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
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. Centrifuge and aliquot serum into plastic vial.
3. Freeze specimen within 30 minutes.

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.

Specimen Minimum Volume
0.4 mL

Reject Due To

<table>
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<td>Gross lipemia</td>
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<td>Gross icterus</td>
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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.

AFH 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 (TMA), 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.

AFH are found in 6% to 10% of aHUS patients, 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 (aHUS) 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

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; 11/2015)

PDF Report
No

Day(s) Performed
Monday

Report Available
2 to 8 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
83520

LOINC® Information
**Test Definition: AFH**  
Factor H Autoantibody, Serum

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