MAYO CLINIC LABORATORIES

Test Definition: LGBBS

Globotriaosylsphingosine, BS

Overview

Useful For

Diagnosing and monitoring of patients with Fabry disease using dried blood spots when a serum specimen is not available

This test is **not intended for** newborn screening followup.

Special Instructions

- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

Serum is the recommended specimen type for monitoring patients with Fabry Disease. For more information see LGB3S / Globotriaosylsphingosine, Serum.

Specimen Required

Supplies:

-Card-Blood Spot Collection (Filter Paper) (T493)

-Card-Postmortem Screening (Filter Paper) (T525)

Container/Tube:

Preferred: Blood Spot Collection (Filter Paper)

Acceptable: PerkinElmer (formerly Ahlstrom) 226 filter paper, Munktell filter paper, Postmortem Screening Card or collected with EDTA, sodium heparin, lithium heparin, or ACD B-containing devices

Specimen Volume: 2 Blood spots

Collection Instructions:

1. Let blood dry completely on filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
2. At least 1 spot should be complete, (ie, unpunched).
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.

Additional Information:

1. For collection instructions, see Blood Spot Collection Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777).
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800).

Forms

Biochemical Genetics Patient Information (T602)

Reject Due To

Shows serum rings	Insufficient specimen	Reject

Specimen Minimum Volume

1 Blood spot

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated (preferred)	10 days	FILTER PAPER
	Frozen	59 days	FILTER PAPER
	Ambient	10 days	FILTER PAPER

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 in 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, kidney 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 heterozygous for 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 has led to significant clinical improvement in affected individuals. For this reason, early diagnosis and treatment are desirable, and early detection of Fabry disease through newborn screening has been implemented in a few US states.

Absent or reduced alpha-GAL A in leukocytes (AGAW / Alpha-Galactosidase, Leukocytes), serum (AGAS / Alpha-Galactosidase, Serum), or blood spots (AGABS / Alpha-Galactosidase, Blood Spot) can reliably diagnose classic or variant Fabry disease in male patients. Molecular genetic testing is the recommended diagnostic test for female patients as alpha-GAL A activity may be in the normal range in an affected female patient. 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 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
Cutoff: < or =0.034 nmol/mL

Interpretation
An elevation of globotriaosylsphingosine is suggestive of Fabry disease.

Cautions
Some patients with Fabry disease may have normal concentrations of globotriaosylsphingosine.

Clinical Reference
1. Alharbi FJ, Baig S, Auray-Blais C, Boutin M, et al: Globotriaosylsphingosine (Lyso-Gb3) as a biomarker for cardiac variant (N215S) Fabry disease. J Inherit Metab Dis. 2018 Mar;41(2):239-247. doi: 10.1007/s10545-017-0127-2.
2. Vardarli I, Rischpler C, Herrmann K, Weidemann F: Diagnosis and screening of patients with Fabry disease. Ther Clin Risk Manag. 2020 Jun 22;16:551-558. doi: 10.2147/TCRM.S247814.
3. Mehta A, Hughes DA: Fabry disease. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2002. Updated January 5, 2017. Accessed November 10, 2020. Available at www.ncbi.nlm.nih.gov/books/NBK1292/

Performance

Method Description
A 3-mm dried blood spot is extracted with internal standard. The extract is subjected to liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. The MS/MS is operated in the multiple reaction monitoring positive mode to follow the precursor to product species transitions for each analyte and internal standard. The ratio of the extracted peak areas to internal standard is determined by LC-MS/MS is used to calculate the concentration of in the sample.(Unpublished Mayo method)

PDF Report
No

Specimen Retention Time
Normal result: 2 months; Abnormal result: Indefinitely

Performing Laboratory Location
Rochester

Fees & Codes

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

82542