Emergencies in Hemophiliacs

Alisa Wray, MD*

*University of California, Irvine, Department of Emergency Medicine, Orange, CA

Correspondence should be addressed to Alisa Wray, MD at awray@uci.edu

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ABSTRACT:

Audience: This modified team-based learning (mTBL) session is appropriate for medical students or emergency medicine residents.

Introduction: Hemophilia is an X-linked recessive disorder leading to a decrease in functional clotting factors; there are two types, hemophilia A and B, with deficiencies in clotting factors VIII and IX respectively. Patients are typically male and suffer from recurrent episodes of bleeding. The prevalence of hemophilia is low; therefore, many residents may not treat a patient with hemophilia during their training. Understanding the management and dosing of treatment factors is essential for emergency physicians.

Objectives: By the end of this session learners will be able to: 1) describe the underlying deficiencies of hemophilia A and B; 2) discuss the complications of hemophilia; 3) formulate an appropriate treatment plan for an acutely bleeding hemophiliac; 4) calculate the appropriate factor dosing for a hemophiliac with acute bleeding.

Method: The format of this education session is a modified TBL.

Topics: Hematology, hemophilia, bleeding emergencies, hemorrhage.

USER GUIDE

List of Resources:

Learner Audience:
Medical students, interns, junior residents, senior residents

Time Required for Implementation:
Instructor Preparation: 20-60 minutes
Learner Responsible Content: 30 minutes
In Class Time: 45-60 minutes

Recommended Number of Learners per Instructor:
15-50

Topics:
Hematology, hemophilia, bleeding emergencies, hemorrhage.

Objectives:
By the end of this session, learners will be able to:

1. Describe the underlying deficiencies of hemophilia A and B.
2. Discuss the complications of hemophilia.
3. Formulate an appropriate treatment plan for an acutely bleeding hemophiliac.
4. Calculate the appropriate treatment dosing for an acutely bleeding hemophiliac.

Linked objectives and methods:
The two learner responsible content articles provide an overview of the background, complications, and treatment for hemophilia, after which learners will be able to describe the underlying deficiencies in hemophilia A and B and discuss the complications and treatment options for hemophilia (objective 1 and 2).

The modified TBL (mTBL) consists of 2 portions, a learning worksheet (hemophilia worksheet, parts A-C) and the group application exercises.

The hemophilia worksheet parts A-C will take approximately 30 minutes for learners to complete. This can be done individually or in small groups. The worksheet will test the learners' understanding of hemophilia and its complications (objectives 1 and 2). Learners will also formulate a treatment plan and calculate factor dosages for acute treatment for a bleeding hemophiliac (objectives 3 and 4).

The group application exercises consist of four cases that focus on emergent treatment in a bleeding hemophiliac. Groups will need to choose the correct factor and calculate dosages for each case. This portion should take approximately 15 minutes.

Recommended pre-reading for instructor:

1. Melendez S. Bleeding and hemophilia in the pediatric ED. ALiEM. https://www.aliem.com/2014/bleeding-hemophilia-pediatric-ed/. Published September 29, 2014. Accessed May 29, 2016.
2. Rezaie S. Hemophilia: what's so bloody funny? R.E.B.E.L.em. http://rebelem.com/hemophilia-whats-bloody-funny/. Published April 13, 2016. Accessed May 29, 2016.
3. Singleton T, Kruse-Jarres R, Leissinger C. Emergency department care for patients with hemophilia and von Willebrand disease. *J Emerg Med*. 2010;39(2):158-165. doi: 10.1016/j.jemermed.2007.12.024
4. Any book chapter on hemophilia

Learner responsible content (LRC):

1. Melendez S. Bleeding and hemophilia in the pediatric ED. ALiEM. https://www.aliem.com/2014/bleeding-hemophilia-pediatric-ed/. Published September 29, 2014. Accessed May 29, 2016.
2. Rezaie S. Hemophilia: what's so bloody funny? R.E.B.E.L.em. http://rebelem.com/hemophilia-whats-bloody-funny/. Published April 13, 2016. Accessed May 29, 2016.
3. Singleton T, Kruse-Jarres R, Leissinger C. Emergency department care for patients with hemophilia and von Willebrand disease. *J Emerg Med*. 2010;39(2):158-165. doi: 10.1016/j.jemermed.2007.12.024

Results and tips for successful implementation:
This TBL was implemented with 30 learners ranging from medical students to senior residents. It was very well received, as learners found the topic important, and they found the exercises high yield. Many had never calculated the dose of factor correction for hemophiliacs previously and they found the practice in a safe didactic session to be beneficial.

- If your learners do not have access to the content prior to the session, they can access the two free open-access medical education sites listed above during the group activity.

- Instructors should assign groups; learners should not self-select. The session is most successful with groups of four to five learners.

Implementation:

1. Three to seven days before the didactic session, instruct learners to read one or more of the above suggested readings. The instructor should also read one or more of the suggested readings.
2. If using the hemophilia worksheet parts A-C as an individual readiness assessment test (iRAT), print one copy of the hemophilia worksheet for each individual. If using the worksheet as a group readiness assessment test (gRAT), print one copy per group. If using it for both iRAT and gRAT, print 1 copy per learner and 1 copy per group.
3. Print one copy of the group application exercises for each group.
4. Print one copy of the hemophilia worksheet parts A-C Answers, and GAE Answers for each instructor.

Content:

- iRAT and gRAT: Hemophilia Worksheet Parts A-C
- GAE
- RAT Key: Hemophilia Worksheet Parts A-C
- GAE Key

References/suggestions for further reading:

1. Melendez S. Bleeding and hemophilia in the pediatric ED. ALiEM. https://www.aliem.com/2014/bleeding-hemophilia-pediatric-ed/. Published September 29, 2014. Accessed May 29, 2016.
2. Singleton T, Kruse-Jarres R, Leissinger C. Emergency department care for patients with hemophilia and von Willebrand disease. *J Emerg Med*. 2010;39(2):158-165. doi:10.1016/j.jemermed.2007.12.024
3. Sahu S, Singh S, Lata I, Kumar M. Revisiting hemophilia management in acute medicine. *J Emerg Trauma Shock*. 2011;4(2):292-212. doi:10.4103/0974-2700.82225
4. Blackman SC, Gonzalez del Rey JA. Hematologic emergencies: acute anemia. *Clin Pediatr Emerg Med*. 2005;6(3):124-137. doi:10.1016/j.cpem.2005.06.001
5. Bhat R, Cabey W. Evaluation and management of congenital bleeding disorders. *Emerg Med Clin North Am*. 2014;32(3):673-690. doi:10.1016/j.emc.2014.04.009
6. Bansal D, Oberoi S, Marwaha RK, Singhi SC. Approach to a child with bleeding in the emergency room. *Indian J Pediatr*. 2012;80(5):411-420. doi:10.1007/s12098-012-0918-2
7. Kulkarni R, Soucie JM. Pediatric hemophilia: a review. *Semin Thromb Hemost*. 2011;37(07):737-744. doi:10.1055/s-0031-1297164
8. Rezaie S. Hemophilia: what's so bloody funny? R.E.B.E.L.em. http://rebelem.com/hemophilia-whats-bloody-funny/. Published April 13, 2016. Accessed May 29, 2016.
9. Fox S. Hemophilia in the ED. Pediatric EM Morsels. http://pedemmorsels.com/hemophilia-ed/. Published May 23, 2014. Accessed May 29, 2016.

Individual Readiness Assessment Test (iRAT) and Group Readiness Assessment Test (gRAT)

The iRAT and gRAT (hemophilia worksheets part A, B and C) start on the following page and be completed individually or as a group.

Hemophilia Worksheet, Part A

	Hemophilia A	Hemophilia B	von Willebrands
How is it inherited			
Most Commonly Affects: Males, Females or Both?			
Factor Deficiency			
Prevalence			
% of Hemophilia Cases			n/a
Prolonged PT, PTT or Bleeding time?			
Treatment?			

Hemophilia Worksheet, Part B: FACTOR LEVELS & BLEEDING

Normal plasma levels of factor VIII or IX range from _____to_____**%**.

Persons with < _____**%** factor VIII or IX activity are considered to have SEVERE hemophilia. Frequent bleeding episodes are (pick one) *common / uncommon*. Bleeding can occur (pick one) *spontaneously / after minor trauma / only after significant trauma or surgery***.** The most common location of bleeding is _____.

Persons with _____**%** factor VIII or IX activity are considered to have MODERATE hemophilia. Persons may experience bleeding (pick one) *spontaneously / after minor trauma / only after significant trauma or surgery*, but should not bleed (pick one) *spontaneously / after minor trauma / only after significant trauma or surgery.*

Persons with more than _____**%** factor VIII or IX activity are considered to have MILD hemophilia. These patients typically bleed (pick one) *spontaneously / after minor trauma / only after significant trauma or surgery.*

The FIVE major sites of serious bleeding.
(think life, limb, function threatening)

1.
2.
3.
4.
5.

The joints most commonly affected by bleeding:

1.
2.
3.

THESE ALL REQUIRE IMMEDIATE ASSESSMENT AND TREATMENT AS THEY ARE CHARAZTERIZED BY BLEEDING INTO AN ENCLOSED SPACE, COMPRESSION OF VITAL TISSUE, POTENTIAL LOSS OF LIFE LIMB OR FUNCTION.

What is the most common cause of death in patients with hemophilia?

Of note, repeated hemarthrosis is a risk factor for future hemarthrosis, as this leads to thickened synovial tissue and friable blood vessels.

Hemophilia Worksheet, Part C: FACTOR TREATMENT OPTIONS

Severity of Bleed	Example of Bleed *(e.g. location or bleeding or type of trauma)*	Goal Factor Activity %	Repeat Dosing?
Mild			
Moderate			
Severe			

FACTOR TYPES:

Match the 3 types of factor replacements to the correct definition.
Options: *Intermediate Purity, Recombinant, Purified*

- _____**:** Non-human product
- _____: Human product, only contains factor VIII
- _____: Human product, contains factor VIII, also contains vWF

1° PPX vs 2° PPX

- **Primary Prophylaxis:** Scheduled factor replacement dosing, typically done at home or outpatient for severe hemophiliacs to reduce the likelihood of spontaneous bleeding.
- **Secondary Prophylaxis**: Emergent or scheduled dosing of factor replacement in response to an injury or in anticipation of a surgery, ie, replacement for an acute need.

LEARNER MATERIALS

HEMOPHILIA A Treatment Options

Factor ____

Treatment of choice for moderate to severe disease in Hemophilia ____
Factor VIII = Each U/kg = an Increase of Factor activity by ____
____ U/kg = an Increase of Factor activity to 100%

DDAVP

Use in patients that have known Factor Activity >10%, who have mild bleeds
Use in patients who can tell you it has worked for them before
DOSE: ____mcg/kg/dose IV

Cryoprecipitate

Contains Factor VIII and vWF
Use only if not other options available
DOSE: 1 bag per ____ kg of body weight

TXA or Amiocaproic Acid

Helps stabilize clot formation
Only for mucosal bleeds
NEVER in patients with renal bleeds or renal insufficiency.
TXA DOSE**:** ____ mg/kg IV or____mg/kg PO q 6-8 hrs, can be used topically as well

HEMOPHILIA B Treatment Options

Factor ____

Treatment of choice for moderate to severe disease in Hemophilia ____
Factor IX = Each U/kg = an Increase of Factor activity by ____
____U/kg = an Increase in Factor activity to 80%

TXA or Amiocaproic Acid

Helps stabilize clot formation
Only for mucosal bleeds
NEVER in patients with renal bleeds or renal insufficiency.
TXA DOSE**:** ____ mg/kg IV or____mg/kg PO q 6-8 hrs, can be used topically as well

Fresh Frozen Plasma

Contains Factor IX
Only use if you have NO other options, as can lead to _____
DOSE: ____mL/kg initially

TREAT

Instructions: Fill in the ____, then use this sheet to help answer the group application questions below.

1. Factor Level:
    a. Option A: The patient knows their factor activity level
    b. Option B: Patient Does Not Know their factor level→**Assume a factor level of ____**
    c. Option C: In the ED always assume factor level of 0%
2. Consider the degree of bleed, how much activity do you need to get them to?
3. Patient's Weight
4. Which factor are you giving? Hemophilia A or B?
5. Calculate out how much to give the patient.

    Desired Factor Level% – Patients Factor Activity% = How much Factor they need%

    Factor VIII = Each U/kg = an Increase of Factor activity by ____
    ____ U/kg = 50% correction (for minor bleeds)
    ____ U/kg = 100% correction (for major bleeds)

    Factor IX = Each U/kg = an Increase of Factor activity by ____
    ____U/kg = 50% correction (for minor bleeds)
    ____ U/kg = 100% correction (for severe bleeds)

FACTOR NEEDED = Wt in kg x How much Factor they need% x U/kg to get to 100%

MATH: Patient has a "severe bleed", they do not know their activity level.

Goal 100% - 0% Unknown = Need 100% Factor Activity Level Change

Factor VIII = Each U/kg = an Increase of Factor activity by ____
Factor IX = Each U/kg = an Increase of Factor activity by ____

For a 50 kg patient:

Hemophilia A: 50kg x ____U/kg = ____U needed to get to 100%
Hemophilia B: 50kg x ____U/kg = ____U needed to get to 100%

6. DO NOT WAIT TO HAVE A DIAGNOSIS, IF THE PATIENT THINKS THEY HAVE A BLEED, DOSE. GET CONFIRMATORY TESTS LATER AND CALL HEMATOLOGY AFTER 1ST DOSE IS GIVEN.
7. If the family bring their factor with them use it! It will save time, and for patients with inhibitors the factor they bring may be the only one that works for them!
8. Do not waste factor, it is expensive use the closest vial size to the recommended dose, and give the whole vial. Giving too much factor will ensure it lasts longer.
9. Ask the patient or parents questions, they will likely know more than you about their illness and can answer questions.
10. **Factor needs to be given in its own line, it cannot be given with anything else! Typically, you will use a butterfly needle to give it.**

Hemophilia Group Application Exercises (GAE)

A 13-year-old male presents with bleeding gums, he states that he has intermittent nose bleeds, and that he believes his family has an unknown bleeding disorder. Which of the following disorders is most likely?

35 y/o M with hemophilia A presents with right knee pain. He says that he believes he is bleeding in his knee. He weighs 80 kg, and believes his factor level is <2%. How much factor must be used to reach 40% activity?

A 12 y/o M with hemophilia B presents with complaints of getting hit in the flank by a basketball just prior to arrival. He states that he has severe pain on that side. He doesn't know his factor level. He weights 35kg. How much factor should the patient receive?

A 22 y/o M with Hemophilia A presents with complaints of gum bleeding x 2 hours. He states that he was unable to give himself factor at home but is concerned. He states that he has a factor level of 5% and requests that you raise his level to 50%. He states that he weighs 75kg.

BONUS: ACQUIRED HEMOPHILIA Information

These are patients with inhibitors to clotting factors making treatment more difficult.

Usually Caused by:

1. Malignancies (CLL, Adenocarcinomas)
2. Pregnancy or Postpartum State
3. Autoimmune Disorders (SLE, RA)
4. Idiopathic

If you are unsure if the patient has Factor Inhibitors, you can perform the
Clotting Factor Mixing Test

Mix normal plasma with the patient's serum
If the patient is Normal and does not have Acquired Hemophilia= aPTT will normalize
If the patient has Acquired Hemophilia or Factor Inhibitors = aPTT remains prolonged

Low titers of inhibitor: treat with Factor VIII concentrates

High titers of inhibitor: treat with factor VIIa concentrates or prothrombin complexes (PCCs)

TREATMENT FOR PATIENTS WITH INHIBITORS:

Recombinant Factor VIIa: "bypasses" the inhibitors.

Dose: 90-150 mcg/kg
Has a short half-life and may require multiple additional doses

Factor Eight Inhibitor Bypassing Agent: is a plasma-derived bypassing agent.

Dose: 50 U/kg
Caution: Must be given slowly, because rapid infusion can cause excessive clotting (e.g. stroke, limb ischemia, etc).

REFERENCES & READING:

1. Melendez S. Bleeding and Hemophilia in the Pediatric ED. ALiEM. https://www.aliem.com/2014/bleeding-hemophilia-pediatric-ed/. Published September 29, 2014. Accessed May 29, 2016.

2. Singleton T, Kruse-Jarres R, Leissinger C. Emergency department care for patients with hemophilia and von Willebrand disease. *JEM*. 2010;39(2):158-165. doi:10.1016/j.jemermed.2007.12.024.

3. Sahu S, Singh S, Lata I, Kumar M. Revisiting hemophilia management in acute medicine. *J Emerg Trauma Shock*. 2011;4(2):292–12. doi:10.4103/0974-2700.82225.

4. Blackman SC, Gonzalez del Rey JA. Hematologic Emergencies: Acute Anemia. *Clinical Pediatric Emergency Medicine*. 2005;6(3):124-137. doi:10.1016/j.cpem.2005.06.001.

5. Bhat R, Cabey W. Evaluation and Management of Congenital Bleeding Disorders. *Emergency Medicine Clinics of North America*. 2014;32(3):673-690. doi:10.1016/j.emc.2014.04.009.

6. Bansal D, Oberoi S, Marwaha RK, Singhi SC. Approach to a Child with Bleeding in the Emergency Room. *Indian J Pediatr*. 2012;80(5):411-420. doi:10.1007/s12098-012-0918-2.

7. Kulkarni R, Soucie JM. Pediatric Hemophilia: A Review. *Semin Thromb Hemost*. 2011;37(07):737-744. doi:10.1055/s-0031-1297164.

8. Rezaie S. Hemophilia: What's so Bloody Funny? - R.E.B.E.L. EM - Emergency Medicine Blog. REBELem. http://rebelem.com/hemophilia-whats-bloody-funny/. Published April 13, 2016. Accessed May 29, 2016.

9. Fox S. Hemophilia in the ED. PedEMMorsels. http://pedemmorsels.com/hemophilia-ed/. Published May 23, 2014. Accessed May 29, 2016.

INSTRUCTOR MATERIALS

Answer keys to all exercises with explanations, are on the following pages.

Learners: please do not proceed.

Hemophilia Worksheet, Part A Key

	Hemophilia A	Hemophilia B	von Willebrands
How is it inherited	x-linked recessive	x-linked recessive	Type I and II AD Type III AR
Most Commonly Affects: Males, Females or both?	Males Females affected if mom is carrier and dad has disease or if XO (Turners)	Males Females affected if mom is carrier and dad has disease or if XO (Turners)	Both
Factor Deficiency	Factor VIII deficiency	Factor IX deficiency	vWF required for plt adhesion
Prevalence	1/5000	1/30,000	1/100 asymptomatic 1/10,000 symptomatic
% of Hemophilia Cases	80%	20%	n/a
Prolonged PT, PTT or Bleeding time?	PTT	PTT	PTT Bleeding Time
Treatment?	Factor VIII	Factor IX	DDAVP, aminocaproic acid, tranexamic acid, and factor replacement

Hemophilia Worksheet, Part B Key: FACTOR LEVELS & BLEEDING

Normal plasma levels of factor VIII or IX range from **50% to 150%**..

Persons with **<1%** factor VIII or IX activity are considered to have SEVERE hemophilia. Frequent bleeding episodes are (pick one) **common**. Bleeding can occur (pick one) **spontaneously.** The most common location of bleeding is **into the joints**.

Persons with **1-5%** factor VIII or IX activity are considered to have MODERATE hemophilia. Persons may experience bleeding (pick one) **after minior trauma**, but should not bleed (pick one) **spontaneously.**

Persons with more than **5%** factor VIII or IX activity are considered to have MILD hemophilia. These patients typically bleed (pick one) **only after significant trauma or surgery**.

The FIVE major sites of serious bleeding.
(think life, limb, function threatening)

6. **INTRACRANIAL/SPINAL CORD**
7. **AIRWAY**
8. **GI/INTRA-ABDOMINAL**
9. **LIMB COMPARTMENTS**
10. **OCULAR**

The most frequent joint bleeds are:

4. **ELBOWS**
5. **KNEES**
6. **ANKLES**

THESE ALL REQUIRE IMMEDIATE ASSESSMENT AND TREATMENT AS THEY ARE CHARAZTERIZED BY BLEEDING INTO AN ENCLOSED SPACE, COMPRESSION OF VITAL TISSUE, POTENTIAL LOSS OF LIFE LIMB OR FUNCTION.

What is the most common cause of death in patients with hemophilia?
INTRACRANIAL HEMORRHAGE

Of note, repeated hemarthrosis is a risk factor for future hemarthrosis, as this leads to thickened synovial tissue and friable blood vessels.

Hemophilia Worksheet, Part C Key: FACTOR TREATMENT OPTIONS

Severity of Bleed	Example of Bleed *(e.g. location or bleeding or type of trauma)*	Goal Factor Activity %	Repeat Dosing?
Mild	Minor trauma, hemarthrosis	30-40%	Single dose ok!
Moderate	Oral or mucosal bleeding Epistaxis Prophylaxis before surgical/dental procedure	50-80%	Consider observation and repeat dosing to activity 50% q12 x 1
Severe	Severe Trauma, Head, Neck or Abdomen trauma	80-100%	Repeat to 50% activity q12

FACTOR TYPES:

Match the 3 types of factor replacements to the correct definition.

- **Recombinan**t: Non-human product
- **Purified**: Human product, only contains factor VIII
- **Intermediate purity**: Human product, contains factor VIII, also contains vWF

1° PPX vs 2° PPX

- **Primary Prophylaxis:** Scheduled factor replacement dosing, typically done at home or outpatient for severe hemophiliacs to reduce the likelihood of spontaneous bleeding.
- **Secondary Prophylaxis:** Emergent or scheduled dosing of factor replacement in response to an injury or in anticipation of a surgery, ie replacement for an acute need.

INSTRUCTOR MATERIALS

HEMOPHILIA A Treatment Options

Factor VIII

Treatment of choice for moderate to severe disease in Hemophilia **A**
Factor VIII = Each U/kg = an Increase of Factor activity by **2%**
50 U/kg = an Increase of Factor activity to 100%

DDAVP

Use in patients that have known Factor Activity >10%, who have mild bleeds
Use in patients who can tell you it has worked for them before
DOSE: **0.3** mcg/kg/dose IV

Cryoprecipitate

Contains Factor VIII and vWF
Use only if not other options available
DOSE: 1 bag per **6** kg of body weight

TXA or Amiocaproic Acid

Helps stabilize clot formation
Only for mucosal bleeds
NEVER in patients with renal bleeds or renal insufficiency.
TXA DOSE**:** **10** mg/kg IV or **25** mg/kg PO q 6-8 hrs, can be used topically as well

HEMOPHILIA B Treatment Options

Factor IX

Treatment of choice for moderate to severe disease in Hemophilia **B**
Factor IX = Each U/kg = an Increase of Factor activity by **1%**
80 U/kg = an Increase in Factor activity to 80%

TXA or Amiocaproic Acid

Helps stabilize clot formation
Only for mucosal bleeds
NEVER in patients with renal bleeds or renal insufficiency.
TXA DOSE**:** **10** mg/kg IV or **25** mg/kg PO q 6-8 hrs, can be used topically as well

Fresh Frozen Plasma

Contains Factor IX
Only use if you have NO other options, as can lead to **volume overload**
DOSE: **15** mL/kg initially

INSTRUCTOR MATERIALS

TREAT

Instructions: Fill in the ____, then use this sheet to help answer the group application questions below.

11. Factor Level:
    a. Option A: The patient knows their factor activity level
    b. Option B: Patient Does Not Know their factor level→**Assume a factor level of <u>0%</u>**
    c. Option C: In the ED always assume factor level of 0%
12. Consider the degree of bleed, how much activity do you need to get them to?
13. Patient's Weight
14. Which factor are you giving? Hemophilia A or B?
15. Calculate out how much to give the patient.

    Desired Factor Level% – Patients Factor Activity% = How much Factor they need%

    Factor VIII = Each U/kg = an Increase of Factor activity by **<u>2%</u>**
    <u>25</u> U/kg = 50% correction (for minor bleeds)
    <u>50</u> U/kg = 100% correction (for major bleeds)

    Factor IX = Each U/kg = an Increase of Factor activity by **<u>1%</u>**
    <u>50</u> U/kg = 50% correction (for minor bleeds)
    <u>100</u> U/kg = 100% correction (for severe bleeds)

<u>FACTOR NEEDED = Wt in kg x How much Factor they need% x U/kg to get to 100%</u>

MATH: Patient has a "severe bleed", they do not know their activity level.

Goal 100% - 0% Unknown = Need 100% Factor Activity Level Change

Factor VIII = Each U/kg = an Increase of Factor activity by **<u>2%</u>**
Factor IX = Each U/kg = an Increase of Factor activity by **<u>1%</u>**

For a 50 kg patient:
Hemophilia A: 50kg x <u>50U/kg</u> = <u>2500U</u> needed to get to 100%
Hemophilia B: 50kg x <u>100U/kg</u> = <u>5000U</u> needed to get to 100%

16. DO NOT WAIT TO HAVE A DIAGNOSIS, IF THE PATIENT THINKS THEY HAVE A BLEED, DOSE. GET CONFIRMATORY TESTS LATER AND CALL HEMATOLOGY AFTER 1ST DOSE IS GIVEN.
17. If the family bring their factor with them use it! It will save time, and for patients with inhibitors the factor they bring may be the only one that works for them!
18. Do not waste factor, it is $$$$, use the closest vial size to the recommended dose, and give the whole vial. Giving too much factor will ensure it lasts longer.
19. Ask the patient or parents questions, they will likely know more than you about their illness and can answer questions.
20. **Factor needs to be given in its own line, it can not be given with anything else! Typically, you will use a butterfly needle to give it.**

Group Application Exercises Key

A 13 yo M presents with bleeding gums, he states that he has intermittent nose bleeds, and that he believes his family has an unknown bleeding disorder. Which of the following disorders is most likely?

von Willebrand's disease (vWD) is the most common inherited bleeding disorder, with a prevalence of roughly 1/100. With vWD disease, platelets are normal in number, morphology, and other functions, but their adhering properties are diminished. Classic symptoms of vWF include easy bruising, gingival bleeding, epistaxis, hematuria, heavy menses, hematomas and hemarthroses. Laboratory values are not always useful for diagnosis, prothrombin time (PT), partial thromboplastin time (PTT), platelets and wWF levels can all be normal; bleeding time is occasionally prolonged. Treatment of bleeding in vWD includes desmopressin acetate (DDAVP), factor VIII, cryoprecipitate, antifibrinolytics, estrogens and topical agents such as fibrin glue or thrombin spray.

35 y/o M with hemophilia A presents with right knee pain. He says that he believes he is bleeding in his knee. He weighs 80 kg, and believes his factor level is <2%. How much factor must be used to reach 40% activity?

1600U

Remember: Factor VIII = Each U/kg = an Increase of Factor activity by **2%**
25 U/kg = 50% correction (for minor bleeds)
50 U/kg = 100% correction (for major bleeds)

GOAL 40% - 0% Activity Level= 40%
80 kg x 40% x 50U/kg = 80 x .4 x 50 = 1600

A 12 y/o M with hemophilia B presents with complaints of getting hit in the flank by a basketball just prior to arrival. He states that he has severe pain on that side. He doesn't know his factor level. He weights 35kg. How much factor should the patient receive?

3500U

Remember: Factor IX = Each U/kg = an Increase of Factor activity by **1%**
50 U/kg = 50% correction (for minor bleeds)
100 U/kg = 100% correction (for severe bleeds)

GOAL 100% - 0% Activity = 100% change
35kg x 100% x 100U/kg = 35 x 1 x 100 = 3500

INSTRUCTOR MATERIALS

A 22 y/o M with Hemophilia A presents with complaints of gum bleeding x 2 hours. He states that he was unable to give himself factor at home but is concerned. He states that he has a factor level of 5% and requests that you raise his level to 50%. He states that he weighs 75kg.

1688U

Remember: Factor VIII = Each U/kg = an Increase of Factor activity by **2%**

25 U/kg = 50% correction (for minor bleeds)
50 U/kg = 100% correction (for major bleeds)

GOAL 50% - 5% Activity Level= 45%
75 kg x 45% x 50U/kg = 75 x .45 x 50 = 1688

BONUS: ACQUIRED HEMOPHILIA Information

These are patients with inhibitors to clotting factors making treatment more difficult.

Usually Caused by:

5. Malignancies (CLL, Adenocarcinomas)
6. Pregnancy or Postpartum State
7. Autoimmune Disorders (SLE, RA)
8. Idiopathic

If you are unsure if the patient has Factor Inhibitors, you can perform the
Clotting Factor Mixing Test

Mix normal plasma with the patients serum
If the patient is Normal and does not have Acquired Hemophilia= aPTT will normalize
If the patient has Acquired Hemophilia or Factor Inhibitors = aPTT remains prolonged

Low titers of inhibitor: treat with Factor VIII concentrates

High titers of inhibitor: treat with factor VIIa concentrates or prothrombin complexes (PCCs)

TREATMENT FOR PATIENTS WITH INHIBITORS:

Recombinant Factor VIIa: "bypasses" the inhibitors.

Dose: 90-150 mcg/kg
Has a short half-life and may require multiple additional doses

Factor Eight Inhibitor Bypassing Agent: is a plasma-derived bypassing agent.

Dose: 50 U/kg
Caution: Must be given slowly, because rapid infusion can cause excessive clotting (e.g. stroke, limb ischemia, etc).

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