Overview

Useful For
Diagnosis of Fabry disease in males

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

Genetics Test Information
Enzyme testing is useful in identifying affected males.

Highlights
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.

This test is used for the diagnosis of Fabry disease in males only.

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

This test is not suitable for carrier detection in females. It is recommended that molecular testing (FABRZ / Fabry Disease, Full Gene Analysis) be performed for diagnosis in females.

Testing Algorithm
The following algorithms are available in Special Instructions:

- Fabry Disease: Newborn Screen-Positive Follow-up
- Fabry Disease 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 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
Test Definition: AGA
Alpha-Galactosidase, Leukocytes

**Advisory Information**
Enzyme levels for carriers are usually within the normal range. Order FABRZ / Fabry Disease, Full Gene Analysis for carrier testing.

**Shipping Instructions**
For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 72 hours of draw to be stabilized. Specimen received after 72 hours could have falsely normal results. Draw specimen Monday through Thursday only and not the day before a holiday. Specimen should be drawn 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)

**Specimen Volume:** 6 mL

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

**Specimen Minimum Volume**
5 mL

**Reject Due To**

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<tr>
<th>Condition</th>
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<tr>
<td>Hemolysis</td>
<td>Mild OK; Gross reject</td>
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<tr>
<td>Lipemia</td>
<td>NA</td>
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<tr>
<td>Icterus</td>
<td>NA</td>
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<tr>
<td>Other</td>
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**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
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<tbody>
<tr>
<td>Whole Blood ACD</td>
<td>Refrigerated (preferred)</td>
<td>72 hours</td>
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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 glycosylphospholipids in tissues throughout the body, in particular, the kidney, heart, and brain. Fabry disease is due to mutations within the GLA gene, and more than 630 mutations have been identified in individuals diagnosed with Fabry disease. Severity and onset of symptoms are dependent on the amount of residual enzyme activity. The classic form of Fabry disease occurs in males 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 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.

Males with residual a-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 end stage renal disease (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 have normal levels of alpha-Gal A. Therefore, molecular genetic analysis of the GLA gene (FABRZ / Fabry Disease, Full Gene Analysis) 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. 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, 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) allows for detection of the disease-causing mutation in males and females.

The following algorithms are available in Special Instructions:

- Fabry Disease: Newborn Screen-Positive Follow-up
- Fabry Disease Testing Algorithm

**Reference Values**

> or =23.1 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
Deficiency of alpha-galactosidase A (alpha-Gal A) is diagnostic for Fabry disease in males.

Urine sediment analysis (CTSA / Ceramide Trihexosides and Sulfatides, Urine) for the accumulating trihexoside substrate is also recommended.

Carrier females usually have alpha-galactosidase levels in the normal range; therefore, molecular sequence analysis of the GLA gene (FABRZ / Fabry Disease, Full Gene Analysis) is recommended as the appropriate diagnostic test for females.

Cautions
Carrier detection using enzyme levels is unreliable in females. Mutation analysis (FABRZ / Fabry Disease, Full Gene Analysis) is the recommended test.

Individuals with pseudodeficiency alleles can show reduced alpha-galactosidase A enzyme activity with this assay.

Clinical Reference

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 Feb;81[2]:157-171)

PDF Report
No

Day(s) and Time(s) Test Performed
**Test Definition: AGA**

**Alpha-Galactosidase, Leukocytes**

Wednesday; Varies

**Analytic Time**

8 days

**Maximum Laboratory Time**

15 days

**Specimen Retention Time**

WBC homogenate stored 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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