HEALTH BASICS

Complement

Complement is a group of blood proteins that helps immune defenses identify and remove threats.

WHAT IT IS
A network of proteins supporting immune defenses

WHERE IT COMES UP
Blood tests, immune disorders, kidney disease, and certain treatments

WHY IT MATTERS
Abnormal activity can affect infection, inflammation, or tissue damage

WHAT IT IS NOT
Not a disease or diagnosis

WHO TO ASK
Your primary care clinician or relevant specialist

HOW IT IS CHECKED
C3, C4, CH50, AH50, or specialized blood tests

Overview

Complement is part of the immune system. It is a network of more than 30 proteins found mainly in the blood and on cell surfaces. Many are made by the liver.

These proteins normally circulate in an inactive form. When the immune system detects a possible threat, complement proteins can switch on in a chain reaction called a cascade . This helps immune cells recognize microbes, increases inflammation where it is needed, and can damage the outer membrane of certain bacteria.

Complement is not a disease or a diagnosis. It is a normal body system. You may see the term on a blood test, in information about an immune or kidney condition, or when discussing medicines that block part of the complement system.

A single complement result rarely explains what is happening by itself. Results are interpreted alongside your health history, symptoms from any underlying condition, examination findings, and other tests.

How it works

Complement can be activated through three main routes:

These routes begin differently but join at a central protein called C3 . Activated C3 produces fragments with several jobs. One fragment, C3b, coats a target so immune cells can recognize and remove it more easily. This coating process is called opsonization .

The cascade can then activate C5 . Small fragments, especially C3a and C5a, help attract immune cells and promote inflammation. Other fragments combine to form the membrane attack complex , also called C5b-9. This structure can make holes in the membranes of certain bacteria.

Complement must be carefully controlled. Protective proteins on healthy cells stop the cascade from damaging the body's own tissues. Other regulators limit how long and where activation continues.

Several blood tests examine different parts of this system. C3 and C4 tests measure the amount of those individual proteins. A CH50 test assesses whether the classical pathway can complete its chain reaction. An AH50 test performs a similar check for the alternative pathway.

Specialized tests can measure individual proteins, protein function, complement activation products, or C1 inhibitor. C1 inhibitor is a regulatory protein involved in complement and other blood-protein systems.

- The classical pathway , often triggered when antibodies attach to a target
- The lectin pathway , triggered when proteins recognize certain sugars on microbes
- The alternative pathway , which provides ongoing surveillance and can become active on unprotected surfaces

Why it matters for your health

Complement helps protect against infection, particularly infection caused by certain bacteria. If an inherited or acquired problem leaves part of the system missing or unable to work, protection against particular infections may be reduced.

Complement also helps clear antibody-containing clusters known as immune complexes . If these clusters remain in tissues, they may contribute to inflammation. This is one reason complement tests are sometimes used when assessing or monitoring autoimmune conditions such as systemic lupus erythematosus.

Low C3 or C4 can mean that complement proteins are being used up by active immune processes. Low levels can also result from reduced production, protein loss, or an inherited

deficiency. The pattern matters: low C3 alone may suggest something different from low C3 and C4 together.

Normal C3 and C4 results do not show that every complement protein works normally. Functional tests such as CH50 or AH50 may be needed when a specific deficiency is suspected.

Raised complement levels are usually less specific. C3 and C4 can increase during inflammation because the liver makes more of them. A high result does not identify a particular condition.

Some medicines intentionally block complement. They are used for selected conditions in which uncontrolled complement activity contributes to tissue injury. Blocking complement can increase susceptibility to serious infections, particularly meningococcal infection. People receiving these medicines need a treatment-specific vaccination, monitoring, and emergency plan from their specialist team.

What can go wrong

Complement deficiency means that a complement protein is missing, present at a low level, or does not work properly. Some deficiencies are inherited. Others develop because of another health condition.

Deficiencies involving early parts of the classical pathway can be associated with autoimmune disease or repeated infections. Deficiencies involving C3 can interfere more broadly with clearing bacteria. Deficiencies involving C5 through C9 are particularly associated with infections caused by Neisseria , including meningococcal infection.

A missing or poorly functioning C1 inhibitor can cause hereditary or acquired angioedema. Angioedema is sudden swelling under the skin or in tissues lining the mouth, throat, or digestive tract. This is different from a typical allergic reaction, even though the swelling can look similar.

Complement may also become overactive or poorly regulated. This can contribute to tissue injury in conditions such as paroxysmal nocturnal haemoglobinuria, atypical haemolytic uraemic syndrome, and C3 glomerulopathy. These are separate medical conditions, not symptoms or forms of "complement."

Complement levels may fall when proteins are consumed during active immune-complex disease. They may also be affected by severe infection, liver disease, kidney-related protein loss, and some other illnesses. The test result alone cannot distinguish among these possibilities.

Seek emergency care for swelling of the tongue or throat, difficulty breathing, confusion, a rapidly spreading purple or dark rash, or severe illness with fever and neck stiffness. These signs can occur in conditions associated with complement problems, but they have many other possible causes.

Contact a clinician promptly for a new abnormal complement result accompanied by fever, reduced urination, blood in the urine, marked swelling, or rapidly worsening illness. An isolated abnormal result without urgent symptoms is usually handled through routine follow-up.

What you can do

If complement appears on your test report, check which test was performed. C3, C4, CH50, and AH50 answer different questions. Ask what the result was being used to investigate or monitor.

Useful questions include:

Keep copies of results so changes over time can be reviewed. Record serious or repeated infections and any family history of complement deficiency, unexplained swelling, or meningococcal disease. This information may help determine whether specialist assessment is appropriate.

There is no home test for complement function. There is also no established food or supplement that reliably "boosts" a specific complement protein. Do not start supplements solely to change a complement result.

If you take a complement-blocking medicine, carry any treatment alert information provided by your clinical team. Follow the medicine-specific infection plan and know how to obtain urgent help. Do not stop the medicine because of a test result unless the prescribing team tells you to do so.

- Was the result outside this laboratory's reference range?
- Does the pattern suggest protein consumption, reduced production, or deficiency?
- Should the test be repeated or paired with another complement test?
- Could a recent infection or known liver, kidney, or autoimmune condition affect it?
- Does your personal or family history suggest a functional or genetic test?

Common questions

Does low complement mean my immune system is weak?

Not necessarily. A low result may reflect increased use of complement during inflammation rather than an inherited immune deficiency. The type of test, the pattern of results, and your wider medical information are needed for interpretation.

Can complement be normal when a deficiency is present?

Yes. C3 and C4 measure only two proteins. Someone can have normal amounts of these proteins but a problem elsewhere in the cascade. CH50, AH50, or individual protein tests may be used when suspicion remains.

Why might my test be repeated?

Complement levels can change during illness and treatment. Repeating a test can confirm an unexpected result, show a trend, or help assess activity in a condition already being monitored.

Is complement the same as antibodies?

No. Antibodies are proteins made by immune cells to recognize specific targets. Complement is a separate protein network. Antibodies can activate one complement pathway, but complement can also be activated without them.

Can I request complement screening if I feel well?

Complement testing is not usually a general health screen. It is most useful when there is a specific reason, such as certain recurrent infections, unexplained angioedema, suspected immune-complex disease, or monitoring of a known condition.

Sources

- MedlinePlus Medical Test: Complement Blood Test - overview of complement testing, C3, C4, and total complement activity
- Merck Manual Professional Edition: Overview of the Complement System - complement pathways, functions, and regulation
- Merck Manual Professional Edition: Complement Deficiencies - clinical associations and laboratory assessment of complement deficiencies
- Centers for Disease Control and Prevention: Meningococcal Disease and Patients Receiving Complement Inhibitors - infection risk and clinical considerations during complement-blocking treatment



- Merle NS, Church SE, Fremeaux-Bacchi V, Roumenina LT. "Complement System Part I: Molecular Mechanisms of Activation and Regulation." Frontiers in Immunology. 2015;6:262. - peer-reviewed review of complement activation and control
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