hemophilia B). (Level 3) [4]**
17. Further evaluation is necessary if the patient's symptoms continue longer than three days. The presence of inhibitors, septic arthritis, or fracture should be considered if symptoms and findings persist.
18. **Rehabilitation must be stressed as an active part of the management of acute joint bleeding episodes. (Level 2) [4,6,7]**
    - As soon as the pain and swelling begin to subside, the patient should be encouraged to change the position of the affected joint from a position of comfort to a position of function, gradually decreasing the flexion of the joint and striving for complete extension.
    - This should be done as much as possible with active muscle contractions. Gentle passive assistance may be used initially and with caution if muscle inhibition is present.
    - Early active muscle control must be encouraged to minimize muscle atrophy and prevent chronic loss of joint motion.
    - Active exercises and proprioceptive training must be continued until complete pre-bleed joint range of motion and functioning are restored and signs of acute synovitis have dissipated [8].
    - If exercises are progressed judiciously, factor replacement is not necessarily required before exercising.

TABLE 5-1: DEFINITION OF RESPONSE TO TREATMENT OF ACUTE HEMARTHROSIS [1]

Excellent	Complete pain relief within 8 hours and/or complete resolution of signs of bleeding after the initial injection and not requiring any further replacement therapy within 72 hours.
Good	Significant pain relief and/or improvement in signs of bleeding within approximately 8 hours after a single injection, but requiring more than one dose of replacement therapy within 72 hours for complete resolution.
Moderate	Modest pain relief and/or improvement in signs of bleeding within approximately 8 hours after the initial injection and requiring more than one injection within 72 hours but without complete resolution.
None	No or minimal improvement, or condition worsens, within approximately 8 hours after the initial injection.

Note: The above definitions of response to treatment of an acute hemarthrosis relate to inhibitor negative individuals with hemophilia. These definitions may require modification for inhibitor positive patients receiving bypassing agents as hemostatic cover or patients who receive factor concentrates with extended half-lives.

Arthrocentesis

1. **Arthrocentesis (removal of blood from a joint) may be considered in the following situations:**
    - **a bleeding, tense, and painful joint which shows no improvement 24 hours after conservative treatment**
    - **joint pain that cannot be alleviated**
    - **evidence of neurovascular compromise of the limb**
    - **unusual increase in local or systemic temperature and other evidence of infection (septic arthritis) (Level 3) [4,9,10]**
2. Inhibitors should be considered as a reason for persistent bleeding despite adequate factor replacement. The presence of inhibitors must be ruled out before arthrocentesis is attempted.

3. The early removal of blood should theoretically reduce its damaging effects on the articular cartilage [10]. If there is a large accumulation of blood, it will also decrease pain.
4. Arthrocentesis is best done soon after a bleed under strictly aseptic conditions.
5. **When necessary, arthrocentesis should be performed under factor levels of at least 30–50 IU/dl for 48–72 hours. Arthrocentesis should not be done in circumstances where such factor replacement is not available. In the presence of inhibitors, other appropriate hemostatic agents should be used for the procedure, as needed. (Level 3) [4]**
6. A large bore needle, at least 16-gauge, should be used.
7. The joint should be immobilized with mild compression.
8. Weight-bearing should be avoided for 24–48 hours.
9. Physiotherapy should be initiated as described above.

5.2 Muscle hemorrhage

1. Muscle bleeds can occur in any muscle of the body, usually from a direct blow or a sudden stretch.
2. A muscle bleed is defined as an episode of bleeding into a muscle, determined clinically and/or by imaging studies, generally associated with pain and/or swelling and functional impairment e.g. a limp associated with a calf bleed [1].
3. Early identification and proper management of muscle bleeds are important to prevent permanent contracture, re-bleeding, and formation of pseudotumours.
4. 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 femorocutaneous, crural, and femoral nerve palsy)
   - the superior-posterior and deep posterior compartments of the lower leg (risk of posterior tibial and deep peroneal nerve injury)
   - the flexor group of forearm muscles (risk of Volkmann's ischemic contracture)
5. Bleeding can also occur in more superficial muscles such as the biceps brachii, hamstrings (triceps surae), gastrocnemius, quadriceps, and the gluteal muscles.
6. Symptoms of muscle bleeds are:
   - aching in the muscle
   - maintenance of the limb in a position of comfort
   - severe pain if the muscle is stretched
   - pain if the muscle is made to actively contract
   - tension and tenderness upon palpation and possible swelling
7. **Raise the patient's factor level as soon as possible, ideally when the patient recognizes the first signs of discomfort or after trauma. If there is neurovascular compromise, maintain the levels for five to seven days or longer, as symptoms indicate (refer to Tables 7-1 and 7-2). (Level 3) [11-13]**
8. Rest the injured part and elevate the limb.
9. Splint the muscle in a position of comfort and adjust to a position of function as pain allows.
10. Ice/cold packs may be applied around the muscle for 15-20 minutes every four to six hours for pain relief if found beneficial. Do not apply ice in direct contact with skin.
11. **Repeat infusions are often required for two to three days or much longer in case of bleeds at critical sites causing compartment syndromes and if extensive rehabilitation is required. (Level 5) [14,15]**

12. **The patient should be monitored continuously for neurovascular compromise; fasciotomy may be required in some such cases. (Level 5) [16,17]**
13. Hemoglobin level should be checked and corrected if needed as muscle bleeds can result in significant blood loss.
14. **Physiotherapy should begin as soon as pain subsides and should be progressed gradually to restore full muscle length, strength, and function. (Level 4) [12,18]**
15. Factor coverage during this process is prudent, unless the physiotherapist is experienced with hemophilia management. Serial casting or splinting may be required. Supportive bracing will be required if there has been nerve damage.
16. Increasing pain during physical therapy can suggest re-bleeding and should be regularly evaluated [19].

Iliopsoas hemorrhage

1. This type of muscle hemorrhage has a unique presentation. Signs may include pain in the lower abdomen, groin, and/or lower back and pain on extension, but not on rotation, of the hip joint. There may be paresthesia in the medial aspect of the thigh or other signs of femoral nerve compression such as loss of patellar reflex and quadriceps weakness. The symptoms may mimic acute appendicitis, including a positive Blumberg's sign.
2. **Immediately raise the patient's factor level. Maintain the levels for five to seven days or longer, as symptoms indicate (refer to Tables 7-1 and 7-2). (Level 4) [20-22]**
3. **Hospitalize the patient for observation and control of pain. Maintain *strict* bed rest. Ambulation with crutches is *not* permitted, as ambulation requires contraction of the muscle. (Level 4) [20-22]**
4. **It is useful to confirm the diagnosis and monitor recovery with an imaging study (ultrasonography, CT scan, or MRI). (Level 4) [20-22]**
5. **Limit the patient's activity until pain resolves and hip extension improves. A carefully supervised program of physiotherapy is key to restoring full activity and function and preventing re-bleeding. Restoration of complete hip extension before returning to full activity is recommended. (Level 4) [20-22]**
6. If residual neuromuscular deficits persist, further orthotic support may be necessary.

5.3 Central nervous system hemorrhage/head trauma

1. *This is a medical emergency. Treat first before evaluating.*
2. All post-traumatic head injuries, confirmed or suspected, and significant headaches must be treated as intracranial bleeds. Sudden severe pain in the back may be associated with bleeding around the spinal cord. Do not wait for further symptoms to develop or for laboratory or radiologic evaluation.
3. ***Immediately* raise the patient's factor level when significant trauma or early symptoms occur. Further doses will depend on imaging results. Maintain factor level until etiology is defined. If a bleed is confirmed, maintain the appropriate factor level for 10-14 days (refer to Tables 7-1 and 7-2). (Level 4) [23,24]**
4. **Intracranial hemorrhage may be an indication for prolonged secondary prophylaxis (three to six months), especially where a relatively high risk of recurrence has been observed (e.g. in the presence of HIV infection). (Level 3) [23,25,26]**
5. **Immediate medical evaluation and hospitalization is required. A CT scan or MRI of the brain should be performed. Neurological consultation should be sought early. (Level 4) [27,28]**
6. Severe headache may also be a manifestation of meningitis in immunocompromised patients.

5.4 Throat and neck hemorrhage

1. *This is a medical emergency because it can lead to airway obstruction. Treat first before evaluating.*
2. ***Immediately* raise the patient's factor level when significant trauma or symptoms occur. Maintain the factor levels until symptoms resolve (refer to Tables 7-1 and 7-2). (Level 4) [15,29,30]**
3. **Hospitalization and evaluation by a specialist is essential. (Level 5) [15]**
4. To prevent hemorrhage in patients with severe tonsillitis, treatment with factor may be indicated, in addition to bacterial culture and treatment with appropriate antibiotics.

5.5 Acute gastrointestinal (GI) hemorrhage

1. ***Immediately* raise the patient's factor levels. Maintain the factor level until hemorrhage has stopped and etiology is defined (refer to Tables 7-1 and 7-2). (Level 4) [31,32]**
2. Acute gastrointestinal hemorrhage may present as hematemesis, hematochezia, or malena.
3. For signs of GI bleeding and/or acute hemorrhage in the abdomen, medical evaluation and possibly hospitalization are required.
4. Hemoglobin levels should be regularly monitored. Treat anemia or shock, as needed.
5. Treat origin of hemorrhage as indicated.
6. EACA or tranexamic acid may be used as adjunctive therapy for patients with FVIII deficiency and those with FIX deficiency who are *not* being treated with prothrombin complex concentrates.

5.6 Acute abdominal hemorrhage

1. An acute abdominal (including retroperitoneal) hemorrhage can present with abdominal pain and distension and can be mistaken for a number of infectious or surgical conditions. It may also present as a paralytic ileus. Appropriate radiologic studies may be necessary.
2. ***Immediately* raise the patient's factor levels. Maintain the factor levels (refer to Tables 7-1 and 7-2) until the etiology can be defined, then treat appropriately in consultation with a specialist. (Level 4) [15,29,30]**

5.7 Ophthalmic hemorrhage

1. This is uncommon unless associated with trauma or infection.
2. ***Immediately* raise the patient's factor level. Maintain the factor level as indicated (refer to Tables 7-1 and 7-2). (Level 4) [15,29,30]**
3. Have the patient evaluated by an ophthalmologist as soon as possible.

5.8 Renal hemorrhage

1. **Treat painless hematuria with complete bed rest and vigorous hydration (3 litres/m² body surface area) for 48 hours. Avoid DDAVP when hydrating intensively. (Level 4) [33]**
2. **Raise the patient's factor levels (refer to Tables 7-1 and 7-2) if there is pain or persistent gross hematuria and watch for clots and urinary obstruction. (Level 4) [33,34]**
3. **Do not use antifibrinolytic agents. (Level 4) [33]**
4. Evaluation by an urologist is essential for evaluation of a local cause if hematuria (gross or microscopic) persists or if there are repeated episodes.

5.9 Oral hemorrhage

1. Early consultation with a dentist or oral and maxillofacial surgeon is essential to determine the source of bleeding. The most common causes are:
   - dental extraction
   - gingival bleeding often due to poor oral hygiene
   - trauma
2. Local treatments must be considered to treat the hemorrhage. These may include:
   - direct pressure on the area using a damp gauze swab, maintained for at least 15 minutes
   - sutures to close the wound
   - application of local hemostatic agents
   - antibiotics, especially in gingival bleeding due to poor oral hygiene
   - use of EACA or tranexamic acid as a mouthwash
3. An appropriate dose of regular paracetamol/acetaminophen will help control the pain.
4. **Antifibrinolytic agents should not be used systemically in patients with FIX deficiency that are being treated with large doses of prothrombin complex concentrates or in patients with inhibitors being treated with activated prothrombin complex concentrates (APCC). (Level 4) [35,36]**
5. Factor replacement may be required as directed by the hemophilia centre.
6. **Oral EACA or tranexamic acid should be used if appropriate. (Level 4) [37,38]**
7. Advise the patient to avoid swallowing blood.
8. Advise the patient to avoid using mouthwashes until the day after the bleeding has stopped.
9. Advise the patient to eat a soft diet for a few days.
10. Evaluate and treat for anemia as indicated.

5.10 Epistaxis

1. Place the patient's head in a forward position to avoid swallowing blood and ask him to gently blow out weak clots. Firm pressure with gauze soaked in ice water should be applied to the anterior softer part of the nose for 10-20 minutes.
2. Factor replacement therapy is often not necessary unless bleeding is severe or recurrent [15,29].
3. Antihistamines and decongestant drugs are useful for bleeds specifically related to allergies, upper respiratory infections, or seasonal changes.
4. If bleeding is prolonged or occurs frequently, evaluate for anemia and treat appropriately.
5. EACA or tranexamic acid applied locally in a soaked gauze is helpful.

6. Consult with an otolaryngologist if the bleed is persistent or recurrent. Anterior or posterior nasal packing may be needed to control bleeding.
7. Epistaxis can often be prevented by increasing the humidity of the environment, applying gels (e.g. petroleum jelly or saline drops/gel) to the nasal mucosa to preserve moisture, or administering saline spray.

5.11 Soft tissue hemorrhage

1. Symptoms will depend on the site of hemorrhage.
2. Factor replacement therapy is not necessary for most superficial soft tissue bleeding. The application of firm pressure and ice may be helpful [15,29].
3. Evaluate the patient for severity of hemorrhage and possible muscular or neurovascular involvement. Rule out possible trauma to spaces containing vital organs, such as the head or abdomen.
4. Open compartmental hemorrhage, such as in the retroperitoneal space, scrotum, buttocks, or thighs, can result in extensive blood loss. Treat with factor immediately if this situation is suspected.
5. Hemoglobin levels and vital signs should be regularly monitored.

5.12 Lacerations and abrasions

1. Treat superficial lacerations by cleaning the wound, then applying pressure and steri-strips.
2. **For deep lacerations, raise the factor level (refer to Tables 7-1 and 7-2), and then suture. (Level 4) [15,29,30]**
3. Sutures may be removed under cover of factor concentrate.

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