aHUS Complement Profile

Versiti proudly offers complement testing for Atypical Hemolytic Uremic Syndrome.

Atypical Hemolytic Uremic Syndrome (aHUS) presents as a group of signs and symptoms, including non-immune hemolytic anemia, thrombocytopenia, and organ dysfunction (primarily renal impairment). The onset of symptoms is generally sudden and severe. Incidence of aHUS in the U.S. is an estimated 1-2 per million per year. Approximately 60% of aHUS cases are diagnosed in children versus 40% in adults. Without immediate and aggressive treatment, progression to end-stage renal disease and death may result.[5]

The complement system is the primary defense system against microbes or foreign cells in the human body. It is composed of at least 30 different proteins that operate in a synergy to affect pathogen clearance. The system also possesses several control proteins to slow or arrest the cascade. aHUS is caused by uncontrolled activation of the alternative pathway in the complement system, and is typically due to a deficiency in the quantity or function of the control proteins or enhanced activity of a complement system component. Such defects can be either acquired or inherited.

C3: Complement protein C3 is the central component of the complement system. Complement activation is associated with consumption of C3. Reduced serum concentrations of C3 may be seen in some patients with aHUS.

C4: Diminished serum concentrations of C4 are observed primarily in activation of the classical pathway by immune complexes. C4 levels may be useful in distinguishing systemic activation of the classical versus alternative complement pathways.

Factor H (CFH): CFH is a regulatory protein of the alternative pathway of the complement system. Decreased CFH plasma levels and/or mutations in CFH have been associated with a number of complement-mediated diseases, including aHUS.[1]

Factor H Autoantibody: Patients can develop autoantibodies to Factor H. These autoantibodies may clear Factor H protein from circulation or otherwise reduce control of the complement system. CFH autoantibodies account for approximately 6% of aHUS cases.[1]

Factor I (CFI): CFI is a control protein of the complement system, that regulates complement activation by cleaving cell-bound or fluid phase C3b and C4b.[5] Levels less than 60% of normal are indicative of a quantitative deficiency.[1]

Factor B (CFB): CFB circulates in the blood as a single chain polypeptide. Upon activation of the alternative pathway, it is cleaved by complement factor D yielding the noncatalytic chain Ba and the catalytic subunit Bb. The active subunit Bb is a serine protease which associates with C3b to form the alternative pathway C3 convertase.3 Reduced CFB levels are indicative of alternative pathway activation.[1]

CD46 (membrane cofactor protein, MCP): CD46 is important for cell surface inactivation of the complement system. It is normally present on all white blood cells. CD46 expression is measured using flow cytometry. Very low expression of CD46 is detected in patients with homozygous CD46 deficiency. Patients with a heterozygous CD46 deficiency will have CD46 expression approximately 50% of the normal range.[1]

Indications for testing:

Suspicion of aHUS.

Test method:

See individual tests.

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Specimen requirements:

C3, C4, Factor B, Factor I, Factor H, Factor H Autoantibody (ordered as profile or individually in any combination): Two 2ml Serum aliquots (red top – no serum separator). Sample should be centrifuged, serum taken off the clot and frozen within 2 hours of draw. Send on dry ice. Frozen serum stable up to 6 months. Avoid freeze/thaw cycles.

CD46 (MCP) Expression: 3ml whole blood collected in K2 EDTA (lavender top). Whole blood specimen stable up to 24 hours.

SHIP

Shipping requirements:

C3, C4, Factor B, Factor I, Factor H, Factor H Autoantibody (ordered as profile or individually in any combination): Place frozen specimen and requisition in plastic bags, seal and insert in a Styrofoam container with 5 lbs dry ice. Seal the Styrofoam container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines.

CD46 (MCP) Expression: Whole blood sample must be received by Versiti within 24 hours of collection. Do not freeze. Place room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in a sturdy carboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Testing performed as needed, Mon-Fri only. Please call the lab before sending sample (800-245-3117, ext. 6250).

Ship to:

Client Services/Hemostasis Laboratory
638 N. 18th Street
Milwaukee, WI 53233
800-245-3117, ext. 6250

ORDER

Required forms:

Please complete all pages of the requisition form.

CPT Codes/Billing/Turnaround time:

Turnaround Time: 7-10 days

CPT codes: For recommended CPT codes, visit the versiti.org/test-catalog

Order Code: 1500

References:

1. Loirat, C. and Frémeaux-Bacchi, V: Atypical hemolytic uremic syndrome, Orphanet Journal of Rare Diseases 2011, 6:60 doi:10.1186/1750-1172-6-60
2. Taylor, C. M., et al Clinical Practice Guidelines for the management of atypical Haemolytic Uraemic Syndrome in the United Kingdom. British Journal of Haematology, 148: 37–47. doi: 10.1111/j.1365-2141.2009.07916.x
3. Tawadrous, H., et al: A novel mutation in the complement factor B gene (CFB) and atypical hemolytic uremic syndrome. Pediatr Nephrol. 2010 May; 25(5):947-51.
4. Westra, et al. A new era in the diagnosis and treatment of atypical haemolytic uraemic syndrome. Neth J Med. 2012 Apr;70(3):121-9.
5. Noris, M, and Remuzzi, G: Atypical Hemolytic–Uremic Syndrome, N Engl J Med 2009; 361:1676-1687
6. Nester, C.M., Thomas, C.P.: Atypical hemolytic uremic syndrome: what is it, how is it diagnosed, and how is it treated? Hematology Am Soc Hematol Educ Program. 2012; 2012:617-25.
7. Kavanagh D., Goodship T.H., Richards A.: Atypical hemolytic uremic syndrome. Semin Nephrol. 2013 Nov; 33(6):508-30.

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