

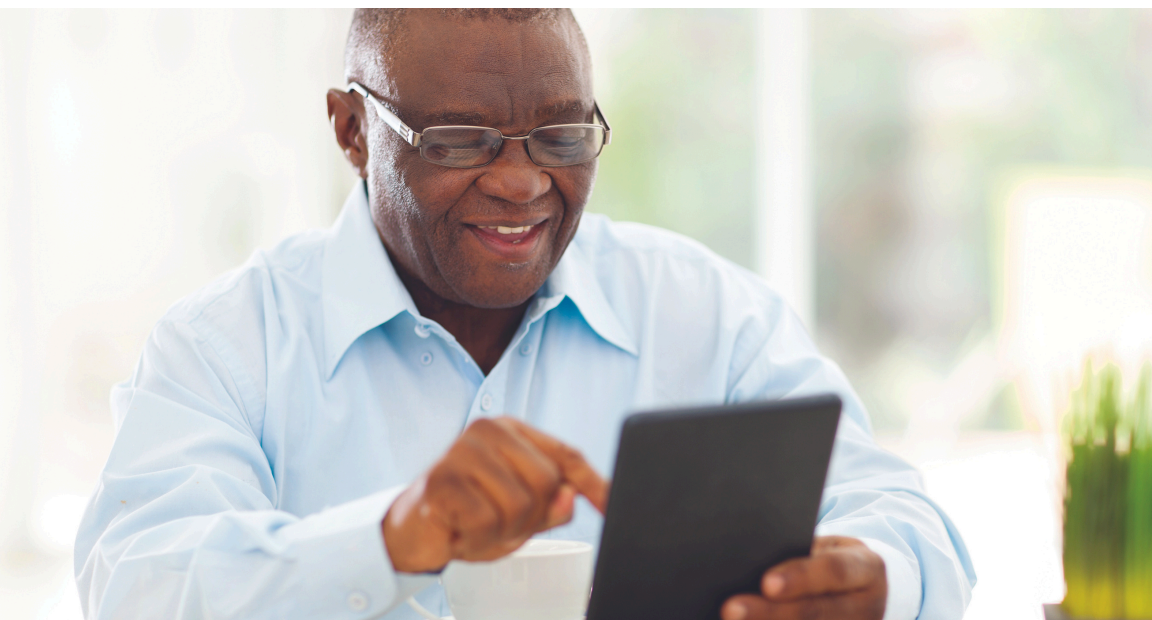


NATIONAL  
**BLEEDING DISORDERS**  
FOUNDATION

# FACTS ABOUT INHIBITORS

Know the basics & get screened





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The information contained in this publication is general information only. NBDF does not give medical advice or engage in the practice of medicine. NBDF under no circumstances recommends particular treatments for specific individuals and in all cases recommends that you consult your physician or local treatment center before pursuing any course of treatment.

#### **TIP FOR USING THIS BROCHURE**



Not sure what some of the terms mean?

Words in **orange** are explained in more detail in the Glossary at the back.

## GET EDUCATED ABOUT INHIBITORS

Hemophilia prevents blood from clotting normally. If you have hemophilia, you are not alone. About 20,000 people in the US also have this bleeding disorder. During the past several decades, treatments to help stop and prevent bleeds have improved. The outlook for living with hemophilia is better than ever. Yet complications still exist. One of them is the development of inhibitors.

### THIS BROCHURE will help you learn about:

- What inhibitors are and how they form
- Who is most likely to develop an inhibitor
- Why yearly testing for inhibitors is so important
- How to understand test results

## WHY DO I NEED TO KNOW ABOUT INHIBITORS?

Inhibitors are proteins in the blood that inactivate infused clotting factor. This stops the factor product from working, so bleeding episodes continue.

People with hemophilia A, hemophilia B or von Willebrand disease (VWD) type 3 can have an inhibitor and not even know it. Inhibitors don't develop in everyone with a bleeding disorder, but can have a serious impact on those who have one. Complications can include uncontrollable bleeding and development of joint disease.

Inhibitors can be hard to detect. Many people do not show symptoms of an inhibitor. When discovered early, there is a greater possibility of successfully eliminating the inhibitor.

**AS OF 2015, NBDF's MEDICAL AND SCIENTIFIC ADVISORY COUNCIL (MASAC) RECOMMENDS that all people with hemophilia should get tested for inhibitors at least once a year.**

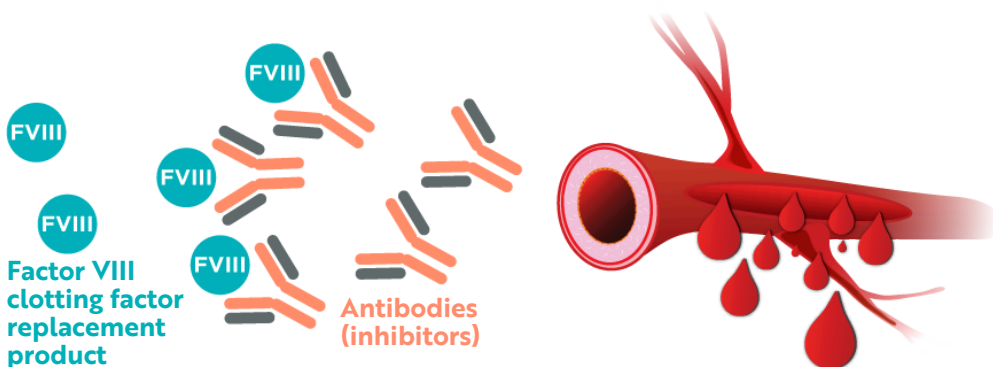
## WHAT IS AN INHIBITOR?

Normally, the body's immune system fights off bacteria, viruses and other foreign substances that can cause illness. These substances are called **antigens**. When the body detects these antigens, it creates **antibodies** to fight them.

Sometimes, however, the immune system builds antibodies to attach things that were meant to help the body, such as certain medications. An inhibitor is a type of antibody that attacks clotting factor replacement treatment.

**INHIBITORS ARE A TYPE OF ANTIBODY that result when your body's immune system targets clotting factor replacement products as foreign substances, or antigens.**

When this happens, the infused clotting factor for either hemophilia A (factor VIII) or hemophilia B (factor IX), is inactivated or unable to effectively perform its job in stopping bleeding. Inhibitors do not affect the location, frequency or severity of bleeds, but they do make them more difficult to control.



## WHEN DO INHIBITORS OCCUR?

Although many people with inhibitors develop them during childhood or their first 50 exposures to infused clotting factor, recent research has shown that they can develop at any time. They often occur within the first 50 exposures to clotting factor. In fact, recent research has shown that in some patients, including those over age 40, the inhibitor was not detected until after more than 150 exposures to clotting factor.



## WHO IS MOST LIKELY TO DEVELOP AN INHIBITOR?

An estimated 30% of people with hemophilia will develop an inhibitor; however, it is more likely for certain groups. Various studies looking at either the number of inhibitors in the study population or the number of new inhibitors in a study population, have found a range of results depending on a patient's severity of hemophilia, where the study was conducted and the size of the study. This is why you may see a range of estimates for how many people with hemophilia have inhibitors. While further research is needed, some estimates are below.





**Among people with severe hemophilia A,  
about 20-30 in 100 may develop an inhibitor**



**Among people with hemophilia B,  
about 3 in 100 may develop an inhibitor**



## THOSE WITH AN INCREASED RISK OF DEVELOPING AN INHIBITOR INCLUDE:

-  People with severe hemophilia
-  People who are black or Hispanic
-  People who have a family member with an inhibitor
-  People with certain genetic mutations of hemophilia

## HOW DO YOU KNOW IF YOU HAVE AN INHIBITOR?

For people who do not have inhibitors, injuries will heal soon after treatment with factor concentrate. For people who do have inhibitors, this is not the case. People who have an inhibitor may not get better after receiving regular clotting factor treatment or the bleed may take longer to resolve. Signs of an inhibitor include frequent bleeds while on a regular treatment schedule, sometimes called breakthrough bleeds, and lack of response to treatment.



**MANY PEOPLE WITH INHIBITORS DO NOT HAVE ANY SYMPTOMS.**

**The only way to know for sure is to get tested.**

During an annual visit at your hemophilia treatment center (HTC) or if you think you have signs of an inhibitor, your medical provider may run a blood test. The Bethesda inhibitor assay, is the most common test used to diagnose inhibitors.

# WHAT DOES A POSITIVE TEST RESULT MEAN?

A positive result of the Bethesda assay means that an inhibitor is present and working against the infused factor. There can be false positive test results and a second test is sometimes needed to confirm an inhibitor diagnosis. The amount of the inhibitor in a person’s blood is called a titer. The degree to which inhibitors affect a person with hemophilia is measured in **Bethesda units**.

The amount of inhibitor you have depends on the number of Bethesda units measured in your blood:

If you have **more than 5 Bethesda units**, you have a **high-titer inhibitor**.

If you have **less than 5 Bethesda units**, you have a **low-titer inhibitor**.

# A CLOSER LOOK AT TEST RESULTS

What is your titer?	What does it mean?	What are some possible side effects?
<b>Less than 5</b> Bethesda units	<ul style="list-style-type: none"> <li>You have a low-titer inhibitor</li> <li>Your body does not have a strong response against the clotting factor product</li> </ul>	<ul style="list-style-type: none"> <li>Continue using factor VIII (8) or factor IX (9) products to control bleeds</li> <li>You may need to increase the dose of your clotting factor product</li> </ul>
<b>More than 5</b> Bethesda units	<ul style="list-style-type: none"> <li>You have a high-titer inhibitor.</li> <li>Your body has a strong response against the factor, so traditional treatments do not work</li> </ul>	<ul style="list-style-type: none"> <li>Factor VIII (8) and factor IX (9) products no longer work to control bleeds.</li> <li>You will need different treatments</li> </ul>

If you have an inhibitor, your doctor will talk to you about specific treatment options. Ask your doctor for more information when you get your results.

## GLOSSARY

**Antibodies** protect the body from bacteria, viruses and other invaders. They are formed by the immune system in response to a foreign substance that enters the body.

**Antigens** are foreign substances that cause the immune system to form antibodies.

**Bethesda units** (BUs) measure how strong your inhibitor is.

**High-titer inhibitor** means your body has a strong response against the clotting factor. Your test results are more than 5 Bethesda units.

**Low-titer inhibitor** means your body has a low response against the clotting factor. Your test results are less than 5 Bethesda units.







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**STEPSFORLIVING.BLEEDING.ORG**  
TODAY





## **DISCUSS AN INHIBITOR TEST WITH YOUR DOCTOR ONCE A YEAR.**

Some people have no symptoms of inhibitors. That's why it is so important to get tested, at least once a year.

Take a moment now to add a reminder on your smartphone or calendar to ask your hematologist about an inhibitor test at your next annual visit. Make sure to write down any questions you may have for your doctor about inhibitors in advance and bring them to your appointment.

## **LOOKING FOR MORE INFORMATION?**

VISIT **BLEEDING.ORG** AND  
**STEPSFORLIVING.BLEEDING.ORG**

**MY NEXT APPOINTMENT IS:**

## **ON OUR WEBSITES, YOU CAN:**

- 💧 Get information on living with a bleeding disorder at all life stages
- 💧 Find a hemophilia treatment center near you
- 💧 Learn more in NBDF's companion booklet called "Living with an Inhibitor: Your Guide to Managing Hemophilia with Inhibitors".

**NOTES/QUESTIONS FOR YOUR HEALTHCARE PROVIDER:**

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**The National Bleeding Disorders Foundation (NBDF)** is dedicated to finding better treatments and cures for inheritable bleeding disorders and to preventing the complications of these disorders through education, advocacy and research. Established in 1948, the National Bleeding Disorders Foundation has chapters throughout the country. Its programs and initiatives are made possible through the generosity of individuals, corporations and foundations as well as through a cooperative agreement with the Centers for Disease Control and Prevention (CDC).