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March is Bleeding Disorder Awareness Month!

Key Inforbits:

- What is Bleeding Disorder Awareness Month?
- What are the most common bleeding disorders?
- Non-Pharmacologic Treatment Options for Bleeding Disorders.
- New Drugs Approved for Bleeding Disorders.

What is Bleeding Disorder Awareness Month?

Bleeding Disorder Awareness Month has been observed every March since 2016. The goal is to increase awareness of inheritable blood and bleeding disorders in the hopes of education and to bring information to the attention of policymakers, industry representatives, and healthcare professionals. It is important to raise awareness of blood disorders because they affect 3 million people nationwide [1]. Bleeding disorders can be inherited, affect the way blood clots, and affect the overall hemostasis of the blood[2] It is important to recognize the different types of bleeding disorders to get the proper care.

What are the most common bleeding disorders?

- Hemophilia

  There are 2 types of Hemophilia: Type A and Type B. The type of hemophilia that a person has is based on what clotting factor in the blood is lacking; Type A lacks factor VIII and Type B lacks factor IX.[3] This rare genetic blood disorder comes from a defect in the X chromosome. Because the mutation is found on the X chromosome, men are more at risk of having hemophilia since men only carry one X chromosome. Before the 1980's, the only treatment for hemophilia was blood transfusions from a blood donor. Since then, there have been synthetic blood factors that have been developed over time to make treatment of hemophilia much safer and more drugs continue to come to market. The table below provides a comparison of the different types of hemophilia:

Table 1: Hemophilia Comparison[4]		
Criteria	**Type A Hemophilia**	**Type B Hemophilia**
Epidemiology	Affects 12/100,000 males in the US and there are 400 boys born with hemophilia A each year Although a genetic disorder, about 1/3 cases have no family history Prolonged bleeding from minor cuts, dental procedures, and injuries.	Occurs in 1/5,000 live births Affects between 30,000 to 33,000 people in the United States Four times less common than hemophilia A Although genetic, 1/3 of cases are caused by spontaneous mutation Prolonged bleeding from minor cuts, dental procedures, and injuries.
Levels of Severity	Mild (6% to 49% of factor VIII): prolonged bleeding after serious injury, trauma, or surgery. The first episode may not happen until adulthood. Women may experience heavy menstrual bleeding or hemorrhage after childbirth Moderate (1% to 5% of factor VIII): prolonged bleeding after injuries Severe (<1% of factor VIII): prolonged bleeding after injuries and spontaneous bleeds often into joints and muscles	Mild (6% to 49% of factor IX): prolonged bleeding after serious injury, trauma, or surgery. The first episode may not happen until adulthood. Women may experience menorrhagia, heavy menstrual bleeding, or hemorrhage after childbirth Moderate (1% to 5% of factor IX): prolonged bleeding after injuries and spontaneous bleeds Severe (<1% of factor IX): prolonged bleeding after injuries and frequent spontaneous bleeds often into joints and muscles
Diagnosis	Diagnosed based on clotting factor tests, hemophilia genetics, and worsening of symptoms Males are diagnosed usually after circumcision	Diagnosed based on clotting factor tests.
Treatment Goals	Treatments vary, but overall are aimed at replacing factor VIII	Concentrated factor IX product or recombinant factor products: Recombinant factor products do not need human derived donor

		sourced plasma and are made using DNA technology. Prophylaxis: optimal therapy for children with severe disease. Aminocaproic acid: This is an antifibrinolytic that is recommended before dental procedures as prophylaxis and for treatment of nose and mouth bleeds. It is also recommended that a dose of clotting factor is given before the aminocaproic acid to help form a clot and keep it from breaking down.

- Von Willebrand Disease[5]

  Von Willebrand Disease (VWD) is the most common inheritable bleeding disorder, affecting 3.2 million people in the United States. For people with VWD, they are typically missing or low in the von Willebrand factor, which is a clotting protein that binds to factor VIII to help form a platelet plug. As a result, these people are unable form the platelet plug, or formation is delayed. Overall, VWD affects 1 in 100 men and women equally, though may be more symptomatic in women. Symptoms include:

  - Frequent nose bleeds that last longer than 10 minutes
  - Bleeding from cuts/injuries that last longer than 10 minutes
  - Bruising easily
  - Being treated for anemia
  - Heavy bleeding after any surgery
  - Having family with similar symptoms or has been diagnosed with VWD or hemophilia
  - For women: heavy menstrual bleeding or heavy bleeding after childbirth or a miscarriage

  There are three types of VWD that are hereditary and one that is not. The types are as shown in Table 2:

https://www.ihtc.org/vwd-inheritance-patterns

Table 2: Types of Von Willebrand Disease			
Type 1	**Type 2**	**Type 3**	**Acquired**
60-80% of patients Low levels of von Willebrand Factor 20-50% of normal Mild symptoms Type 1C • Von Willebrand Factor has increased clearance and prolongs bleeding	15-30% of patients Normal von Willebrand Factor, but less functional Mild to moderate symptoms Four subtypes depending on how the von Willebrand Factor is defective: Type 2A, 2B, 2M, and 2N	5-10% of patients Very low or no von Willebrand Factor May also be low in factor VIII Severe symptoms Spontaneous bleeds into joints and muscles	Results after diagnosis of an autoimmune disease or after some medications

VWD is diagnosed with a von Willebrand Factor antigen test, clotting time, and platelet function. Once diagnosed with VWD, more tests are run to decipher the specific type. Treatment will depend on the type and severity. Options include desmopressin, tranexamic acid, hormonal therapy for women with heavy menstrual bleeding, or factor concentrates.[16]

- Other Factor Deficiencies:[1]

  These deficiencies are rare disorders, where a specific clotting factor protein is low, missing, or defective. Most of these disorders were discovered within the past 60-70 years. Treatments depends on the missing protein. People can have deficiencies for factors I, II, V, VII, X, XI, XII, and XIII. Of these factors, factor VII deficiency is the most common, while factor XIII deficiency is the rarest. Each of these disorders is considered rare. Some people are treated with factor concentrates while others are treated with fresh frozen plasma.

Non-Pharmacologic Approaches for Bleeding Disorders

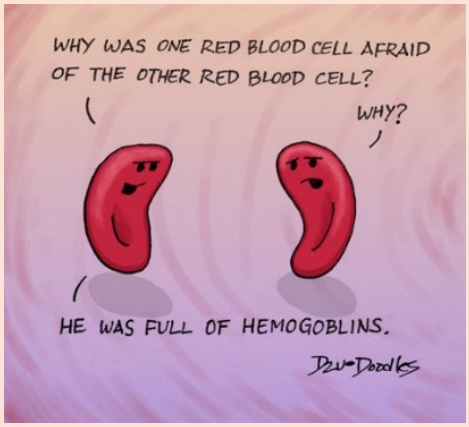
- Hemophilia Prevention: there is currently no non-pharmacologic treatment recommended for the treatment of prophylaxis of hemophilia. Although there are no non-pharmacologic recommendations, it is important to inform the patient that hemophilia is a lifelong condition and to inform them of the symptoms mentioned above, and to seek medical attention if any of these symptoms occur.

New Drugs Approved for Bleeding Disorders

Table 3: New Medications to Treat Hemophilia[6-10]

Drug Name & FDA Approval Date	Mechanism of Action	Indications for use	Common Adverse Effects	Contraindications	Formulations & Route of Administration	Average Cost
Altuviiio (Antihemophilic Factor (Recombinant) 02/23/2023	Replaces Factor VIII which is necessary for clot formation and the maintenance of homeostasis[4]	Used for prophylaxis, on-demand treatment, and perioperative management of patients with hemophilia A	Headaches Arthralgias	Hypersensitivity (anaphylaxis) to hemolytic factor	Once weekly IV administration	$6.31 per unit
Roctavian (valoctocogene roxaparvovec-rvox) 6/29/2023	Adeno-associated virus stereotype 5 based gene therapy designed to introduce a functional copy of a transgene that encodes for factor VIII.	Treatment of severe hemophilia Type A with factor VIII < 1 IU/dL without antibodies to the adeno-associated virus stereotype 5	Nausea Increased AST & ALT levels Fatigue Increased creatine phosphokinase Increased lactate dehydrogenase	Active infection or uncontrolled chronic infection Known hepatic fibrosis or cirrhosis Hypersensitivity to mannitol	IV through a peripheral catheter with an in-line 0.22-micron polyvinylidene fluoride filter Dosed at 1ml/min which can be increased every 30 minutes by 1mL/min to a maximum of 4mL/min	$2.9 million BioMarin Pharm
Hemgenix (etranacogene dezaparvovec-drlb) 11/22/2022	Adeno-associated virus stereotype 5 based gene therapy containing a codon-optimized DNA sequence of the gain-of-function Padua variant of factor IX.	Treatment of hemophilia Type B who are currently using prophylaxis treatment, have historical life-threatening hemorrhage, or have repeated serious bleeding episodes	Increased serum kinase Increased AST & ALT levels Antibody development Fatigue Headache Malaise Flu-like symptoms	No contraindications are listed per the manufacturer	IV through a peripheral catheter with an in-line 0.22-micron polyvinylidene fluoride filter Dosed at 2mL/kg as a single one time dose	$3.5 million CSL Behring

The last "dose" …



https://twitter.com/DzuDoodles/status/1056923002064674817?photo=1

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