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ORIGIN, TREATMENT AND PREVENTION OF THROMBOPHILIA DISEASE

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Abstract:

Thrombophilia refers to a group of conditions where the blood clots more easily than normal. This can lead to unwanted blood clots (called thromboses) forming within blood vessels. These blood clots can cause problems such as deep vein thrombosis (DVT) or pulmonary embolism. See the separate leaflets called Deep Vein Thrombosis and Pulmonary Embolism for more details.

Keywords: Thrombophilia, called platelets, thromboses

The body has a natural clotting process in the blood, which is altered in thrombophilia.
The normal clotting process is called hemostasis. It helps to stop bleeding if you have an injury such as a cut. When a blood vessel is injured, the clotting process is triggered. This is called the clotting cascade. It is a chain reaction of different chemicals in the blood which are called clotting factors. The clotting cascade makes the blood solidify into a clot, which sticks to the injured part of the blood vessel. Small particles in the blood, called platelets, also help to form the clot.
There are also natural chemicals in the blood which act against the clotting system, to stop the blood clotting too much.
Thrombophilia occurs if the normal balance of the clotting system is upset. There may be too much of a clotting factor, or too little of a substance that opposes clotting.
Thrombophilia can cause unwanted blood clots (thromboses). This does not mean that every person with thrombophilia will develop a blood clot. But, it means that you have a higher risk than normal of having clots. The extra risk will depend on the type of thrombophilia that you have.

What is a thrombosis?
A blood clot that forms within a blood vessel is known medically as a thrombus. Thrombosis is the process that occurs to form a thrombus. A thrombus can block a blood vessel - this blockage is now also known as thrombosis. The word thromboses is the plural version of thrombosis (that is, more than one).

What are the different types of thrombophilia?
Thrombophilia's can be classified into inherited or acquired. The inherited ones are genetic and may be passed on from parent to child.
Acquired thrombophilia's are not inherited, meaning they have nothing to do with your genes. Usually, acquired thrombophilias become apparent in adulthood. They can happen as a result of other medical problems that have developed, or they might be due to problems with the immune system.
It is possible to have a mixed thrombophilia, due partly to genetic and partly to non-genetic factors.
The different types of thrombophilia are explained in more detail later in this leaflet.

What are the symptoms of thrombophilia?
There are no symptoms unless the thrombophilia results in a blood clot (thrombosis).
Many people with thrombophilia do not develop a blood clot and have no symptoms at all.

What are the symptoms of blood clots?
Blood clots can form in arteries and veins. Arteries are blood vessels that take blood away from the heart to the organs and tissues of the body. Veins are blood vessels that bring blood back to the heart, from the rest of the body.

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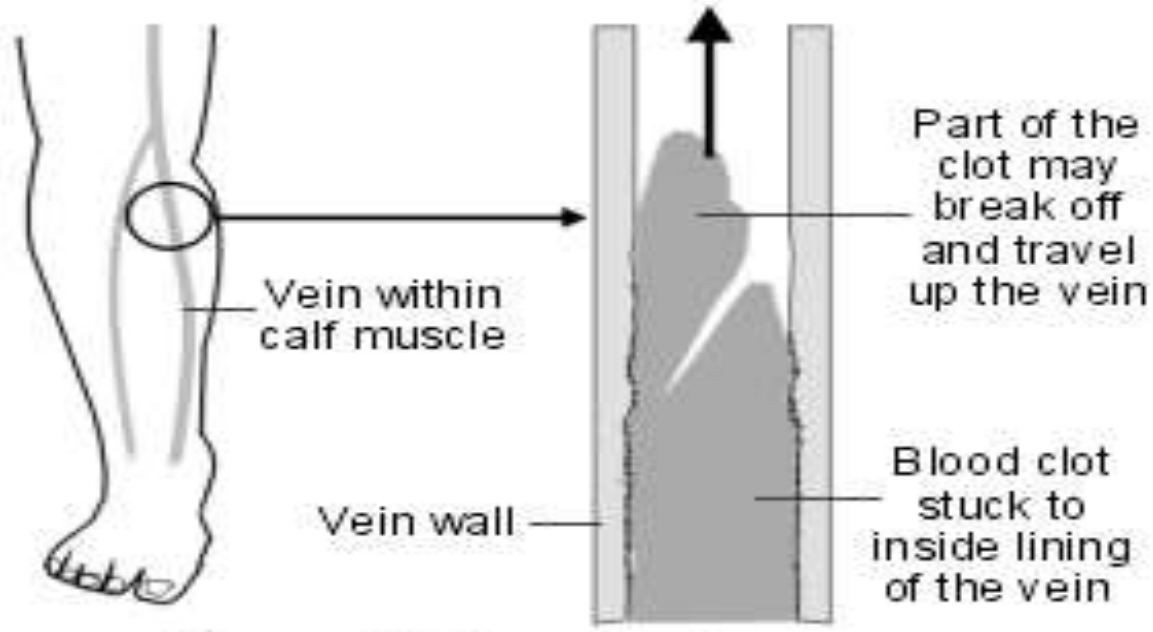

Deep vein thrombosis

A blood clot in a vein is the most common problem with thrombophilia - this is called venous thrombosis. Possible symptoms are:

- Pain and swelling in a leg. This occurs if you have a blood clot in a large vein in a leg. This is commonly known as a deep vein thrombosis (DVT). A DVT can occur in any vein in your body but most often affects a leg vein.
- The blood clot may travel to the heart and on into a lung, causing a pulmonary embolism. Possible symptoms are chest pain, pain on deep breathing, shortness of breath or, rarely, collapse.
- Some types of thrombophilia can cause a blood clot in an unusual site such as the brain, gut or liver. This can cause symptoms in the head or the tummy (abdomen). A blood clot in the liver veins is called Budd-Chiari syndrome.

A blood clot in an artery can occur with some types of thrombophilia. This is called arterial thrombosis. Depending on which artery is affected, a blood clot in an artery can cause a stroke, a heart attack or problems with the placenta during pregnancy. So the possible symptoms of arterial thrombosis due to thrombophilia are:

- Having a stroke at a relatively young age.
- Repeated miscarriages.
- Pregnancy problems: pre-eclampsia, reduced fetal growth or, rarely, fetal death (a stillbirth, or intrauterine death).
- A heart attack.

It is important to remember that all of these conditions can be due to causes other than thrombophilia. For example, smoking, high blood pressure, diabetes and high cholesterol are the main risk factors for developing problems such as heart attack and stroke.
For this reason, not everyone with a stroke or heart attack is tested for thrombophilia, as it is not a common cause.

How is thrombophilia diagnosed?
Thrombophilia may be suspected if a blood relative had a blood clot at a young age (under 40 years). It may also be suspected if you develop a blood clot which would not be expected, given your age and general health.
One of the most important things is that thrombophilia testing is not done routinely on everyone who has a blood clot. Only certain people need to have these tests - where the result will change how you are treated. The tests are expensive and sometimes it is not known how the result will affect your chances in the future of having a blood clot. This can be quite difficult to understand, but often, if you have just had a blood clot, you will have blood-thinning (anticoagulant) treatment in any case. This will happen whether or not you have a thrombophilia. If you have had an unprovoked blood clot once (meaning it happened without obvious cause), you will be classed as having a higher risk of a blood clot in the future anyway. This will be the case whether or not you have a positive thrombophilia test.

How to test for thrombophilia
Thrombophilia is diagnosed by blood tests.

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Tests are done some weeks or months after having a DVT or pulmonary embolism, as the presence of these conditions can affect the results. Usually you have to wait until you have been off blood-thinning medication (anticoagulants), such as warfarin, for 4-6 weeks. If you have recently been pregnant, the tests may have to be delayed by eight weeks. This is because the results in pregnancy can be much harder to understand.
A sample of blood is taken and a number of different tests will be done on it, to check different parts of the clotting process. Usually, the tests are done in two stages. The first test is a thrombophilia screen which is some basic clotting tests. If the results of this suggest that thrombophilia is possible then another blood sample will be taken for more detailed tests.
You may be referred to a doctor specialising in blood conditions (a haematologist). The doctor will usually ask about your history and family history. This will help with interpreting the test results.

Can all thrombophilias be diagnosed on tests?
It is likely that there are some kinds of thrombophilia which we cannot yet identify or test for. This is because there are some people or families who have more blood clots than would normally be expected, yet test negative on the thrombophilia tests. In this situation, you might be advised to have treatment as for thrombophilia, even if you do not have a definite diagnosis.
Therefore, negative tests do not exclude the possibility that you have an inherited increased risk of having blood clots.

Who should be tested for thrombophilia?
Current guidelines suggest that thrombophilia testing should be considered in the following situations:

- If you have a venous thrombosis or pulmonary embolus under the age of 40.
- If you have repeated episodes of venous thrombosis or pulmonary embolus or inflamed veins (thrombophlebitis).
- If you have a venous thrombosis in an unusual site - for example, the tummy (abdomen) or the brain - in some circumstances, as these can be caused by other conditions.
- Unexplained thromboses in newborn babies.
- Babies or children with a rare condition called purpura fulminans.
- If you develop skin necrosis, in which patches of skin are lost due to clots in or under the skin, due to medicines such as warfarin.
- If you have an arterial thrombosis occurring under the age of 40 years.
- If you are a blood relative of someone with certain types of high-risk thrombophilia - such as protein C and protein S deficiencies, in some circumstances.
- Some pregnant women who have had a thrombosis in the past due to a mild provoking factor. (However, a pregnant woman with a history of unprovoked thrombosis does not need testing, as she needs blood-thinning medication (anticoagulants) anyway in pregnancy.)
- If you have a family history of venous thrombosis in at least two relatives.
- If you have certain blood test results: an unexplained prolonged activated partial thromboplastin time (aPTT) - an abnormal result on a certain type of blood clotting test. Some people with other medical conditions (because these can sometimes be linked to thrombophilia):
  - Recurrent miscarriage.
  - Fetal death.
  - Idiopathic thrombocytopenic purpura (ITP) - a condition affecting blood platelets.
  - Systemic lupus erythematosus (SLE), also referred to as lupus.

Even if there is a known thrombophilia in the family, you may not be tested for it if it is mild and you have not had a blood clot yourself. This is because you are asymptomatic (you have no symptoms). Knowing if you have this inherited defect will not change how you are treated; you probably won't need anticoagulants because it is not known how much your risk of abnormal blood clotting is increased. Treatment with anticoagulant medication has to be carefully assessed, as its use also has certain risks, such as bleeding.

What is the treatment for thrombophilia?
The first step is for you and your doctor to consider how much risk there is of you developing a blood clot. This risk depends on a combination of things, such as:

- What type of thrombophilia you have (some are more high-risk for blood clot than others).
- Your age, weight, lifestyle and other medical conditions.
- Whether you are pregnant or have recently given birth.
- Whether you have already had a blood clot.
- Your family history - whether any close relatives have had a blood clot.

This information will help your doctor to assess how much risk you have of developing a blood clot and what type of blood clot could occur. Then you and your doctor can discuss the pros and cons of taking treatment and, if needed, what type of treatment to take.
Possible treatments for thrombophilia are:

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Low-dose aspirin

Low-dose aspirin inhibits the action of platelets, so can help to prevent blood clots. It may also help prevent miscarriage or pregnancy problems, in some types of thrombophilia.

Anticoagulant treatment

Anticoagulation is often called 'thinning' of the blood. However, it does not actually thin the blood. It alters certain chemicals in the blood to stop blood clots forming so easily - in effect, it slows down the clotting process. It doesn't dissolve a blood clot either (as some people incorrectly think). The body's own healing mechanisms can then get to work to break up any existing blood clot.

Anticoagulation can greatly reduce the chance of a blood clot forming. Anticoagulant medication is commonly used to treat a venous thrombosis (such as a DVT) or a pulmonary embolism.

In thrombophilia, anticoagulant medication may be advised if:

- You have had a blood clot, to prevent another one.
- You have not had a blood clot but have a high risk of developing one.
- You have a temporary situation that puts you at high risk of a blood clot. This may be the case if you are pregnant, within six weeks after childbirth, or are immobile for a long period.

Anticoagulant medicines are either given by injection (for example, heparin) or can be taken as a tablet. Warfarin is the most commonly used tablet anticoagulant medicine. Other anticoagulants taken in tablet form include apixaban, edoxaban, dabigatran and rivaroxaban.

Warfarin is the usual anticoagulant. However, it takes a few days for warfarin tablets to work fully. Therefore, heparin injections (often given just under the skin) are used alongside warfarin in the first few days (usually five days) for immediate effect if you currently have a blood clot. If you are starting warfarin and don't have a blood clot (that is, it is just to prevent one), you won't need heparin injections first.

The aim is to get the dose of warfarin just right so the blood will not clot easily. Too much warfarin may cause bleeding problems. To get the dose right, you will need a regular blood test, called International Normalised Ratio (INR), whilst you take warfarin. The dose is adjusted on an individual basis according to the result of this blood test. The INR is a blood test that measures your blood clotting ability. You need the tests quite often at first but then less frequently once the correct dose is found.

An INR of 2.5 is usually the aim if you take warfarin to prevent a blood clot in thrombophilia or to treat a DVT or pulmonary embolism. However, anywhere in the range 2-3 is usually OK. If you have had recurrent DVTs, or have had a pulmonary embolism whilst on warfarin, you might need a higher INR (even 'thinner' blood). INR blood tests can usually be done in an outpatient clinic, or sometimes by your GP. You may be advised to take warfarin on a lifelong basis to prevent blood clots if you have thrombophilia. Or, you may have short-term treatment for your current DVT or pulmonary embolism (usually 3-6 months).

Heparin is an injectable anticoagulant. Standard heparin is given intravenously (IV), which means directly into a vein - usually in the arm. This type of heparin is given in hospital and monitored with blood tests.

Low molecular weight heparin (LMWH) is injected into the skin on the lower tummy (abdomen). It can be given at home, either by a district nurse, or you can be taught to self-inject (or a carer can do it for you). It does not need blood tests to monitor it. Different doses are used for prevention (prophylaxis) and treatment of an existing blood clot. There are different brands of heparin injection; the common ones you might see used are Clexane® and Fragmin®.

How to treat thrombophilia in pregnancy

If you are pregnant or planning a pregnancy, discuss this with your doctor, and tell your midwife and doctor specialising in pregnancy and childbirth (obstetrician) about the thrombophilia. Treatment for thrombophilia may be different in pregnancy because:

- Some women with certain types of thrombophilia are advised to take low-dose aspirin while pregnant, to help prevent miscarriage or pregnancy problems.
- The pregnancy itself increases the risk of a venous thrombosis - this applies to the whole pregnancy and especially to the six weeks after childbirth. So you may be advised to start anticoagulant treatment while pregnant or after childbirth. This will depend on the type of thrombophilia and your medical history.
- If you were taking warfarin, you will normally be advised to change to heparin instead. This is because heparin is safer for the unborn baby (there is a significant chance that warfarin could cause fetal abnormalities). Both heparin and warfarin are safe for breast-feeding.

Prevention of DVT

Certain situations can temporarily put you at high risk of having a blood clot, and in these situations you may be advised to take extra treatment for a while. Examples are pregnancy and after childbirth, severe illness, major

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surgery, or anything which immobilises you, such as travel or an operation. Special stockings such as flight socks or compression stockings may also be advised to help prevent a DVT.

General advice for people with thrombophilia

- If you are having any medical treatment or surgery, tell your doctor/nurse/pharmacist about the thrombophilia.
- Be aware of the warning symptoms of a blood clot - obtain medical help immediately if you suspect one (see above for symptoms).
- Avoid lack of fluid in the body (dehydration) by drinking adequate amounts of fluid. Dehydration can contribute to blood clots forming.
- Keep active and avoid being immobile for long periods - immobility helps cause blood clots in the legs (DVTs).
- Caution with medication: some medications increase the risk of a blood clot. For example, the combined oral contraceptive (COC) pill or patch, and tablet forms of hormone replacement therapy (HRT). You may be advised to avoid certain medications, or to change to one which does not affect blood clotting.
- Keep to a healthy weight - being overweight or obese increases the risk of blood clots in legs.
- To keep blood vessels healthy (arteries in particular), do not smoke. This is important if you have thrombophilia of a type that can cause blood clots in arteries, as smoking also promotes arterial blood clots.

Often there are no complications with thrombophilia. Many forms of thrombophilia are mild, so that the outlook (prognosis) for many people with thrombophilia means that they have no problems from their condition. Also, treatment can successfully prevent complications in many cases.

A pulmonary embolism, stroke, heart attack or a blood clot in the brain or tummy (abdomen) can all be life-threatening conditions. Early treatment can be life-saving and it reduces complications. It is therefore important to be aware of the symptoms and seek treatment immediately if you suspect any kind of blood clot.

As mentioned above, some types (not all) of thrombophilia may increase the chance of problems in pregnancy. Your doctor can advise - it will depend on the type of thrombophilia and it also varies between individuals. However, many women with thrombophilia do have successful pregnancies.

There may also be complications due to blood-thinning (anticoagulant) treatment. Aspirin, heparin and warfarin can have side-effects, mainly unwanted bleeding, such as internal bleeding from the stomach lining. For this reason, it is important for you and your doctor to weigh up the pros and cons of taking treatment. Your individual situation and preferences need to be taken into account.

Testing relatives

If you or your family have an inherited (genetic) form of thrombophilia, you *may* be asked to consider tests for yourself or your close relatives. This is to see if you or others in the family have the same condition. However, the benefits of looking for people with thrombophilia who have not had a blood clot have not yet been proven. This is why there are clear guidelines on who should be tested.

What are the different types of thrombophilia?

This section explains the more common types of thrombophilia, although it does not cover every condition.

Factor V Leiden

This is pronounced 'factor 5 lyden'. It is fairly common in people of European origin - about 1 in 20 Europeans have the factor V Leiden gene. This gene affects the factor V part of the clotting cascade, making the clotting process go on longer. It increases the risk of a blood clot in a vein by about eight times. That is still a relatively low risk, so most people with factor V Leiden do not develop problems. Some people inherit two factor V Leiden genes - one gene from each parent (known as 'homozygous factor V Leiden'). This is less common but makes the risk much higher - around eighty times the normal risk.

Prothrombin 20210

Prothrombin is a clotting factor, and people with the 20210 gene have a change in their prothrombin which makes the blood clot more easily. About 1 in 50 people of European origin have this gene; it is more common in people of South European origin. It increases your risk of having a blood clot in a vein to twice the normal risk. This is a relatively low risk, so most people with prothrombin 20210 do not develop a blood clot.

Protein C deficiency

Protein C is a natural anticoagulant chemical in the blood. The deficiency can be genetic, or due to other conditions such as kidney disease. With inherited protein C deficiency, the risk of a blood clot forming varies between families. This is because each family has a different alteration in the protein C gene. The best guide to your level of risk is whether you or your relatives have had a blood clot. If a child inherits two genes with protein C deficiency (one from each parent - this is very rare), they will have a more severe problem. They will get blood clots in the skin soon after birth (a condition called purpura fulminans). This is

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treated with protein C concentrates and blood-thinning (anticoagulant) medication.

Protein S deficiency

Protein S is also a natural anticoagulant chemical in the blood. Protein S deficiency is rare. The risk of a blood clot forming varies between families. The best guide to your risk is to look at whether other relatives have had a blood clot.

Antithrombin deficiency

Antithrombin is another of the natural anticoagulant chemicals in the blood. There are different types of antithrombin deficiency, both genetic and due to other diseases. The inherited form is rare, affecting about 1 in 2,000 people.

Antithrombin deficiency is a fairly severe type of thrombophilia. The risk of having a blood clot varies between families but can be increased by 25-50 times the normal risk. With this condition, a blood clot can occur not only in the legs or lung but also in the veins of the arms, gut, brain or liver. About 1 in 2 people with antithrombin deficiency develop a blood clot before the age of 30 years. Others, however, may reach elderly age without problems.

With this condition, if you do develop a blood clot, you may be advised to take long-term warfarin medication. However, this must be decided on an individual basis. Also, treatment with antithrombin concentrates can be given when there is a higher risk of having a blood clot - for example, if you are having major surgery.

With pregnancy, anticoagulant treatment with heparin is usually needed. Treatment with antithrombin concentrates can also be used.

Note: children can have antithrombin deficiency; parents need to be aware so that they can detect signs of a blood clot. Although most children don't develop a blood clot, they are at risk of them in situations such as surgery. Some newborn babies develop blood clots too. Anticoagulant treatment or antithrombin concentrate may be needed. Parents who have antithrombin deficiency themselves and are expecting a child, should discuss this with their doctor.

Dysfibrinogenaemia

This is a rare genetic defect where a clot-dissolving chemical called fibrinogen does not work normally. There may be increased clotting, increased bleeding or both.

Combined inherited thrombophilias

Some people inherit more than one thrombophilia gene - for example, factor V Leiden plus prothrombin 20210. With combined thrombophilias, the risk of developing a blood clot is multiplied and there is a much greater risk than with either condition alone.

Acquired thrombophilias are not inherited, and usually start in adulthood.

Antiphospholipid syndrome (APS). This is also known as Hughes' syndrome. It is caused by certain immune system chemicals (antibodies) in the blood, which are called antiphospholipid antibodies. APS can cause a blood clot to form in arteries and small blood vessels, as well as in veins. APS can affect pregnancy in some cases. Many women with APS do not have problems in pregnancy. However, APS may cause miscarriage, or other problems - growth restriction of the fetus, pre-eclampsia or, rarely, fetal death. These problems can be reduced by treatment.

APS can be treated with low-dose aspirin, which is helpful in pregnancy. If you have had a blood clot then warfarin is usually advised instead (or heparin if you are pregnant). Read more in our leaflet about antiphospholipid syndrome .

Other acquired conditions

Other conditions can increase the risk of a blood clot. Some doctors classify these as thrombophilias. Examples are certain disorders affecting platelets, some bone marrow disorders, some kidney problems, inflammatory bowel disease and advanced cancer.

LITERATURE:

1. *Mitchell RS, Kumar V, Abbas AK, Fausto N (2007). "Chapter 4". Robbins Basic Pathology (Eighth ed.). Philadelphia: Saunders. ISBN 978-1-4160-2973-1.*
2. ^ Jump up to:[a b c d e f g h i j k l] *Heit JA (2007). "Thrombophilia: common questions on laboratory assessment and management". Hematology Am. Soc. Hematol. Educ. Program. **2007** (1): 127–35. doi:10.1182/asheducation-2007.1.127. PMID 18024620.*
3. ^ Jump up to:[a b c d] *Kyrle PA, Rosendaal FR, Eichinger S (December 2010). "Risk assessment for recurrent venous thrombosis". Lancet. **376** (9757): 2032–9. doi:10.1016/S0140-6736(10)60962-2. PMID 21131039. S2CID 31610364.*
4. ^ Jump up to:[a b c d] *Dahlbäck B (July 2008). "Advances in understanding pathogenic mechanisms of thrombophilic disorders". Blood. **112** (1): 19–27. doi:10.1182/blood-2008-01-077909. PMID 18574041.*
5. ^ Jump up to:[a b c d e f g] *Rosendaal FR, Reitsma PH (July 2009). "Genetics of venous thrombosis". J. Thromb. Haemost. 7 Suppl 1:*

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-16, November 2022
ISSN: 2749-3644

301–4. doi:10.1111/j.1538-7836.2009.03394.x. PMID 19630821.

6. **^** *Scarvelis D, Wells PS (October 2006). "Diagnosis and treatment of deep-vein thrombosis". CMAJ.* ***175*** *(9): 1087–92. doi:10.1503/cmaj.060366. PMC 1609160. PMID 17060659.*