



**PROTHROMBIN  
GENE MUTATION**

# THROMBOPHILIA

Information for Patients



## **INTRODUCTION**

**Thrombophilia** (Hypercoagulability) is a condition in which a person forms blood clots more than normal. Blood clots may occur in the arms or legs (e.g., **deep vein thrombosis – DVT**), the lungs (e.g., **pulmonary embolism – PE**) or other organs. Blood clots can cause swelling, pain, or shortness of breath. Other symptoms of blood clots include dizziness, headache, changes in vision, lack of concentration, confusion, slurred speech, numbness, tingling, and weakness in the arms or legs. Blood clots may become life threatening if not recognized and treated early.

Some forms of thrombophilia are inherited from one or both parents. This is called **inherited thrombophilia**. Examples include:

- ◆ **Factor V Leiden**
- ◆ **Prothrombin gene mutation**
- ◆ **Antithrombin deficiency**
- ◆ **Protein C deficiency**
- ◆ **Protein S deficiency**

Other forms of thrombophilia develop after birth. This is called **acquired thrombophilia**. Examples include:

- ◆ **Antiphospholipid syndrome**
- ◆ **Hyperhomocysteinemia**

Things that may trigger or cause blood clots to form include: surgery, trauma (injury) or fractures, bed rest or sitting or lying still for several hours at a time, cancer and chemotherapy, intravenous catheters, estrogen use, pregnancy, or air travel. Sometimes, blood clots happen without an identifiable trigger or cause.

## ***PROTHROMBIN GENE MUTATION***

**Prothrombin gene mutation** is the second most common cause of inherited thrombophilia in the United States. It is present in about 2% of Caucasians. It is caused by a change or mutation in the gene for the blood clotting protein called **prothrombin** (which is also called Factor II). People with the prothrombin gene mutation have higher than normal levels of prothrombin in their blood, making them prone to blood clots, most common in the veins.

The prothrombin gene mutation can be inherited from one or both parents. This means that if one parent has it, then each child has a 50:50 chance of inheriting it.

Most people with the prothrombin gene change have inherited one copy of the abnormal prothrombin gene from one parent. People with one copy of this gene have about a five times greater chance of getting a blood clot than someone without the prothrombin gene change. The good news is that most people who have inherited one copy of the abnormal prothrombin gene will never get a blood clot during their lifetime.

About one percent of people with the prothrombin gene change have inherited two copies of the abnormal prothrombin gene, one from each parent. These people have up to 50 times higher risk of getting a blood clot

Rarely, the prothrombin gene change is inherited along with Factor V Leiden. If an individual has both the prothrombin gene change and Factor V Leiden, the onset of blood clots may be earlier or more severe.

## ***Diagnosis***

The diagnosis of prothrombin gene mutation is made by a genetic or DNA test done in a blood sample.

## ***Treatment***

The primary goal of treatment is to prevent blood clots. The treatment you receive will depend on your: history of previous blood clots, overall health, symptoms, and need for other medications or surgical procedures. The duration of treatment will vary depending on your individual medical history, and the presence of other health problems. Your treatment plan should be discussed with your primary doctor or hematologist. Some people with thrombophilia will never need treatment. Your doctor may recommend treatment with anticoagulant medications (blood thinners), such as **heparin, low-molecular weight heparin, or warfarin** to help prevent blood clots.

## ***Prevention***

People who have thrombophilia can reduce their risk of getting a blood clot by:

- ◆ **Exercising regularly** – Exercise improves the body's ability to dissolve clots that have formed and helps prevent blood from clotting inside the veins.
- ◆ **Avoiding becoming overweight or obese** – Overeating increases levels of the hormone insulin. Insulin can interfere with the normal clotting controls. Obesity can also cause poor circulation in the veins, leading to a higher risk of clotting.
- ◆ **Avoiding long periods of immobility during illness or when traveling** – When people sit or lie down for several hours at a time, the circulation of the blood slows down. This may increase the risk of clotting.
- ◆ **Refraining from cigarette smoking** – Smoking decreases the amount of oxygen in the blood and may damage vessel walls, potentially leading to clot formation.

- ◆ **Seeking medical advice before major surgery** – Blood vessels may be damaged during surgery, leading to a high risk of blood clots. It is important for your doctors to know that you have thrombophilia before planning any surgery.
- ◆ **Seeking medical advice before taking birth control pills or hormone replacement therapy** – Hormones, including birth control pills may increase risk of clotting.
- ◆ **Seeking medical advice when pregnant or planning to become pregnant** - Women with thrombophilia have an increased risk of blood clots during pregnancy, and may also have a higher risk of miscarriage and other complications of pregnancy.

### ***Genetic Testing***

There are many issues around the decision to pursue genetic testing for you or a family member. You and your family will want to consider how this information will be used before having testing done. It is recommended that these issues be discussed with a hematologist, genetic counselor, or other trusted health care provider.

## **ANTICOAGULANT MEDICATIONS**

Anticoagulant medications can cause you to bleed more easily. You may notice that, if you cut yourself, the blood takes longer to clot. You might bruise more easily. If you have any unusual, heavy or prolonged bleeding, severe headaches, visual changes, or stiff neck, call your doctor.

Treatment may include blood thinners (anticoagulant medications) such as heparin, low-molecular weight heparin, warfarin, aspirin, or clopidogrel.

Warfarin has a stronger effect on some people than others. If you take warfarin, your doctor will want to check you frequently with a blood test called the **INR (International Normalized Ratio)** or **Prothrombin Time (PT)**. This test will tell your doctor how well the warfarin is working. Many other medications can make warfarin more or less strong. Ask your doctor before you take a new medicine, even a nonprescription medicine or vitamin.

If you are pregnant, you should not take warfarin. Warfarin can cause birth defects. If you are pregnant or might become pregnant, talk with your doctor.

## **COPING WITH STRESS**

The diagnosis of thrombophilia and the treatment it may require can cause stress for many patients and their families. It is normal to feel a variety of emotions, including shock, fear, and anger. To cope, many people have found it helpful to become involved in support groups that are made up of other people and their families facing similar issues. Please ask your nurse, social worker, or doctor if you wish to receive more information about support groups. Professional counselors are also available as an option if you feel you need to additional help dealing with your illness and its treatment.

## GLOSSARY

**Activated protein C resistance test:** A blood test that can be used to detect Factor V Leiden.

**Alzheimer's disease:** A degenerative disease characterized by progressive brain deterioration and dementia.

**Antibody:** A protein substance normally formed by the body to help defend it against infections and foreign substances.

**Anticardiolipin antibody:** A type of antiphospholipid antibody.

**Anticoagulant:** A substance that prevents excessive blood clotting.

**Anticoagulation medication:** A drug that is given to prevent excessive blood clotting. Sometimes called a blood thinner.

**Antiphospholipid antibody:** An autoantibody that reacts with a normal component of blood cells called phospholipid.

**Antiphospholipid syndrome:** A form of acquired thrombophilia caused by autoantibodies that react with a normal component of blood cells called phospholipid.

**Antithrombin:** A blood protein that prevents excessive blood clotting.

**Antithrombin concentrate:** A medication that contains large amounts of antithrombin.

**Antithrombin deficiency:** A form of inherited thrombophilia caused by a mutation in the gene for the blood protein called antithrombin.

**Autoantibody:** An antibody that reacts with normal components of the body.

**Autosomal dominant:** A pattern of inheritance in which, if one parent has a disorder, then each child has a 50:50 chance of inheriting the disorder.

**Aspirin:** A medication that prevents blood clotting by blocking the effects of platelets.

**Autoimmune disease:** A disorder caused by the production of antibodies that react with normal components of the body

**Betaine:** A medication used to treat severe hyperhomocysteinemia.

**Blood clotting proteins:** Proteins in the blood that are involved in the process of blood clotting.

**Cell:** The basic building blocks of life. Humans are made of many cells of different types.

**Chemotherapy:** A medication used to treat cancer.

**Clopidogrel:** A medication that prevents blood clotting by blocking the effects of platelets.

**Coagulation:** The process by which blood clots.

**Cystathionine beta-synthase (CBS):** A protein that breaks down homocysteine. Deficiency of CBS can cause hyperhomocysteinemia.

**Deep vein thrombosis:** A blood clot that forms in the deep veins of the extremities.

**DNA:** The substance from which the genetic code is made.

**Factor V:** One of the blood clotting proteins.

**Factor V Leiden:** A form of inherited thrombophilia caused by a mutation in the gene for the blood clotting protein, factor V.

**Folate:** One of the B vitamins.

**Folic acid:** A form of the vitamin folate.

**Genetic counselor:** A health care provider that is trained to provide information and counseling about the diagnosis and management of genetic (inherited) disorders.

**Genetic disorder:** An inherited condition passed down in genes through generations in a family.

**Genetic test:** A test that detects variant in DNA.

**Heart attack:** A medical condition that occurs when a blood vessel in the heart is blocked, often by a blood clot.

**Hematologist:** A doctor who specializes in diseases of the blood and bone marrow.

**Heparin:** An anticoagulant medication.



**Heterozygous:** A genetic condition in which a person has inherited one normal copy and one abnormal copy of a gene.

**Homozygous:** A genetic condition in which a person has inherited two copies of a gene variant.

**Homocysteine:** An amino acid that is normally present in blood.

**Homocystinuria:** A severe form of hyperhomocysteinemia.

**Hypercoagulability:** A condition in which a person has an increased tendency to form blood clots. Also called thrombophilia.

**Hyperhomocysteinemia:** A form of acquired thrombophilia resulting from a high level of homocysteine in the blood.

**Hypothyroidism:** A medical condition caused by deficient thyroid activity.

**Inherited thrombophilia:** A form of thrombophilia that runs in families, and can be inherited from one or both parents.

**International Normalized Ratio (INR):** A blood test used to monitor the effects of anticoagulant medications such as warfarin.

**Intravenous catheter:** A tube that is used to infuse medications into the blood through a vein.

**Livedo reticularis:** A blotchy skin condition that is sometimes seen in people with the antiphospholipid syndrome.

**Low-molecular weight heparin:** An anticoagulant medication.

**Lupus:** A medical condition known as systemic lupus erythematosus.

**Lupus anticoagulant test:** A diagnostic test for antiphospholipid syndrome.

**Methionine:** An amino acid found in proteins in the diet.

**Methylene tetrahydrofolate reductase (MTHFR):** A protein that breaks down homocysteine. Deficiency of MTHFR can cause hyperhomocysteinemia.

**Mutation:** A change in a gene from what is considered normal.

**Phospholipid:** A component of blood cells that is involved in the blood clotting process.

**Platelet:** A type of blood cell that assists in blood clotting.

**Primary antiphospholipid syndrome:** Antiphospholipid syndrome in someone who does not have another autoimmune disease.

**Protein:** Essential molecules in the body made up of many amino acids strung together.

**Protein C:** An anticoagulant that is normally found in blood.

**Protein C deficiency:** A form of inherited thrombophilia caused by a low level of protein C in the blood.

**Protein S:** An anticoagulant that is normally found in blood.

**Protein S deficiency:** A form of inherited thrombophilia caused by a low level of protein S in the blood.

**Prothrombin:** A blood clotting protein. Also called factor II.

**Prothrombin time (PT)** – A blood test that measures, in seconds, how quickly blood clots. Used to monitor the effects of anticoagulant medications such as warfarin.

**Prothrombin gene mutation:** A form of inherited thrombophilia caused by a mutation in the gene for the blood clotting protein called prothrombin.

**Pulmonary embolism:** A blood clot forms in the deep veins of the legs or other locations and then travels to the lung.

**Secondary antiphospholipid syndrome:** Antiphospholipid syndrome in someone who also has another autoimmune disease.

**Stroke:** A medical condition that occurs when a blood vessel in the brain is blocked, often by a blood clot.

**Systemic lupus erythematosus:** A medical condition known as Lupus.

**Thrombocytopenia:** A low number of platelets in the blood.

**Thrombophilia:** A condition in which a person has an increased tendency to form blood clots. Also called a hypercoagulable state.

**Warfarin:** An anticoagulant medication.



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