



Bleeding Disorders and Thrombosis Program  
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# Learning about Thrombophilia

- **Thrombophilia** is a medical term. It is used to describe your blood's increased tendency to **clot**.
- There are two types of thrombophilia:
  - **Inherited**-1 or both of your parents passed it down to you.
  - **Acquired**- abnormal clotting related to a specific cause. For example: immobility or infection.
- Please remember even though you are at a higher risk of developing a blood clot it does not mean you will during your life.

## Acquired Thrombophilia

- Some people can have medical conditions that increase their tendency to form a blood clot. Some of these conditions include:
  - severe infection or trauma
  - cancer
  - kidney disease
  - rheumatologic disease (systemic lupus erythematosus or SLE)
  - diabetes
  - major surgical procedures and orthopedic procedures
  - pregnancy
  - use of estrogen containing oral contraceptive pills (OCPs)
  - use of catheters inserted into large veins to deliver medications, nutrition, and other therapies.

# Factor V Leiden

## Heterozygous Abnormal (1 abnormal gene)

- This is the most common genetic form of **thrombophilia**. About 5% of Caucasians have just one abnormal gene. This is called **heterozygous abnormal**.
- This is not a disease. It is a gene that was passed down through one of your parents. Having this **gene** increases your risk of developing a blood clot by 3-5 times more than people without the abnormal gene.
- Having Factor V Leiden does not mean you will develop a blood clot. It just means you have an increased chance of developing a blood clot. There are some preventative things that you can do daily to better your chances of not developing a blood clot. Please see the handout titled: Prevention of forming a blood clot.

## Homozygous Abnormal (2 abnormal genes)

- Is not a disease. It is a gene that was passed down through both of your parents. Having these two genes increases your risk of developing a blood clot 50-80 times over someone without the gene.
- Even though your risk of developing a blood clot is much higher with 2 abnormal genes it does not necessarily mean you will develop a blood clot in your life time. There are some preventative things you can do daily to better your chances of not developing a blood clot. Please see handout titled: Prevention of forming a clot.

## How is a clot formed when you have the abnormal gene Factor V Leiden?

Factor V itself is a clotting factor. Its normal role is to help blood clots form when needed. Normally Factor V listens to Protein C and Protein S. These are regulators of blood clotting. These proteins tell Factor V to turn off and stop forming a clot.

When FV is abnormal, also called Factor V Leiden, it cannot always hear what Protein C is saying. It “resists” being turned off. Eventually, Factor V activity will stop but this is over a longer period. During this time period, blood clots are more likely to develop.

Resources:

[www.fvleiden.org](http://www.fvleiden.org)

# MTHFR Gene Mutations

(Methylenetetrahydrofolate reductase)

## Heterozygous Abnormal (1 abnormal gene):

- Having one abnormal gene is very common in the population. 20-30% of people carry a single mutation.
- It is very unlikely for you to develop a blood clot if you have 1 abnormal gene and a normal homocysteine level.

## Homozygous Abnormal (2 abnormal genes)

- Having 2 abnormal genes may lead to high **homocysteine** levels in your blood. Homocysteine is a substance your body uses to make proteins to build and maintain tissues. Having a high homocysteine level means you may have a small increased risk of developing a blood clot.
- There are ways that may decrease the homocysteine level in the body. Folic acid and Vitamin B have been shown to decrease the homocysteine level in some cases.

## How is a clot formed when you have 2 abnormal genes *and* an elevated homocysteine level?

Methylenetetrahydrofolate reductase (MTHFR) is an **enzyme** found in the cells of your body. It is needed to break down homocysteine found in the proteins you eat. If this gene is not working correctly the body cannot break down the homocysteine. The levels in your body continue to rise. This rise in homocysteine may increase your risk of developing blood clots, mainly clots related to stroke and heart attacks in adults.

# Protein C, Protein S and Antithrombin Deficiency

## Protein C Deficiency:

- Protein C is a protein that regulates the formation of blood clots. When this protein is decreased the body continues to make a blood clot when it is not needed.

## Protein S Deficiency:

- Protein S helps Protein C in regulating the formation of blood clots. When this protein is decreased the body can continue to make a blood clot when it is not needed.

## Antithrombin Deficiency:

- Antithrombin is a naturally occurring blood thinner that is in your body. It helps prevent new blood clot formation when the blood clot is not needed anymore after an injury to a blood vessel. If antithrombin levels are low, a person will have an increased risk of developing too many blood clots.

## Important things to remember:

1. It is rare for your parents to have passed any of these deficiencies down to you. However, if this has indeed happened then you are at a very high risk of developing abnormal blood clots and having them return in adult hood.
2. Some people who are very sick with an infection, kidney or liver disease may have low levels of these proteins for a short amount of time. They will be at risk for blood clots while the levels are low. The level of Protein C, S can also be affected if they are measured while you are on a medicine called Coumadin (Warfarin). If you are found to have a low level this should be repeated when you are off Coumadin.

# Prothrombin Gene Mutation

## Heterozygous Abnormal (1 abnormal gene)

- This is the second most common form of thrombophilia. 3% of Caucasians have 1 abnormal copy of the prothrombin gene.
- It is not a disease. It was passed down through one of your parents. Having prothrombin gene mutation increases your risk of developing a blood clot 2-3 times. It also increases the risk of blood clot reforming after treatment.

## Homozygous Abnormal (2 abnormal genes)

- Having 2 abnormal genes increases your risk of developing a clot dramatically. The risk is about 2-3 times the average person's risk.

## How is a clot formed when you have the Prothrombin Gene Mutation?

All individuals make prothrombin. This is also called Factor II. It is a building block for the protein thrombin. Thrombin is the major protein in blood clots. People who have the mutation in the prothrombin gene make too much of these proteins. This causes an increased tendency of a blood clot to form.

\*Having Prothrombin Gene Mutation does not mean you will develop a blood clot. It means you have an greater risk. There are some preventative things that you can do daily to better your chances of not developing a blood clot. Please see handout titled: Prevention of forming a clot.

Resources:

- <http://www.stopthecLOT.org>

# Prothrombin Gene Mutation and Factor V Leiden

- Having mutations in both prothrombin and Factor V Leiden can occur in the same individual. This increases the risk of blood clots forming by 50-100 times.
- Having Prothrombin Gene Mutation and Factor V Leiden does not mean you will develop a blood clot. It means you have an increased risk. There are some preventative things that you can do daily to better your chances of not developing a blood clot and to decrease the chances of it returning. Please see handout titled: Prevention of forming a clot.

Resources:

<http://www.stoptheclot.org>

## **Elevated Lipoprotein (a)**

- Lipoprotein (a) carries fat around the body to help heal artery damage.
- If you have too much of this protein plaque can build up in your arteries. This ultimately causes a blood clot to form.
- Due to the high levels of Lipoprotein (a) the body cannot effectively break down the clot once it has formed.
- Very high levels of this protein have been reported in children with abnormal clots.



# Antiphospholipid Antibodies and Lupus Anticoagulant

- Sometimes when your body is stressed, the immune system goes into overdrive and produces proteins. These proteins attack normal parts of your body because they recognize them as foreign. These proteins are called auto (self) antibodies. These particular auto antibodies attack a part of the blood clotting system. They interfere with normal building and breaking down of clots.
- Once these antibodies are formed they can increase your risk of developing a blood clot.
- Usually these antibodies go away quickly in children. They can stay in the blood for several years.
- If they are present in high amounts at the time of a new blood clot and if they remain detectable beyond 12 weeks, they can cause uncontrolled blood clotting in the veins or arteries. This condition is called Antiphospholipid Antibody Syndrome.

# Prevention of Forming a Clot

- During high risk situations some people with a history of thrombophilia might need blood thinners. This is done to prevent blood clots from forming.
  - **High Risk Situations:**
    - Pregnancy
    - Major Surgery
      - Orthopedic surgery
      - Surgery requiring long anesthesia
    - Trauma
    - Prolonged bed rest
    - Immobilization of an extremity (cast or traction)
    - Chronic medical illness
      - Kidney disease, cancer, rheumatologic disease
- There is media attention about the development of blood clots in people on long plane flights and long car rides.
  - Any person with blood clots or thrombophilia should get up and stretch every few hours during long plane rides or road trips. This is done to prevent the slowing or stopping of blood flow and possible blood clot formation.
  - They should talk with their doctor before going. Talk with their doctor about the need for a short course of blood thinning medicine.
- Women with a history of thrombophilia need to avoid hormone pills, especially those with estrogen. You should not take these medicines to treat acne. They may be a good choice to prevent pregnancy or control severe bleeding during your cycles. You should talk to your doctor about the risk of forming a blood clot compared to the benefit of using these pills.
  - Birth control pills or hormone replacement therapy increase ALL women's risk for blood clots. This risk is higher if you also have thrombophilia.
  - Women who have had a blood clot in the past will need to be on heparin during pregnancy. Women with certain thrombophilia may also need to be on blood thinners around the last trimester of pregnancy and after delivery.
    - Coumadin is dangerous to the fetus.
  - Discuss options with your doctor if you have thrombophilia.

# Signs and Symptoms to Be Aware of

- Signs and Symptoms of a blood clot in the arm or leg
  - Pain, heaviness
  - Swelling
  - Reddish/purple discoloration of the affected arm or leg
  - Sudden onset after injury or prolonged bed rest
- Signs and Symptoms of Pulmonary Embolism (blood clot that has traveled to the lungs)
  - Difficulty breathing
  - Chest pain that gets progressively worse
  - Fever
- Signs and symptoms of stroke and cerebral sinovenous thrombosis (CVST)
  - Headache
  - Speech Problems
  - Arm or leg weakness or paralysis
  - Seizures

## Definitions of Medical Terms

- 1. Acquired Thrombophilia:** Abnormal clotting related to a specific cause such as an infection, immobility, or prolonged hospital stay.
- 2. Auto Antibodies:** Are produced when the immune system recognized something in the body as foreign.
- 3. Blood Clot or Thrombus:** A clump of blood that has formed in your veins or arteries causing blood not to flow normally.
- 4. Enzymes:** Proteins that break down things in the body i.e: they help break down food and other chemicals in the body.
- 5. Gene:** A unit of heredity that is passed down from the baby's parents. They are instruction manuals for our body.
- 6. Heterozygous Abnormal:** 1 gene that does not function normally in the body.
- 7. Homozygous Abnormal:** 2 genes that do not function normally in the body.
- 8. Inherited Thrombophilia:** Genetically passed down to the child from one or both parents.
- 9. Pulmonary Embolism:** A blood clot that breaks off of a clot formed in the body and travels to the lungs causing difficulty breathing, chest pain and fever. This can be potentially fatal.
- 10. Stroke:** or "brain attack" occurs when a blood clot obstructs an artery or vein in the brain causing headache, speech problems, arm or leg weakness or paralysis and sometime seizures.
- 11. Thrombophilia:** A medical term used to describe an increased tendency for a person to form a blood clot.