HEALTH BASICS

Complement component 4

Complement component 4 is an immune-system protein measured in blood to assess complement activity.

WHAT IT IS
A blood protein in the complement immune system

WHERE IT COMES UP
Blood tests for immune, swelling, or infection concerns

WHY IT MATTERS
Helps show complement use, deficiency, or reduced production

WHAT IT IS NOT
Not a disease or diagnosis

WHO TO ASK
Primary care clinician, rheumatologist, allergist, or immunologist

HOW IT IS CHECKED
Serum C4 blood test, often with C3 and CH50

Overview

Complement component 4, usually shortened to C4 , is a protein in the complement system. This system is a network of proteins that helps your immune system respond to infections, damaged cells, and substances it recognizes as foreign.

C4 is not a disease and does not cause symptoms by itself. It is most often discussed because of a blood test result. Clinicians may measure it while investigating an autoimmune condition, repeated or unusual infections, or unexplained episodes of swelling.

A C4 result cannot confirm a diagnosis on its own. It needs to be interpreted with your symptoms, medical history, examination, and other tests. Your laboratory's reference range also matters because testing methods and ranges can differ.

C4 is different from CD4 , which is a type of immune cell commonly measured in people with HIV. It is also different from C4d , a breakdown product sometimes examined in tissue samples, including transplant biopsies.

How it works

Much of the C4 circulating in your blood is made by the liver. It travels in an inactive form until part of the complement system is triggered.

The complement system can be activated through several routes, called pathways. C4 takes part in the classical pathway , which can respond to antibodies attached to a target. It also takes part in the lectin pathway , which recognizes certain patterns on microbes.

When activated, C4 is split into smaller pieces. One piece, called C4b, attaches to a nearby surface and helps form an enzyme that activates more complement proteins. This creates a chain reaction that can:

The body normally controls this process carefully. Regulatory proteins help keep complement activity focused on the intended target and limit damage to healthy tissue.

A standard C4 blood test measures the amount of C4 protein. It does not directly show how well the entire complement system works. A CH50 test checks the overall function of the classical complement pathway. An AH50 test examines the alternative pathway, which does not use C4.

- Mark microbes or damaged cells for removal
- Support inflammation and immune-cell activity
- Help build structures that damage certain microbes

Why it matters for your health

A C4 result can provide a clue about whether complement proteins are being used up, produced in lower amounts, or affected by an inherited difference. It can also help clinicians decide which additional tests may be useful.

Low C4 may occur when the classical pathway is highly active. For example, immune complexes-groups of antibodies attached to their targets-can activate complement and use C4 faster than it is replaced.

Clinicians may follow C4 alongside C3 in someone with a known autoimmune condition such as systemic lupus erythematosus. Changes can support the overall assessment, but they do not always match disease activity. A normal result does not rule out lupus, and a low result does not establish that diagnosis.

C4 is also used when investigating hereditary angioedema related to C1 inhibitor deficiency. This is an inherited condition that can cause episodes of deeper swelling. C4 is often low in affected people, but diagnosis requires more specific tests, including the amount and function of C1 inhibitor. Some other forms of hereditary angioedema may have normal C4.

What can go wrong

An abnormal C4 result points to several possible situations. It does not show which one applies without further assessment.

Autoimmune and immune-complex conditions: C4 can be consumed during complement activation. This may happen in systemic lupus erythematosus, some forms of blood-vessel inflammation called vasculitis, and cryoglobulinemia, in which certain blood proteins clump in cooler temperatures.

Hereditary angioedema due to C1 inhibitor deficiency: Reduced control of the classical complement pathway can lead to persistently low C4. C4 is a screening clue rather than a stand-alone diagnostic test.

Inherited complement deficiency: A person can inherit a reduced amount or impaired function of C4. Complement deficiencies may be associated with certain infections or autoimmune conditions. A concentration test alone may not identify the exact inherited change.

Reduced production: Because the liver makes complement proteins, significant liver dysfunction can contribute to low levels. Poor nutritional status or severe protein loss may also affect blood protein measurements, although these findings are not specific to C4.

Laboratory and timing factors: Results may be affected by how a sample is collected, handled, or stored. The clinical meaning may also differ depending on whether testing occurs during an active illness or at another time.

A high C4 result is usually less specific than a low one. C4 can rise as part of the body's response to inflammation. The result does not identify the cause or prove that a particular disease is present.

An isolated abnormal result is generally suitable for routine follow-up. Seek emergency help for trouble breathing or sudden swelling of the tongue or throat. These are emergencies because of the possible underlying allergic reaction or angioedema, not because of the C4 number itself.

What you can do

There is no useful home test for C4, and there is no food, supplement, or self-care method proven to correct an abnormal result. The practical step is to understand why the test was ordered and how it fits with your other findings.

Questions you can ask include:

Keep a copy of the result with the date, measurement units, and reference range. Comparing numbers from different laboratories can be misleading if their methods or ranges are different.

If swelling is being investigated, record when it happens, which body areas are affected, how long it lasts, and whether hives occur. Note any breathing, voice, swallowing, or abdominal symptoms. This record can help distinguish among different causes of swelling.

Routine follow-up is appropriate for an abnormal C4 result when you otherwise feel well. Do not stop prescribed medicines because of the result unless the clinician responsible for them advises you to do so.

- Was my C4 below, within, or above this laboratory's range?
- Were C3, CH50, C1 inhibitor, or other related tests checked?
- Is the result being used for diagnosis, monitoring, or both?
- Should the test be repeated to confirm a pattern?
- Could a current illness or liver problem affect the result?

Common questions

Does low C4 mean I have lupus?

No. Low C4 can occur in lupus, but it also has other causes. Some people with lupus have normal C4. Diagnosis is based on a wider clinical assessment and other laboratory findings.

Can C4 diagnose hereditary angioedema?

Not by itself. A low level can support further investigation, especially for hereditary angioedema caused by C1 inhibitor deficiency. Tests of C1 inhibitor amount and function are needed. A normal C4 does not exclude every form of hereditary angioedema.

What is the difference between C3 and C4?

Both are complement proteins, but they take part in different stages and pathways. Comparing them can provide more information than either result alone. For example, low C4 with normal C3 may suggest a different pattern of complement activation than low levels of both.

Do I need to fast for a C4 blood test?

Fasting is not usually required for C4 alone. Follow the instructions provided for your appointment because other blood tests ordered at the same time may require fasting.

Is a low C4 result inherited?

Sometimes, but many low results are acquired rather than inherited. Functional complement tests, repeat measurements, family history, and specialist testing can help investigate a

possible inherited deficiency.

Can C4 levels change over time?

Yes. Levels may change with inflammation, complement activity, liver function, treatment, and the condition being monitored. A trend is often more useful than comparing one result with an unrelated test from another laboratory.

Sources

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