Test Definition: C2

C2 Complement, Functional, with Reflex, Serum

Overview

Useful For

Investigation of a patient with a low (absent) hemolytic complement, with reflex testing to C3 and C4, if appropriate

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
C4	Complement C4, S	Yes	No
C3	Complement C3, S	Yes	No

Testing Algorithm

If the C2 result is less than 20 U/mL, then C3 and C4 testing will be performed at an additional charge.

Method Name

Turbidimetric Measurement of Liposome Lysis

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

This test is for assessment of complement C2 and includes assessment of C3 and C4 as reflex testing. Unless a deficiency has already been identified, initial assessment should begin with the total complement assay (COM / Complement, Total, Serum), which is a screen for suspected complement deficiencies and should be performed before ordering individual complement component assays. A deficiency of an individual component of the complement cascade will result in an undetectable total complement level.

Specimen Required

Patient Preparation:

Fasting: 12 hours, preferred but not required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

Collection Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL serum

Collection Instructions:

1. Immediately after specimen collection, place the tube on wet ice and allow specimen to clot.
2. Centrifuge at 4 degrees C and aliquot serum into a plastic vial.
3. Within 30 minutes of centrifugation, freeze specimen. Specimen must be placed on dry ice if not frozen immediately.

Note: If a refrigerated centrifuge is not available, it is acceptable to use a room temperature centrifuge, provided the specimen is kept on ice before centrifugation, and immediately afterward, the serum aliquoted and frozen.

Specimen Minimum Volume

Serum: 0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen	21 days	

Clinical & Interpretive

Clinical Information

Complement proteins are components of the innate immune system. There are 3 pathways to complement activation: 1) the classical pathway, 2) the alternative (or properdin) pathway, and 3) the lectin (or mannan binding lectin) pathway. The classical pathway of the complement system is composed of a series of proteins that are activated in response to the presence of immune complexes. A single IgM molecule or 2 IgG molecules are sufficient to trigger activation of the recognition complex initiated by C1q. This activation process triggers a cascade that includes an amplification loop. The amplification loop in mediated by C3, with cleavage of a series of proteins, and results in 3 main end products: 1) anaphylatoxins that promote inflammation (C3a, C5a), 2) opsonization peptides that are chemotactic for neutrophils (C3b) and facilitate phagocytosis, and 3) the membrane attack complex, which promotes cell lysis.

The absence of early components (C1, C2, C3, C4) of the complement cascade results in the inability of immune complexes to activate the cascade. Patients with deficiencies of the early complement proteins are unable to generate lytic activity or to clear immune complexes. These patients have increased susceptibility to infections with encapsulated microorganisms. They may also have symptoms that suggest autoimmune disease, of which complement deficiency may be an etiologic factor.

Although rare, C2 deficiency is the most common inherited complement deficiency. Homozygous C2 deficiency has an estimated prevalence ranging from 1 in 10,000 to 1 in 40,000 (the prevalence of heterozygotes is 1 in 100 to 1 in 50).

Half of the homozygous patients are clinically normal.

However, discoid lupus erythematosus or systemic lupus erythematosus (SLE) occurs in approximately one-third of patients with homozygous C2 deficiency. Patients with SLE and a C2 deficiency frequently have a normal anti-double stranded DNA titer. Clinically, many have lupus-like skin lesions and photosensitivity, but immunofluorescence studies may fail to demonstrate immunoglobulin or complement along the epidermal-dermal junction.

Other diseases reported to be associated with C2 deficiency include dermatomyositis, glomerulonephritis, vasculitis, atrophoderma, cold urticaria, inflammatory bowel disease, and recurrent infections.

The laboratory findings that suggest C2 deficiency include a hemolytic complement of nearly zero, with normal values for C3 and C4.

Reference Values

> or =34 U/mL

Interpretation

Low levels of complement may be due to inherited deficiencies, acquired deficiencies, or due to complement consumption (eg, as a consequence of infectious or autoimmune processes).

Absent (or low) C2 levels in the presence of normal C3 and C4 values are consistent with a C2 deficiency.

Low C2 levels in the presence of low C3 and C4 values are consistent with a complement-consumptive process.

Low C2 and C4 values, in the presence of normal values for C3 is suggestive of C1 esterase inhibitor deficiency.

Cautions

As with all complement assays, proper specimen handling is of utmost importance to ensure that the complement system is not activated before clinical testing.

Clinical Reference

1. Gaither TA, Frank MM. Complement. In: Henry JB, ed. Clinical Diagnosis and Management by Laboratory Methods. 17th ed. WB Saunders Company; 1984:879-892
2. O'Neil KM. Complement deficiency. Clin Rev Allergy Immunol. 2000;19(2):83-108
3. Frank MM. Complement deficiencies. Pediatr Clin North Am. 2000;47(6):1339-1354
4. Agnello V. Complement deficiency states. Medicine. 1978;57(1):1-23
5. Buckley D, Barnes L. Childhood subacute cutaneous lupus erythematosus associated with homozygous complement 2 deficiency. Pediatr Dermatol. 1995;12(4):327-330
6. Willrich MAV, Braun KMP, Moyer AM, Jeffrey DH, Frazer-Abel A. Complement testing in the clinical laboratory. Crit Rev Clin Lab Sci. 2021;58(7):447-478. doi:10.1080/10408363.2021.1907297
7. Nandakumar V, Braun KMP, Willrich MAV. Challenges for complement functional assays in the clinical laboratory: From test validation to clinical interpretation. J Immunol Methods 2025;537:113824
8. Moyer AM, Sridharan M, Willrich MA. Complement defects. In: Schmitz JL, Detrick B, O'Gorman MRG, eds. Manual of molecular and clinical laboratory immunology, Vol. 2. Wiley, 2024:796-812

Performance

Method Description
Testing is performed on the Binding Site Optilite turbidimetric analyzer with the Optilite CH50 Reagent kit using modified manufacturer's instructions. C2 activity is measured by mixing patient serum with C2-deficient serum. The lytic activity of the serum mixture is tested against sensitized, labeled liposomes.(Package insert: Optilite CH50 Reagent, The Binding Site Group, Ltd.; INS095.OPTA, 08/2024)

PDF Report
No

Day(s) Performed
Tuesday, Friday

Report Available
1 to 3 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
86161
86160 x 2 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
C2	C2	93977-7

	Complement,Functional,w/Reflex,S	

Result ID	Test Result Name	Result LOINC® Value
C2FX	C2 Complement,Functional,S	93977-7
INT53	Interpretation	69048-7