

Congenital thrombophilia

The term *congenital thrombophilia* covers a range of conditions that are inherited by someone at birth. This means that their blood is stickier than normal, which increases the risk of blood clots and thrombosis.

Factor V Leiden and Prothrombin 20210 are the most common thrombophilias among people of European origin. Other congenital thrombophilias include Protein C Deficiency, Protein S Deficiency, and Antithrombin Deficiency.

Factor V Leiden

Factor V Leiden is by far the most common congenital thrombophilia. In the UK it is present in 1 in 20 individuals of European origin. It is rare in people of Black or Asian 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 and the clotting process goes on for longer. This makes you more prone to blood clots, which can lead to **Venous Thrombosis**.

The risk of venous thrombosis is about eight times greater if you have Factor V Leiden than for those without it. However Factor V Leiden does not increase the risk of arterial thrombosis, so there is no increased risk of heart attacks or strokes.

Inheritance

A single dose of Factor V Leiden (inherited from one parent) is known as *heterozygous Factor V Leiden*. But as Factor V Leiden is relatively common, some individuals have a double dose, which means that they have inherited it from both parents.

A double dose is known as *homozygous Factor V Leiden*, and it affects 1 in 1600 people of European origin.

Factor V Leiden and venous thrombosis

Most individuals with Factor V Leiden have a low risk of venous thrombosis unless one or more additional risk factors is present.

The risk of having a venous thrombosis is about eight times greater for an individual with *heterozygous* Factor V Leiden. However this risk is still relatively low and most individuals with the condition are not affected.

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

Factor V Leiden and pregnancy

It is important that women with Factor V Leiden who are pregnant discuss this with their obstetrician as they have an increased risk of venous thrombosis during pregnancy. Some evidence suggests that they may also have a slightly higher risk of miscarriage and placental problems.

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 to *fibrin strands*, which make up part of a clot.

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

Prothrombin 20210 is present in 2 in 100 people of European origin. This means that the risk of having a venous thrombosis is twice that of someone without the condition.

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

Inheritance of Prothrombin 20210

Prothrombin 20210 is inherited in an *autosomal dominant* way. This means that if you have it, there is a 50:50 chance that your children will inherit it.

There are a few individuals with a double dose, known as *homozygous* Prothrombin 20210, which means that they have inherited the condition from both parents - but this is extremely rare.

Some people with Factor V Leiden also have Prothrombin 20210.

Prothrombin 20210 and venous thrombosis

If you have Prothrombin 20210 you have a low risk of venous thrombosis unless one or more additional risk factors is present.

The risk of venous thrombosis with 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

It is important that women with Prothrombin 20210 who are pregnant discuss this with their obstetrician. As well as an increased risk of venous thrombosis, women with Prothrombin 20210 may have a slightly higher risk of placental problems during pregnancy.

Testing for Prothrombin 20210

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

Testing other family members

If you have Prothrombin 20210 then testing is recommended for close blood relatives including brothers and sisters and sons and daughters, as there is a 50:50 chance that they will inherit the condition.

Because individuals with congenital thrombophilia 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 the age of 13.

Protein C deficiency

Protein C is one of the natural anticoagulants found in the blood. Those who have insufficient Protein C are more likely to have a venous thrombosis. It is uncertain whether there may also be a very slight risk of arterial thrombosis.

Inheritance of Protein C deficiency

Protein C is inherited in an *autosomal dominant* way. This means that if you have it, there is a 50:50 chance that your children will inherit it.

There is an extremely rare chance (less than one in a million) of a child being born with a double dose of Protein C deficiency. This is known as *homozygous* Protein C deficiency. Babies born with this condition have skin thromboses soon after birth and require Protein C concentrates or other anticoagulants to keep them healthy and free from 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 in individuals with 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 the family with Protein C deficiency. If no one in your family has had a venous thrombosis, then the risk is probably low

unless other risk factors are present. The risk of venous thrombosis increases when one or more additional risk factors are present.

If a number of family members with Protein C deficiency have had a venous thrombosis, the risk is greater. This risk can be reduced through prevention.

Protein C deficiency and pregnancy

It is important that women with Protein C deficiency who are pregnant discuss this with their obstetrician. As well as an increased risk of venous thrombosis, women with Protein C deficiency may have a slightly higher risk of placental problems during pregnancy. These include having a smaller baby or pre-eclampsia.

Testing for Protein C deficiency

There are a number of tests to detect Protein C deficiency and these may 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 present in the blood.

Testing other family members

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

Because individuals with congenital thrombophilia 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 the age of 13.

Protein S deficiency

Protein S is one of the natural anticoagulants found in the blood. Those who have insufficient Protein S are more likely to have a venous thrombosis. It is uncertain whether there may also be a very slight risk of arterial thrombosis.

Inheritance of Protein S deficiency

Protein S deficiency is inherited in an *autosomal dominant* way. This means that if you have it, there is a 50:50 chance that your children will inherit it.

Other causes of Protein S deficiency

Protein S levels in the blood fall naturally during pregnancy and when women use the combined oral contraceptive pill, or certain types of hormone replacement therapy (HRT). This is a factor in the increased risk of venous thrombosis in pregnant women, and those taking combined oral contraceptives and 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 no one has had a venous thrombosis, then the risk is probably low, unless other risk factors are present. The risk of venous thrombosis increases when one or more additional risk factors are present.

If a number of family members with Protein S deficiency have had a venous thrombosis, the risk is greater. This risk can be reduced through prevention.

Protein S deficiency and pregnancy

It is important that women with Protein S deficiency who are pregnant discuss this with their obstetrician. As well as an increased risk of venous thrombosis, women with Protein S deficiency may have a slightly higher risk of placental problems during pregnancy. These include having a smaller baby or pre-eclampsia.

Testing for Protein S deficiency

There are a number of tests to detect Protein S deficiency and these may 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 present in the blood, or how much free Protein S is present.

Testing other family members

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

Because individuals with congenital thrombophilia 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 the age of 13.

Antithrombin deficiency

Antithrombin (previously known as antithrombin III) is one of the natural anticoagulants found in the blood. People who have insufficient antithrombin are more likely to have a venous thrombosis. It is uncertain whether there may also be a very slight risk of arterial thrombosis.

Inheritance of antithrombin deficiency

Antithrombin deficiency is inherited in an *autosomal dominant* way. This means that if one parent has it, there is a 50:50 chance (1 in 2) that a child will inherit it.

A single dose (inherited from one parent) is known as *heterozygous* antithrombin deficiency. There is an extremely rare chance of inheriting a double dose of antithrombin deficiency, known as *homozygous* antithrombin deficiency. In this situation the foetus does not survive.

Other causes of antithrombin deficiency

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

Antithrombin deficiency and venous thrombosis

Of all the congenital thrombophilias, *heterozygous* antithrombin deficiency is associated with the greatest risk of venous thrombosis. As many as 1 in 2 individuals 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, about half of all women with antithrombin deficiency will 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.

One of the best guides to risk is to look at other members of the family with antithrombin deficiency. If none of them has had a venous thrombosis, then the risk is probably low unless other risk factors are present. The risk of venous thrombosis increases when one or more additional risk factors are present.

If a number of family members with antithrombin deficiency have had a venous thrombosis, the risk is greater. This risk can be reduced through prevention.

Antithrombin deficiency and pregnancy

It is important that women with antithrombin deficiency who are pregnant discuss this with their obstetrician. As well as an increased risk of venous thrombosis, women with antithrombin deficiency may have a slightly higher risk of placental problems during pregnancy. These include having a smaller baby or pre-eclampsia.

Testing for antithrombin deficiency

There are a number of tests to detect antithrombin deficiency and these may 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.

Testing other family members

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

Because individuals with congenital thrombophilia 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 the age of 13.

Other congenital thrombophilias

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

Dysfibrinogenaemia

Individuals 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.

Inheritance

Dysfibrinogenaemia is inherited in an *autosomal dominant* way. This means that if one parent has it, there is a 50:50 chance (1 in 2) that a child will inherit it.

Dysfibrinogenaemia and venous thrombosis

The risk of venous thrombosis depends on the type of dysfibrinogenaemia.

The risk of venous thrombosis increases when one or more additional risk factors are present.

This risk can be reduced through prevention.

Dysfibrinogenaemia and pregnancy

It is important that women with dysfibrinogenaemia who are pregnant discuss this with their obstetrician, as they are at increased risk of venous thrombosis during pregnancy.

Preventing venous thrombosis

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

- Leading a physically active life
- Eating a healthy, balanced diet
- Avoiding becoming overweight or obese
- Avoiding long periods of immobility during illness or when travelling
- Stopping cigarette smoking.

Those with congenital thrombophilia should also seek medical advice before major surgery, or when they are likely to be immobile for a long period, as this increases the risk of venous thrombosis.

Women should also seek medical advice before taking oral contraception or hormone replacement therapy, and when pregnant or planning to become pregnant.

More advice on healthy living can be found at www.dh.gov.uk

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