Test Definition: LGB3S

Globotriaosylsphingosine, Serum

Overview

Useful For

Diagnosis and monitoring of Fabry disease

Genetics Test Information

This test is used to diagnose and monitor patients with Fabry disease.

Testing Algorithm

The following algorithms are available:

-Fabry Disease: Newborn Screen-Positive Follow-up

-Fabry Disease Diagnostic Testing Algorithm

Special Instructions

- Fabry Disease Diagnostic Testing Algorithm
- Fabry Disease: Newborn Screen-Positive Follow-up
- Biochemical Genetics Patient Information

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

This test **should not be used** to determine carrier status. Order FABRZ / Fabry Disease, Full Gene Analysis, Varies for carrier testing.

Necessary Information

1. Patient's age is required.

2. Reason for testing is required.

Specimen Required

Collection Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	90 days	
	Refrigerated	48 hours	

Clinical & Interpretive

Clinical Information

Fabry disease is an X-linked recessive lysosomal storage disorder caused by a deficiency of the enzyme alpha-galactosidase A (alpha-Gal A). Reduced enzyme activity results in accumulation of glycosphingolipids in the lysosomes throughout the body, in particular, the kidney, heart, and brain. Severity and onset of symptoms are dependent on the residual enzyme activity. Symptoms may include acroparesthesias (pain crises), multiple angiokeratomas, reduced or absent sweating, corneal opacity, renal insufficiency leading to end-stage kidney disease, and cardiac and cerebrovascular disease. There are renal and cardiac variant forms of Fabry disease that may be underdiagnosed. Female patients who are carriers of Fabry disease can have clinical presentations ranging from asymptomatic to severely affected, and they may have alpha-Gal A activity in the normal range. The estimated incidence varies from 1 in 3000 infants detected via newborn screening to 1 in 10,000 male patients diagnosed after onset of symptoms.

Unless irreversible damage has already occurred, treatment with enzyme replacement therapy leads to significant clinical improvement in affected individuals. For this reason, early diagnosis and treatment are desirable. 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, 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 male and female patients. Molecular genetic testing is the recommended diagnostic test for female patients as alpha-galactosidase activity may be in the normal range in those affected.

The glycosphingolipid, globotriaosylsphingosine (LGb3), may be elevated in symptomatic patients and supports a diagnosis of Fabry disease. It may also be helpful as a tool for monitoring disease progression as well as determining treatment response in known patients. In addition, measurement of LGb3, may provide additional diagnostic information in the evaluation of uncertain cases, such as in asymptomatic heterozygous female patients, individuals with novel *GLA* variants of unclear clinical significance, as well as asymptomatic patients identified by family screening.

Reference Values

< or =1.0 ng/mL

Interpretation

Elevation of globotriaosylsphingosine is diagnostic for Fabry disease.

Cautions

Carrier detection using globotriaosylsphingosine (LGb3) is unreliable.

Some patients with Fabry disease may, and all individuals with pseudodeficiency of alpha-galactosidase enzyme, have normal concentrations of LGb3.

Clinical Reference

1. Aerts JM, Groener JE, Kuiper S, et al: Elevated globotriaosylsphingosine is a hallmark of Fabry disease. Proc Natl Acad Sci USA. 2008 Feb 26;105(8)2812-2817
2. Mehta A, Hughes DA: Fabry disease. In: Adam MP, Everman DB, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2002. Updated January 27, 2022. Accessed January 17, 2023. Available at www.ncbi.nlm.nih.gov/books/NBK1292/
3. 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
4. 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
5. Weidemann F, Beer M, Kralewski M, Siwy J, Kampmann C: Early detection of organ involvement in Fabry disease by biomarker assessment in conjunction with LGE cardiac MRI: results from the SOPHIA study. Mol Genet Metab. 2019 Feb;126(2):169-182

Performance

Method Description

Internal standard is added to the serum. Globotriaosylsphingosine (LGb3) is extracted from the serum prior to injection onto a liquid chromatography tandem mass spectrometry (LC-MS/MS) system. Following chromatographic isolation, the concentration is measured by MS/MS analysis in the selected reaction monitoring positive mode. The ratio of extracted peak area to internal standard is utilized to calculate the concentration of LGb3 in the sample.(Unpublished Mayo

method)

PDF Report
No

Day(s) Performed
Thursday

Report Available
8 to 14 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
82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LGB3S	Lyso-GB3, S	90234-6

Result ID	Test Result Name	Result LOINC® Value
BG708	Reason for Referral	42349-1
65532	Lyso-GB3, S	90234-6
113176	Interpretation (LGB3S)	59462-2
113177	Reviewed By	18771-6