Thrombosis UK
Awareness • Research • Care

INHERITED THROMBOPHILIA

WHAT IS INHERITED THROMBOPHILIA?

The term genetic or inherited thrombophilia covers a range of sticky blood conditions that increase the risk of blood clots (also known as thrombosis) in the veins and are inherited - i.e. someone is born with this.

Because inherited thrombophilias are genetic, the prevalence varies in people of different ethnic backgrounds. **Factor V Leiden** and **Prothrombin 20210** are the most common thrombophilias among people of European origin. Other genetic thrombophilias include **protein C deficiency**, **protein S deficiency** and, **antithrombin deficiency**.

People with genetic thrombophilias do not tend to have problems until they are adults, because children have much less sticky blood. Individuals are not usually tested until they are old enough to understand why the blood sample is being taken. This is usually after age 13.

PREVENTING VENOUS THROMBOSIS

Anyone who has a genetic thrombophilia can reduce the risk of venous thrombosis by making lifestyle changes like:

- Avoiding long periods of not moving around during illness or when travelling
- Leading a physically active life
- Avoiding becoming overweight or obese
- Stopping smoking
- Eating a healthy, well balanced diet

If you have genetic thrombophilia, you should get medical advice before major surgery or when you are likely to be unable to move around for a long period.

if you are a woman with inherited thrombophilia, you should get medical advice if considering taking oral combined contraception. However, there are other forms of contraception that can be used. The use of oral hormone replacement therapy also increases the risk of clots but transdermal e.g. patches don't, and are safe in those with inherited thrombophilia.

FACTOR V LEIDEN

Factor V Leiden is by far the most common genetic thrombophilia. In the UK it is present in 1 in 20 individuals of European ethnic origin. It is rare in people of Afro-Caribbean or Asian ethnic origin.

Factor V Leiden is caused by a change in the gene for Factor V, which helps the blood to clot. To stop a clot spreading, a natural blood thinner, known as protein C, breaks down Factor V.

If you have Factor V Leiden, the Factor V molecule in the blood is more resistant to being broken down by Protein C and the clotting process goes on for longer. This makes you more prone to blood clots, which can lead to **venous thrombosis.**

This risk of clots in the veins is about eight times greater for people who have Factor V Leiden than for those who don't. However, Factor V Leiden does not increase the risk of arterial thrombosis, so there is no increased risk of heart attacks or strokes.

Inheriting Factor V Leiden

If you inherit Factor V Leiden from one parent, this is known as heterozygous Factor V Leiden. But as Factor V Leiden is relatively common, some individuals inherit it from both parents and this is known as homozygous Factor V Leiden. It affects 1 in 1600 people of European origin.

Factor V Leiden and venous thrombosis

The risk of having a venous thrombosis is about eight times greater if you have **heterozygous** Factor V Leiden than for someone without Factor V Leiden. However, this risk is still relatively low and most people with the condition do not have blood clots.

The risk of venous thrombosis is much higher if you have **homozygous** Factor V Leiden. It is about 80 times greater than for those without the condition.

Factor V Leiden and pregnancy

If you are pregnant and have Factor V Leiden, it is important that you discuss this with your midwife as you have an increased risk of venous thrombosis during pregnancy.

PROTHROMBIN 20210

Prothrombin is one of the blood-clotting factors. It circulates in the blood and, when activated, is converted to thrombin. Thrombin causes fibrinogen, another clotting factor, to convert fibrin strands, which make up the major part of a clot.

The condition known as Prothrombin 20210 is due to a mutation of the prothrombin gene. If you have the condition, you will tend to have slightly stickier blood due to higher prothrombin levels.

Prothrombin 20210 is present in 2 in 100 people of European origin.

Prothrombin 20210 does not increase the risk of arterial thrombosis, so there is no increased risk of heart attacks or strokes.

Inheriting Prothrombin 20210

Prothrombin 20210 is inherited in an 'autosomal dominant way'. This means that if one parent has it, there is a 50:50 chance that you will inherit it. If you do inherit it, is known as heterozygous Prothrombin 20210.

There are a few cases where both parents have the gene, which would make it certain that their child would inherit homozygous Prothrombin 20210. However, this is very rare.

Prothrombin 20210 and venous thrombosis

If you have Prothrombin 20210, you have a low risk of venous thrombosis unless you have one or more extra risk factors.

The risk of venous thrombosis if you have Prothrombin 20210 is about twice that of someone without the condition. However, this risk is relatively low and most people with the condition are not affected.

However, if you have Prothrombin 20210 as well as Factor V Leiden or Protein S, the risk of thrombosis is substantially increased.

Prothrombin 20210 and pregnancy

If you have Prothrombin 20210 and are pregnant, you should discuss this with your midwife.

Testing for Prothrombin 20210

As it is a common condition, Prothrombin 20210 is usually included as part of standard thrombophilia testing. It is detected through a genetic test – a blood sample is taken and the DNA is examined to look for the mutation (inherited defect) in the prothrombin gene.

Testing other family members

If you have Prothrombin 20210, it is not recommended in the UK that close blood relatives are tested because it is such a low risk thrombophilia.

PROTEIN C DEFICIENCY

Protein C is one of the natural anticoagulants found in the blood. If you do not have enough protein C, you are more likely to have a venous thrombosis. It is uncertain whether there may also be a very slight risk of arterial thrombosis.

Inheriting protein C deficiency

Protein C is inherited in an 'autosomal dominant' way. This means that if one parent has it, there is a 50:50 chance that you will inherit it.

It is extremely rare for both parents to have it (less than one in a million). If a child does inherit it from both parents, this is known as homozygous protein C deficiency. Babies born with this condition have multiple thromboses especially in the skin soon after birth and need protein C concentrates and/or other anticoagulants to keep them healthy and free from further thrombosis.

Other causes of protein-C deficiency

Occasionally, medical conditions, such as kidney disease, can cause low levels of protein C.

Protein C deficiency and venous thrombosis

The risk of venous thrombosis is increased if you have protein C deficiency, but the level of risk varies. This is because each family with the condition has a different mutation within the protein C gene, which affects the level of risk.

One of the best guides to risk is to look at other members of your family who have protein C deficiency.

If nobody in your family has had a venous thrombosis, the risk is probably low unless you have other risk factors.

If a number of family members with protein C deficiency have had a venous thrombosis, the risk is greater. However, you can reduce this risk by taking preventive measures.

Protein C deficiency and pregnancy

If you have protein C deficiency and are pregnant, you should discuss this with your midwife. You should also be seen by a haematologist or obstetric physician with an interest in thrombosis to discuss whether you need anticoagulants during and/or after pregnancy due to the increased risk of venous thrombosis.

Testing for protein C deficiency

There are a number of tests to detect protein C deficiency and these vary between different laboratories. Sometimes a hospital may send the test to a specialist laboratory.

Usually a test is carried out to measure the amount of protein C that is working in the blood. This is known as a functional protein C assay. Other tests may measure the total amount of protein C in the blood. Lastly, it is now usual to have a genetic test to find the defect in the Protein C gene.

Testing other family members

Testing close blood relatives of people with a protein C deficiency is sometimes recommended, including siblings and children, as there is a 50:50 chance that they will inherit the condition.

Because people with genetic thrombophilias do not tend to have problems until they are adults, children are not usually tested until they are old enough to understand why the blood sample is being taken. This is usually after age 13. However if the gene defect is known within the family, a buccal smear (a cotton bud rubs the inside of the mouth) is all that is required to see if the individual concerned is affected.

PROTEIN S DEFICIENCY

Protein S is one of the natural anticoagulants found in the blood. If you do not have enough protein S, you are more likely to have a venous thrombosis.

Other causes of protein S deficiency

Protein S levels in the blood fall naturally during pregnancy and when women used the combined oral contraceptive pill or oral hormone replacement therapy (HRT). This is a factor in the increased risk of venous thrombosis in pregnancy and those taking combined oral contraceptives and oral HRT.

Occasionally other medical conditions, such as kidney disease, can cause low levels of protein S.

Protein S deficiency and venous thrombosis

The risk of venous thrombosis is increased if you have protein S deficiency, but the level of risk varies. This is because each family with the condition has a different mutation within the protein-S gene, which affects the level of risk.

One of the best guides to risk is to look at other members of the family with protein S deficiency. If nobody in your family has had a venous thrombosis, the risk is probably low unless you have other risk factors.

If a number of family members with protein S deficiency have had a venous thrombosis, the risk is greater. You can reduce this risk by taking preventive measures.

Protein-S deficiency and pregnancy

If you have protein S deficiency and are pregnant, you should discuss this with your midwife or other physician.

Testing for protein S deficiency

There are a number of tests to detect protein S deficiency and these vary between different laboratories. Sometimes a hospital may send the test to a specialist laboratory.

Usually a test is carried out to measure the amount of protein S that is working in the blood. This is known as a functional protein S assay. Other tests may measure the total amount of protein S in the blood, or how much free protein S is present.

A genetic test to find the fault in the Protein S gene is now advised too.

Testing other family members

Testing is occasionally recommended for close blood relatives of people with a protein S deficiency, including siblings and offspring, as there is a 50:50 chance that they will inherit the condition.

Because people with genetic thrombophilias do not tend to have problems until they are adults, children are not usually tested until they are old enough to understand why the blood sample is being taken. This is usually after age 13. However, it is possible to look at a child without causing pain from taking blood by doing a buccal smear (a cotton bud in the mouth).

ANTITHROMBIN DEFICIENCY

Antithrombin (previously known as antithrombin III) is one of the natural anticoagulants found in the blood. If you do not have enough antithrombin, you are more likely to have a venous thrombosis. It is uncertain whether there may also be a very slight risk of arterial thrombosis.

Inheriting antithrombin deficiency

Antithrombin deficiency is inherited in an 'autosomal dominant' way.

This means that if a parent has it, there is a 50:50 chance that a child will inherit it.

If it is inherited from one parent, this is known as heterozygous antithrombin deficiency. It is extremely rare for both parents, to have it and if a feotus inherits it, it is known as homozygous antithrombin deficiency. This is very rare indeed.

Other causes of antithrombin deficiency

Occasionally, medical conditions, such as kidney disease, the long-term use of heparin and being very unwell can cause low levels of antithrombin.

Antithrombin deficiency and venous thrombosis

Of all the genetic thrombophilias, heterozygous antithrombin deficiency is associated with the greatest risk of venous thrombosis. As many as 50% of people with antithrombin deficiency will have a venous thrombosis before the age of 50 if they do not follow advice to reduce the risks.

During pregnancy, up to half of all women with antithrombin deficiency may have a venous thrombosis if they do not receive thromboprophylaxis to reduce the risk. This involves giving small amounts of anticoagulant drugs to prevent blood clots.

The level of risk varies between individuals with antithrombin deficiency. This is because each family with the condition has a different mutation within the antithrombin gene, which affects the level of risk.

One of the best guides to risk is to look at other members of your family with antithrombin deficiency. If nobody in your family has had a venous thrombosis, the risk is probably low unless you have other risk factors.

If several family members with antithrombin deficiency have had a venous thromboses at a young age then, the risk is greater. You can reduce this risk by taking preventive measures.

Antithrombin deficiency and pregnancy

We advise women with antithrombin deficiency to talk to a haematologist with an interest in thrombosis before getting pregnant so any future pregnancy can be planned safely.

If you have antithrombin deficiency and are pregnant, you should discuss this with your midwife, but also should be receiving advice from a consultant who is an expert on thrombosis. The main anticoagulant used in pregnancy is heparin, indeed this is the only safe anticoagulant in pregnancy. The problem for those with antithrombin deficiency is that heparin works as a blood thinner by making antithrombin work harder. Those with antithrombin deficiency will need much bigger doses of heparin than normally used to get the same blood thinning effects as someone without antithrombin deficiency. This means the blood levels of the effect of heparin need to be monitored in pregnancy.

Pre-implantation genetics

For the last 10 years pre-implantation genetics has become available for those with antithrombin deficiency. Essentially this means that if a man or a woman come from a badly affected family of antithrombin deficiency then they can go through a process whereby the family have IVF – in vitro fertilization- and the resultant eggs are checked for antithrombin deficiency and only the normal eggs are used. This means any future children do not have antithrombin deficiency.

While this sounds relatively simple, it can be a complex and prolonged process. If you are interested then talk to your Haematologist.

Testing for antithrombin deficiency

There are a number of tests to detect antithrombin deficiency and these vary between different laboratories. Sometimes a hospital may send the test to a specialist laboratory.

Usually a test is carried out to measure the amount of antithrombin that is working in the blood. This is known as a functional antithrombin assay. Other tests may measure the total amount of antithrombin present in the blood.

But there is now increasing emphasis on finding the genetic defect in those with antithrombin deficiency because there is now understanding of how the different mutations in the antithrombin gene affect the individual.

Testing other family members

Testing is often recommended for close blood relatives of people with antithrombin deficiency, including brothers and sisters and sons and daughters, as there is a 50:50 chance that they will inherit the condition.

Because people with genetic thrombophilias do not tend to have problems until they are adults, children are not usually tested until they are old enough to understand why the blood sample is being taken. This is usually after age 13. However genetic testing from a buccal smear (a cotton wool bud stroked in the mouth) can be used to get DNA from the inside of the mouth for genetic testing.

OTHER GENETIC THROMBOPHILIAS

There are a few other rare conditions that are associated with venous thrombosis. These include dysfibrinogenaemia.

Dysfibrinogenaemia

People with dysfibrinogenaemia have an abnormal fibrinogen molecule in the blood. Some people with this condition have a tendency to bleed more, others have a tendency to thrombosis, and some have both.

Inheriting dysfibrinogenaemia

Dysfibrinogenaemia is inherited in an 'autosomal dominant' way. This means that if a parent has it, there is a 50:50 chance that you will inherit it.

Dysfibrinogenaemia and venous thrombosis

The risk of thrombosis depends on the type of dysfibrinogenaemia.

The risk of venous thrombosis increases if you have one or more other risk factors. You can reduce this risk by taking preventive measures.

Dysfibrinogenaemia and pregnancy

If you have dysfibrinogenaemia and are pregnant, you should discuss this with your midwife as you are at increased risk of venous thrombosis during pregnancy, and should be reviewed by an expert in thrombosis.

Helping a lot by donating a little

There are a number of ways you can help us:

- **Make a donation** and help us to support vital research being carried out in the UK.
- **Become a volunteer** and help us explain to others what we are doing.
- **Or why not have some fun** and organise a fundraising event in your area? You could host a coffee morning, organise a quiz night or take part in a fun run.

For more information on how to help us

Write to: PO Box 1242, Chew Magna, Bristol, BS40 8WG

Email: admin@thrombosisuk.org

or visit our website: www.thrombosisuk.org

Links to support groups

Thrombosis UK (www.thrombosisuk.org)

Email: admin@thrombosisuk.org

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