CONDITION

Factor XII (hageman factor) deficiency

Factor XII deficiency is a usually inherited condition that prolongs clotting tests without causing abnormal bleeding.

WHAT IT IS
Inherited low activity of blood-clotting factor XII

BODY SYSTEM
Blood and circulation

MAIN SYMPTOMS
Usually none, no unusual bruising, no abnormal bleeding

WHAT CAUSES IT
Usually inherited F12 gene changes

HOW IT IS DIAGNOSED
aPTT, mixing study, factor XII activity assay

MAIN TREATMENT
Usually none; test-aware planning

CAN IT BE CURED?
No, inherited factor level remains low

IS IT AN EMERGENCY?
No, not by itself

LONG-TERM OUTLOOK
Normal lifespan and daily life for most people

Overview

Factor XII deficiency is a rare blood-clotting condition. Factor XII, also called Hageman factor, is a protein made by the liver and carried in the blood.

Factor XII helps start the "contact activation" pathway measured by the activated partial thromboplastin time, or aPTT. If you have very little factor XII activity, your aPTT can be much longer than normal.

This result can look concerning, but factor XII deficiency does not usually cause abnormal bleeding. Factor XII is important to clotting in a test tube, but it is not essential for stopping bleeding inside the body. Other pathways can form a stable clot after an injury.

The condition is often found by chance during tests before surgery or while investigating

another health issue. Identifying the cause can prevent delays, repeated testing, or unnecessary treatment intended to "correct" the aPTT.

Factor XII deficiency is different from hemophilia and deficiencies of factors VIII, IX, or XI, which can cause bleeding.

Symptoms

Most people with factor XII deficiency have no symptoms and may not know they have it.

The condition does not usually cause:

A prolonged aPTT is a laboratory finding, not a symptom. When factor XII deficiency is the cause, the result does not show how likely you are to bleed.

If you have unusual bleeding as well as low factor XII activity, another cause should be considered. Possibilities include a different clotting-factor deficiency, a platelet problem, medicine use, or liver disease.

- Frequent nosebleeds
- Easy or unexplained bruising
- Heavy bleeding from small cuts
- Bleeding into joints or muscles
- Excessive bleeding after dental work, childbirth, or surgery

Causes and risk factors

Factor XII deficiency is usually inherited. Changes in the F12 gene reduce the amount or activity of factor XII.

It is generally inherited in an autosomal recessive pattern. A person with severe deficiency usually receives an altered gene copy from each parent. The parents are often carriers without related health problems.

Someone with one altered copy may have a moderately reduced factor XII level and a normal or mildly prolonged aPTT. Two altered copies may cause very low activity and a much longer aPTT.

The condition affects people of any sex. Having a close biological relative with factor XII deficiency increases the chance of carrying the same gene change.

Occasionally, reduced factor XII activity is acquired because of an illness or, rarely, an antibody

that interferes with factor XII. Sample or testing problems can also cause an unexpected result. A new abnormal aPTT therefore needs proper assessment rather than being assumed to be inherited.

Diagnosis

Factor XII deficiency is often suspected after an unexpectedly prolonged aPTT, which measures how long a blood sample takes to clot under laboratory conditions.

Typical findings include:

Other possible causes of a prolonged aPTT include deficiencies of factors VIII, IX, or XI; anticoagulant medicines; lupus anticoagulant like warfarin or apixaban ; and contamination of the sample with heparin.

A mixing study helps distinguish between these causes. Your plasma is mixed with normal plasma. If the aPTT returns toward normal, a clotting factor is probably missing. If it stays prolonged, an interfering substance may be present.

A factor XII activity assay confirms low activity. Other clotting factors may also be tested to rule out a deficiency that could cause bleeding.

Genetic testing can identify some F12 gene changes but is not always necessary when the clotting-test pattern and factor assay are clear. It may help when the diagnosis is uncertain or a family wants information about inheritance.

Your bleeding history remains important. A very long aPTT caused only by factor XII deficiency does not predict excessive surgical bleeding.

- A prolonged aPTT
- A normal prothrombin time, or PT
- No personal history of abnormal bleeding
- A normal platelet count, unless another condition is present

Treatment and management

Most people do not need treatment or factor replacement because factor XII deficiency does not usually cause bleeding.

The main part of management is ensuring the result is correctly documented and interpreted. Keep a copy of your laboratory results or specialist letter for surgery, dental treatment,

emergency care, or future assessments.

A prolonged aPTT may cause a procedure to be postponed while its cause is investigated. Once isolated factor XII deficiency is confirmed, the abnormal result alone does not usually indicate extra bleeding risk.

Fresh frozen plasma contains clotting factors but is generally not needed simply to shorten the aPTT. Blood products have potential risks and should not be used only to make a laboratory number normal.

Factor XII deficiency can affect anticoagulant monitoring. The aPTT may not reliably measure unfractionated heparin when the starting result is already very long. If anticoagulation is needed, the care team can use another method, such as a suitable anti-factor Xa test.

Treatment for acquired low factor XII focuses on any underlying condition. A separate bleeding disorder, blood clot, or other medical problem should be managed independently.

Complications

Isolated factor XII deficiency does not usually cause bleeding complications. Practical difficulties are more likely to arise from misunderstanding the abnormal aPTT.

These may include delayed surgery, repeated tests, or unnecessary plasma treatment. Clear documentation can reduce these problems.

Older reports suggested that factor XII deficiency might increase the risk of harmful blood clots. Later research has not established isolated inherited deficiency as a cause of thrombosis in people.

You can still develop a blood clot for unrelated reasons, such as major surgery, prolonged immobility, cancer, pregnancy, or another clotting condition. Factor XII deficiency should not be assumed to protect against these risks.

Studies have also explored possible links between low factor XII and pregnancy loss, but the evidence is uncertain. Pregnancy care should be based on your full medical and pregnancy history rather than this result alone.

Prevention

Inherited factor XII deficiency cannot be prevented. It results from gene changes present from birth, not from diet, exercise, infection, or anything a parent did during pregnancy.

Lifestyle changes cannot raise an inherited factor XII level. No special diet or activity

restriction is usually needed.

If the condition runs in your family, genetic counselling can explain inheritance and the limits of testing. Testing relatives is a personal decision. It may be useful before a planned procedure or for someone with an unexplained prolonged aPTT, but it is not usually urgent.

Acquired reductions cannot always be prevented. Managing an associated condition may improve the level in some cases.

Living with it and what to expect

Inherited factor XII deficiency is lifelong. Factor activity stays low, although measurements can vary between laboratories or over time. The prolonged aPTT is also likely to remain.

For most people, the condition does not affect energy, growth, fertility, physical activity, work, or lifespan. Children can usually attend school and take part in ordinary activities without restrictions.

You generally do not need regular factor infusions or repeated clotting tests when well. Follow-up may be needed if the diagnosis is uncertain, another clotting abnormality is present, or your health changes.

Tell relevant healthcare professionals about the diagnosis before surgery or anticoagulant treatment. The important concern is not an expected bleeding problem, but that your aPTT may be misleading.

A medical information card, health-record note, or copy of your results can help. It should state that factor XII deficiency causes a prolonged aPTT without the usual bleeding tendency.

If you later develop unusual bleeding, seek a fresh assessment rather than assuming it is related to factor XII deficiency.

When to get medical help

Arrange routine medical follow-up if you have an unexplained prolonged aPTT, were told your factor XII level is low without confirmatory testing, or had a planned procedure delayed because of the result. This is usually not an emergency.

Discuss the condition in advance of major surgery, pregnancy care, or anticoagulant treatment. This allows time to confirm the diagnosis and plan how clotting tests will be interpreted.

Get urgent medical help for significant or unexplained bleeding, including blood in vomit, black stools, heavy bleeding that does not stop, or a severe headache after a head injury. These are

not expected features of isolated factor XII deficiency and may have another cause.

Seek emergency care for possible blood-clot symptoms, including sudden shortness of breath, chest pain, coughing up blood, or painful one-sided leg swelling. Factor XII deficiency does not rule out an unrelated clot.

Common questions

Does factor XII deficiency make me bleed?

Usually not. Even people with very low activity generally do not have abnormal bleeding. If you are bleeding unusually, another cause should be investigated.

Why is my aPTT so long if my blood clots normally?

The aPTT relies heavily on factor XII to start clotting in a test tube. Inside the body, other pathways can start clotting after an injury. The test can therefore be very abnormal while everyday clotting remains effective.

Can I have surgery or dental treatment?

Isolated factor XII deficiency does not usually increase bleeding during procedures. Document the diagnosis beforehand so the prolonged aPTT is understood. Your bleeding history, medicines, procedure, and other conditions still matter.

Does factor XII deficiency cause blood clots?

Current evidence does not clearly show that inherited factor XII deficiency causes harmful clots. You can still have the same clotting risks as other people, and a suspected clot needs normal assessment.

Do my family members need to be tested?

Testing is not usually urgent because the condition rarely causes health problems. It may help relatives with an unexplained prolonged aPTT or an upcoming procedure. Genetic counselling can help your family decide whether testing would be useful.

Can I take blood thinners if I need them?

Factor XII deficiency does not automatically prevent anticoagulant treatment. However, the aPTT may not reliably monitor certain medicines, so the treatment team may need another laboratory method.

Sources



- National Organization for Rare Disorders. Factor XII Deficiency . NORD Rare Disease Database.
- Orphanet. Hereditary factor XII deficiency . Orphanet rare condition summary.
- Merck Manual Professional Edition. Uncommon Hereditary Coagulation Disorders .
- Renné T, Schmaier AH, Nickel KF, Blombäck M, Maas C. "In vivo roles of factor XII." Blood . 2012;120(22):4296-4303. doi:10.1182/blood-2012-07-292094.