CONDITION

Congenital protein C or S deficiency

An inherited shortage or dysfunction of proteins that normally help prevent harmful blood clots.

WHAT IT IS
Inherited blood-clotting tendency caused by deficient natural anticoagulant proteins

BODY SYSTEM
Blood, heart and circulation

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

WHAT CAUSES IT
Inherited changes affecting natural anticoagulant proteins

HOW IT IS DIAGNOSED
Repeat protein C or S blood tests, sometimes genetic testing

MAIN TREATMENT
Anticoagulants; protein C replacement for severe deficiency

CAN IT BE CURED?
No - inherited clotting tendency remains lifelong

IS IT AN EMERGENCY?
Sometimes - signs of deep vein thrombosis or pulmonary embolism

LONG-TERM OUTLOOK
Often a normal life with appropriate clot prevention

Overview

Congenital protein C or S deficiency is an inherited condition that increases the chance of developing abnormal blood clots. "Congenital" means present from birth, although many people do not have symptoms until adulthood or never develop symptoms at all.

Protein C and protein S are natural anticoagulants like warfarin or apixaban . This means they help control clotting so that a clot does not keep growing after bleeding has stopped. Protein S helps activated protein C work properly. If either protein is missing, present at a low level, or not working normally, the balance shifts toward clot formation.

The main concern is venous thromboembolism, or VTE. This includes deep vein thrombosis, known as DVT, usually in a leg, and pulmonary embolism, known as PE, when part of a clot travels to the lungs.

Most inherited protein C or S deficiency is passed down through families in a pattern where one altered gene copy can increase clot risk. The risk is not the same for everyone. It is affected by the specific deficiency, family history, age, previous clots, pregnancy, surgery, immobility and other health factors.

Rarely, a baby inherits severely altered gene copies from both parents. Severe protein C deficiency can then cause widespread clotting and skin damage shortly after birth. This is very different from the more common form involving one altered gene copy.

Symptoms

The deficiency itself usually does not cause day-to-day symptoms. Symptoms appear if a blood clot develops.

A DVT most often affects one leg. Possible symptoms include:

A pulmonary embolism may cause sudden breathlessness, chest pain that can worsen with a deep breath, coughing, a fast heartbeat, dizziness or fainting. Some people cough up blood, although this is less common.

Clots can occasionally form in other veins, including veins in the abdomen or brain. Symptoms depend on the location and need prompt assessment.

In severe congenital protein C deficiency, symptoms may begin in the newborn period. Purpura fulminans causes painful dark red, purple or black skin patches because small blood vessels in the skin become blocked. Clots may also affect other organs. This requires emergency specialist care.

Protein C or S deficiency is not generally considered an established cause of heart attack or stroke in the same way it causes venous clots. Those events often have other causes that need separate assessment.

- New swelling, pain, tenderness or warmth in one leg
- Red or darker skin over the affected area
- A heavy or tight feeling in the leg

Causes and risk factors

Protein C deficiency results from an altered `PROC` gene. Protein S deficiency results from an altered `PROS1` gene. These genes provide instructions for making the relevant proteins.

A person with one altered gene copy may have lower protein levels or a protein that does not function properly. Having the genetic change does not mean a clot will definitely occur.

Situations that can further increase clot risk include:

Low protein C or S results are not always inherited. Liver disease, severe infection, vitamin K deficiency and some medicines can lower protein levels or affect test results. Protein S also falls naturally during pregnancy. These are acquired changes rather than congenital deficiency.

- A previous DVT or pulmonary embolism
- A strong family history of clots, especially at younger ages
- Major surgery, injury or a hospital stay
- Long periods of limited movement
- Pregnancy and the weeks after birth
- Estrogen-containing contraception or menopausal hormone therapy
- Active cancer
- Increasing age
- Other inherited or acquired clotting risk factors

Diagnosis

Testing is usually considered after a clot when the result could affect future care, or when there is a significant family history. Testing everyone who has a blood clot is not always useful because the result may not change treatment.

Protein C can be assessed with an activity test, which measures how well it works. An antigen test can measure how much protein is present. Protein S testing may include free protein S antigen, total antigen and a functional activity test. Free protein S is the portion available to help control clotting.

A single abnormal result does not always confirm congenital deficiency. Results can be affected by:

Testing may therefore need to be repeated at a suitable time. Anticoagulant medicine should not be stopped just to arrange testing unless the clinician managing it has made a safe plan.

Genetic testing can sometimes identify a change in `PROC` or `PROS1`. It may be useful when severe deficiency is suspected or when a known family variant is being investigated. A negative genetic test does not always rule out the condition.

Testing relatives is an individual decision. It may be more useful when a confirmed result would change decisions about pregnancy, estrogen use, surgery or clot prevention. Testing children requires particular care because normal protein levels change with age and because results may not alter childhood care.

- A recent blood clot or serious illness
- Pregnancy or recent childbirth
- Liver disease or vitamin K deficiency
- Warfarin and some other anticoagulants
- Estrogen-containing medicines
- The testing method used by the laboratory

Treatment and management

Treatment depends mainly on whether you have had a blood clot and on your future risk. An abnormal blood test alone does not automatically mean lifelong treatment is needed.

A DVT or pulmonary embolism is treated with an anticoagulant. These medicines are often called blood thinners, although they do not literally thin the blood. They reduce the blood's ability to form or extend a clot while the body gradually breaks the clot down.

How long treatment continues is based on factors such as:

Some people need anticoagulation for a limited period. Others may be advised to continue it long term because their chance of another clot is high. The deficiency is one part of this decision, not the only part.

Warfarin lowers protein C and protein S before it fully lowers some clotting proteins. In rare cases, this temporary imbalance can contribute to warfarin-related skin damage. Clinicians account for this when starting treatment, particularly in someone with known deficiency. Do not start, stop or change an anticoagulant without medical guidance.

People who have never had a clot are not routinely given lifelong anticoagulation solely because of mild inherited deficiency. Short-term preventive treatment may be considered during high-risk periods such as major surgery, prolonged immobility, pregnancy or after childbirth.

Pregnancy planning should include a review of personal and family clot history. Some anticoagulants are unsuitable during pregnancy, while certain heparin medicines can be used because they do not cross the placenta. The plan is tailored to the level of risk.

Severe congenital protein C deficiency may require protein C concentrate to replace the missing protein. Anticoagulation and other specialist treatments may also be needed. Protein S concentrate is not routinely available as a standard replacement treatment.

- Whether the clot followed surgery, immobility or another temporary trigger
- Whether the clot occurred without a clear trigger
- The location and severity of the clot
- Previous clots and family history
- Bleeding risk and treatment preferences
- Other health conditions

Complications

The main complication is venous thromboembolism. A pulmonary embolism can interfere with blood flow through the lungs and strain the heart. Prompt treatment lowers the risk of serious harm.

After a DVT, some people develop post-thrombotic syndrome. This can cause persistent leg swelling, aching, heaviness or skin changes because the clot has damaged the vein and its valves.

A small proportion of people who have had a pulmonary embolism develop long-lasting high blood pressure in the lung arteries, called chronic thromboembolic pulmonary hypertension. Ongoing unexplained breathlessness after treatment should be reviewed.

Clots can recur, especially after a previous unprovoked clot or when several risk factors are present. Anticoagulants reduce this risk but can cause bleeding. Follow-up therefore includes balancing clot prevention against bleeding risk.

Severe protein C deficiency can cause repeated skin injury, loss of tissue, organ damage and clots in multiple locations. Early specialist treatment is important.

Prevention

The inherited deficiency itself cannot be prevented. It results from a genetic change that is present from birth.

Not every clot can be prevented, but risk can sometimes be reduced. Tell healthcare professionals about confirmed protein C or S deficiency before surgery, a hospital admission

or pregnancy. They can assess whether preventive anticoagulation or other measures are appropriate.

During travel or other long periods of sitting, regular movement and avoiding dehydration may be sensible. Travel-related medicine or compression stockings are not needed by everyone, so these should be based on your overall risk rather than the blood-test result alone.

Smoking, excess weight and limited activity can add to cardiovascular or clotting risk, but they do not cause the inherited deficiency. Sustainable physical activity and management of other health conditions support general circulation.

Before using estrogen-containing contraception or menopausal hormone therapy, discuss the inherited deficiency and any personal or family history of clots. Non-estrogen options may be more suitable for some people.

Living with it and what to expect

Many people with congenital protein C or S deficiency live active lives and never develop a clot. Others first learn they have the condition after a DVT, pulmonary embolism or family investigation.

The underlying deficiency generally remains throughout life. Its presence does not mean that clotting risk is constant. Risk may rise temporarily during surgery, illness, immobility, pregnancy or the period after birth.

If you take long-term anticoagulation, follow-up usually covers bleeding symptoms, kidney or liver health when relevant, interactions with other medicines, and whether treatment remains appropriate. Some anticoagulants need regular blood tests; others do not require routine clotting-level monitoring but still need medical review.

Physical activity is usually encouraged after recovery from a clot, with timing based on symptoms and medical advice. People taking anticoagulants may need to consider bleeding risk when choosing contact sports or activities with a high chance of serious injury.

Carry an up-to-date medicine list and make sure healthcare professionals know if you take an anticoagulant. Before dental work, surgery or invasive tests, the team may need to plan around the medicine. Anticoagulants should not be paused without an agreed plan.

Family members may wonder whether they should be tested. A haematology or genetics appointment can help explain inheritance, the limits of testing and whether a result would change care. A parent with one altered gene copy can pass it to a child, but the severity and clot history may differ between relatives.

The outlook is usually good when clots are recognised and treated and higher-risk situations are planned for. People with severe protein C deficiency need lifelong specialist care and may have a more complicated course.

When to get medical help

Seek emergency medical help for possible pulmonary embolism, especially:

A newborn with rapidly developing purple, dark red or black skin patches needs emergency assessment.

Get urgent same-day medical advice for new one-sided leg swelling, pain, warmth or skin colour change. These symptoms do not always mean DVT, but they need prompt assessment.

If you take an anticoagulant, seek urgent help for significant bleeding, vomiting or coughing blood, black stools, severe unexplained headache, or a major injury. Emergency assessment is especially important after a head injury.

Routine follow-up is appropriate for treatment reviews, pregnancy planning, questions about contraception or hormone therapy, and planning before surgery or long travel. Also arrange a review if ongoing leg swelling or breathlessness continues after a treated clot.

- Sudden or unexplained shortness of breath
- Chest pain, particularly pain that worsens with breathing
- Coughing up blood
- Fainting, severe dizziness or a very fast heartbeat

Common questions

Is protein C or S deficiency the same as having a blood clot?

No. It is an inherited tendency that can make venous clots more likely. Some people with the deficiency never develop a clot.

Which is worse, protein C deficiency or protein S deficiency?

Neither is always worse. Risk is shaped by how much protein function is affected, whether you have had a previous clot, your family history and other risk factors. Severe protein C deficiency affecting both gene copies is a distinct and serious condition that often begins in infancy.

Do I need blood thinners for life?

Not necessarily. People who have never had a clot often do not need lifelong anticoagulation.

After a clot, treatment length is based on why it happened, the chance of another clot and the risk of bleeding.

Can protein C or S levels return to normal?

Levels may look low temporarily because of pregnancy, illness, liver problems or medicines. In a confirmed congenital deficiency, the inherited tendency remains even if later test results differ because of testing conditions.

Can I have a healthy pregnancy?

Many people with the condition have successful pregnancies. Pregnancy and the period after birth increase clot risk, so planning before pregnancy is important. The prevention plan is based on previous clots, family history and the specific deficiency.

Can I pass this condition to my children?

Yes. The more common forms involving one altered gene copy can be passed from parent to child. A child who inherits the change may have a different clot history from the parent. Genetic counselling can explain the inheritance pattern in your family.

Sources

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