MAYO CLINIC LABORATORIES

Test Definition: AFH

Factor H Autoantibody, Serum

Overview

Useful For

Detection and quantification of antibodies to factor H

Monitoring patients with known factor H autoantibodies

Aiding in the differential diagnosis of thrombotic microangiopathy and C3 glomerulopathies

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL
Collection Instructions:
1. Immediately after specimen collection, place the tube on wet ice.
2. After sample has clotted on wet ice, centrifuge at 4 degrees C and aliquot serum into a plastic vial.
3. Freeze specimen within 30 minutes of centrifugation. Sample must be placed on dry ice if not frozen immediately.
Additional Information: If the specimen is to be shared with AHUSD / Atypical Hemolytic Uremic Syndrome Complement Panel, Serum and Plasma, **only serum collected in a red-top tube is acceptable.**
NOTE: If a refrigerated centrifuge is not available, it is acceptable to use a room temperature centrifuge, provided the sample is kept on ice before centrifugation, and immediately afterward, the serum aliquoted and frozen..

Specimen Minimum Volume

0.4 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Frozen (preferred)	28 days	
	Ambient	14 days	
	Refrigerated	28 days	

Clinical & Interpretive

Clinical Information

Complement factor H (FH) is an important regulator of cell-bound activated C3b, and most importantly of activated C3b in the fluid phase. It is estimated that C3 activation takes place at a rate of 1% to 2%, thus constant activity of FH and other regulators is essential to retain control of complement's alternative pathway. Anti-factor H (AFH) is an autoantibody that interferes with the ability of FH to bind the C3 convertase, therefore allowing unrestricted amplification of C3b in the complement cascade.

Anti-factor H is predominantly seen in children between the ages of 9 and 13 years but can also affect adults. AFH is found in atypical hemolytic uremic syndrome (aHUS) and in C3 glomerulopathies. AHUS is a form of thrombotic microangiopathy, a condition that can cause small blood vessels in the kidneys to become damaged and inflamed as a result of clots forming in the vessels. The clots clog the glomeruli of the kidneys and can cause problems with the kidney's ability to filter and eliminate waste products. Compared to typical HUS, which is caused by Shiga toxin-producing bacterial infection, aHUS is a diagnosis of exclusion, associated with genetic variants in the complement alternative pathway or acquired autoantibodies that contribute to uncontrolled activation of the complement system. C3 glomerulopathies (C3G) are rare kidney diseases resulting from complement deposition in the kidney (mostly C3 fragments) and causing glomerular damage. C3G may have autoimmune or genetic causes and is attributed mostly to dysfunction of the complement alternative pathway.

Anti-factor H are found in 6% to 10% of patients with aHUS, and the presence or absence of AFH can be a determinant of whether immunosuppressive therapy is warranted versus complement-blocking therapy.(1) Deletion of the *CFHR1* gene, with or without other *CFHR* genes, can result in predisposition to generation of AFH; however, not all individuals with *CFHR1* deletion develop AFH, and conversely, some individuals with the autoantibody do not have a *CFHR1* deletion.(2) Most commonly, the deletion encompasses both the *CFHR1* and *CFHR3* genes. The allele frequency of the *CFHR3/CFHR1* deletion varies among populations, from 0% in Japanese and South American populations to 54.7% in Nigeria; similarly, the frequency of homozygosity for the deletion ranges from 0% up to 33% in Nigeria.(3) Interestingly, while AFH are much more common in aHUS cohorts from India, accounting for approximately 50% of cases, the population frequency of homozygous *CFHR1* deletion is 9.5%, which is not significantly higher than in other populations.(4,5) The mechanism that results in AFH formation in the presence of the deletion remains unknown. Most of the autoantibodies inhibit FH function by binding and blocking the C-terminus, impairing its ability to bind endothelial cell surfaces, sialic acids, and

C3b; however, in some individuals, the AFH may recognize other regions, such as the N-terminal SCR1-4.

Reference Values

<15.8 U/mL

Interpretation

Absent (<15.8 U/mL): Antibodies to factor H are not detected.

Present (> or =15.8 U/mL): Antibodies to factor H are detected. Clinical correlation recommended.

Cautions

Healthy individuals may see false-positive results for anti-factor H (AFH) since the diseases where AFH is pathogenic are so rare.

Positive AFH results can occur in healthy individuals and in IgA nephropathy. AFH could be an incidental finding in patients with diseases other than atypical hemolytic uremic syndrome and C3 glomerulopathies (C3G). This is most likely due to the multifactorial nature of the diseases and differences in penetrance for genetic variants.

Results should be interpreted in the context of other complement assays and other laboratory tests in the evaluation of thrombotic microangiopathies or C3G.

Use of caution is suggested on a finding of AFH in the clinical setting.

This assay to measure AFH is not standardized to European methods and results obtained by other laboratories can only be compared qualitatively.

Clinical Reference

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3. Holmes LV, Strain L, Staniforth SJ, et al. Determining the population frequency of the CFHR3/CFHR1 deletion at 1q32. PLoS One. 2013;8(4):e60352. doi:10.1371/journal.pone.0060352
4. Sinha A, Gulati A, Saini S, et al. Prompt plasma exchanges and immunosuppressive treatment improves the outcomes of anti-factor H autoantibody-associated hemolytic uremic syndrome in children. Kidney Int. 2014;85(5):1151-1160. doi:10.1038/ki.2013.373
5. Durey MA, Sinha A, Togarsimalemath SK, Bagga A. Anti-complement-factor H-associated glomerulopathies. Nat Rev Nephrol. 2016;12(9):563-578. doi:10.1038/nrneph.2016.99
6. Blanc C, Togarsimalemath SK, Chauvet S, et al. Anti-factor H autoantibodies in C3 glomerulopathies and in atypical hemolytic uremic syndrome: one target, two diseases. J Immunol. 2015;194(11):5129-5138. doi:10.4049/jimmunol.1402770
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9. Dragon-Durey MA, Blanc C, Roumenina LT, et al. Anti-factor H autoantibodies assay. Methods Mol Biol. 2014;1100:249-56. doi:10.1007/978-1-62703-724-2_20

Performance

Method Description

The anti-factor H enzyme-linked immunoassay assay for the quantitation of antibodies to complement factor H is a 3-step procedure. In the first step, standards, controls, and diluted patient specimens are incubated with human recombinant complement factor H immobilized on a microwell plate. During this incubation, antibodies to factor H (AFH) present in the standards, controls, and patient sample will bind to the factor H-coated microwell plate. After incubation, a wash cycle removes the unbound material. In the second step, anti-human IgG conjugated to horseradish peroxidase (HRP) is added to the wells and incubated. The conjugate reacts with the AFH bound to the microwell plate. After incubation, a wash cycle removes the excess conjugate. In the third step, a chromogenic enzyme substrate is added to the wells and incubated. The bound HRP-conjugate reacts with the substrate forming a blue color. The enzyme reaction is stopped by dispensing an acidic solution into the wells, changing the color of the solution from blue to yellow. The color intensity of the reaction mixture is measured spectrophotometrically at 450 nm and is directly proportional to the amount of AFH present in the patient specimens, standards, and controls.(Package insert: Anti-Faktor H. GA Generic Assays GmbH; 05/2022)

PDF Report

No

Day(s) Performed

Monday

Report Available

2 to 8 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

Test Definition: AFH

Factor H Autoantibody, Serum

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

83520

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AFH	Factor H Autoantibody, S	101863-9

Result ID	Test Result Name	Result LOINC® Value
AFH	Factor H Autoantibody, S	101863-9