Overview

Useful For
Confirmation of diagnosis of Pompe disease (as a follow-up to biochemical analyses)

Reflex Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
<tr>
<td>CULFB</td>
<td>Fibroblast Culture for Genetic Test</td>
<td>Yes</td>
<td>No</td>
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</table>

Testing Algorithm

If skin biopsy is received, fibroblast culture for genetic test will be added and charged separately.

See Newborn Screen Follow-up for Pompe Disease in Special Instructions.

For more information, see Newborn Screening Act Sheet Pompe Disease: Decreased Acid Alpha-Glucosidase in Special Instructions.

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screening Act Sheet Pompe Disease: Decreased Acid Alpha-Glucosidase
- Newborn Screen Follow-up for Pompe Disease
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name
Polymerase Chain Reaction (PCR) Followed by DNA Sequence Analysis

NY State Available
Yes

Specimen

Specimen Type
Varies

Shipping Instructions
Specimen preferred to arrive within 96 hours of collection.

Specimen Required
Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1740 for instructions for testing patients who have received a bone marrow transplant.
Submit only 1 of the following specimens:

**Preferred:**

**Specimen Type:** Whole blood

**Container/Tube:**

**Preferred:** Lavender top (EDTA) or yellow top (ACD)

**Acceptable:** Any anticoagulant

**Specimen Volume:** 3 mL

**Collection Instructions:**

1. Invert several times to mix blood.
2. Send specimen in original tube.

**Specimen Stability Information:** Ambient (preferred)/Refrigerated

**Specimen Type:** Cultured fibroblasts

**Container/Tube:** T-75 or T-25 flask

**Specimen Volume:** 1 Full T-75 or 2 full T-25 flasks

**Specimen Stability Information:** Ambient (preferred)/Refrigerated 24 hours

**Specimen Type:** Skin biopsy

**Supplies:** Eagle’s minimum essential medium with 1% penicillin and streptomycin (T115) tubes are available upon request.

**Container/Tube:** Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.

**Specimen Volume:** 4-mm punch

**Specimen Stability Information:** Refrigerated (preferred)/Ambient

**Specimen Type:** Blood spot

**Supplies:** Whatman Protein Saver 903 Paper or Ahlstrom 226 filter paper or Blood Spot Collection Card (T493)
Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: Ahlstrom 226 filter paper, or Blood Spot Collection Card

Specimen Volume: 2 to 5 Blood Spots on collection card

Collection Instructions:

1. An alternative blood collection option for a patient >1 year of age is finger stick.

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.

3. Do not expose specimen to heat or direct sunlight.

4. Do not stack wet specimens.

5. Keep specimen dry

Specimen Stability Information: Ambient (preferred)/Refrigerated

Additional Information:

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

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

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

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. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521) 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

Blood: 1 mL
Blood Spots: 5 punches-3 mm diameter

Reject Due To

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.
Pompe disease, also known as glycogen storage disease type II, is an autosomal recessive condition caused by deficiency of acid alpha-glucosidase. Enzyme insufficiency results in symptoms such as muscle weakness, cardiomyopathy, and respiratory problems. Mutations in the GAA gene (which encodes acid alpha-glucosidase) are associated with Pompe disease.

The diagnosis of this heterogeneous condition relies on both clinical and laboratory evaluation. Clinically, the condition is categorized into infantile and late-onset forms based on age of onset, organ involvement, and rate of progression. The infantile form (or classic Pompe disease) is the most severe form and is characterized by early onset and rapid progression of cardiac, liver, and muscle problems resulting in death within the first year. The infantile variant form has a similar age of onset but a milder clinical presentation. On the less severe end of the spectrum is the late-onset form with childhood, juvenile, or adult onset. The rate of progression and severity of symptoms is quite variable, particularly in the late-onset forms. The incidence varies by clinical type and ethnic population; the combined incidence is approximately 1 in 40,000 individuals.

Biochemical testing of acid alpha-glucosidase in blood spot specimens or fibroblasts is useful for individuals with a suspected diagnosis of Pompe disease (GAABS / Acid Alpha-Glucosidase, Blood Spot). When clinical manifestations and results of that analysis are supportive of a diagnosis of Pompe disease, mutation analysis of the GAA gene is warranted.

Over 250 different mutations have been identified in this gene including point mutations and large deletions. GAA full gene sequencing provided by this test will detect 2 mutations in approximately 83% to 93% of individuals with confirmed GAA enzyme deficiency. Identification of mutations provides confirmation of the diagnosis and allows for subsequent testing of at risk family members.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of Pompe disease may have a mutation that is not identified by this method (eg, large genomic deletions or duplications, promoter mutations). The absence of a mutation(s), therefore, does not eliminate the possibility of positive carrier status or the diagnosis of Pompe disease. For carrier testing, it is important to first document the presence of a GAA gene mutation in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.
Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

**Clinical Reference**


**Performance**

**Method Description**

Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the GAA gene. (Unpublished Mayo method)

**PDF Report**

No

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

Performed weekly, varies

**Analytic Time**

14 days

**Maximum Laboratory Time**

20 days

**Specimen Retention Time**

Whole Blood: 2 weeks (if available) Extracted DNA: 3 months

**Performing Laboratory Location**

Rochester

**Fees and Codes**

Fees
Test Definition: GAAZ
Pompe Disease Full Gene Analysis

- 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
81406-GAA (glucosidase, alpha; acid) (eg, glycogen storage disease type II [Pompe disease]), full gene sequence
Fibroblast Culture for Genetic Test
88233-Tissue culture, skin or solid tissue biopsy (if appropriate)
88240-Cryopreservation (if appropriate)

LOINC® Information

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