



The Factor V Leiden Mutation and Blood Clots

What is the Factor V Leiden Mutation?

Factor V (five) is a protein that helps our blood clot normally. The *factor V Leiden mutation* is a variation that makes it slightly harder to control factor V activity. As a result, people with the factor V Leiden mutation have an increased risk of abnormal *venous blood clotting* (blood clotting in veins). The mutation does not cause increased bleeding.

The factor V Leiden mutation was first identified in the city of Leiden in the Netherlands. It is present in about 5% of healthy Caucasians (including Hispanics) and about 1% of African-Americans. It is rarely found in Asians.¹

Inheritance of the Factor V Leiden Mutation

The factor V Leiden mutation is inherited in a *simple Mendelian dominant* fashion. This means that we have two copies of the factor V gene and it takes only one copy with the Leiden mutation to increase the risk for abnormal blood clotting. We inherit one factor V gene from each parent. If we get a normal gene from one parent and an abnormal gene from the other, we are *heterozygous* for the factor V Leiden mutation. This means that one of the two factor V genes is abnormal. If we get abnormal genes from each parent, we are *homozygous*, with two abnormal genes.

If one parent is heterozygous for the factor V Leiden mutation and the other is normal, each child has a 50% chance of inheriting the mutation. Each sibling of a person who is heterozygous has a 25% chance of being heterozygous. Whenever a person is discovered to be either heterozygous or homozygous, all close relatives may be tested for the mutation.

Health Risks of the Factor V Leiden Mutation

Among people *without* the factor V Leiden mutation, the possibility of suffering a venous blood clot is 0.16% (1.6 per thousand). People who are heterozygous for the factor V Leiden mutation have a 0.6% (6 per thousand) chance, or about 3.75 times normal. The risk for people who are homozygous is near 50%, or 80 times normal.

Venous blood clots usually form in the large deep leg veins, where they cause pain, swelling, and a sensation of heat. If left untreated, leg clots lead to a painful long-term disability condition called *post-phlebotic syndrome*. More serious still, pieces of leg clots may break off and travel through the heart to the arteries of the lungs where they are called *pulmonary emboli*. About 30% of pulmonary emboli are fatal within an hour. All are debilitating as they cause shortness of breath.

The possibility for developing clots is increased for those with additional risk factors. For example, women who have the heterozygous factor V Leiden mutation and who take *birth control pills* or *hormone replacement therapy after menopause* increase their odds for a clot to 30 times normal. Other risks include surgery, obesity, smoking, or immobilization, such as sitting for four hours or longer.

The factor V Leiden mutation does not appear to increase the risk of heart attacks or strokes.

Diagnosing the Factor V Leiden Mutation

There are two blood tests for the factor V Leiden mutation, both of which can be performed on about 10 mL or two teaspoonfuls of blood taken from an arm vein. The first is a rapid screening test called the *activated protein C resistance* test or APCR. This name comes from the fact that the factor V Leiden mutation causes factor V to resist the normal controlling influence of another blood protein called *protein C*.

If the activated protein C resistance test is positive, the *factor V Leiden mutation test* should be performed. This is a more specialized test done on the patient's DNA. It takes about a week to perform, and it confirms the results of the APCR test.

Treating the Factor V Leiden Mutation

People who are either heterozygous or homozygous for the factor V Leiden mutation may not need regular therapy, although they should avoid circumstances that increase their risk of thrombosis. For example, a woman who is heterozygous may choose against birth control or hormone replacement therapy after discussing the risks and benefits with her physician. All people who have the factor V Leiden mutation should exercise, stay well hydrated, and should avoid smoking and immobilization.

Many doctors may prescribe protective *anticoagulant* (blood-thinning) therapy during unavoidable periods of increased risk. For example, a factor V Leiden mutation patient, either heterozygous or homozygous, may be instructed to use *heparin* injections for a few days after major surgery.

Patients who have had a blood clot may be placed on long-term anticoagulant therapy such as Coumadin pills. Some factor V Leiden mutation people may need to take Coumadin indefinitely. This well-known drug requires monthly laboratory monitoring. Please read more information on [Coumadin](#) in this web site.

For those who want to learn more on factor V Leiden, please see the [factor V Leiden](#) web site.

For more information, contact the UAB Coagulation Service

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¹ Dowling NF, Austin H, Dilley A, Whitsett C, Evatt BL, Hooper WC. The epidemiology of venous thromboembolism in Caucasians and African-Americans: The GATE Study. *J Thrombos Haemostas* 2003; 1; 80-87.