CONDITION

Congenital antithrombin III deficiency

Congenital antithrombin III deficiency is an inherited condition that increases the risk of harmful blood clots.

WHAT IT IS
Inherited shortage or dysfunction of a natural anticlotting protein

BODY SYSTEM
Blood and circulation

MAIN SYMPTOMS
Leg swelling, leg pain, chest pain, breathlessness

WHAT CAUSES IT
Inherited SERPINC1 gene change

HOW IT IS DIAGNOSED
Antithrombin activity and antigen blood tests

MAIN TREATMENT
Anticoagulants and selected use of antithrombin concentrate

CAN IT BE CURED?
No - inherited gene change remains

IS IT AN EMERGENCY?
Sometimes - sudden breathlessness or chest pain

LONG-TERM OUTLOOK
Usually good with clot prevention and prompt treatment

Overview

Congenital antithrombin III deficiency is an inherited condition that makes blood more likely to form harmful clots. It is now usually called hereditary antithrombin deficiency . Antithrombin III and antithrombin refer to the same protein.

Antithrombin is made mainly by the liver. It limits clotting by blocking thrombin and other clotting proteins. If there is too little antithrombin, or it does not work properly, this natural control is weakened.

The main concern is venous thromboembolism , or VTE. This includes a blood clot in a deep vein, called deep vein thrombosis or DVT, and a clot that travels to the lungs, called pulmonary embolism or PE.

The condition itself usually does not cause day-to-day symptoms. Some people first learn they have it after a blood clot, while others are tested because a close relative has the condition. Having the deficiency increases clot risk, but it does not mean that a clot is certain.

Symptoms

Antithrombin deficiency does not usually produce symptoms unless a clot forms.

A DVT most often develops in a deep vein of the leg. Possible symptoms include:

A pulmonary embolism happens when part of a clot reaches the lungs. Symptoms may include sudden shortness of breath, chest pain that can worsen with a deep breath, coughing up blood, a fast heartbeat, dizziness, or fainting.

Clots can occasionally form in less common places, such as veins in the abdomen or brain. Symptoms depend on the vein involved and can include persistent severe abdominal pain or a new, unusual, intense headache. These symptoms have many possible causes, so they need medical assessment rather than self-diagnosis.

Some people with hereditary antithrombin deficiency never develop a recognised clot. Others may have more than one clot over their lifetime, particularly when other risk factors are present.

- Swelling in one leg
- Pain or tenderness, often in the calf or thigh
- Warm or discoloured skin over the affected area
- A feeling of heaviness or tightness

Causes and risk factors

Congenital antithrombin deficiency is usually caused by a change in the SERPINC1 gene. This gene provides instructions for making antithrombin.

There are two broad forms:

The condition is usually inherited in an autosomal dominant pattern. This means one altered copy of the gene can cause the condition. In a family with this inheritance pattern, each child of an affected parent has a 1 in 2 chance of inheriting the gene change. The severity and clot history can still differ between relatives.

Other factors can add to the inherited risk. These include surgery, a major injury, prolonged

immobility, hospital admission, pregnancy, the weeks after giving birth, and medicines containing oestrogen. Cancer and increasing age can also increase clot risk.

Not every low antithrombin result is inherited. Antithrombin can fall because of severe liver disease, loss of protein through the kidneys, widespread abnormal clotting, serious illness, or certain treatments. An acute clot and some medicines can also affect testing.

- Type I deficiency: the body makes too little antithrombin
- Type II deficiency: the amount may be near normal, but the protein does not work properly

Diagnosis

Diagnosis begins with blood tests, but the timing and interpretation matter.

An antithrombin activity test checks how well the protein works. If activity is low, an antithrombin antigen test can measure how much protein is present. Low activity and a low antigen level suggest type I deficiency. Low activity with a normal or near-normal antigen level can suggest type II deficiency.

A low result is usually confirmed with repeat testing. Testing during an acute clot, serious illness, pregnancy, or certain anticoagulant treatments may not give a reliable picture. Some anticoagulants like warfarin or apixaban can also interfere with particular laboratory methods. A clinician or haematology team may therefore arrange testing at a more suitable time.

The assessment may include:

Genetic testing can support the diagnosis and help with family testing, but it is not always required. A result should be interpreted alongside the blood tests and family history.

Testing everyone after a routine blood clot is not always useful. It is more likely to be considered when the result could change treatment, pregnancy planning, or decisions for close relatives.

- Your personal and family history of blood clots
- Repeat antithrombin activity and antigen tests
- Tests for acquired causes of low antithrombin
- Genetic testing for a SERPINC1 change in selected cases

Treatment and management

Treatment focuses on treating blood clots and reducing the chance of future clots. It does not

remove the inherited gene change.

A DVT or pulmonary embolism is usually treated with an anticoagulant , often called a blood thinner. These medicines do not literally thin the blood. They reduce clot formation and stop an existing clot from growing while the body gradually breaks it down.

Heparin is one type of anticoagulant, and it relies partly on antithrombin to work. In someone with marked antithrombin deficiency, the expected response to heparin may be reduced. The healthcare team can monitor treatment and choose an appropriate approach.

After a clot, the length of anticoagulant treatment is based on factors such as:

Some people may be advised to continue anticoagulation for an extended period. People who have never had a clot are not automatically given lifelong anticoagulants because these medicines can cause bleeding.

Antithrombin concentrate replaces the missing or poorly functioning protein for a limited time. It may be used in selected high-risk situations, such as around major surgery or childbirth, or when a clot is difficult to treat because heparin is not working as expected. It is not usually used as continuous long-term treatment.

Pregnancy requires individual planning because pregnancy and the period after birth both raise clot risk. The safest anticoagulant options also differ during pregnancy and breastfeeding. Ideally, planning takes place before pregnancy with maternity and haematology teams.

- Whether the clot had a temporary trigger
- The location and seriousness of the clot
- Previous clots and family history
- Ongoing clot risks
- The risk of bleeding from treatment

Complications

The main complication is venous thromboembolism. A clot can return, particularly if anticoagulation is stopped or another strong risk factor develops.

A DVT can sometimes damage the valves inside a leg vein. This can cause post-thrombotic syndrome , with long-term swelling, aching, skin changes, or ulcers.

After a pulmonary embolism, most people recover, but some continue to experience breathlessness or reduced exercise tolerance. Rarely, unresolved clots lead to persistently high pressure in the lung arteries, called chronic thromboembolic pulmonary hypertension.

Anticoagulants reduce clot risk but increase the chance of bleeding. Minor bruising or bleeding can occur, while internal or uncontrolled bleeding is more serious. The balance between preventing clots and avoiding bleeding is reviewed over time.

Pregnancy and the weeks after birth are higher-risk periods for venous clots. A personal history of VTE adds to that risk.

Prevention

The inherited condition itself cannot currently be prevented. A person is born with the gene change, even if it is not discovered until later.

However, some blood clots may be prevented. The most useful step is to have a plan for situations that temporarily raise risk. This can include surgery, hospital admission, pregnancy, childbirth, a leg cast, or long periods of limited movement.

Tell healthcare professionals about the deficiency before an operation or hospital treatment. Preventive anticoagulation may be appropriate in some situations, but it must be balanced against bleeding risk.

Medicines containing oestrogen, including some contraceptives and menopausal hormone treatments, can further increase venous clot risk. Discuss alternatives and personal risks before starting or stopping them.

If you already take an anticoagulant, take it as directed and arrange advice before procedures or new medicines. Do not stop it on your own because an interruption can leave you without expected protection.

Close relatives may choose to discuss testing, especially when the result could affect contraception, pregnancy planning, surgery, or clot prevention during other high-risk periods.

Living with it and what to expect

Hereditary antithrombin deficiency is lifelong, but it does not usually cause continuous illness or limit everyday activity by itself. Many people go for long periods without a clot, and some never have one.

The condition does not usually worsen steadily over time. What changes is the level of clot risk. It may rise temporarily during surgery, illness, pregnancy, reduced mobility, or exposure to oestrogen.

If you have had a clot, follow-up may focus on how well you are recovering, how long

anticoagulation should continue, and whether you have symptoms such as persistent leg swelling or breathlessness. If you take long-term anticoagulants, reviews may also cover bleeding, kidney or liver health, interactions, and plans for procedures.

Keep a record of the diagnosis and your current medicines. It can be useful to know which laboratory tests confirmed the condition and whether a SERPINC1 gene change was found. Consider carrying an anticoagulant alert card or medical identification if you take blood-thinning treatment.

Routine physical activity is generally compatible with the condition. If you take an anticoagulant, activities with a high risk of major injury may need extra consideration because of bleeding risk.

Family members can have different experiences even when they carry the same gene change. One person's clot history cannot predict exactly what will happen to another.

When to get medical help

Call emergency services for symptoms that may indicate a pulmonary embolism, including:

Stroke symptoms are also an emergency. These include sudden facial drooping, arm weakness, speech difficulty, loss of vision, or a severe new neurological problem.

Seek urgent same-day medical assessment for new swelling, pain, warmth, or colour change in one leg, particularly when symptoms appear after surgery, travel, illness, or reduced mobility.

If you take an anticoagulant, emergency assessment is needed for uncontrolled bleeding, vomiting blood, black stools, a major injury, or a significant blow to the head. Sudden severe headache, weakness, or confusion also needs emergency care.

Arrange routine follow-up to discuss pregnancy plans, contraception containing oestrogen, an upcoming operation, persistent symptoms after a clot, or concerns about anticoagulant side effects. These situations need planning but are not usually emergencies when you otherwise feel well.

- Sudden or severe difficulty breathing
- Chest pain, especially with breathing
- Coughing up blood
- Fainting, severe dizziness, or collapse

Common questions

Is antithrombin III the same as antithrombin?

Yes. Antithrombin III is the older name. Most laboratories and healthcare professionals now use antithrombin . It is not related to antithrombin medications or antibodies; it is a natural protein that controls clotting.

Does a low antithrombin result mean I inherited the condition?

Not always. Antithrombin can be temporarily or persistently low because of an acute clot, severe illness, liver disease, kidney protein loss, or certain treatments. Repeat activity and antigen tests, taken at an appropriate time, help distinguish inherited deficiency from an acquired low level.

Will I definitely develop a blood clot?

No. The condition raises the likelihood of a venous clot, but it cannot predict exactly who will have one or when. Your personal clot history and temporary risks such as surgery, pregnancy, or immobility help guide prevention decisions.

Can I use birth control or hormone replacement therapy?

Some oestrogen-containing treatments increase venous clot risk and may not be the preferred option for someone with hereditary antithrombin deficiency. Other hormonal and non-hormonal choices are available. The safest option should be considered using your clot history and treatment needs.

Can I have a healthy pregnancy?

Many people with antithrombin deficiency have successful pregnancies. Pregnancy and the weeks after birth increase clot risk, so advance planning is important. Care may involve a maternity specialist and a haematology team, with a prevention plan tailored to personal and family history.

Should my family members be tested?

Testing may be useful for first-degree relatives such as parents, siblings, and adult children, particularly if the result would affect decisions about pregnancy, oestrogen, surgery, or clot prevention. Testing children requires careful consideration because the result may not change care until later.

Sources

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