



NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

FACTOR V (F5)

DEFICIENCY

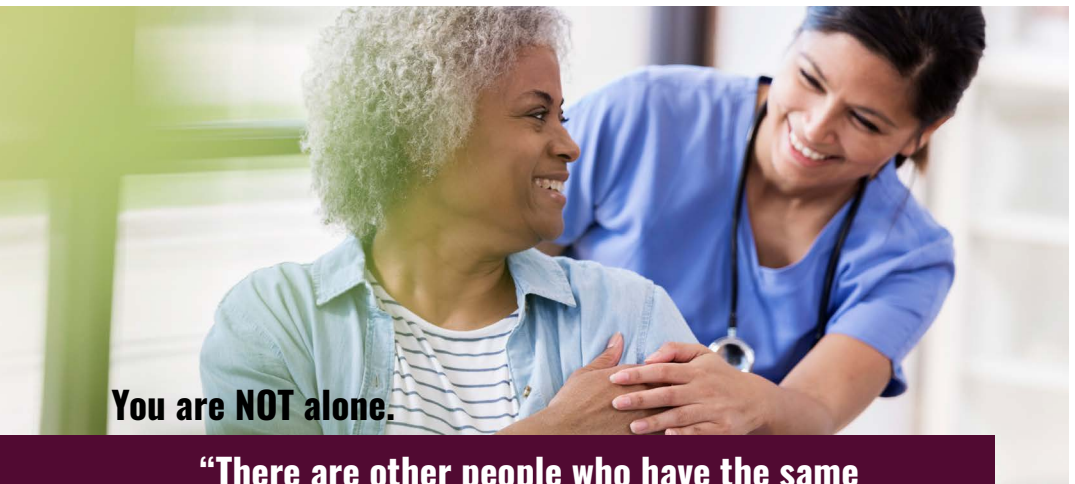
YOU ARE NOT ALONE



Factor V Deficiency

WHAT YOU SHOULD KNOW

Whether you are newly diagnosed with **Factor V Deficiency (FV Deficiency)** or have been diagnosed for some time, it is common to go through many ups and downs. We want to share information and some resources about this condition that can help you on your path to improved health and quality of life. When you are first given a new diagnosis, one as rare as FV Deficiency, it is understandable to have many emotions or to feel overwhelmed. The good thing is that you're not alone. There are other people who have the same condition and lead full lives that are enriched by becoming closer to other people who are traveling on a similar path. **With the care of an experienced team, you will find support from your healthcare providers as well as from the vibrant and caring bleeding disorders community.** You can be involved in this community and build meaningful relationships with your new extended family.



You are NOT alone.

“There are other people who have the same condition and lead full lives. They have had their lives enriched by becoming closer to other people who are traveling on a similar path.”

The **National Hemophilia Foundation (NHF)** is here to provide you with education and support as you manage your bleeding disorder, whether you are a child, a teen, or an adult. In this spirit, NHF and the bleeding disorders community have selected some of the most frequently asked questions and answers below to empower you.



What Is Factor V Deficiency?

FV Deficiency is a very rare bleeding disorder. Also known as Owren's disease or parahemophilia, it was first described in a patient in Norway with frequent nosebleeds and heavy menstrual periods.

Bleeding disorders are a group of medical conditions that share an inability or decreased ability to form a stable blood clot. When the body is injured, an area bleeds, and a clot is formed to stop the bleeding. Clot formation is a multistep process called coagulation. When the blood clots properly, the blood clot is held together firmly at the

site of the injury to prevent ongoing blood loss. People with a bleeding disorder are unable to form strong clots, which can lead to continued bleeding. Improper clotting can be caused by abnormalities in either blood components called platelets, blood clotting proteins (also called clotting factors), or both. Platelets are small colorless disc-shaped pieces of cells that help blood clot normally. Platelets act like first responders and stop bleeding by clumping and forming plugs in blood vessel injuries.

“Bleeding disorders are a group of medical conditions that share an inability or decreased ability to form a stable blood clot.”

This initial plug is strengthened by the formation of a mesh-like network of fibers called fibrin that is generated by a series of clotting proteins. If one or more of the blood components is defective, deficient, or even absent, blood clotting is affected. **Factor V** (also called proaccelerin) is one of the clotting factors that is an important part of this process. FV Deficiency results from not having enough FV protein or having FV protein that doesn't work properly. With FV Deficiency, your blood clot may not be strong enough to stop you from bleeding. **FV Deficiency affects about 1 in a million people.** It should not be confused with Factor V Leiden, a genetic disorder that is more common than FV Deficiency and increases the risk of forming blood clots, termed a clotting disorder.



How does someone get Factor V Deficiency?



If you have FV Deficiency, that means that you have a lower-than-normal level of FV clotting factor. The normal level of FV in the blood ranges from 50% to 200%. An FV level lower than 15% of the normal amount would give you a diagnosis of FV Deficiency. Still, there are some patients with levels between 15% and 60% who have experienced bleeding. This is likely due to differences between the tests done at different laboratories. Unlike some other bleeding disorders, the symptoms that you may experience with FV Deficiency are not always related to the level of FV in your blood.¹ **Some people who have very low FV levels have mild symptoms; in other words, the level does not always correlate well with the bleeding symptoms.** FV Deficiency can be inherited, meaning that it is passed on from biological parents to a child at the time of conception. It equally affects both males and females.



For someone to inherit FV Deficiency, they receive a copy of the defective gene from both biological parents. This means that both biological parents are either affected by or are carriers of the defective gene.

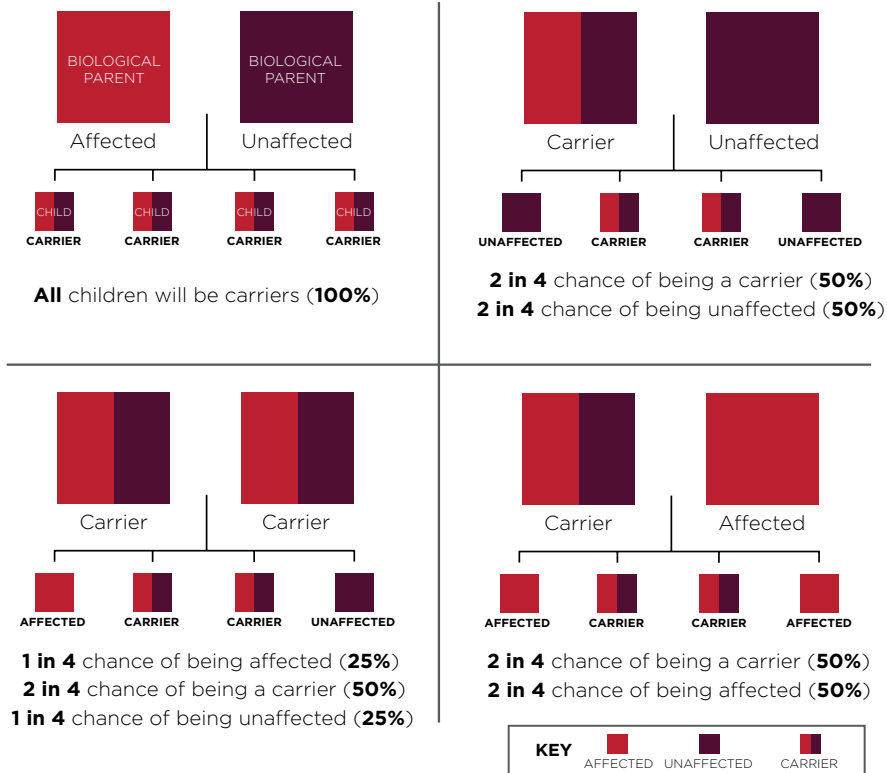


A carrier has only one copy of a defective gene. Carriers usually do not have bleeding problems, but as mentioned above, they may have FV levels between 15% and 60% and still experience bleeding (though usually not severe).



This pattern of inheritance is called autosomal recessive. It is different from other forms of inheritance that are associated with some other bleeding disorders, like hemophilia. The different forms of autosomal recessive inheritance are illustrated on the next page.

Family Inheritance of an Autosomal Recessive Disorder



SUMMARY

If you are **AFFECTED** with FV Deficiency, you probably inherited one defective gene from each of your biological parents.

If you are a **CARRIER** of FV Deficiency, you inherited only one copy of a defective gene from a biological parent.

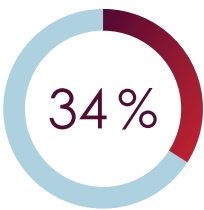
You can use the same logic to work out the likelihood of your children being impacted by FV Deficiency, depending on your and your partner's genes. Genetic testing and counseling are available if you are interested in figuring out where the deficiency came from or who else in the family might be at risk of having the same condition.

Sometimes a person might develop FV Deficiency rather than being born with it; this is termed an acquired deficiency and is rarer than the inherited form. To date, there have only been around 200 cases reported worldwide. Acquired FV Deficiency happens when your body makes an antibody that interferes with your FV, causing it to not work correctly or at all. If you hear your healthcare professional talk about an "inhibitor" to your FV, that is the name given to the antibody that is stopping your FV from working. In most cases, acquired FV Deficiency is caused by certain antibiotics, blood transfusions, surgical procedures, or other medical conditions (e.g., some cancers, tuberculosis).^{2,3} Twenty percent of acquired FV Deficiency cases are idiopathic, meaning that the cause is unknown. Around 60% of people with acquired FV Deficiency have bleeding events, with a wide range of symptoms similar to that seen with hereditary FV Deficiency.⁴

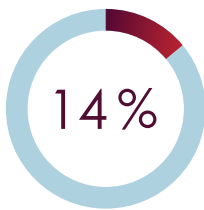
What are the symptoms of Factor V Deficiency?

The symptoms of FV Deficiency may depend upon how much FV you have circulating in your blood or how well it functions. **As noted earlier, sometimes this is not the case and the severity of bleeding does not always reflect FV levels in your blood.**

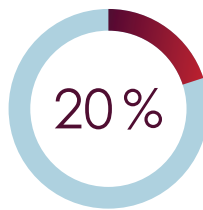
Symptoms can begin at any age and range from no symptoms at all to severe symptoms. In general, symptoms are mild and include nose bleeds, bruising, bleeding gums, poor wound healing, and bleeding in the joints (although this is rarer and is usually due to trauma). Excessive bleeding following surgery, trauma, or childbirth is common. Women may also experience very heavy or prolonged menstrual periods. FV Deficiency may also be suspected in women who have had multiple miscarriages.⁵ If you have FV levels that are not able to be detected in the laboratory test, you are considered to have a severe deficiency. The more severe form of FV Deficiency is noticeable in newborns, with excessive bleeding at the belly button. Severe symptoms may include bleeding in the brain, lungs, or gut, although this is rare for this deficiency.



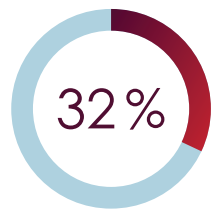
experience minor bleeding, not caused by injury (bruising, nose bleeds, gum bleeds, or heavy menstruation).



experience major bleeding, not caused by injury (umbilical, brain, joint, muscle, or gut bleeds).



experience excessive bleeding after trauma (sports injury leading to joint or muscle bleeding, surgery).



experience no symptoms at all.⁶

If you are a carrier and experience bleeding symptoms, it is important to seek medical care from a hematologist (a doctor who specializes in the study of blood) or contact a Hemophilia Treatment Center (HTC). By process of elimination, the bleeding disorder specialist will rule out more common bleeding disorders before concluding that FV Deficiency is the cause of your bleeding symptoms.



Classification of Factor V Deficiency^{6,7}



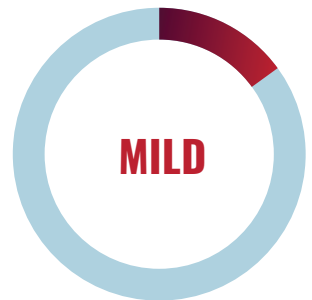
Undetectable level (<1%)

Increased risk of bleeding inside the skull, lungs, joints, muscles, or the gut. All of which may be life threatening.



1% - 10%

Nosebleeds, easily bruised, bleeding of the gums, heavy or prolonged menstrual periods.



≥ 10%

Often don't show symptoms but can have problems with bleeding during trauma, a surgical procedure, or pregnancy and childbirth.



How is Factor V Deficiency diagnosed?

Diagnosing FV Deficiency is challenging because it is rare and because symptoms may be mild and not appear until later in life. Common laboratory tests may also show that the results are normal. Diagnosis of FV Deficiency is based on a variety of laboratory tests on a sample of your blood. First, the time it takes for your blood to form a clot is measured. These tests are called the prothrombin time (PT) and the activated partial thromboplastin time (aPTT), and the results are usually given as a number of seconds. If the results are high, this means that your blood takes longer than usual to clot, and you will be diagnosed with a bleeding disorder. Your plasma (the liquid portion of blood) will then be mixed with pooled plasma from individuals without a bleeding disorder with normal FV levels (called a mixing study). If the clotting time becomes normal (due to the normal level of FV provided from this pooled plasma), it confirms that you have a missing clotting factor.⁸ Other tests will be done to find out what type of bleeding disorder you have. For a firm diagnosis of FV Deficiency a specific test to calculate the activity of FV can be done.⁹

The diagnosis of acquired FV Deficiency is more challenging. If the clotting time in the mixing study (described above) does not become normal, you may have something interfering with your clotting factor, such as an antibody. A Bethesda assay can detect whether there are any antibodies in your blood that would interfere with your FV.

People with abnormal FV levels should also have their FVIII checked to rule out FVIII Deficiency, which is a separate bleeding disorder inherited at the same time.

What are the treatments for

Factor V Deficiency?

There are different treatment options for FV Deficiency. It is important to consider the benefits and the risks of any treatment. For optimal care, you should find a specialized doctor, called a hematologist, who is experienced in treating FV Deficiency. These doctors, by and large, work at HTC's. If your doctor is not experienced in treating FV Deficiency, please make sure they speak to the nearest HTC. Treatment of FV Deficiency is usually only needed to prevent (prophylaxis) severe bleeds before surgery and dental procedures or to treat major bleeding from trauma.

Fresh frozen plasma (FFP) is the usual treatment for FV Deficiency. FFP is given into your veins (intravenously). Plasma is the liquid portion of blood that contains all the clotting factors. However, FFP is usually not treated to kill viruses so there is a risk of infectious disease. Viral-inactivated FFP is available in some countries, which reduces infectious disease risk, but is typically not used in the United States.

A disadvantage of having repeated cycles of FFP is that the concentration of each individual clotting factor is low, so a large volume of plasma is needed to replace the missing factor. As FFP contains all the other clotting factors, there is a risk of having too many clotting factors, which can lead to fluid overload, which can put stress on the heart or lead to lung injury with swelling of the extremities.

Occasionally FFP can trigger an immediate allergic reaction, similar to a severe allergic reaction to a bee sting, causing a rash, hives, swelling of the lips or throat, wheezing/shortness of breath, or very low blood pressure (anaphylaxis). FFP can also lead to your body making antibodies against FV, although this is rare.⁹ Another plasma product called Octaplas, which is hypoallergenic, can be used to treat bleeds associated with FV Deficiency.

If you have acquired FV Deficiency, FFP treatment will not be successful as your antibodies will stop the FV from working.

Another treatment possibility is platelet transfusions that contain FV. About 75% of FV is circulating in the blood, with only 25% of FV is in the platelets. This treatment is advantageous because when the platelets arrive at the injury site, the FV is right where it needs to be. If you have acquired FV Deficiency, platelet transfusion is also advantageous because your antibodies do not have the ability to interfere with FV before it has done its job.

Platelet transfusions have a small risk of passing on infections or causing allergic reactions. If the platelets aren't a good match to your own, your body may reject them. This can usually be overcome by selecting replacement platelets that closely match your own.

Heavy menstrual bleeding (long-lasting heavy periods) in women with FV Deficiency may be controlled with hormonal therapy. Hormonal therapies include pills that usually contain estrogen (e.g., levonorgestrel), intrauterine devices (IUDs), or implants under the skin (e.g., Norplant/Nexplanon).¹⁰ Medicines that prevent too much bleeding (e.g., tranexamic acid) can be taken for the first five days of the period to control heavy bleeding. If the patient is past childbearing age, removal of the lining of the uterus (endometrial ablation) is an option that usually improves symptoms.

For the most current list of FDA-approved treatments for all bleeding disorders, including FV Deficiency, **visit www.hemophilia.org/healthcare-professionals/guidelines-on-care/products-licensed-in-the-us**.

Your healthcare provider will work with you to develop an ideal treatment plan based on your bleeding history and the type and severity of the bleeding disorder that you have.

What special precautions need to be taken when considering pregnancy? _____



Although rare, miscarriage and recurrent miscarriages have been reported in women with inherited FV Deficiency. Miscarriages can be the first symptom for women with FV Deficiency.⁵ Meeting with your hematologist is essential before becoming pregnant. It is important to work closely with a hematologist who is experienced in the treatment of FV Deficiency. With treatment to maintain an adequate level of FV in your blood during pregnancy, it is possible to carry a baby to full term. Your hematologist can guide your women's health doctor (OB/GYN) to help develop a treatment plan during pregnancy, labor, delivery, and postpartum (up to four to six weeks after delivery). HTC hematologists will also be able to provide care to your baby and provide testing as needed.

“It is important to work closely with a hematologist who is experienced in the treatment of Factor V Deficiency”

ADVICE FROM OTHER FV COMMUNITY MEMBERS



Research events with NHF and your local chapter. Let yourself grieve and go through the process. Get involved, join your community.”

FV Patient



Be your own advocate. Always ask questions because all doctors don't know about ultra-rare bleeding disorders.”

FV Patient



Fight and advocate for your treatment.”

FV Patient



You're living. Try not to worry so much. Be content with what you have.”

FV Patient



It's so much worse for other people. Keep a positive attitude!”

FV Patient

Where else can I obtain additional information?

You are now part of a family known as the bleeding disorders community. You are not alone, and you can turn to other members of this community for support if needed.



Know how to navigate disclosing your or your child's bleeding disorder to daycare, school, work, emergency rooms, and non-hematology specialists.



Learn more about advocating for appropriate treatment in an emergency room (ER) or with other healthcare providers who may not know much about FV Deficiency. Always carry your treatment plan letter provided by your HTC when traveling or going to the ER.



Find out where to connect with others with bleeding disorders locally.

Resources:

The National Hemophilia Foundation

- **Factor V:** <https://www.hemophilia.org/bleeding-disorders-a-z/types/other-factor-deficiencies/factor-v>
- **Steps for Living – The basics of bleeding disorders:** <https://stepsforliving.hemophilia.org/>
- **Webinar by Sweta Gupta – Basics of Factor 5 Deficiency:** <https://www.hemophilia.org/educational-programs/education/online-education/basics-of-factor-5-deficiency>
- **HANDI toll-free hotline:** 1-800-42-HANDI

HemAware bleeding disorders magazine <https://hemaware.org/>

- **Pregnancy planning and bleeding disorders:** <https://hemaware.org/womens-health/pregnancy-planning-and-bleeding-disorders>

Comprehensive Health Education Services

- **Rare bleeding disorders:** <https://ches.education/rare-bleeding-disorders>

Foundation for Women & Girls with Blood Disorders

- **Clinics and services for women and girls with bleeding disorders and sickle cell disease:** <https://www.fwgbd.org/clinics>

Hemophilia Federation of America

- **The learning central:** <https://www.hemophiafed.org/the-institute/>

Mayo Clinic

- **Autosomal Recessive Inheritance Pattern:** <https://www.mayoclinic.org/autosomal-recessive-inheritance-pattern/img-20007457>

National Institutes of Health

- **Genetic and Rare Diseases Information Center:** <https://rarediseases.info.nih.gov/diseases/2237/factor-v-deficiency>
- **MedlinePlus - Factor V Deficiency:** <https://medlineplus.gov/genetics/condition/factor-v-deficiency/>

The World Federation of Hemophilia

- **What are rare clotting factor deficiencies?:** <http://www1.wfh.org/publication/files/pdf/1337.pdf>

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This booklet is intended for informational purposes only. It is not intended to be used to make healthcare coverage or treatment determinations. NHF's Medical and Scientific Advisory Council (MASAC) recommends that the product and corresponding treatment regimen used by an individual should remain a decision between patient and physician.

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