## Overview

### Useful For

Evaluation of patients with a clinical presentation suggestive of Pompe disease (muscle hypotonia, weakness, or cardiomyopathy) outside of the newborn screening setting

### Highlights

This test is used to diagnose Pompe disease and is based upon a ratio calculated between the creatine (Cre) and creatinine (Crn) ratio and the activity of acid-alpha glucosidase (GAA).

This test can help differentiate true cases of infantile and late onset Pompe disease from false-positive cases such as carriers and pseudodeficiency of GAA enzyme.

A positive test result supports the utility of follow-up molecular genetic analysis of the *GAA* gene.

### Testing Algorithm

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

### Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screen Follow-up for Pompe Disease
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions

### Method Name

Flow Injection Analysis-Tandem Mass Spectrometry (FIA-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Whole blood

### Advisory Information

Due to reference range differences, this test is the appropriate test for patients older than 6 weeks of age. For patients 6 weeks of age or younger, order PD2T / Pompe Disease Second-Tier Newborn Screening, Blood Spot.

### Specimen Required

**Supplies:** Card-Blood Spot Collection (Filter Paper) (T493)

**Container/Tube:**

**Preferred:** Card-Blood Spot Collection (Filter Paper)

**Acceptable:** Ahlstrom 226 filter paper, Munktell filter paper, Whatman Protein Saver 903 paper, or blood collected in

tubes containing ACD, EDTA, or heparin and dried on filter paper

**Specimen Volume:** 3 blood spots

**Collection Instructions:**

1. Let blood dry completely on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.

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

3. Do not stack wet specimens.

4. Keep specimen dry.

**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 in required.** Please document on the request form or electronic order that a copy is on file. An Informed Consent for Genetic Testing (T576) is available in Special Instructions.

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

1 blood spot

## Reject Due To

| | |
|---|---|
| Blood spot | Shows serum rings or has multiple layers |

## Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Whole blood | Refrigerated (preferred) | 56 days | FILTER PAPER |
| | Frozen | 56 days | FILTER PAPER |
| | Ambient | 7 days | FILTER PAPER |

## Clinical and Interpretive

### Clinical Information

Pompe disease, also known as glycogen storage disease type II, is an autosomal recessive disorder caused by a deficiency of the lysosomal enzyme acid alpha-glucosidase (GAA; acid maltase) due to mutations in the *GAA* gene. The estimated incidence is 1 in 40,000 live births. In Pompe disease, glycogen that is taken up by lysosomes during physiologic cell turnover accumulates, causing lysosomal swelling, cell damage and, eventually, organ dysfunction. This leads to progressive muscle weakness, cardiomyopathy, and, eventually, death. Patients with Pompe disease, especially those with infantile, childhood, and juvenile onset, can have elevations of serum enzymes (such as creatine kinase) secondary to cellular dysfunction. Delayed diagnosis of symptomatic patients with later onset Pompe disease is not unusual due to nonspecific and overlapping presentation (such as proximal muscle weakness and respiratory insufficiency) with more common neuromuscular diseases.

The clinical phenotype of Pompe disease lies on a spectrum, with differing clinical phenotypes dependent on age of onset and residual enzyme activity. Complete loss of enzyme activity causes onset in infancy leading to death, typically within the first year of life when left untreated. Juvenile and adult-onset forms, as the names suggest, are characterized by later onset and longer survival. All disease variants are eventually associated with progressive muscle weakness and respiratory insufficiency. Cardiomyopathy is associated almost exclusively with the infantile form. Treatment with enzyme replacement therapy is available, making prompt diagnosis of Pompe disease desirable, as early initiation of treatment may improve prognosis.

The ratio calculated between the creatine (Cre):creatinine (Crn) ratio as the numerator and the activity of GAA as the denominator can differentiate true cases of infantile and late-onset Pompe disease from false-positive cases such as carriers and pseudodeficiency of GAA enzyme. This determination can be performed in a timely fashion and provide better guidance in the decision to submit samples for further confirmatory testing by molecular genetic analysis (GAAZ / Pompe Disease, Full Gene Analysis).

### Reference Values

An interpretive report will be provided.

### Interpretation

An interpretive report (including acid alpha-glucosidase (GAA) activity and [Creatine/Creatinine]/GAA ratio, if applicable) is provided.

The quantitative measurements of informative metabolites and related ratios are evaluated using the Collaborative Laboratory Integrated Reports (CLIR) system. The report is in text form only, indicating if the applicable ratio is normal or abnormal and whether or not the CLIR postanalytical tool is informative for Pompe disease. Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. To verify a preliminary diagnosis, independent biochemical (ie, in vitro enzyme assay) or molecular genetic analyses are required, many of which are offered within Mayo Clinic's Division of Laboratory Genetics and Genomics. Recommendations for additional biochemical testing and confirmatory studies (enzyme assay, biomarker testing, molecular analysis) are provided in the interpretative report.

### Cautions

For asymptomatic individuals, this test may not detect some late-onset and variant forms of Pompe disease.

Carrier status (heterozygosity) for Pompe disease cannot be reliably detected.

A positive test result is strongly suggestive of a diagnosis but requires follow-up molecular genetic analysis of the *GAA* gene, which is best coordinated by local genetics providers.

## Clinical Reference

1. Pascual JM, Roe CR: Systemic Metabolic Abnormalities in Adult-onset Acid Maltase Deficiency. JAMA Neurol 2013;70(6):756-763

2. Tortorelli S, Eckerman JS, Orsini JJ, et al: Moonlighting newborn screening markers: The incidental discovery of a second tier test for Pompe disease Genet Med Epub ahead of print: 2017 Nov 2. doi: 10.1038/gim.2017.190

## Performance

## Method Description

Dried blood spots are processed using 2 analytical protocols with postanalytical integration of all test results.

Protocol 1:

A dried blood spot is extracted by the addition of methanol with known concentrations of isotopically labeled amino acids and acylcarnitines, which are used as internal standards. The extract is derivatized by the addition of 3M HCl in n-butanol. From the residual blood spot a second extraction and derivatization is performed and analyzed concurrently by electrospray tandem mass spectrometry (ESI-MS/MS) for creatine and creatinine.(Turgeon C, Magera M, Allard P, et al: Combined newborns screening for succinylacetone, amino acids, and acylcarnitines in dried blood spots. Clin Chem 2008;54[4]:657-664)

Protocol 2:

Two 3-mm dried blood spots are excised from a single specimen and placed into individual plates. One spot is treated with a solution containing substrate and internal standard for acid sphingomyelinase (ASM), beta-glucocerebrosidase (ABG), alpha-glucosidase (GAA), alpha-galactosidase (GLA), galactocerebrosidase (GALC) and alpha-L-iduronidase (IDUA). The enzyme plate is sealed and incubated overnight. Following the incubation the enzyme plate is purified by liquid-liquid extraction. The second dried blood spot is extracted with methanol containing d4-C26 lysophosphatidylcholines (LPC) on day 2 of the procedure. The LPC extracts and enzyme products are combined and analyzed concurrently by ESI-MS/MS.(Tortorelli S, Turgeon C, Gavrilov D, et al: Simultaneous testing for 6 lysosomal storage disorders and X-adrenoleukodystrophy in dried blood spots by tandem mass spectrometry. Clin Chem 2016;62[9]:1248-1254)

## PDF Report

No

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

Monday through Saturday; 4 p.m.

Sunday; 1 p.m.

## Analytic Time

2 days

## Maximum Laboratory Time

3 days

## Specimen Retention Time

Indefinitely

## 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

83789

### LOINC® Information

| Test ID | Test Order Name | Order LOINC Value |
|---|---|---|
| PDBS | Pompe Disease, BS | 63416-2 |

| Result ID | Test Result Name | Result LOINC Value |
|---|---|---|
| 602290 | Interpretation | 59462-2 |
| 602300 | Reviewed By | 18771-6 |