MAYO CLINIC LABORATORIES

Test Definition: AGAS

Alpha-Galactosidase, Serum

Overview

Useful For

Diagnosis of Fabry disease in male patients

Preferred screening test (serum) for Fabry disease

This test is **not useful for** patients undergoing a work up for a meat or meat-derived product allergy.

Genetics Test Information

Serum is the preferred screening specimen for Fabry disease.

Enzyme testing is useful in identifying affected male patients.

Testing Algorithm

The following algorithms are available:

-Fabry Disease: Newborn Screen-Positive Follow-up

-Fabry Disease Diagnostic Testing Algorithm

For more information, see Newborn Screening Act Sheet Fabry Disease: Decreased Alpha-Galactosidase A.

Special Instructions

- Informed Consent for Genetic Testing
- Fabry Disease Diagnostic Testing Algorithm
- Fabry Disease: Newborn Screen-Positive Follow-up
- Biochemical Genetics Patient Information
- Newborn Screening Act Sheet Fabry Disease: Decreased Alpha-Galactosidase A
- Informed Consent for Genetic Testing (Spanish)

Method Name

Fluorometric

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

If testing needed for assessment of meat or meat-derived product allergy, order either ALGAL / Galactose-Alpha-1,3-Galactose (Alpha-Gal), IgE, Serum or APGAL / Galactose-Alpha-1,3-Galactose (Alpha-Gal) Mammalian Meat Allergy Profile, Serum.

Carrier detection using enzyme levels is unreliable for female patients as results may be within the normal values. For testing carrier status, order FABRZ / Fabry Disease, Full Gene Analysis, Varies.

Additional Testing Requirements

Urine sediment analysis (CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine) for the accumulating trihexoside substrate and measurement of globotriaosylsphingosine (LGB3S / Gobotriaosylsphingosine, Serum) are also recommended.

Necessary Information

Sex of patient is required for interpretation of results.

Specimen Required

Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2.Biochemical Genetics Patient Information (T602)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

0.2 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	14 days	
	Refrigerated	24 hours	

Clinical & Interpretive

Clinical Information

Fabry disease is an X-linked lysosomal storage disorder resulting from deficient activity of the enzyme alpha-galactosidase A (alpha-Gal A) and the subsequent deposition of glycosylsphingolipids in tissues throughout the body; in particular, in the kidney, heart, and brain. Variants within the *GLA* gene cause Fabry disease and more than 630 variants have been identified. Severity and onset of symptoms are dependent on the amount of residual enzyme activity. The classic form of Fabry disease occurs in male patients who have less than 1% alpha-Gal A activity. Symptoms usually appear in childhood or adolescence and can include acroparesthesias (burning pain in the extremities), gastrointestinal issues, multiple angiokeratomas, reduced or absent sweating, corneal opacity, and proteinuria. In addition, progressive renal involvement leading to kidney failure, also called end-stage renal (kidney) disease (ESRD), typically occurs in adulthood, followed by cardiovascular and cerebrovascular disease. The estimated incidence varies from 1 in 3000 infants detected via newborn screening to 1 in 10,000 males diagnosed after onset of symptoms.

Male patients with residual alpha-Gal A activity greater than 1% may present with 1 of 3 variant forms of Fabry disease with onset of symptoms later in life: a renal variant associated with ESRD but without the pain or skin lesions; a cardiac variant typically presenting in the sixth to eighth decade with left ventricular hypertrophy, cardiomyopathy and arrhythmia, and proteinuria, but without ESRD; and a cerebrovascular variant presenting as stroke or transient ischemic attack. The variant forms of Fabry disease may be underdiagnosed.

Female patients who are carriers of Fabry disease can have clinical presentations ranging from asymptomatic to severely affected. Measurement of alpha-Gal A activity is not generally useful for identifying carriers of Fabry disease, as many of these individuals have normal levels of alpha-Gal A. Therefore, molecular genetic analysis of the *GLA* gene (FABRZ / Fabry Disease, Full Gene Analysis, Varies) is recommended to detect carriers.

Unless irreversible damage has already occurred, treatment with enzyme replacement therapy has led to significant clinical improvement in affected individuals. In addition, some (adult) patients may be candidates for oral chaperone therapy. For this reason, early diagnosis and treatment are desirable, and in a few US states, early detection of Fabry disease through newborn screening has been implemented.

Absent or reduced alpha-Gal A in blood spots (AGABS / Alpha-Galactosidase, Blood Spot), leukocytes (AGAW / Alpha-Galactosidase, Leukocytes), or serum (AGAS / Alpha-Galactosidase, Serum) can indicate a diagnosis of classic or variant Fabry disease. Molecular sequence analysis of the *GLA* gene (FABRZ / Fabry Disease, Full Gene Analysis, Varies) allows for detection of the disease-causing variant in both male and female patients. The biomarkers globotriaosylsphingosine (LGB3S / Globotriosylsphingosine, Serum) and ceremide trihexosides (CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine) are typically elevated in symptomatic patients with Fabry disease and may aid in the diagnostic evaluation of female patients and individuals with a variant of uncertain significance in *GLA*.

See Fabry Disease Testing Algorithm and Fabry Disease: Newborn Screen-Positive Follow-up

Reference Values

0.074-0.457 U/L

Note: Results from this assay are not useful for female carrier determination. Carriers usually have levels in the normal

range.

Interpretation

Deficiency (<0.016 U/L) of alpha-galactosidase in properly submitted specimens is diagnostic for Fabry disease in male patients. If concerned about specimen integrity, recheck using leukocyte testing (AGAW / Alpha-Galactosidase, Leukocytes).

Cautions

Individuals with pseudodeficiency allelic variants can show reduced alpha-galactosidase A enzyme activity with this assay.

Clinical Reference

1. Desnick RJ, Ioannou YA, Eng CM: Alpha-galactosidase A deficiency: Fabry disease. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed February 18, 2022. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546984
2. De Schoenmakere G, Poppe B, Wuyts B, et al: Two-tier approach for the detection of alpha-galactosidase A deficiency in kidney transplant recipients. Nephrol Dial Transplant. 2008 Dec;23(12):4044-4048. doi: 10.1093/ndt/gfn370
3. Mehta A, Hughes DA: Fabry Disease. In: Pagon RA, Adam MP, Ardinger HH, et al: eds. GeneReviews [Internet]. University of Washington, Seattle; 2002. Updated January 27, 2022. Accessed February 18, 2022. Available at www.ncbi.nlm.nih.gov/books/NBK1292/
4. Laney DA, Bennett RL, Clarke V, et al: Fabry disease practice guidelines: Recommendations of the National Society of Genetic Counselors. J Genet Couns. 2013 Oct;22(5):555-564. doi: 10.1007/s10897-013-9613-3
5. Laney DA, Peck DS, Atherton AM, et al: Fabry disease in infancy and early childhood: a systematic literature review. Genet Med. 2015 May;17(5)323-330. doi: 10.1038/gim.2014.120
6. Ferreira S, Auray-Blais C, Boutin M, et et al: Variations in the GLA gene correlate with globotriaosylceramide and globotriaosylsphingosine analog levels in urine and plasma. Clin Chim Acta. 2015 Jul 20;447:96-104. doi: 10.1016/j.cca.2015.06.003
7. Nowak A, Beuschlein F, Sivasubramaniam V, et al: Lyso-Gb3 associates with adverse long-term outcome in patients with Fabry disease. J Med Genet. 2022 Mar;59(3):287-293. doi: 10.1136/jmedgenet-2020-107338

Performance

Method Description

Alpha-galactosidase is a lysosomal enzyme active at an acidic pH. The enzyme hydrolyzes artificial substrates such as 4-methylumbelliferyl and alpha-*D* galactopyranoside. The 4-methylumbelliferone liberated is measured by fluorometry.(Desnick RJ, Allen KY, Desnick SJ, et al: Fabry's disease: enzymatic diagnosis of hemizygotes and heterozygotes. Alpha-galactosidase activities in plasma, serum, urine, and leukocytes. J Lab Clin Med. 1973 Feb;81[2]:157-171; Cowan T, Pasquali M: Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

PDF Report

No

Day(s) Performed
Monday, Thursday

Report Available
8 to 15 days

Specimen Retention Time
1 month

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 Regional Manager. 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
82657

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AGAS	Alpha-Galactosidase, S	1813-5

Result ID	Test Result Name	Result LOINC® Value
50578	Specimen	31208-2
50579	Specimen ID	57723-9
50580	Source	31208-2
50581	Order Date	82785-7
50582	Reason For Referral	42349-1
50583	Method	85069-3
50590	Alpha-Galactosidase,S	1813-5
50584	Interpretation	59462-2
50585	Amendment	48767-8
50586	Reviewed By	18771-6
50587	Release Date	82772-5