

What is an inhibitor?

- Inhibitors are antibodies that are developed by the immune system (the body's natural defense system) because it sees the clotting factor that is being infused as a foreign substance.
- The immune system then thinks that this foreign substance needs to be destroyed.
- The antibodies that are formed neutralize the factor before the factor has time to work.

What are the symptoms of an inhibitor?

- A bleed does not quickly improve with a normal dose of factor
- A normal dose of factor treatment seems less and less effective
- Bleeding continues to be more and more difficult to control
- Breakthrough bleeding despite compliance with prophylactic infusions

Who is at risk for developing an inhibitor?

- Inhibitors occur more often in individuals with severe Hemophilia than with moderate or mild, and more often in Hemophilia A than in Hemophilia B
- Approximately 25-30% of severe Hemophilia A patients develop inhibitors
- Only 2-5% of Hemophilia B patients develop inhibitors
- Most inhibitors develop during the first 50 exposures (or infusions) of factor

How is an inhibitor diagnosed?

- A blood test called a **Bethesda Assay** is performed. The amount of inhibitor in a person's blood is measured in **Bethesda Units (BU)**.
 - **High Titer = More than 5 BU.** These inhibitors act more strongly and more quickly destroy infused factor. Must use a bypassing agent to stop bleeding
 - **Low Titer = Less than 5 BU.** These inhibitors act more weakly and more slowly destroy infused factor. May be able to use factor VIII (8) or factor IX (9) to overcome the inhibitor.

What are the treatment options for inhibitors?

- **Treating bleeds**
 - Recombinant factor VIIa (NovoSeven™)
 - Activated prothrombin complex concentrates (aPCCs) (FEIBATM)
- **Getting rid of the inhibitor**
 - Immune tolerance induction therapy (ITI)
 - High dose factor VIII (8) or IX (9)
 - Immunosuppression (selected cases)

What is immune tolerance induction therapy (ITI)?

- Daily high doses of factor over a period of weeks, months, or years
- Given with the goal of “teaching” the body to tolerate the factor and not see that factor product as foreign
- Often the patient is given bypassing agents as their prophylaxis regimen in addition to the high doses of factor product
 - Given to help prevent or control bleeding as the ITI will likely not give much factor coverage until the body learns to not recognize this as foreign anymore