

Overview

Useful For

Diagnosis of Fabry disease in male patients

Verifying abnormal serum alpha-galactosidase results in male patients with a clinical presentation suggestive of Fabry disease

Genetics Test Information

Fabry disease is caused by deficient activity of the enzyme alpha-galactosidase A and results in damage to multiple organs including the kidney, heart, and brain.

Treatment with enzyme replacement therapy is available for individuals with Fabry disease.

Testing Algorithm

The following are available in Special Instructions:

[-Fabry Disease: Newborn Screen-Positive Follow-up](#)

[-Fabry Disease Diagnostic Testing Algorithm](#)

[-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

Flow Injection Analysis-Tandem Mass Spectrometry

NY State Available

Yes

Specimen

Specimen Type

Whole Blood ACD

Advisory Information

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

Shipping Instructions

For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 96 hours of collection to be stabilized. Collect specimen Monday through Thursday only and not the day before a holiday.

Specimen should be collected and packaged as close to shipping time as possible.

Specimen Required

Container/Tube:

Preferred: Yellow top (ACD solution B)

Acceptable: Yellow top (ACD solution A) or lavender top (EDTA)

Specimen Volume: 6 mL

Collection Instructions: Send specimen in original tube. Do not transfer blood to other containers.

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 in Special Instructions:

[-Informed Consent for Genetic Testing](#) (T576)

[-Informed Consent for Genetic Testing-Spanish](#) (T826)

2. [Biochemical Genetics Patient Information](#)(T602) in Special Instructions

Specimen Minimum Volume

2 mL

Reject Due To

Gross hemolysis	Reject
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Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood ACD	Refrigerated (preferred)	4 days	
	Ambient	72 hours	

Clinical and 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. Alterations within the *GLA* gene cause Fabry disease and more than 630 genetic alterations 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 end-stage renal 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.

Females 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 will have normal levels. Therefore, molecular genetic analysis of the *GLA* gene (FABRZ / Fabry Disease, Full Gene Analysis, Varies) is recommended as the most appropriate diagnostic test to detect carriers.

Unless irreversible damage has already occurred, treatment with enzyme replacement therapy (ERT) has led to significant clinical improvement in affected individuals. In addition, some adult patients may be candidates for an 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 (this test), or serum (AGAS / Alpha-Galactosidase, Serum) can indicate a diagnosis of classic or variant Fabry disease. The biomarkers globotriaosylsphingosine (LGBWB / Globotriaosylsphingosine, Blood) and ceramide trihexosides (CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine) may be elevated in patients with Fabry disease and may aid in the diagnostic evaluation of females. 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.

Reference Values

> or =10.32 nmol/hour/mg protein

An interpretative report will be provided.

Note: Results from this assay do not reflect carrier status because of individual variation of alpha-galactosidase enzyme levels.

Interpretation

Values below the reference range are consistent with a diagnosis Fabry Disease.

When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing and in vitro, confirmatory studies (enzyme assay, molecular analysis), name and phone number of key contacts who may provide these studies, and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

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: Galactosidase A deficiency: Fabry disease. In: Valle D, Beaudet AL, Vogelstein B, et al. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill. Accessed 2/14/19. Available at <https://ommbid.mhmedical.com/content.aspx?sectionid=225546984&bookid=2709&Resultclick=2>

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;23:4044-4048
3. Mehta A, Hughes DA: Fabry disease. In: Pagon RA, Adam MP, Ardinger HH, et al. eds. *GeneReviews*. [Internet]. University of Washington, Seattle. Updated 2017 Jan 5. Accessed 2/11/2019. 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;22:555-564
5. Laney DA, Peck DS, Atherton AM, et al: Fabry disease in infancy and early childhood: a systematic literature review. *Genet Med*. 2015;17:323-330

Performance

Method Description

The specimens are incubated with a mix of substrate and internal standard for acid sphingomyelinase (ASM), beta-glucocerebrosidase (ABG), acid alpha-glucosidase (GAA), alpha-galactosidase (GLA), galactocerebrosidase (GALC) and alpha-L-iduronidase (IDUA). The sample is then purified by liquid-liquid extraction. The extract is evaporated and reconstituted before analysis by tandem mass spectrometry. (Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Specimens are processed Monday through Sunday.

Assay is performed: Varies

Analytic Time

5 days

Maximum Laboratory Time

10 days

Specimen Retention Time

WBC homogenate; 1 month

Performing Laboratory Location

Rochester

Fees and 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 U.S. Food and Drug Administration.

CPT Code Information

82657

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
AGAW	Alpha-Galactosidase, Leukocytes	24049-9

Result ID	Test Result Name	Result LOINC Value
606261	Alpha-Galactosidase, Leukocytes	24049-9
606262	Interpretation	59462-2
606263	Reviewed By	18771-6