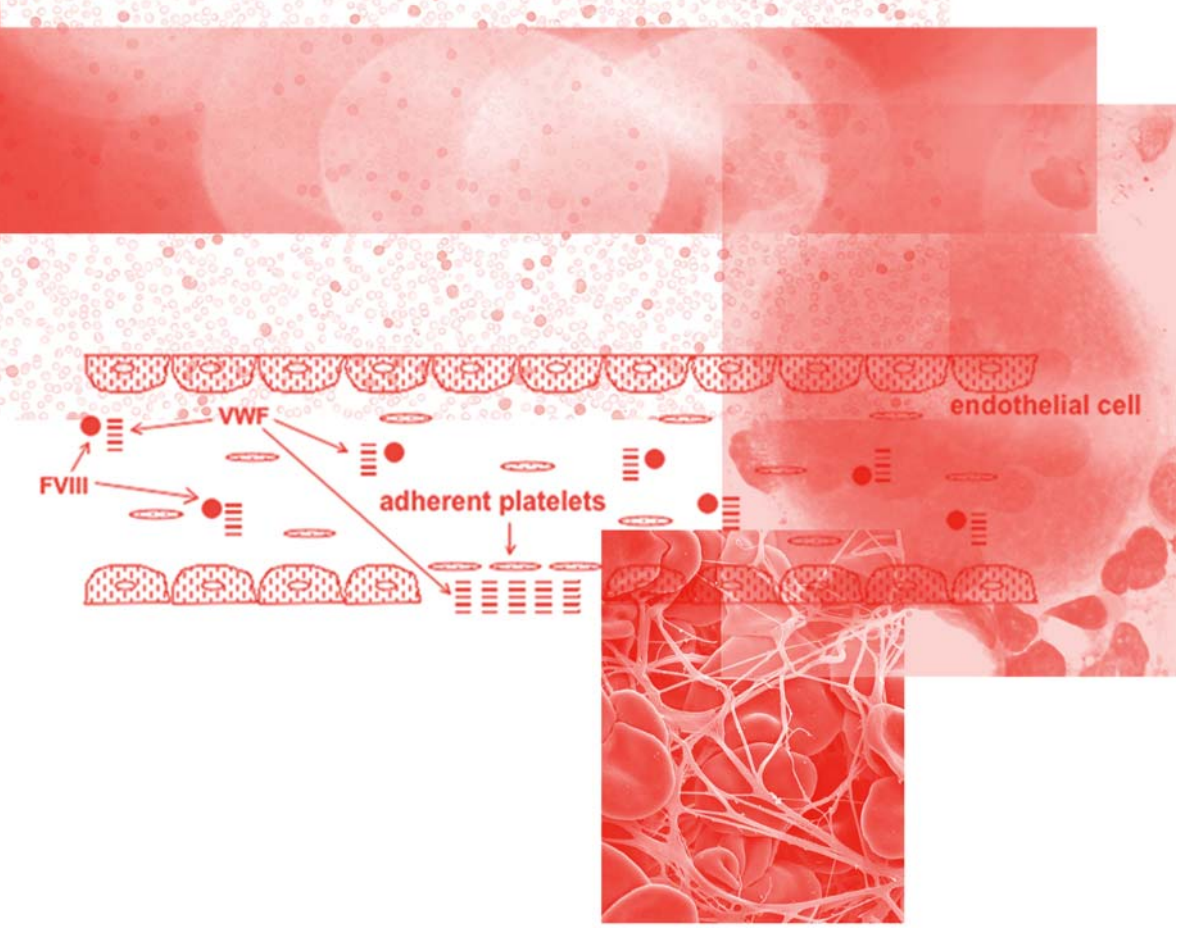
IN BRIEF

YOUR GUIDE TO

von Willebrand Disease



If you often have large, lumpy bruises; frequent or difficult-to-stop nosebleeds; bleed a lot after a fairly minor cut; or are a woman who has very heavy or long menstrual periods, you should ask your doctor about an inherited bleeding disorder called von Willebrand disease (VWD). Named for Dr. Erik von Willebrand, a Finnish doctor who first described the condition in 1926, VWD affects your blood's ability to clot and can lead to heavy, hard-to-stop bleeding after an injury. The bleeding from VWD can lead to damage of your internal organs or even be life threatening, but this is rare.

In VWD, you either have low levels of a certain protein in your blood or the protein doesn't work the way it should. The protein is called von Willebrand factor (VWF). It is made in the walls of your blood vessels and released into your blood.

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Normally, when one of your blood vessels is injured, you start to bleed. As soon as this happens, small cells in your blood that are called platelets clump together to plug the hole in the blood vessel and stop the bleeding. Von Willebrand factor acts like glue to help the platelets stick together and form a blood clot.

Von Willebrand factor also carries with it clotting factor VIII (8), another important protein that helps your blood clot. Factor VIII is the protein that is inactive or missing in hemophilia, another clotting disorder.

Von Willebrand disease, like hemophilia, is an inherited bleeding disorder, but VWD is more common and usually milder. In fact, VWD is the most common of all the inherited bleeding disorders. It occurs in about 1 out of every 100 to 1,000 people. It also affects both males and females, while hemophilia mainly affects males.

There are three major types of von Willebrand disease.

- In type 1 VWD, you have a low level of the von Willebrand factor, and you may have lower levels of factor VIII than normal. This is the mildest and most common form of VWD. About 3 out of every 4 people with VWD have type 1 VWD.
- In type 2 VWD, the von Willebrand factor does not work the way it's supposed to. Type 2 VWD is divided into subtypes 2A, 2B, 2M, and 2N. Each type is caused by different gene mutations and treated differently. This makes knowing the exact type of VWD that you have very important.
- In type 3 VWD, you usually have no von Willebrand factor and low levels of factor VIII. Type 3 is the most serious form of VWD, but very rare.

Von Willebrand disease cannot be cured, but it can be treated. Early diagnosis is important, and with the right treatment plan, even people with type 3 VWD can be helped to live active lives.

What Causes von Willebrand disease?

Von Willebrand disease is almost always inherited. Your parents pass the gene for the disease on to you. You can develop types 1 or 2 VWD when only one of your parents carries the gene for it. You usually inherit type 3 VWD only if both of your parents pass the gene on to you. Your symptoms may be different from your parent's.

Some people develop a form of the disease later in life as a result of other medical conditions. This is called Acquired von Willebrand Syndrome (AVWS).

What Are the Signs and Symptoms of von Willebrand Disease?

The signs and symptoms of VWD depend on the type and severity of the disease. Many people have such mild symptoms that they may not know they have the disorder. Some people have the gene for the disease but don't have any symptoms.

If you have *type 1 or type 2 VWD*, you may have the following mild to moderate symptoms:

- Frequent large bruises from minor bumps or injuries.
- Frequent or difficult-to-stop nosebleeds.
- Extended bleeding from the gums after a dental procedure.
- Heavy or extended menstrual bleeding in women.*
- Blood in your stools from bleeding in your intestines or stomach.
- Blood in your urine from bleeding in your kidneys or bladder.
- Heavy bleeding after a cut or other accident.
- Heavy bleeding after surgery.

*Heavy menstrual bleeding is the most common symptom in women. If it isn't treated, it can lead to iron deficiency and anemia. (Not all heavy menstrual bleeding is due to VWD.)

If you have *type 3 VWD,* you may have any or all of the symptoms listed above, as well as the following:

- Severe bleeding episodes for no reason. These bleeding episodes can be life threatening if not treated right away.
- Bleeding into soft tissue or joints, causing severe pain and swelling.

How is von Willebrand Disease Diagnosed?

Von Willebrand disease is sometimes difficult to diagnose. People with type 1 or type 2 VWD may not have major bleeding problems; as a result, they may not be diagnosed until they have heavy bleeding after surgery or some other trauma.

On the other hand, type 3 VWD can cause major bleeding problems during infancy and childhood. As a result, children with type 3 VWD are usually diagnosed during their first year of life.

To find out if you have VWD, your doctor will take a complete medical history and do a physical exam. For the history, he or she will likely want to know about your personal and family history -– in particular:

- Any episodes of bleeding from a small wound that lasted more than 15 minutes or started up again within the first seven days following the injury.
- Any episodes of extended, heavy or repeated bleeding after surgery or dental extractions that required medical attention.
- Any episodes of bruising with little or no apparent trauma, especially if you could feel a lump under the bruise.
- A nosebleed that occurred for no apparent reason and lasted more than 10 minutes despite pressure on the nose or a nosebleed that needed medical attention.
- Any episode of blood in your stool for no apparent reason.
- Any heavy menstrual bleeding in women (usually with clots or lasting longer than 7 to 10 days).
- Any history of muscle or joint bleeding.

- Any medicines you've taken that might cause bleeding or increase the risk of bleeding – for example, aspirin, other nonsteroidal anti-inflammatory drugs (NSAIDs), clopidogrel (Plavix ®), warfarin, or heparin.
- Any history of liver or kidney disease, blood or bone marrow disease, or high or low blood platelet counts.

The doctor will also do a physical examination to look for:

- Unusual bruising or other signs of recent bleeding.
- Evidence of liver disease or anemia.

No single test exists for diagnosing VWD. As a result, your doctor will order a combination of blood tests to diagnose the disease. These tests may include:

- Von Willebrand factor antigen. This test measures the amount of von Willebrand factor in your blood.
- Von Willebrand factor ristocetin (ris-toe-SEE-tin) cofactor activity. This test shows how well the von Willebrand factor works.
- Test for factor VIII clotting activity. Some people with von Willebrand disease have low levels of factor VIII activity, while others have normal levels.
- Von Willebrand factor multimers. This test is performed if one or more of the 3 tests above are abnormal. It shows the makeup or structure of the von Willebrand factor. It helps your doctor diagnose what type of VWD you have.
- Platelet function test. This test measures how well your platelets are working.

Your doctor may order these tests more than once to confirm the diagnosis. He or she may also refer you to a hematologist (a doctor who specializes in treating blood diseases) to confirm the diagnosis and for follow-up care.

Early diagnosis is important to make sure you are treated effectively and can live a normal, active life.

How is von Willebrand Disease Treated?

Your doctor will decide what treatment you need, based on the type of VWD you have and how severe it is. Most cases of von Willebrand disease are mild, and you may need treatment only if you have surgery, tooth extraction, or an accident.

Treatments for von Willebrand disease include medicines to:

- Increase release of von Willebrand factor and factor VIII into the bloodstream.
- Replace von Willebrand factor.
- Prevent breakdown of clots.
- Control heavy menstrual bleeding in women.

Specific treatments include:

- Desmopressin (DDAVP). This is a synthetic hormone that you usually take by injection or nasal spray. It makes your body release more von Willebrand factor and factor VIII into your bloodstream. DDAVP works for most patients with type 1 and some with type 2 VWD.

Tips for Living with von Willebrand Disease

It's important that you try to prevent bleeding and stay healthy. You should:

- Avoid over-the-counter medicines that can affect blood clotting, including aspirin, Ibuprofen, and other nonsteroidal anti-inflammatory drugs (NSAIDs).
- Always check with your doctor before taking any medicines.
- Tell your doctor or dentist that you have von Willebrand disease. Your dentist can talk to your doctor about whether you need medicine before dental work to reduce bleeding.
- Consider wearing a medical ID bracelet or necklace if you have a serious form of VWD (for example, type 3 VWD), so that in case of serious injury or accident the doctors caring for you will know you have VWD.
- Exercise regularly and maintain a healthy weight. Exercise helps keep muscles flexible. It also helps prevent damage to muscles and joints. Always stretch before exercising.

  Some safe exercises or activities are swimming, biking, and walking. Football, hockey, wrestling, and lifting heavy weights are not safe activities if you have bleeding problems. Always check with your doctor before starting any exercise program.

- VWF replacement therapy. This involves getting an infusion of a concentrate of von Willebrand factor and factor VIII into a vein in your arm. This treatment can be used if you:
  - ❑ Can't take DDAVP or need extended treatment.
  - ❑ Have type 1 VWD that doesn't respond to DDAVP.
  - ❑ Have type 2 or type 3 VWD.
- Oral contraceptives, or birth control pills, can help women who have heavy menstrual bleeding. The hormones in the pills can increase the amount of VWF and factor VIII in the bloodstream.
- Antifibrinolytic drugs help prevent the breakdown of blood clots. They are used mostly to stop bleeding after minor surgery, tooth extraction, or an injury. They may be used alone or together with DDAVP and replacement therapy.
- Fibrin glue is medicine that is placed directly on a wound to stop the bleeding.

Frequently Asked Questions

1. Is there a cure for von Willebrand disease?

   No, von Willebrand disease is a lifelong disorder. However, most people have a mild form that causes little or no change in their lives. Even those with type 3 von Willebrand disease can live normal, active lives once they are treated.

2. Who should know that I have von Willebrand disease?

   People like your doctor, dentist, employee health nurse, gym trainer, and sports coach should be aware of your condition. If you have a severe form of VWD (for example, type 3

VWD), consider wearing a medical ID bracelet or necklace that states you have von Willebrand disease. In case of an accident or emergency, this will be very helpful to the health care team treating you.

Since your parents, brothers and sisters, and children may also have von Willebrand disease, you should consider telling them about your diagnosis and suggesting they consider getting tested.

3. Who should know that my child has von Willebrand disease?

   Anyone who is responsible for your child should know about his or her condition. For example, his or her teacher, school nurse, daycare provider, coach, or any after-school program leader should know, particularly if your child has one of the more severe forms of VWD (for example, type 3 VWD).

4. Is von Willebrand disease life threatening?

   Most people with von Willebrand disease have a mild form of the disease, which usually does not cause bleeding that is life threatening. But any bleeding that can't be controlled can be life threatening. Some people with severe forms of von Willebrand disease need to seek emergency treatment to stop bleeding before it becomes life threatening.

5. Do all people who have the gene for von Willebrand disease have bleeding problems?

   No. Some people carry the genes for the disease but do not have symptoms. They still can pass the disease on to their children.

6. How will I know if I have von Willebrand disease?

   The first step is a thorough history and physical examination. If you or anyone in your family has a history of bleeding, your doctor can order a number of blood tests to find out whether you have the disease. These tests will check how quickly your blood clots and the levels of clotting factors in your blood. Your doctor can use these test results to diagnose your exact type of VWD.

For Women Only

Heavy menstrual bleeding is often the main symptom of von Willebrand disease for women. Doctors call this menorrhagia. They define it as:

- bleeding with clots larger than about 1-inch in diameter
- anemia or low blood iron
- need to change pad or tampon more than every hour

Of course, heavy menstrual bleeding can also be a sign of a gynecological disorder, so it's important to have a complete gynecological exam before you seek testing for VWD.

If you have VWD and heavy menstrual bleeding, there are treatments to help you. They include:

- Combined oral contraceptives. They increase VWF and factor VIII in your blood and reduce menstrual blood loss. They are the most often recommended birth control method for women with VWD.
- A levonorgestrel intrauterine device. This is a contraceptive device that contains progestin.
- Aminocaproic acid or tranexamic acid are antifibrinolytic drugs. They can reduce bleeding by slowing the breakdown of blood clots.
- Desmopressin (DDAVP).

For some women who no longer want children, endometrial ablation is performed. This procedure, which destroys the lining of your uterus, has been shown to reduce menstrual blood loss in women with VWD.

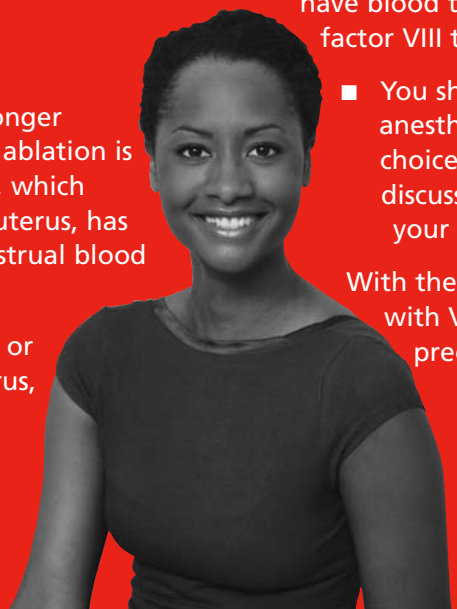
If you need a hysterectomy, or surgical removal of the uterus, for another reason, it will do away with menstrual bleeding altogether and possibly improve your quality of life. However, hysterectomy carries its own risk of bleeding complications.

Pregnancy can be a challenge for women with VWD. Although blood levels of VWF and factor VIII tend to increase during pregnancy, women with VWD can have bleeding complications during delivery. They also are likely to have heavy bleeding for an extended period after delivery.

However, there are things you can do to minimize the chances of complications in pregnancy:

- Consult a hematologist and an obstetrician who specializes in high-risk pregnancies before you become pregnant.
- Consider using a center that specializes in high-risk obstetrics and has a hematologist with expertise in bleeding disorders on the staff for prenatal care and delivery.
- Before you have any invasive procedure, such as amniocentesis, ask your doctor whether anything needs to be done to prevent serious blood loss.
- During your third trimester, you should have blood tests to measure VWF and factor VIII to help plan for delivery.
- You should also meet with an anesthesiologist to review your choices for anesthesia and to discuss taking medicine to reduce your bleeding risk.

With these precautions, most women with VWD can have successful pregnancies.



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