

HEREDITARY THROMBOPHILIA

Introduction

Thrombophilia is an increased tendency to develop blood clots in blood vessels due to an abnormality in the blood. There are different types of blood clots:

- Venous thrombosis is the most common cause of potentially life-threatening blood clots in the lungs (also called pulmonary embolism), clots in the deep leg veins, arm veins, kidney veins, or any other veins.
- Arterial thrombosis is a clot in the arteries. These clots can cause life-threatening complications such as heart attack (myocardial infarction), stroke, and transient ischemic attacks (TIA).

Hereditary Thrombophilia

Some people are born with thrombophilia (inherited) either as a result of inheriting an abnormal gene from one parent (heterozygous), inheriting the same abnormal gene from both parents (homozygous), or from a genetic mutation that occurred after conception (spontaneous mutation). People can also inherit more than one abnormal gene (compound heterozygous). People with hereditary thrombophilia have either an inability of the body to produce adequate amounts of normal protein, or the body produces abnormal protein, which does not function normally. A person may have more than one type of hereditary thrombophilia, or may have both hereditary and acquired thrombophilia. The following is a description of some hereditary thrombophilias that are fairly common.

Factor V Leiden: Factor V Leiden (FVL) is the most common form of hereditary thrombophilia in Caucasian populations (found in 3-5% of people of northern European descent). Heterozygous FVL (inheriting one gene from one parent) is much more common than homozygous FVL (inheriting two genes, one from each parent). FVL predisposes to mainly venous thrombosis. FVL is confirmed by a DNA blood test that looks for the mutation in the factor V gene.

Antithrombin III Deficiency. ATIII is a protein made in the liver. ATIII deficiency is usually mild to moderate (heterozygous). Complete (homozygous) ATIII deficiency is thought to be incompatible with life. ATIII deficiency can predispose to both mostly venous (occasionally arterial) thrombosis. Testing for ATIII deficiency is done by a blood test that measures the amount of ATIII activity in the blood. Acquired ATIII deficiency can also be seen in people with liver disease, some kidney diseases, at the time of an acute clot, pregnancy, and in people on heparin.

Protein C Deficiency. Protein C (PC) is a protein made in the liver that helps to control (decrease) the formation of blood clots. PC deficiency may be severe (homozygous) (rare) or mild/moderate (heterozygous)(more common). PC deficiency may be due to the liver producing either less protein or a dysfunctional protein. PC deficiency is more often a cause of venous thrombosis rather than arterial thrombosis. Testing for PC deficiency is done by a blood test that measures the amount of PC activity in the blood. PC deficiency can also be an acquired disorder seen with liver disease, vitamin K deficiency, at the time of an acute clot, pregnancy, and in people who are taking Coumadin.



Protein S Deficiency. Protein S (PS) is a protein also made in the liver that helps to control (decrease) the formation of blood clots. PS deficiency occurs as a severe (homozygous)(rare) or mild/moderate (heterozygous)(more common) form and may be due to the liver making either less protein or a dysfunctional protein. PS deficiency can predispose to either mostly venous (occasionally arterial) thrombosis (venous thrombosis is more common with PS deficiency). Testing for PS deficiency is done by a blood test that measures the amount of PS activity in the blood. PS deficiency can also be an acquired disorder seen with liver disease, vitamin K deficiency, at the time of acute clot, pregnancy, and in people who take Coumadin.

Prothrombin Gene Mutation. Prothrombin is a protein made by the liver that aids in forming clots. The prothrombin gene mutation causes increased production of prothrombin and is a relatively common abnormality, which can cause mainly venous thrombosis. Testing for the prothrombin gene mutation is done by a blood DNA test.

Hyperhomocysteinemia. Hyperhomocysteinemia (HHC) is an increase in the amount of homocysteine (a component of protein) in the blood. Severe HHC is rare. Mild HHC in adults is common and may be associated with both arterial and venous blood clots. Testing for HHC is done by a blood test that measures blood levels of homocysteine. Higher blood homocysteine levels can also be related to deficiency of folic acid or vitamin B12. Mild HHC can be corrected by taking small doses of folic acid or by eating foods containing adequate amounts of folic acid.

Elevated LP(a) (also known as lipoprotein a). An elevated LP(a) is associated with both venous and arterial clots. Some of the rare inherited thrombophilias include abnormalities in fibrinogen and the fibrinolytic pathway.

Testing: Who, Why, When?

Anybody who develops a thrombosis before the age of 55 should be tested for thrombophilia, as they have the highest likelihood of having one or more types of inherited thrombophilia. If you have a family history of anybody in your family (blood relatives) who has been diagnosed with a specific hereditary thrombophilia, you should be tested for the type of thrombophilia found in your family members.

Testing is important because if you are found to have a thrombosis and are diagnosed with a thrombophilia, your doctor can recommend lifestyle changes, treatment options and/or medications to help prevent future clots. If you have been diagnosed with a thrombophilia, and have not yet had a clot, your doctor can give you helpful information regarding when treatment may be necessary to prevent a clot. Remember, even if you have not yet had a clot, but are diagnosed with a thrombophilia, there are steps you can take to help reduce your risk of developing a clot. Having a diagnosis of a thrombophilia is not a guarantee you will have a clot at some time in your life and many people with thrombophilia never develop blood clots.

Testing for thrombophilia can be affected by many different factors. These factors can interfere with testing and cause false-positive or false-negative results. Some of these factors include acute and chronic illnesses (liver disease, kidney disease, infection), and medications such as heparin, Coumadin, and estrogen. Therefore, testing for thrombophilia is not optimal if performed at the time of an acute clot, other illnesses, or while taking blood thinner medications (such as Coumadin or heparin). People with a clot should be tested after an appropriate course of anticoagulant therapy and discontinuation of anticoagulants for 3-4 weeks.



If you have had an episode of an early clot, you may have more than one blood abnormality that significantly increases your risk for developing clots. Therefore, full and complete assessment should be done which includes comprehensive laboratory testing.

You should consider testing for thrombophilia for any of the following reasons:

- You are diagnosed with an early clot (before age 55)
- You have a history of an early clot or someone in your family (a blood relative) has had a history of an early clot
- You have a personal or family history of a clot and are scheduled for major surgery, or are considering pregnancy or oral contraceptive use
- You have a family history of diagnosed inherited thrombophilia

Treatment Options

Anybody diagnosed with a clot will most likely require a period of anticoagulation therapy. Anticoagulation therapy may include treatment with one or more of the following:

- Standard heparin
- Low molecular weight heparin
- Warfarin
- Aspirin
- Thrombolytic medications (clot-dissolving drugs)
- Surgery

The specific course of treatment depends on many factors. These factors include:

- Location and severity of clot
- Personal history of previous clots
- Family history (blood relative) of clots
- Diagnosis of thrombophilia, either acquired or hereditary
- Conditions such as: pregnancy, obesity, illnesses, age

The specific course for treatment will vary. Therefore, it is very important to have a doctor with experience in thrombophilia, and can recommend the best treatment course for your specific situation.

Summary

There are many known causes for the development of blood clots. It is very important for anybody with a personal history of clots or a family history (blood relative) of clots to be tested for thrombophilia. Testing can help establish the reason for clotting, identify people and families at risk for future clots, and helps reduce the incidence of future clotting through preventive measures.

If you have questions regarding this information, please call your CCBBD Nurse Coordinator at (414)257-2424.