Guidelines for Emergency Management of Individuals with Hemophilia

PURPOSE:

Individuals with hemophilia who present to an emergency department for care should receive appropriate, expeditious management. To this end, the St. Jude Hemophilia Treatment Center (HTC) has developed the following guidelines.

TRIAGE:

Triage should be urgent because delays in administration of factor concentrate significantly affect morbidity and mortality in individuals with hemophilia.

ASSESSMENT:

1. Treatment for a suspected bleeding episode is based on clinical history. Physical exam findings may be normal in the early phases of most hemophilic bleeds. Spontaneous bleeding is common in individuals with severe disease (factor levels <1%). ***When in doubt, administer clotting factor replacement therapy***.
2. Treatment decisions should be based on the suspicion of a bleeding-related problem, not the documentation of one.
3. Believe the patient or the parent of a patient. If in their experience they suspect occult bleeding is occurring, administer clotting factor replacement. Patients are almost always aware of their appropriate factor replacement dosing guidelines as advised by their treating hematologist. Electronic versions of these guidelines are also accessible through MILLI (Power chart) or the on-call MD. Refer to patient's most recent hematology clinic note (under "Flow sheet" or "Clinical Documents" tab).

4. Consultation with the St. Jude Hemophilia Treatment Center is strongly advised. However, this should not delay giving factor replacement to the patient. Between 9:00 AM and 5:00 PM, Monday through Friday, contact the clinic at 901-595-5041. For concerns after-hours, or on weekends, or holidays, contact the St. Jude operator at 901-595-3300 and request to speak with the hematology physician on-call.

DIAGNOSTIC STUDIES:

1. Clotting factor replacement therapy should be given promptly ***and before*** any diagnostic studies (X Rays, CT scans, etc.) are performed in the evaluation of a suspected bleeding problem, especially in the case of head trauma or suspected intracranial hemorrhage.
2. For routine joint bleeding, no radiographic studies are indicated.
3. For patients with hemophilia who have illnesses or disorders that necessitate an invasive procedure (lumbar puncture, arterial blood gas) or surgery, factor replacement must be administered in the emergency department beforehand.
4. For an individual with known hemophilia, routine laboratory studies (i.e. PT, aPTT, factor levels) are not indicated in the treatment of a routine bleeding episode unless requested by the patient's hematologist. The clinical severity of a patient's hemophilia is gauged by his baseline clotting factor level, a value that remains constant throughout that person's life.

INDICATIONS FOR FACTOR REPLACEMENT:

1. Suspected bleeding into a joint or muscle.
2. Any significant injury to the head, neck, mouth, or eyes or evidence of bleeding in those areas.
3. Any new or unusual headache, particularly one following trauma.
4. Severe pain or swelling at any site.
5. All open wounds requiring surgical closure, wound adhesive, or steri strips.
6. History of an accident or trauma that might result in internal bleeding.
7. Any invasive procedure or surgery.
8. Heavy or persistent bleeding from any site.
9. Gastrointestinal bleeding.
10. Acute fractures, dislocations, and sprains.

TREATMENT – PRODUCT SELECTION AND DOSING:

Hemophilia A without Inhibitor

The treatment of choice for children with Hemophilia A (Factor VIII deficiency) is recombinant Factor VIII. Plasma-derived concentrate is a suitable alternative in an emergency situation when recombinant Factor VIII is not available. Cryoprecipitate and fresh frozen plasma are no longer recommended for individuals with Hemophilia A, but should be used if a Factor VIII concentrate is not available. Cryoprecipitate is the preferred product over fresh frozen plasma due to its higher concentration of Factor VIII.

Factor VIII and IX Dosing Recommendations:

Site of bleeding	Hemostatic level	Factor VIII dosing units/kg	Factor IX dosing* units/kg
Muscle, soft tissue – minor	40%	20 units/kg	40 units/kg
Mucous membranes (tooth, gums, nose)	40%	20 units/kg	40 units/kg
Urinary tract – persistent	40%	20 units/kg	40 units/kg
Joint – minor to moderate	60%	30 units/kg at hour 0, 12 and 36	60 units/kg at hour 0, 12 and 36
Head, neck, throat, iliopsoas muscle	100%	50 units/kg	100 units/kg

Hemophilia B without Inhibitor

The treatment of choice for children with Hemophilia B (Factor IX Deficiency) is recombinant Factor IX. Plasma-derived concentrate is a suitable alternative in an emergency situation when recombinant Factor IX is not available. Fresh frozen plasma is no longer recommended for treatment of individuals with Hemophilia B, but should be

used if a Factor IX concentrate is not available. Note that cryoprecipitate does NOT contain Factor IX.

*Some patients may require Factor IX concentrate up to 2 units/kg to raise Factor IX levels by 1%. Refer to patient's most recent hematology clinic note for results of Factor IX Recovery Study.

Mild Hemophilia A with Non-Life or Limb Threatening Bleeding

Children with mild Hemophilia A (Factor VIII greater than 5%) who are experiencing non-life or limb threatening bleeding and do not have suspected intracranial bleeding may use desmopressin (DDAVP IV or intranasal) if they have been shown to respond to this treatment previously (Refer to St. Jude electronic medical record for documentation of DDAVP Challenge results). Otherwise treatment is the same as for individuals with Hemophilia A.

- Intravenous DDAVP - The dose of desmopressin is 0.3 mcg/kg intravenously in 30 mL normal saline over 30 minutes.
- Intranasal DDAVP (Stimate™)
    - o The dose of Stimate™ is 1 spray (0.15 mg/inh) in one nostril for children less than 50 kg.
    - o The dose of Stimate™ is 1 spray (0.15 mg/inh) in each nostril for children greater than 50 kg.
    - o Stimate™ should not be used in children less than 2 years of age.
    - o Side effects include headache, flushing, dizziness, and tachyphylaxis.
    - o On days that patients use Stimate™, they should only drink enough fluids to quench thirst (risk for hyponatremia and lowering of seizure threshold).
    - o Do not use Stimate™ for more than 3 days in a row.

Hemophilia A or B with inhibitor

For individuals with inhibitors (antibodies to Factor VIII or Factor IX), treatment decisions may be more complicated. The care of inhibitor patients should be urgently discussed with the patient's hematologist. If an individual with an inhibitor presents in a life- or limb-threatening scenario, the safest immediate action is to administer recombinant Factor VIIa (rFVIIa or Novo Seven) at a dose of 90-200 mcg per kg. In some but not all cases, activated prothrombin complex concentrate (FEIBA) at 75-100 units per kg is an alternative.* The patient or family can also provide information on response to therapeutic bypassing agents.

*Note – In Factor IX patients with a history of inhibitors and anaphylaxis do not give Factor IX-containing products unless bleeding is life threatening.

Site of bleeding	Hemostatic level	Factor VIII dosing units/kg	Factor IX dosing* units/kg
Muscle, soft tissue – minor	40%	20 units/kg	40 units/kg
Mucous membranes (tooth	40%	20 units/kg	40 units/kg

ADDITIONAL GUIDELINES:

1. In any suspected bleeding emergency in which the clotting factor level of an individual is unknown, the factor level should be assumed to be 0%.
2. If a patient with hemophilia or the parent of a child with hemophilia brings clotting factor with them to the emergency department, allow them to utilize it. They should be permitted to reconstitute the product and administer it whenever possible. Individuals with bleeding disorders are encouraged to have an emergency dose of factor concentrate or intranasal DDAVP (Stimate) in their home and to take it with them when they travel. In those situations where a patient does not bring their own clotting factor concentrate, emergency departments must be prepared to provide clotting factor replacement. Emergency departments must have ready access to factor replacement products so that they are available within one hour of the patient's arrival.
3. Dose the factor up to the "closest vial size" and infuse the full content of each reconstituted vial. A moderate excess of factor concentrate will not create a hypercoagulable state but will prolong the therapeutic level of the product administered; thus it is prudent to "round up."
4. The clinician with the most IV experience should perform any venipuncture. Traumatic venipunctures and repeated needle sticks cause painful hematomas that may limit further IV access. In situations where the patient is hemodynamically stable and is not requiring volume replacement, the smallest gauge needle should be utilized for obtaining IV access (25 g butterfly needles in young infants, 23 g butterfly needles in older children and adults). Tourniquets should not be applied tightly to extremities because they may cause bleeding.
5. Factor VIII replacement must be administered intravenously by IV push over 1-5 minutes. Factor IX replacement must be administered intravenously by IV push over 10 minutes.
6. Intramuscular injections should be avoided if at all possible. If they must be given, factor replacement therapy should precede the injection. Parenteral agents should be given intravenously or subcutaneously.
7. Aspirin and aspirin-containing products are contraindicated in individuals with hemophilia. Acetaminophen and/or codeine may be used for analgesia. Non-steroidal anti-inflammatory drugs may be carefully administered to select patients, such as individuals with chronic arthritic pain who are not actively bleeding or being treated for a recent bleeding problem.
8. If a child with hemophilia is bleeding and requires transportation to another facility for definitive care, all efforts should be made to replace the deficient clotting factor before transport.

REFERENCES:

National Hemophilia Foundation Medical and Scientific Advisory Council, Document #175, October 2006

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Urinary tract – persistent	40%	20 units/kg	40 units/kg
Joint – minor to moderate	60%	30 units/kg at hour 0, 12 and	60 units/kg at hour 0, 12 and

Triage Checklist:

When possible, St. Jude Hemophilia Treatment Center staff will notify ED charge nurse of patient's pending arrival, diagnosis, and treatment plan.

Patient presents to triage, states their diagnosis, and reports acute bleed.

Very briefly check history and perform limited physical exam.

If patient brings home supply of factor, obtain IV access, and infuse factor without delay according to treatment guidelines (see attached).

If patient does not have a home supply of factor, order factor STAT from the pharmacy.

Place IV (obtain labs if clinically indicated).

Infuse factor according to treatment guidelines (see attached). (Factor VIII concentrate over 1-5 minutes. Factor IX concentrate over 10 minutes).

Then obtain full history and physical exam.

Discuss case with on-call hematologist.

Order additional studies/tests as needed.

Depending on severity of bleeding, admit patient to inpatient unit or discharge from ED.

Discharge Plan:

1. If the patient does not meet criteria for hospitalization, observe for at least 1 hour from the factor infusion, watching for clinical stability.
2. Discharge home with instructions to return if the child's clinical condition worsens. Examples include:
    a. Active mucosal bleeding
    b. Persistent pain, warmth, swelling, or decreased range of motion in a joint
    c. Headache
    d. Change in level of consciousness
3. The St. Jude Hematology fellow will complete a MILLI Telephone Encounter Note and forward to the Hematology attending physician for review and signature.
4. Send record of ED encounter to the Hematology Department via fax (901-595-2952, attention: Michelle Boals) or MOLLI Inbox (Hematology Attending).
5. Instruct patients to contact the St. Jude Hemophilia Clinic (901-595-5041) to arrange follow up.

Factor VIII Deficiency Treatment Plan

Site of Bleeding: **% correction = units/kg = units**
Round to the nearest vial

MODERATE BLEEDING

Joint **60% = 30units/kg = units**

*Replacement should be given as soon as bleeding is discovered, 12 hours later, and at 36 hours after the initial replacement.

MILD BLEEDING

Muscle **40% = 20units/kg = units**

Minor calf or forearm, Soft tissue, buttocks.

*Severe calf or forearm with swelling, pain, or numbness of hand or foot – requires evaluation for possible nerve or circulation damage.

*Abdominal/back/thigh muscles – requires evaluation for iliopsoas or retroperitoneal bleeding. Requires 100% correction. Notify on-call hematologist.

Mucous Membranes **40% = 20units/kg = units**

Mouth – tooth, tongue, gum.
Nose – Apply pressure for about 20-30 minutes, give factor if no response.

*Use Amicar (50mg/kg/dose, 2gm/dose max) every 6 hours by mouth for 5-10 days.

Urinary Tract: **40% = 20units/kg = units**

Small amount of blood in urine – increase fluids, rest, observe.
For persistent bleeding (greater than 24 hours), moderate amounts of blood, and/or any clots, give replacement.

DO NOT GIVE AMICAR IF THERE IS EVIDENCE OF BLOOD IN THE URINE.

SEVERE BLEEDING

TREAT IMMEDIATELY, ASSUME CHILD IS BLEEDING

CALL TREATMENT CENTER – MAY REQUIRE ED VISIT FOR FURTHER EVALUATION

Head Injury: **100% = 50units/kg = units**
Neck or Throat **100% = 50units/kg = units**
Spine and Femoral Triangle **100% = 50units/kg = units**

Contact Hemophilia Treatment Center for any questions or unusual bleeding: 901-595-5041. Nights and weekends: 901-595-3300. Ask for the Hematologist on call.

Factor IX Deficiency Treatment Plan

Site of Bleeding: **% correction = units/kg = units**
Round to the nearest vial

MODERATE BLEEDING
Joint **60% = 60units/kg = units**

*Replacement should be given as soon as bleeding is discovered, 24 hours later, and at 36 hours after the initial replacement.

MILD BLEEDING
Muscle **40% = 40units/kg = units**
Minor calf or forearm, Soft tissue, buttocks.

*Severe calf or forearm with swelling, pain, or numbness of hand or foot – requires evaluation for possible nerve or circulation damage.

*Abdominal/back/thigh muscles – requires evaluation for iliopsoas or retroperitoneal bleeding. Requires 100% correction. Notify on-call hematologist.

Mucous Membranes **40% = 40units/kg = units**
Mouth – tooth, tongue, gum.
Nose – Apply pressure for about 20-30 minutes, give factor if no response.

*Use Amicar (50mg/kg/dose, 2gm/dose max) every 6 hours by mouth for 5-10 days.

Urinary Tract: **40% = 40units/kg = units**
Small amount of blood in urine – increase fluids, rest, observe.
For persistent bleeding (greater than 24 hours), moderate amounts of blood, and/or any clots, give replacement.

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