Medscape EDUCATION

Evaluation and Management of Hemophilia in the Emergency Department

CME / CE

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Target Audience

This activity is intended for emergency medicine physicians, hem/onc specialists, pediatricians, and nurses.

Goal

The goal of this activity is to increase understanding of the optimal management of patients with hemophilia who present to the emergency department (ED).

Learning Objectives

Upon completion of this activity, participants will:

Have increased knowledge regarding the

- Discuss common complications related to hemophilia.
- Triage and assess hemophilia patients who present to the emergency department.
- Apply latest recommendations for treating hemophilia patients in the emergency department
- Coordinate with other members of the interprofessional team to improve the care for patients with hemophilia who present to the ED

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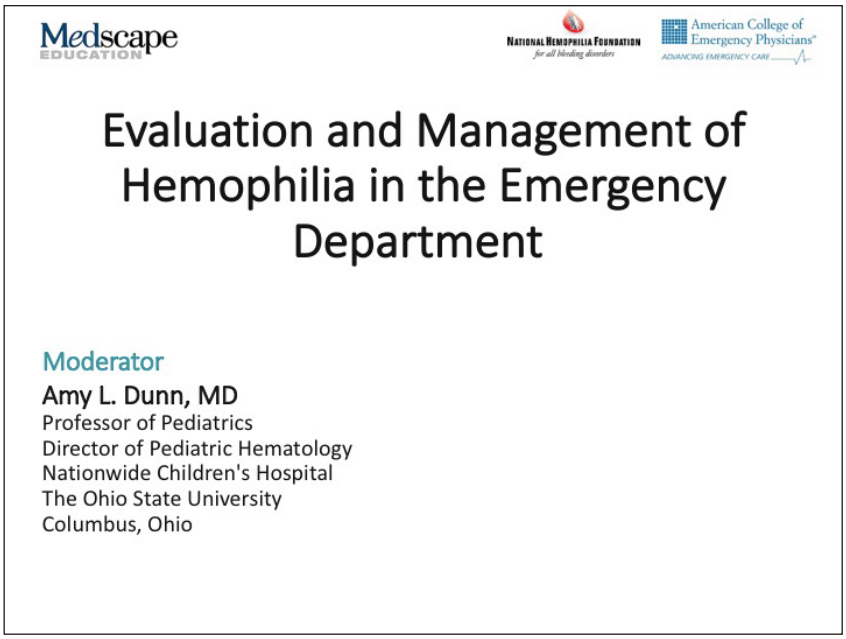
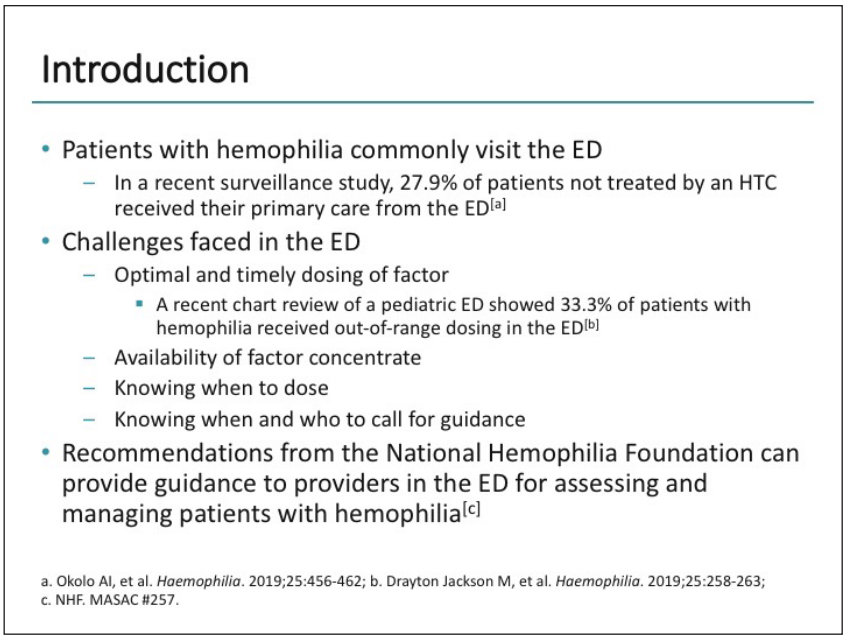


Evaluation and Management of Hemophilia in the Emergency Department

Amy L. Dunn, MD: Hi, I'm Amy Dunn from Nationwide Children's Hospital and The Ohio State University in Columbus, Ohio. Welcome to this program titled, "Evaluation and Management of Hemophilia in the Emergency Department."

Panelists

Amy L. Dunn, MD: Joining me today are Jennifer Maahs from the Indiana Hemophilia and Thrombosis Center in Indianapolis, Indiana; Colin Kaide from The Ohio State University in Columbus, Ohio; and Mohamed Hagahmed from UT Health San Antonio in San Antonio, Texas. Welcome

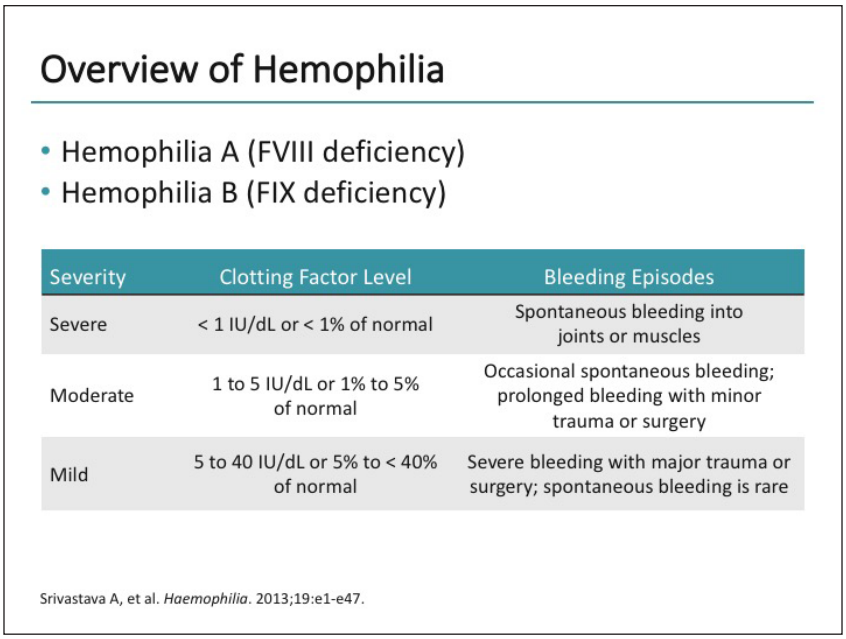


Introduction

Amy L. Dunn, MD: Patients with hemophilia commonly visit the ED. In a recent surveillance study, more than a quarter of patients not treated in HTCs received primary care from the ED. Patients with severe hemophilia usually are knowledgeable about their hemophilia treatment, but those with mild hemophilia often do not know how to infuse or do not have clotting factor at home. Some main challenges that the EDs face include, availability of factor concentrates; optimal and timely dosing — up to one-third of patients may be over- or under-dosed with factor in the ED; knowing when to dose; and knowing when and who to call for guidance.

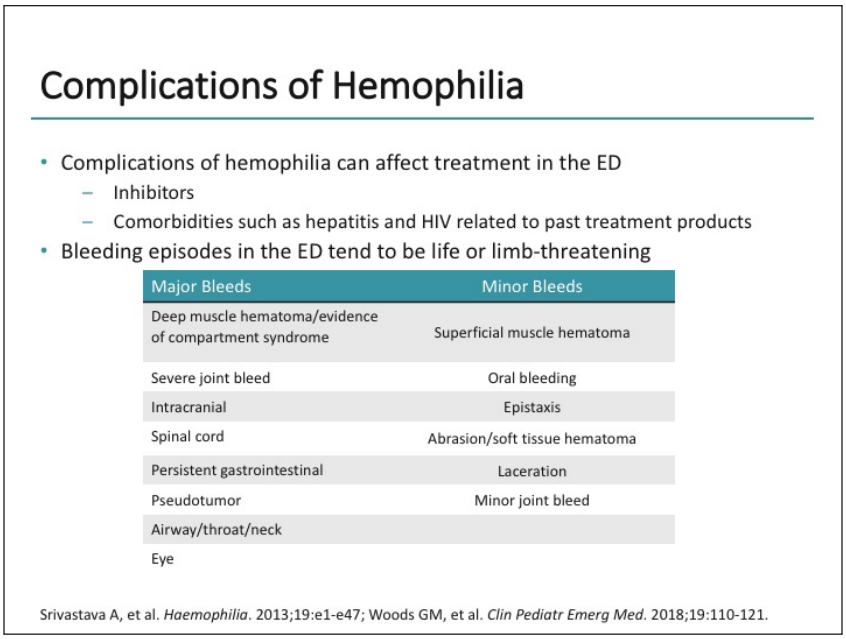
Fortunately, there are resources available to help, including recommendations from the National Hemophilia Foundation that provide guidance to providers in the ED for assessing and managing patients with hemophilia. For this program, our faculty includes a hematologist, a hemophilia nurse practitioner, and 2 ED physicians to discuss optimal strategies for treating patients with hemophilia in the ED.

Jen, could you give us a quick overview of hemophilia?



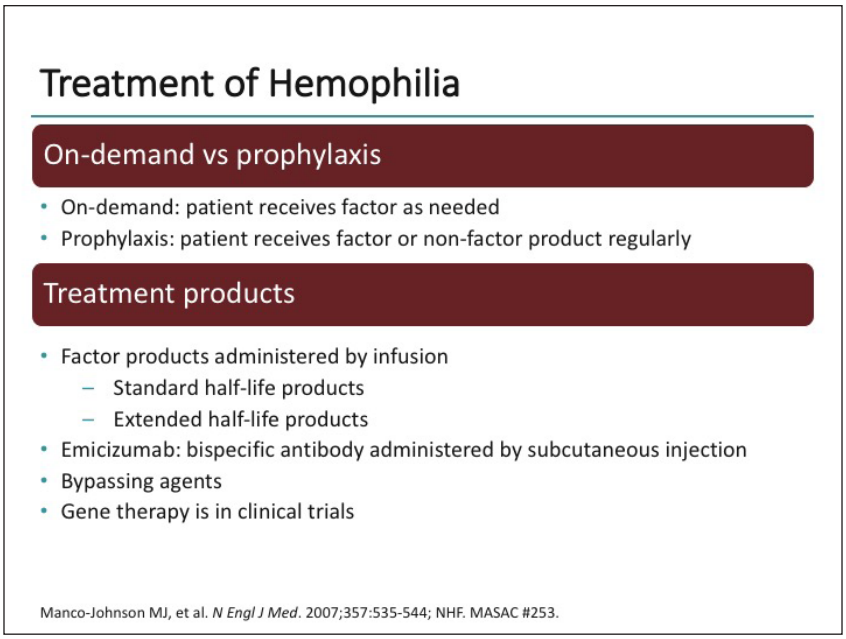
Overview of Hemophilia

Jennifer Maahs, RN-BC, MSN, PNP: There are 2 kinds of hemophilia: hemophilia A characterized by FVIII deficiency and hemophilia B characterized by FIX deficiency. In both of these deficiencies, there are 3 main severities. Severe is patients that make less than 1% clotting FVIII or FIX. Moderate, they have 1% to 5% factor levels, and mild is > 5% to 40%.



Complications of Hemophilia

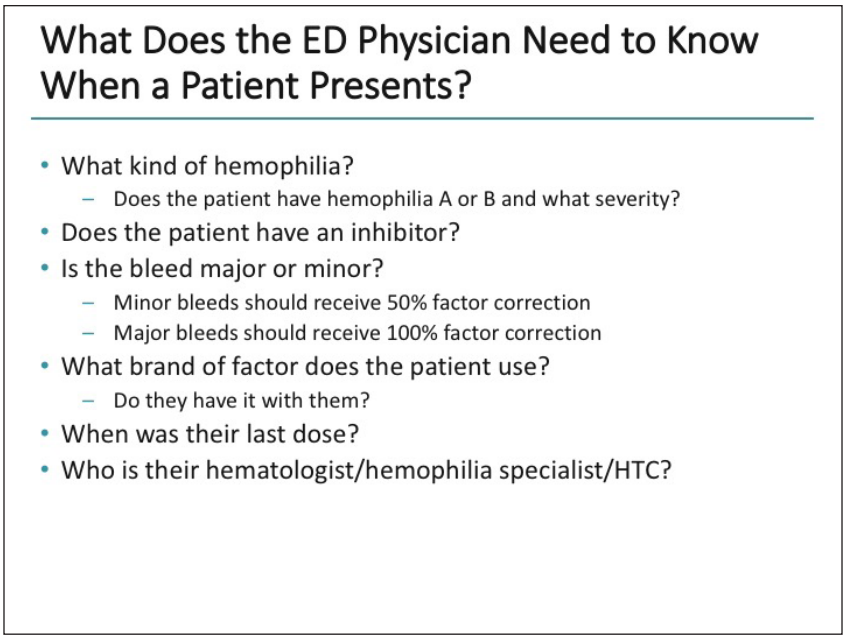
Jennifer Maahs, RN-BC, MSN, PNP: When we talk about the complications in hemophilia and we think about the ED, often we're talking about life- or limb-threatening bleeding episodes. Usually these are related to trauma. When we look at other complications, such as the development of an inhibitor or an antibody to the factor that they receive, this can be problematic because it impacts their ability to respond to treatment once it's given. Comorbidities such as hepatitis C and HIV related to past treatment products also need to be considered when we're developing a hemostasis plan for our patients.



Treatment of Hemophilia

Jennifer Maahs, RN-BC, MSN, PNP: Typically, treatment for patients with hemophilia is either on-demand, which means you treat only when you need to, or a prophylactic regimen, which is a schedule of treatment infusions over a period of a week. Patients may infuse a couple times a week or less than that, depending on the type of factor concentrate that they're receiving.

We have different options for factor concentrate. There are standard half-life products, which are what were previously available for patients. Now, in addition to those standard products, we have products that have an extended half-life, meaning that their prophylactic regimens may be extended. When we talk about inhibitors, we have bypassing agents and non-factor agents, specifically emicizumab. Also gene therapy is really in clinical trials right now.



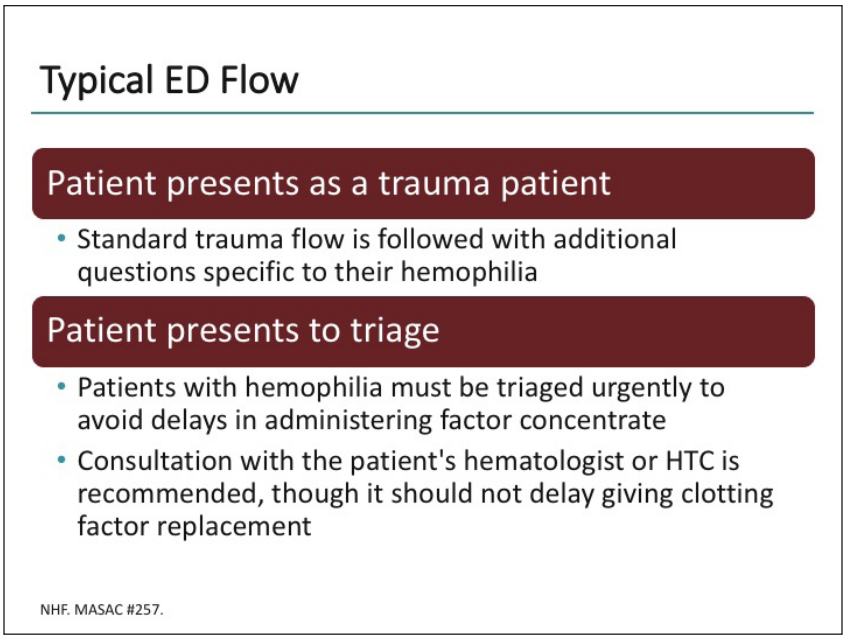
What Does the ED Physician Need to Know When a Patient Presents?

Dr Dunn: Colin, can you tell me about things you need to know as an ED physician when a patient with hemophilia presents to the ED?

Colin G. Kaide, MD: The first thing that I want to know is what kind of hemophilia does the patient have. Are they hemophilia A or B? I like to also find out if they have an inhibitor because that will very significantly impact the way that I'm going to be treating this patient.

Dr Dunn: Mohamed, what sorts of things do you want to know when a patient with hemophilia comes to the ED?

Mohamed Hagahmed, MD: Other important things that I would like to consider when taking their history is 1, whether they have their factor brand with them at hand that I could use. Then, when was the last dose that was given of that factor, and, very important information to know is their hematologist contact information. In terms of the clinical evaluation, I want to make sure that I know whether the bleeding is major or minor because that will determine my plan of attack and whether there is a spontaneous or traumatic bleed.

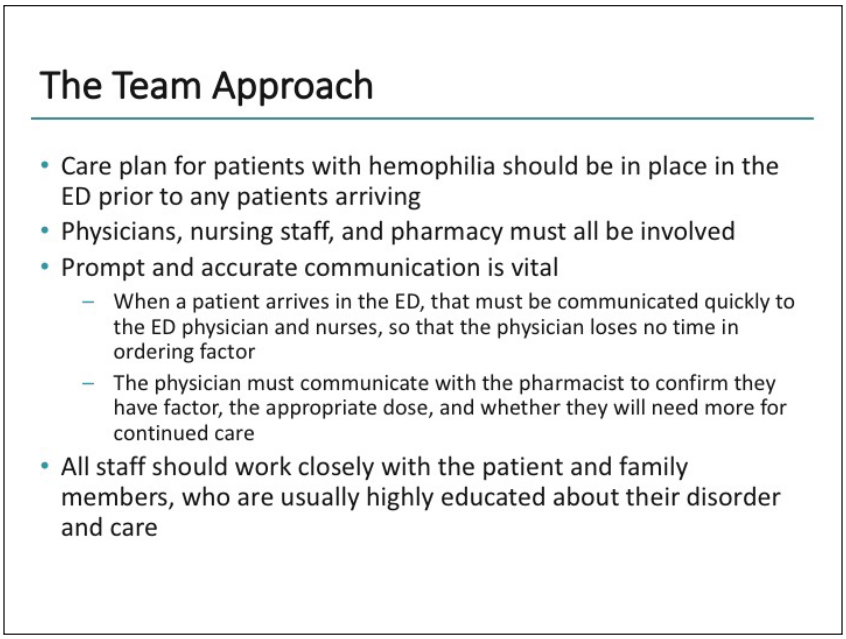


Typical ED Flow

Dr Dunn: Colin, can you talk about the standard flow for trauma in the ED and how that might differ for a patient with hemophilia?

Dr Kaide: If a patient presents as a trauma alert, I'm going to run that trauma in the same way that I would normally do things so that I don't miss anything. However, I'm going to ask a few additional questions upfront — specifically about their hemophilia and about inhibitors and their last dose, as was alluded to just a few minutes ago.

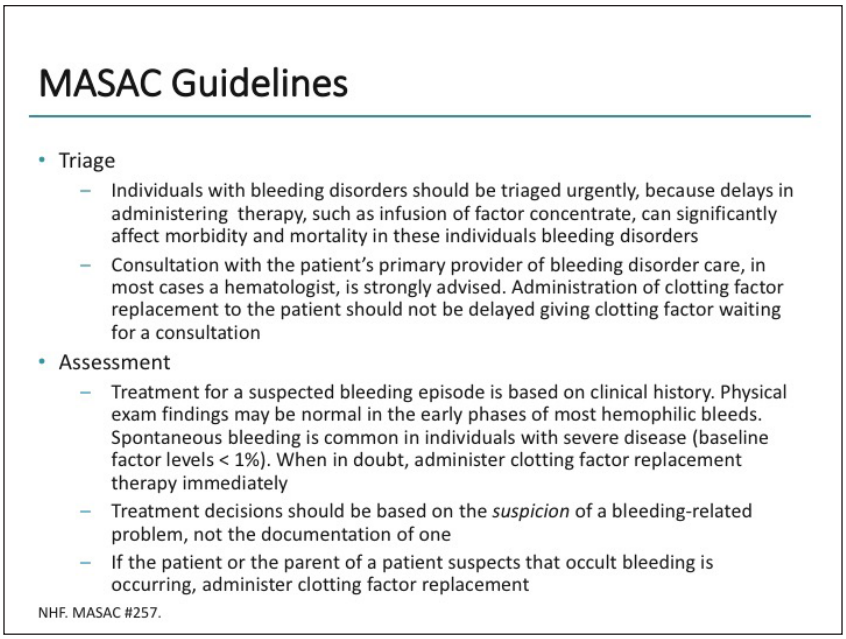
It becomes a little bit more complicated if the person presents to triage and they're not automatically a trauma alert. Then it becomes very important that the people involved in the triage process understand that this patient is essentially just like a patient on anticoagulation. If they have a traumatic injury, they have potential to have very severe bleeding complications. One way that providers can become a little bit more comfortable understanding hemophilia is simply to think about these patients as anti-coagulated patients because we deal with those kinds of patients all the time. They are on a factor Xa or II inhibitor or warfarin. The biggest difference is the longer you are away from the dose of your anticoagulant, the better off you are. But the farther you are away from your dose of your hemophilia agents, the more likely you are to be bleeding as a result of the trauma.



The Team Approach

Dr Dunn: That's really great advice. Mohamed, can you talk about how the team approaches a patient with hemophilia in the ED?

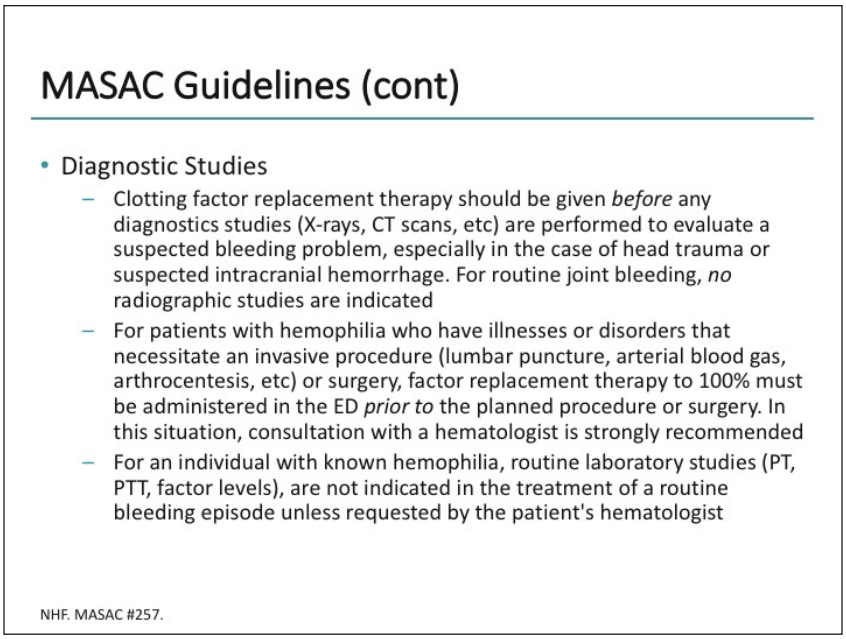
Dr Hagahmed: Even before determining the plan of attack for these patients, it is important that the ED have a care plan for patients with hemophilia before they even arrive in the ED. That includes a close discussion with the nursing staff as well as the pharmacy. When the patient arrives in the ED, it is crucial to quickly communicate that with the physician and also the other staff taking care of that patient. The ED physician must not delay ordering factor replacement therapy — and must discuss that with the pharmacist to ensure they have the appropriate dose and also whether the need will arise for obtaining other doses — as well as availability in the ED in order to care for that patient. Ultimately, patients with hemophilia as well as their family members are great resources. They know their illness and they can provide useful information when it comes to their care.



MASAC Guidelines

Dr Dunn: Jen, can you talk about the Medical and Scientific Advisory Council (MASAC)? What is MASAC and what guidelines can they provide in the ED?

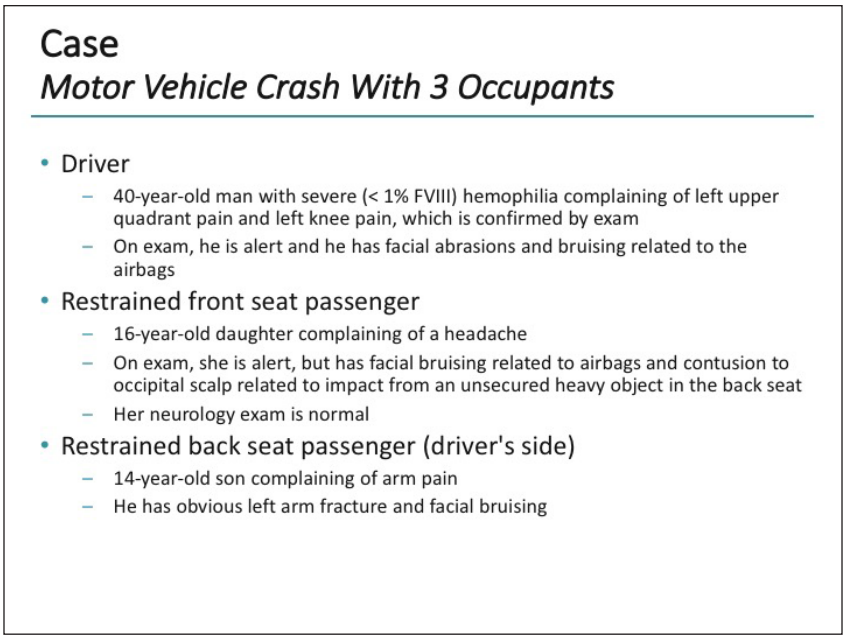
Ms Maahs: The MASAC recommends that patients be treated urgently even if there are no visible signs of bleeding. In addition, the patient's hematologists or HTCs should be consulted. In most cases, screening coagulation studies such as a PT or an aPTT are not needed prior to treatment.



MASAC Guideline (cont)

Ms Maahs: The decision to infuse or not is really based on the suspicion of a bleed, not related to imaging or lab results. If you do feel like imaging is needed, it's important to order/administer factor replacement prior to those tests.

Dr Dunn: To explore some of the issues that arise when treating patients with hemophilia in the ED, we'll explore a case of a motor vehicle crash involving a father with hemophilia and his children.

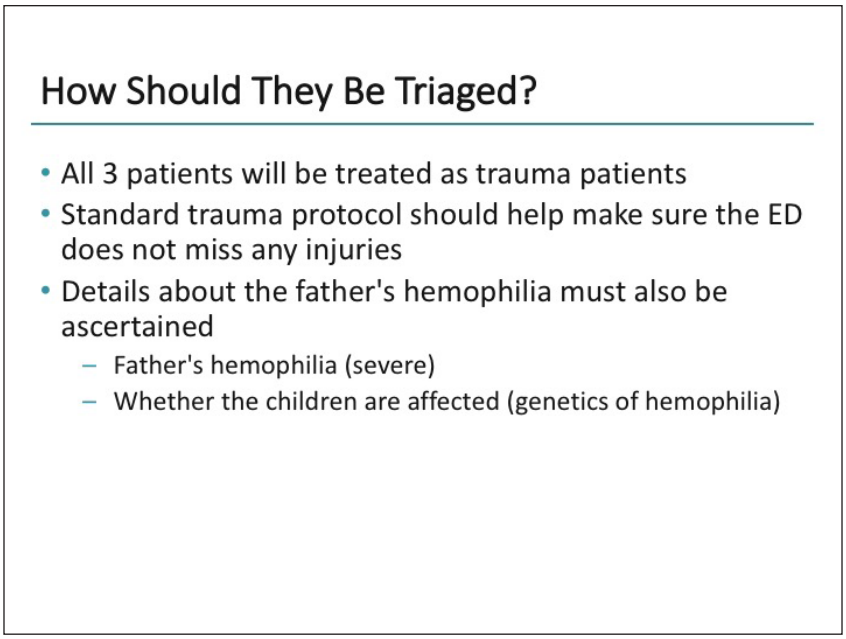


Case: Motor Vehicle Crash With 3 Occupants

Ms Maahs: A small car was traveling through a 4-way intersection at approximately 50 miles per hour when a full-sized truck ran a red light and T-boned the driver's side of the vehicle. The front and side airbags deployed and the 3 occupants of the car arrived at the ED. The driver is a 40-year-old man who was restrained. His medical identification states he has severe — < 1% FVIII — hemophilia. He's complaining of left upper quadrant pain and left knee pain. On exam he's alert. There are facial abrasions and bruising related to the airbags. Exam confirms his left knee is indeed swollen and he has left upper quadrant tenderness.

The restrained front seat passenger is his 16-year-old daughter. She's complaining of a headache, though on exam she is alert. She has facial bruising related to airbags and a contusion to the occipital scalp related to the impact of an unsecured heavy object in the back seat. Her neuro exam is normal.

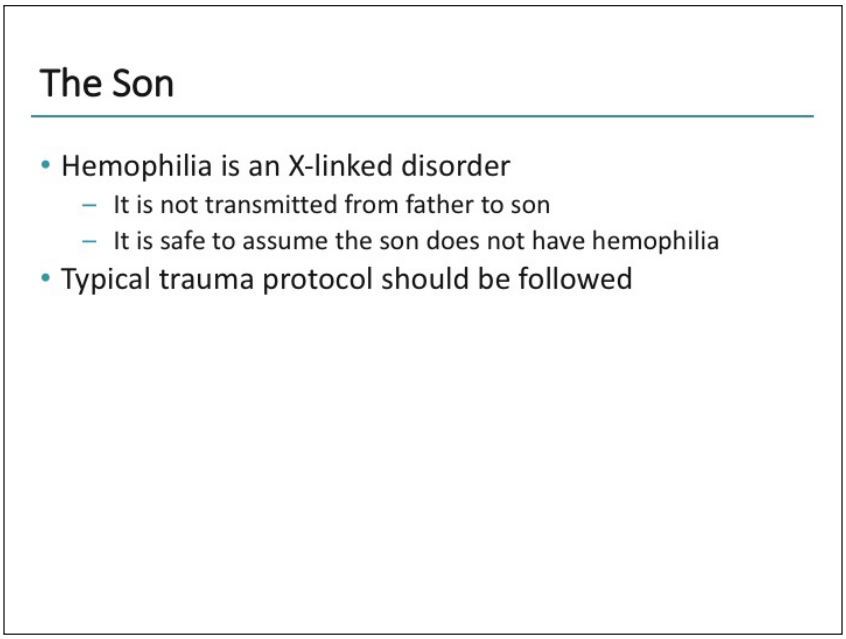
Restrained in the back seat is her 14-year-old brother. He's complaining of arm pain and has an obvious left arm fracture and facial bruising.



How Should They Be Triaged?

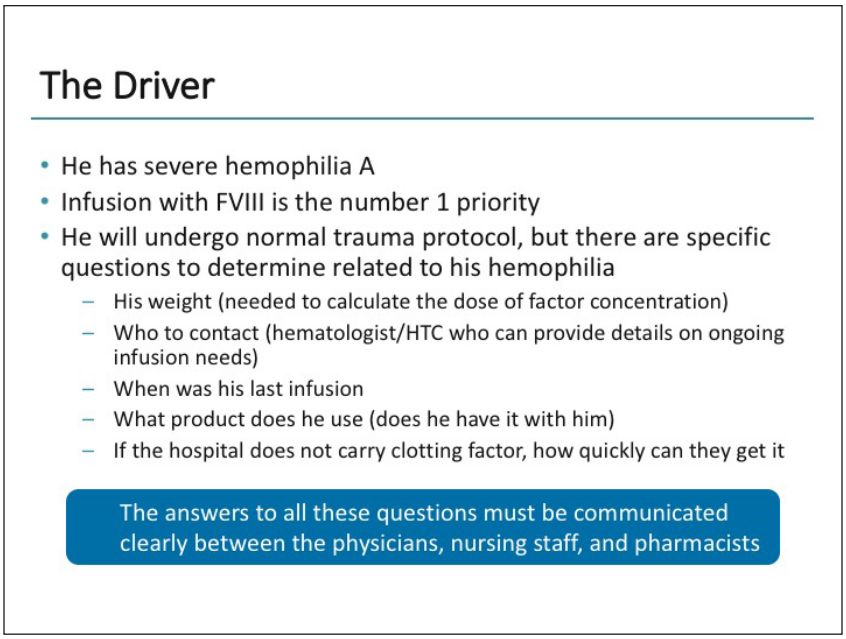
Dr Dunn: ED colleagues, how would you triage these 3 patients and then walk us through their treatment?

Dr Kaide: The first thing I would say is that because these patients are from an injury, they will be treated as trauma patients. And again, if we stick with our standard trauma protocol, we're going to do the things that we need to do in order to make sure we don't miss any injuries. But there are some questions that need to be asked upfront — in particular the details that we talked about earlier with the father's degree of hemophilia. Then we're going to have to address the 2 children who will have different clinical presentations based on their genetics.



The Son

Dr Hagahmed: Let's look at the son. Hemophilia is an X-linked recessive disorder, meaning that it is not transmitted from the father to his son. Therefore, it is safe to assume that the son does not have hemophilia. So, we should proceed with the usual trauma protocol for caring for the son.



The Driver

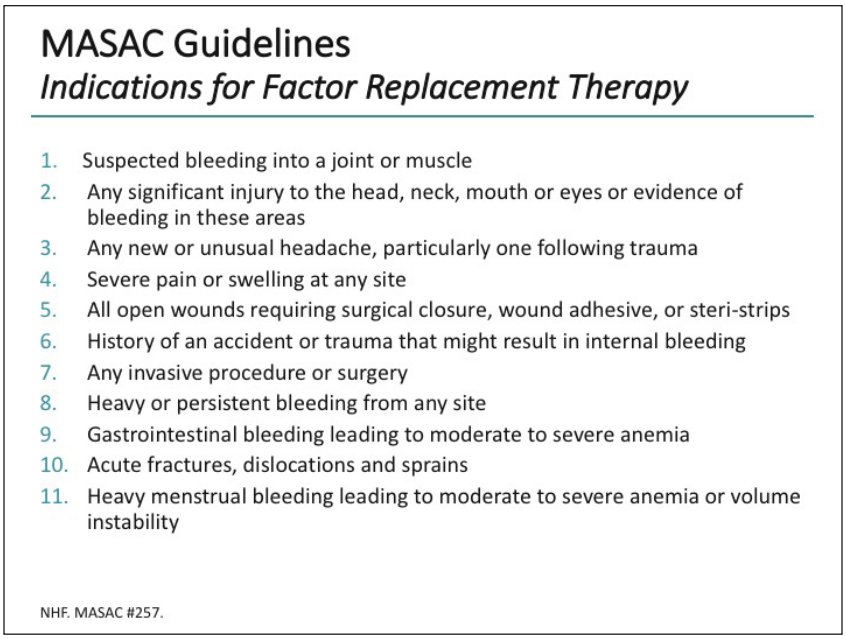
Dr Dunn: What about the driver, Mohamed?

Dr Hagahmed: When it comes to assessing the father, we know that he has severe hemophilia A, so he's an acutely ill patient. In his case, infusion with FVIII is the number 1 priority.

Dr Dunn: We know this patient has severe hemophilia A and infusion with FVIII is the number 1 priority in this situation. But what other things do you need to keep in mind in the ED in this patient?

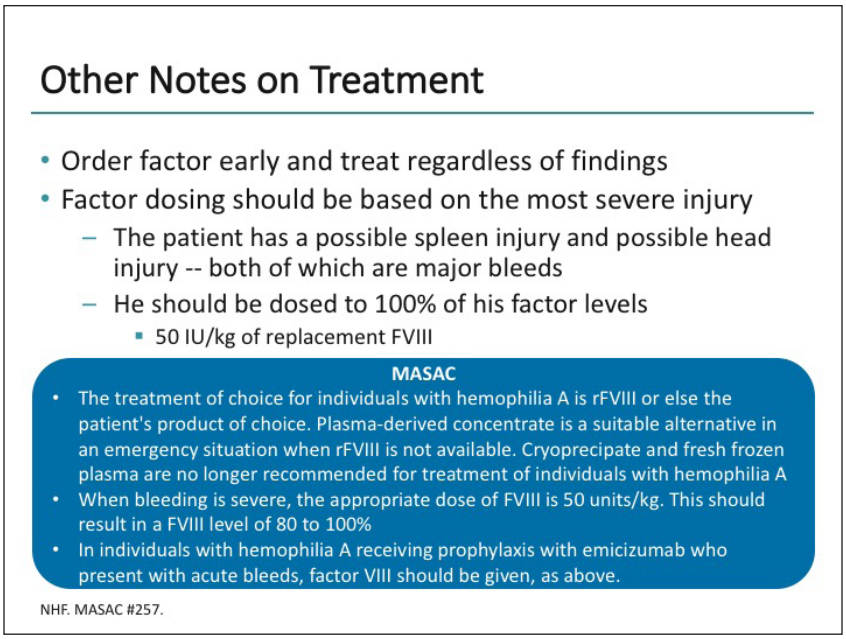
Dr Hagahmed: We need to know his weight. That is crucial for his factor replacement therapy. We also need to know his hematologist — so who to contact for related ongoing infusion needs. We also need to know when was the last time that he used his replacement therapy and does the patient have the product with him as well. Usually these patients travel with their factor when they go on vacation or away from home. If not, then the ED physician should know whether the hospital already has clotting factors onboard and how quickly we can get it to give to this patient. It is very important to communicate this clearly — with the patient, our pharmacists, and also the rest of the nursing stuff.

Otherwise we will undergo the usual trauma protocol for this patient.



MASAC Guidelines: Indications for Factor Replacement Therapy

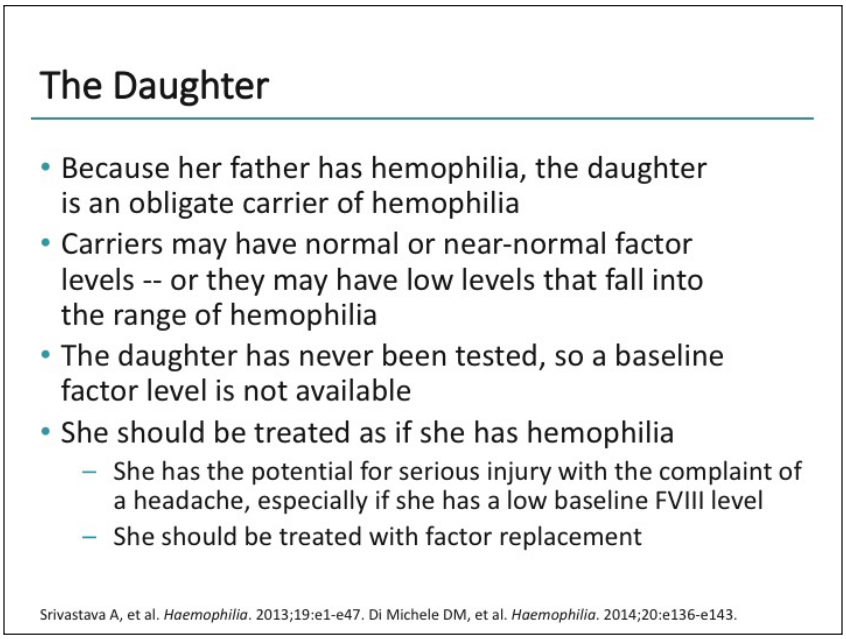
Dr Hagahmed: According to the MASAC guidelines, order factor early and as soon as possible regardless of injury findings. Imaging here is not really crucial when it comes to treating these patients as it further delays factor initiation. Note also that x-rays of the joints to rule out bleeding is not necessary from this case.



Other Notes on Treatment

Dr Kaide: One of the most important things that we have to understand is how we're going to dose the factor. The thing that we take into account is the most serious injury. In this case, this patient has a potential spleen injury and possibly a head injury. So I'm going to need to correct this patient to 100% of his factor levels. In order to do that, I'm going to be giving him 50 IU/kg of replacement FVIII.

Now, if somebody has a more minor injury, the degree of correction can be less. However, in this particular patient, we know that he has some serious injuries and he's going to need to be corrected to 100%.



The Daughter

Dr Dunn: Now that we have the initial treatment for the father, let's turn to the treatment of the daughter.

Dr Kaide: This is going to require a little bit more thought. Based on her genetics, she is an obligate carrier of the disease and carriers can have normal factor levels or pretty close to normal or they can actually dip down into the range where they become clinically hemophiliacs.

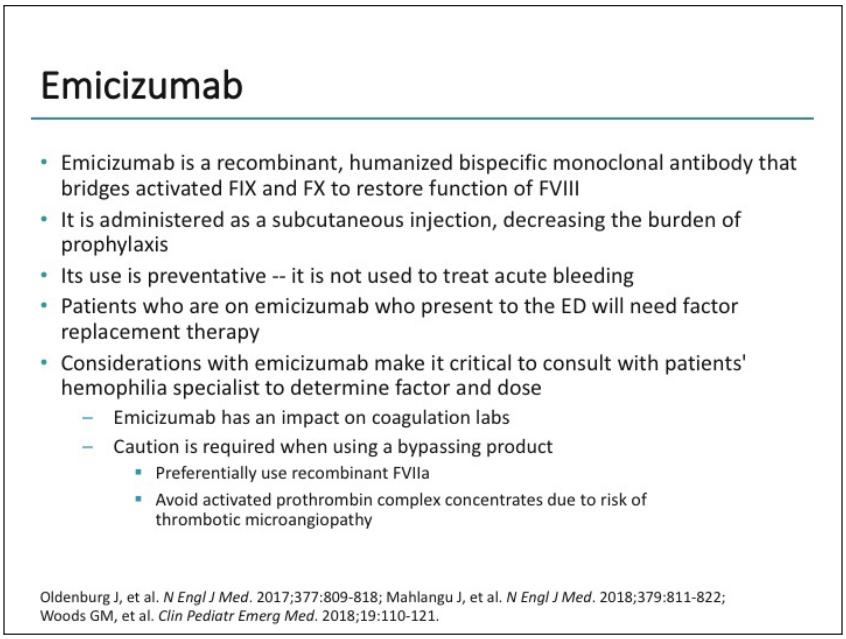
Ms Maahs: I'd like to make a point about carriers. It was previously thought that women only carried hemophilia and were not at risk for bleeding. What we find is that is not true. Many carriers have levels that are lower than the normal range and can be at risk for bleeding during trauma or surgical procedures or even after dental work. When we think about this daughter, we really need to consider what are her bleeding risks and if she, in fact, has mild hemophilia as well, based on her factor level.

Dr Kaide: I don't know what this patient's genetics are going to show me with regards to her factor level, so I'm going to assume that she's going to be in the range where she needs to be treated and I'm going to give her a dose of FVIII.

If she does have normal levels, it's certainly not going to hurt her to give the factor, but if she has mild to moderate hemophilia, not treating has a significant complication. And given her complaints of headache, even if she has a normal neuro exam, she has potential for serious injury. So, in most of these cases we want to default to treatment. We know what her genetics are, but we just don't know what her factor level is and in this particular case it's not that important. We should just go ahead and treat the factor replacement.

Dr Dunn: Is desmopressin indicated in a situation like this?

Dr Kaide: Given the fact that we really don't know much about her levels and that she has potential for more serious injury, I would say no. We typically reserve desmopressin for minor injuries, and the way that works is that it helps to release von Willebrand's factor, which carries FVIII in the blood. We can actually boost that level, but I wouldn't consider that necessarily in a patient who has potential for such serious injury as she does.



Emicizumab

Dr Dunn: The landscape of hemophilia care has really been changing in the last few years, in particular with the advent of the use of emicizumab.

Colin, how would your treatment differ if this father was on emicizumab prophylaxis for his hemophilia?

Dr Kaide: Well, the emicizumab is going to make things better for him, but he's still going to need to be treated just as if he's a regular hemophiliac.

Jen, can you tell us a little bit about emicizumab?

Ms Maahs: Sure. Emicizumab is a new treatment. In fact, it's a very exciting treatment for our patients with FVIII deficiency. It's a subcutaneous injection, which makes it different from their current treatment, which is IV therapy. The use of emicizumab is becoming much more prevalent in our hemophilia A patients. The impact of emicizumab, though, is it's really a preventative treatment, so it can't be used to treat acute bleeding episodes. When these patients do have bleeding, they still need FVIII at the same time.

Dr Dunn: What do you recommend for your patients on emicizumab?

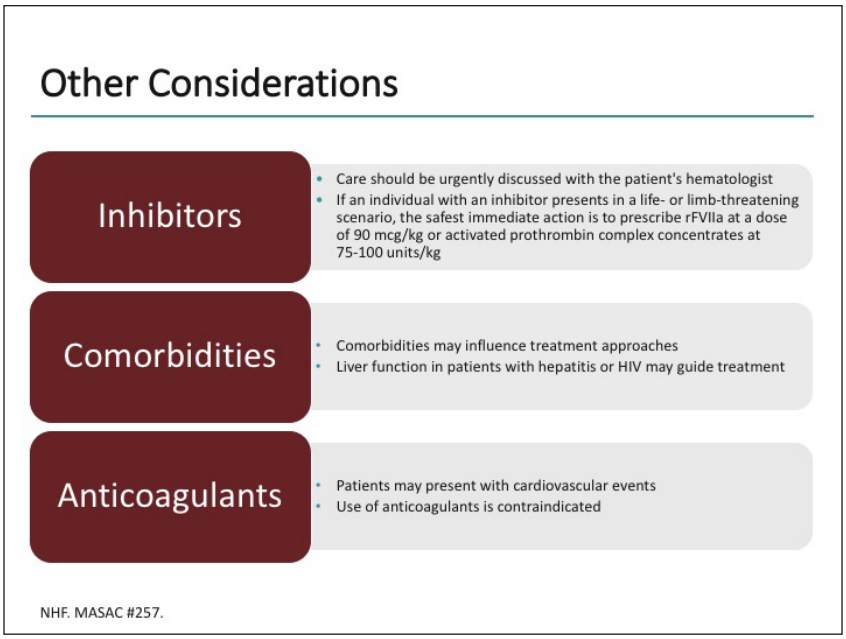
Ms Maahs: What we know about emicizumab is that, when you start infusing FVIII, it's competitive. It knocks the emicizumab off the receptors. Really, those patients, you would treat them like you would treat them with any trauma, he would need that full correction of 50 units per kilo or getting his level up into the normal range without taking into consideration that he's currently on emicizumab.

Dr Dunn: Do patients on emicizumab need additional doses of emicizumab in the ED then?

Ms Maahs: No. Remember this is just a preventative treatment. The patient's going to take it on a scheduled dosing schedule, and so they don't need to get additional doses based on their bleeding issues. Now, if they're due for a dose and they're in the hospital, they do need to continue to get those doses, but it should not be taken into consideration from the standpoint of bleed prevention when they're on FVIII treatment.the standpoint of bleed prevention when they're on FVIII treatment.

Dr Dunn: Also, if you're taking care of a patient on emicizumab, it's important to know that emicizumab impacts certain coagulation laboratories and so these should be interpreted with caution. If you have a patient with an inhibitor and you need to use a bypassing product, you would preferentially use recombinant FVIIa. You want to avoid prothrombin complex concentrates if possible due to a risk of thrombotic microangiopathy. However, this happens typically when doses exceed more than 200 IU/kg/d.

Ms Maahs: One thing that we're finding in our pediatric population is many of them needed a port-a-cath or a central line to give the medication to get the factor concentrate. Now that they're on emicizumab, we're removing the central lines. When you think about how these patients may present in the ED, it may be because the family is unable to give the factor concentrate when they are having bleeding episodes, so that's a little wrinkle that we're seeing now that is becoming an issue in the ED.



Other Considerations

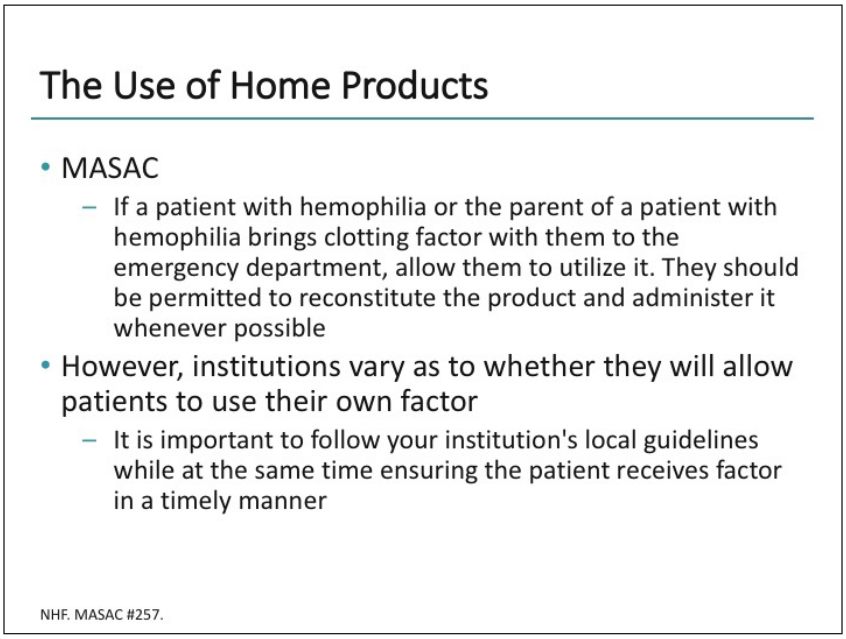
Dr Dunn: There are also important considerations if a patient has an inhibitor in regard to response to treatment. I would strongly recommend that if you are treating a patient with hemophilia who has an inhibitor in the ED, you should discuss that treatment with the hemophilia treatment specialist as soon as possible.

There are also other comorbidities to consider. Many of our older patients acquired HIV or hepatitis through a contaminated clotting factor and understanding their liver function will help guide treatment in the ED.

Ms Maahs: One of the other comorbidities we've also found is that many of our older patients, especially in the mild range, develop cardiovascular disease. They may end up in the ED with some sort of cardiovascular event where decisions need to be made about emergent care.

Dr Dunn: What do the MASAC guidelines say about using anticoagulants in the ED?

Dr Hagahmed: Good question. The MASAC guidelines recommend against using aspirin or aspirin-like products in this patient population.



The Use of Home Products

Dr Dunn: Jen, could you speak to the issue related to when patients bring their own factor to the ED?

Ms Maahs: We all want optimal care for our patients, and when we're talking about a patient in the ED, optimal care usually involves prompt treatment. Many hospitals, especially in rural areas, may not carry factor concentrate. Because of that, we ask patients to carry their products with them when they travel or in the event of an emergency. Many hospitals may have some factor, but it might not be the product that the patient is on, and that becomes a little bit of an issue when a patient gets a different product.

The MASAC guidelines are really in place to support patients bringing their products from home into the ED and being able to use them. However, we know that it can change based on your guidelines of your local institutions

Dr Dunn: For example, in my institution we can only use home products if they are not on our local formulary. What about in your ED, Colin?

Dr Kaide: It comes down to the physician's discretion. If they ask if they can use their product, I will usually tell them yes.

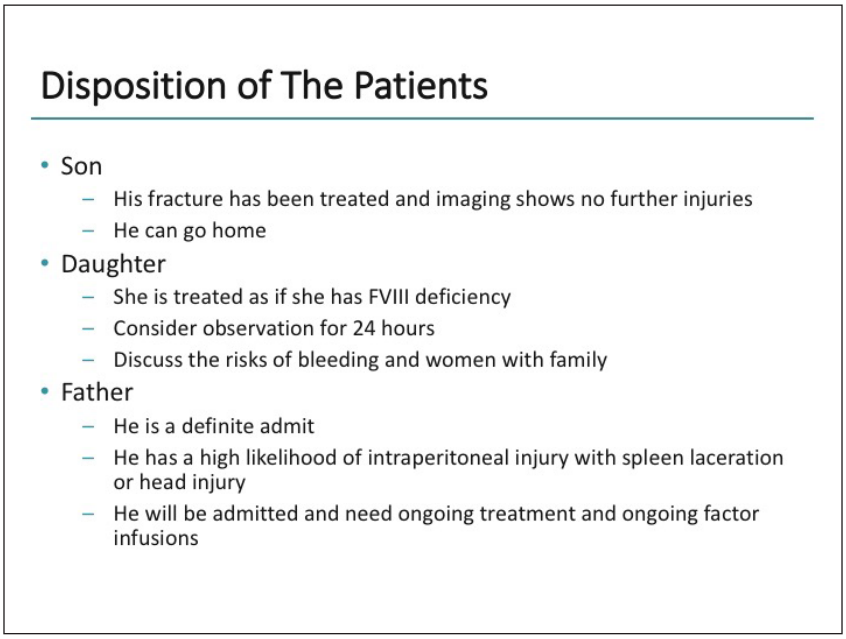
Dr Dunn: How about you. Mohamed?

Dr Hagahmed: We usually have a close discussion with our hematologists who are readily available to us, but we allow the patient to bring their home product with them and use it in ED.

Dr Dunn: Jen, I know that you cover the entire state. What happens for your patients in their home factor use?

Ms Maahs: If they come to our institution, we do carry the products that they need. If they're going locally and if we know ahead of time, we will call and find out if they do carry the product and if not, advise the patient to take their products with them.

Dr Dunn: So I think the bottom line is know your local guidelines and follow those.



Disposition of The Patients

Dr Dunn: Now that all of these patients have had their initial triage and treatment, what sort of disposition would you be looking at for the son, Colin?

Dr Kaide: Well, for the son, I think if his imaging shows that he doesn't have any more serious injuries and I've treated his fracture, I think he can go home. He doesn't really need a lot of observation for this.

Dr Dunn: Colin, since many places you won't be able to get a factor level very quickly, what would you do in disposition for this girl?

Dr Kaide: Well, because I've decided to treat her as if she has FVIII deficiency, I'm going to watch her for a period of time. I may try to observe her for 24 hours and then assess the situation, and when I do decide to send her home, I'm going to make sure she's with reliable people who can watch for signs of complications.

Dr Dunn: Is it safe to do this sort of observation in the local community hospital or should she be transferred to a higher-level facility?

Dr Kaide: I think it kind of depends on your imaging. If I manage this patient and gave an initial dose, and I did all my imaging and everything comes up negative, it might be okay to be able to keep this patient locally. When in doubt, I might want to transfer this patient to someplace that has the capability of doing the ongoing care. It kind of depends upon what resources I have available and what kind of things that I actually find when I do my workup.

Dr Dunn: Yeah. I think this goes back to Mohamed's point earlier where it's really important for your teams to be doing case-based scenarios for patients with hemophilia before they present.

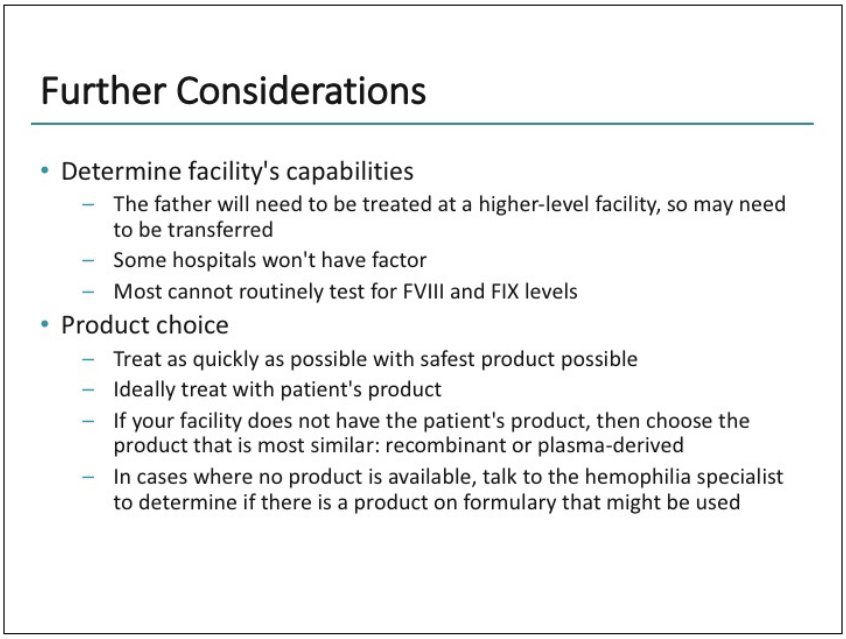
Dr Hagahmed: Right. This is also a crucial important point here that we need to emphasize is the discussion with the patient family members as well, because if they have a close follow-up with their primary care doctor and their hematologist within the next day and the patient's completely hemodynamically stable with a negative ED workup, then they can be safely discharged. Again, we just have to sit down and have a shared decision making with the family and the patient

Dr Dunn: As a hemophilia provider, we really appreciate getting those phone calls from the ED. Even if the imaging is negative, it really helps us plan the next follow-up appropriately for those patients.

Ms Maahs: It would also be a really good time to have a conversation with the family about the risks of women and bleeding. They may not know that their daughter is at risk for having bleeding episodes with trauma, and so encouraging them to get that baseline factor level on her during a nontraumatic time would be very helpful in planning future care for her.

Dr Dunn: Last but not least, certainly, is the father. What would be the disposition for him?

Dr Kaide: Well, he's definitely getting admitted. He has a very high likelihood, hemophilia or not, to have an intraperitoneal injury like a spleen laceration or a head injury. Regardless of the hemophilia state, he's going to be admitted to the hospital, and he's going to need ongoing treatment and ongoing factor infusions.



Further Considerations

Dr Dunn: It sounds like the father is someone who would need to be taken care of in a higher-level facility if possible.

Dr Kaide: Absolutely. If I saw him at a community hospital setting, I would arrange for transfer as quickly as possible. During the downtime while I'm waiting for transfer, I can do all the imaging, but what I really need to think about is to get this person to the factor in the timeliest way possible.

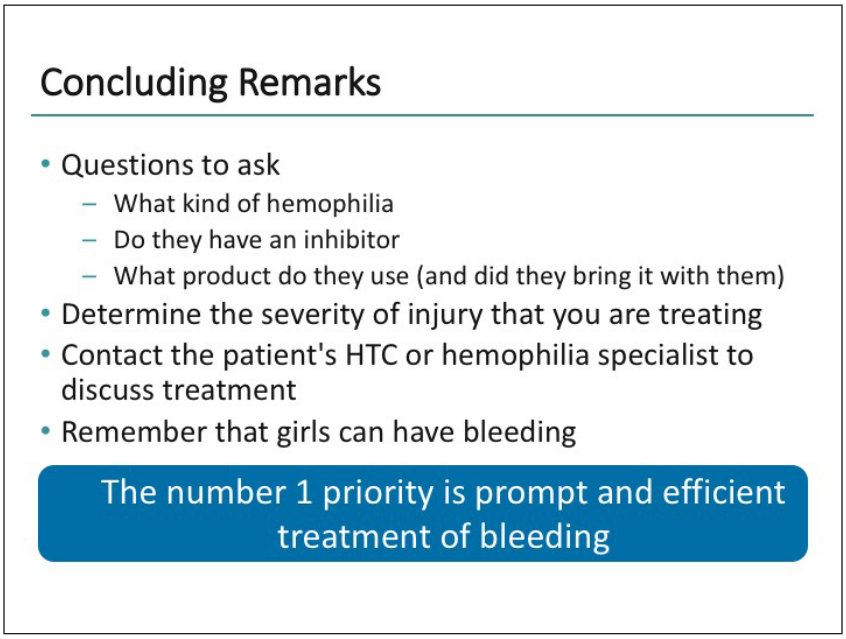
Ms Maahs: Another issue to consider is sometimes hospitals may be able to carry factor, but if they need continuing monitoring such as laboratory studies, most hospitals can't do routine FVIII and IX levels unless you're at a hospital that actually has a treatment center.

Dr Dunn: One last comment about the product choice. I would always recommend that you treat as quickly as possible with the safest product possible. This goes back to knowing what products your facility carries. When you're choosing the factor product to treat these patients with, ideally, you would treat them with the product they use at home. However, if you don't have that product, try to choose the product that is most similar.

For example, if a patient is on a recombinant FVIII concentrate, use another recombinant FVIII concentrate. If they're on a plasma-derived concentrate, use a plasma-derived concentrate. If you have any questions at all, call the hemophilia treatment center and let them guide you, but prompt treatment should still be your goal.

Dr Kaide: Let me ask you, as a practicing emergency physician, we always hope for the best but plan for the worst. Let's say I'm in a situation in a small community hospital and my transportation is significantly delayed because of a snow storm or some other environmental conditions. Let's say I have a bypassing agent available like FVIIa inhibitor bypassing activity. If I have that available at my facility for other uses, is it okay to give that in lieu of actual regular factor replacement, or is that something I shouldn't be getting into? How would I approach that situation where I don't really have the products that I need to have?

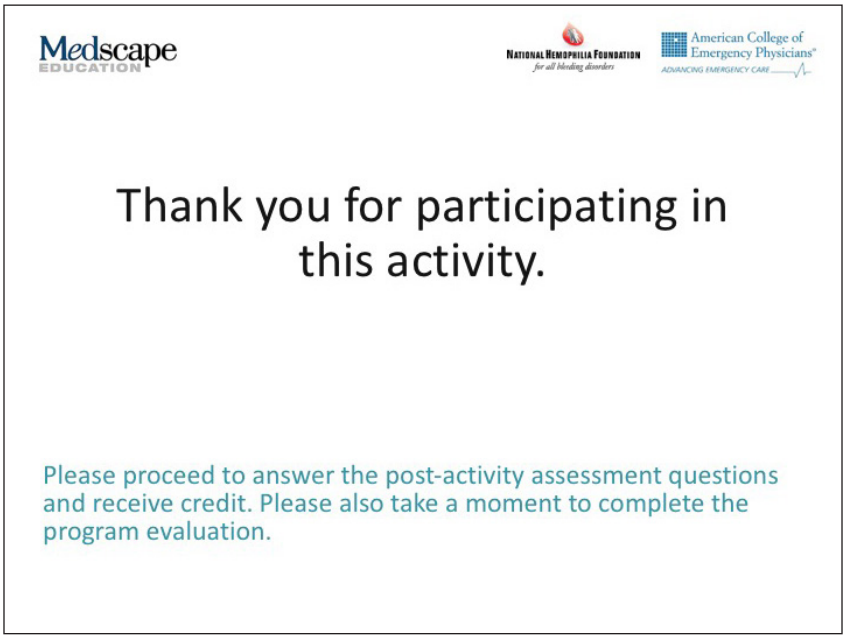
Dr Dunn: It's a great question, and I would definitely recommend at least discussing that with the hemophilia treatment center. There may be a product on the formulary that you're not aware of that could be used for treatment in this situation. Again, going back to knowing what's on your formulary, knowing what you have access to and then also understanding the appropriate doses of these agents for patients with hemophilia is really important.



Concluding Remarks

Dr Dunn: To summarize what we've discussed today, there are some really important things that you need to know if a patient with hemophilia presents to the ED. First and foremost, you need to know what kind of hemophilia they have, whether or not they have an inhibitor, what product they use, the severity of injury that you are treating. It's important to discuss these patients with their hemophilia treatment center. Don't forget, the number 1 priority is prompt and efficient treatment of bleeding. And don't forget that girls can have bleeding too.

I'd like to thank Mohamed, Colin, and Jen for joining me today.



Thank you for participating in this activity.

Dr Dunn: And thank you, the audience, for listening to our case presentation. Please continue on to answer the questions that follow and complete the evaluation.

HCP

Hemophilia is an inherited x-linked bleeding disorder secondary to a deficiency in plasma clotting FVIII or FIX. There are 2 types of hemophilia, hemophilia A, which is more common, and hemophilia B. Severity of hemophilia is usually based off baseline factor activity at initial diagnosis and often predicts risk factors for bleeds and severity once bleeding occurs. [5] Regardless of their severity, patients with hemophilia will have injury associated with the disorder or spontaneous bleeding episodes that require evaluation and treatment in the ED. Due to the necessity of prompt and adequate treatment, all personnel in the ED must have knowledge of the disorder and understand guidelines to appropriately serve this population and decrease the risk for morbidity.

Patients with hemophilia are usually followed closely by a hematology team at an HTC, with education starting at diagnosis that continues in combination with close follow-up in the outpatient hematology clinic. Patients with hemophilia are usually able to maintain outpatient treatment in the clinic or at home, limiting the number of visits to the ED. Most patients only present to the ED when treatment at home is not sufficient or injury was the cause.[11] On presentation, this population is unique due to the importance of fast diagnosis and the need for factor replacement therapy. A delay in either one can ultimately lead to increased morbidity and mortality, which makes the treatment received at the ED a vital part of patients' overall outcome.

For patients presenting to the ED, the first line of evaluation is performed by the triage nurse who examines the patient and determines the level of acuity. Acuity is ranked using the Emergency Severity Index (ESI), a 5-level triage algorithm that categorizes patients in the ED by evaluating patient acuity and resource needs. Level 1 is the most severe and requires immediate response with all available resources, while level 5 is the least severe and indicates less urgency and need of resources. If determined a level 1, the patient is immediately taken to a room where treatment is started. Level 2 patients will be roomed next and so forth, with the potential for level 3 through 5 having a prolonged wait for the next available provider. As a result, accurate assignment of an acuity level is of great importance — incorrectly deeming a critical patient a low level will cause a dangerous delay in evaluation and treatment.

Patients with hemophilia should be considered high acuity (eg, at least level 2) and receive urgent examination and intervention. When the triage nurse discovers the patient has hemophilia during the thorough history of present illness and physical assessment, the nurse should first assess the patient for evidence of a major or a minor bleed.

Types of major bleeds include[5]:

- Hemarthroses
- Deep muscle hematoma
- Compartment syndrome
- Intracranial
- Spinal cord
- Gastrointestinal
- Pseudotumor
- Airway/throat/neck
- Ophthalmic

Types of minor hemorrhages include[5]:

- Superficial muscle hematoma
- Oral bleeding
- Epistaxis
- Abrasion/hematoma
- Laceration

Details of the bleed will be documented and reviewed by the physician once the patient is roomed, helping to determine initial treatment and dose of factor to be administered.

Next, the triage nurse will ask if the patient has started treatment at home or brought factor with them to be administered. Most patients with moderate or severe disease have been trained to initiate treatment at home when a bleed occurs and may be presenting to the ED due to problems with starting an IV, maintaining an IV, or significant pain from the bleeding event. Factor brought from home will be used if permitted by the hospital, as these families are usually well versed and doses are specific for that patient.[11] Patients with mild disease may present to the ED because home infusions have never been a necessity and this is their first experience with a bleeding episode.[11]

If factor is not available, the nurse will document it, and after the patient is roomed, the provider will immediately order factor. The goal is to have the factor available within 1 hour of the patient's arrival, if possible.[5] Guidance on how to order the correct factor will vary by institution. As an example, at our institution, there are guidelines on the intranet developed by our hematology team that outline what replacement to order based on type of emergency along with appropriate dosing. In addition, our ED has onsite pharmacists who can guide and assist in ordering the correct factor.

The triage nurse must also be aware that this patient population may not have obvious signs of bleeding and could be experiencing an occult bleed. There are certain chief complaints that support this concern and prompt further questioning.

These include:

- Significant injury to the head, neck, mouth, or eyes
- Severe pain or swelling at any site
- Accident or trauma that could cause internal bleeding and acute fracture, dislocation, or sprain

Patients with any of the above complaints would also be made a level 2 with immediate room assignment. This first-line assessment and acuity assignment makes the triage nurse a very integral part of the patient's overall outcome. A patient with hemophilia not triaged correctly could delay evaluation and treatment, ultimately leading to unfavorable outcomes.

After the triage nurse has roomed the patient, another nurse takes over care for the patient in conjunction with the physician. This nurse does their own assessment and completes the orders placed by the provider. After factor has been ordered or home factor is available, the nurse would start the process of placing the IV. Literature recommends the most experienced IV therapist should place the IVs or obtain blood draws due to the negative outcomes that could arise from multiple failed attempts, which can lead to hematomas that limit IV.[3] It is also important to limit the number of blood draws and injections. This is because they risk causing further bleeds. Intramuscular hematomas are a common finding in this population and can be sustained after receiving a intramuscular injection.[5]

Once the IV is placed and factor started, consultation with the patient's hematologist should be made by the physician and the need for further work up or testing determined. Mild bleeds are often treated and appropriate plasma level achieved in the ED, allowing the patient to continue home treatment with follow-up in the hematology clinic. Once major bleeds are determined to be stable in the ED, those patients are admitted to the hematology floor where they continue to receive treatment by their specialist. If a patient with a major bleed has presented to a community hospital ED, arrangements should be made after initial factor infusion and stabilization for safe transfer to a facility where further care can be provided.

In our ED, all high level acuity patients are evaluated by a physician rather than a nurse practitioner. However, all clinicians in the ED should understand the presentation of this disease and also the guidelines for treatment due to the possibility of the undiagnosed patient. For example, young children will often present to the ED for unexplained bruising or bleeding and triaged a level 4 or 5. These children are often worked up for non-accidental traumas but consideration of a bleeding disorder must be considered.[11] The clinician would need to get a thorough family history of any bleeding disorders and,

based on that history, order appropriate labs to rule out the diagnosis. These labs include: a complete blood count with platelet count and peripheral blood smear, PT/INR, aPTT, and fibrinogen. Based off lab findings, consultation to the on-call hematologist may be warranted to discuss patient findings. Other common presentations to the ED that may represent an undiagnosed bleeding disorder are complaints of swelling of the joints/muscles and deep tissue hematomas after routine childhood vaccinations.[11] All clinicians must be aware of these common findings in undiagnosed bleeding disorders in order to avoid delay in treatment.

Once the blood level of the clotting factor has been returned to normal for minor bleeds, the nurse will reassess the patient and notify the provider if there are any other concerns or conditions that haven't been addressed due to priority of factor replacement. This assessment may prompt the provider to order further testing or imaging. If the underlying cause of the emergency visit and clotting factor level has been resolved, then the patient will be discharged.

In conclusion, the largest concerns for a patient with hemophilia presenting to the ED is delay in severity recognition and delay in immediate action or treatment. At our institution, thorough education is provided to the nurses to reiterate this importance with known "next steps" in place. Having a good familiarity with the MASAC guidelines and working closely with the patient and family will ensure timely and optimal care.

References

1. Okolo AI, Soucie JM, Grosse SD, et al. Population-based surveillance of haemophilia and patient outcomes in Indiana using multiple data sources. *Haemophilia*. 2019;25:456-462.
2. Drayton Jackson M, Dunn MW, Storey MA, et al. Increasing optimal coagulation factor dosing in the paediatric emergency department: A quality improvement study. *Haemophilia*. 2019;25:258-263
3. National Hemophilia Foundation. MASAC recommendation concerning guidelines for emergency department management of individuals with hemophilia and other bleeding disorders. Document #252. https://www.hemophilia.org/sites/default/files/document/files/252%20ER%20Management.pdf. Accessed November 14, 2019.
4. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. WFH guidelines for the management of haemophilia. *Haemophilia*. 2013;19:e1-e47.
5. Woods GM, Dunn MW, Dunn AL, et al. Emergencies in hemophilia. *Clin Pediatr Emerg*. 2018;19:110-121.
6. Manco-Johnson MJ, Abshire TC, Shapiro AD, et al. Prophylaxis versus episodic treatment to prevent joint disease in boys with severe hemophilia. *N Engl J Med*. 2007;357:535-544.
7. National Hemophilia Foundation. MASAC recommendation concerning products licensed for the treatment of hemophilia and other bleeding disorders. Medical and Scientific Advisory Council Document #253. https://www.hemophilia.org/sites/default/files/document/files/masac253.pdf. Accessed November 14, 2019.
8. Di Michele DM, Gibb C, Lefkowitz JM, et al. Severe and moderate haemophilia A and B in US females. *Haemophilia*. 2014;20:e136-e143.
9. Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab prophylaxis in hemophilia A with inhibitors. *N Engl J Med*. 2017;377:809-818.
10. Mahlangu J, Oldenburg J, Paz-Priel I, et al. Emicizumab prophylaxis in patients who have hemophilia A without inhibitors. *N Engl J Med*. 2018;379:811-822.
11. Singleton T, Kruse-Jarres R, Leissinger C. Emergency department care for patients with hemophilia and von Willebrand disease. *J Emerg Med*. 2010;39:158-165.

Abbreviations

aPTT = activated partial thromboplastin time
CT = computed tomography
ED = emergency department
FIX = factor IX
FVIIa = factor VIIa
FVIII = factor VIII
HIV = human immunodeficiency virus
HTC = hemophilia treatment center
INR = international normalized ration
IV = intravenous
MASAC = Medical and Scientific Advisory Council
NCH = Nationwide Children's Hospital
PT = prothrombin time
PTT = partial thromboplastin time
rVIII = recombinant FVIII