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

If the patient has abnormal newborn screening results for Fabry disease, refer to the appropriate ACMG Newborn Screening ACT Sheet.(1)

Special Instructions

- Informed Consent for Genetic Testing
- Fabry Disease Diagnostic Testing Algorithm
- Fabry Disease: Newborn Screen-Positive Follow-up
- Biochemical Genetics Patient Information
- Hereditary Peripheral Neuropathy Diagnostic Algorithm
- Informed Consent for Genetic Testing (Spanish)

Method Name

Fluorometric

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

If testing is 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.

Enzyme testing is unreliable for female patients as results may be within the normal values even in affected female patients; order GLA / Fabry Disease, *GLA* Gene Sequencing with Deletion/Duplication, Varies.

Additional Testing Requirements

Urine sediment analysis for the accumulating trihexoside substrate and measurement of globotriaosylsphingosine are recommended. Order both CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine and LGB3S / Globotriaosylsphingosine, Serum in conjunction with this test.

Necessary Information

Sex of patient is required for interpretation of results.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

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

Serum: 0.3 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

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 glycosphingolipids in tissues throughout the body; in particular, in the kidney, heart, and brain. Disease-causing variants within the *GLA* gene cause Fabry disease. 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 typically occurs in adulthood, followed by cardiovascular and cerebrovascular disease.

Male patients with residual alpha-Gal A activity greater than 1% are at risk for a late-onset form of Fabry disease. Clinical manifestations may include adult-onset cardiac disease with left ventricular hypertrophy, cardiomyopathy, arrhythmia, and proteinuria; kidney failure without skin lesions or pain; or cerebrovascular disease presenting as stroke or transient ischemic attack. The variant forms of Fabry disease may be underdiagnosed.

Female patients with Fabry disease can have clinical presentations ranging from asymptomatic to severely affected. Measurement of alpha-Gal A activity is not generally useful for identifying female individuals with Fabry disease, as many of them will have normal levels. Therefore, molecular genetic analysis of the *GLA* gene (GLA / Fabry Disease, *GLA* Gene Sequencing with Deletion/Duplication, Varies) is recommended.

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 (PLSD / Lysosomal and Peroxisomal Disorders Screen, 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 (GLA / Fabry Disease, *GLA* Gene Sequencing with Deletion/Duplication, 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*.

For more information 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. ACMG Newborn Screening ACT Sheets. Accessed October 10, 2025. Available at www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx?hkey=9d6bce5a-182e-42a6-84a5-b2d88240c508
2. 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 October 10, 2025. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546984
3. Mehta A, Hughes DA. Fabry disease. In: Adam MP, Feldman J, Mirzaa GM, et al. eds. GeneReviews [Internet]. University of Washington, Seattle; 2002. Accessed October 10, 2025. 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;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;17(5):323-330. doi:10.1038/gim.2014.120
6. Ferreira S, Auray-Blais C, Boutin M, et al. Variations in the GLA gene correlate with globotriaosylceramide and globotriaosylsphingosine analog levels in urine and plasma. Clin Chim Acta. 2015;447:96-104. doi:10.1016/j.cca.2015.06.003
7. Nowak A, Beuschlein F, Sivasubramaniam V, Kasper D, Warnock DG. Lyso-Gb3 associates with adverse long-term outcome in patients with Fabry disease. J Med Genet. 2022;59(3):287-293. doi:10.1136/jmedgenet-2020-10733

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;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

Test Definition: AGAS

Alpha-Galactosidase, Serum

Day(s) Performed
Tuesday, Friday

Report Available
2 to 5 days

Specimen Retention Time
1 month

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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
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
50590	Alpha-Galactosidase,S	1813-5
50584	Interpretation	59462-2
50586	Reviewed By	18771-6