Overview

Useful For
Diagnosis of Fabry disease in male patients
Preferred screening test (serum) for Fabry disease

Genetics Test Information
Serum is the preferred screening specimen.

Enzyme testing is useful in identifying affected males.

Testing Algorithm
The following algorithms are available in Special Instructions:

- 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 in Special Instructions.

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

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.

Additional Testing Requirements
Urine sediment analysis (CTSA / Ceramide Trihexosides and Sulfatides, 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 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

3. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume
0.2 mL

Reject Due To

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<td>Gross icterus</td>
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Specimen Stability Information

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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. 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 end-stage renal disease (ESRD) typically occurs in adulthood, followed by cardiovascular and cerebrovascular disease. The estimated incidence varies from 1 in 3,000 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 (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 (AGA / 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 ceramide trihexosides (CTSA / Ceremide Trihexosides and Sulfatides, Urine) may be elevated in patients with Fabry disease and may aid in the diagnostic evaluation of female patients and in individuals with a variant of uncertain significance in GLA.

See Fabry Disease Testing Algorithm and Fabry Disease: Newborn Screen-Positive Follow-up in Special Instructions.

Reference Values

0.074-0.457 U/L

Note: Results from this assay are not useful for 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 (AGA / Alpha-Galactosidase, Leukocytes).

Cautions

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


Performance

Method Description

PDF Report
No

Day(s) and Time(s) Test Performed
Varies

Analytic Time
8 days

Maximum Laboratory Time
15 days

Specimen Retention Time
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

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