Test Definition: PDBS

Pompe Disease, Blood Spot

Overview

Useful For

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

Testing Algorithm

For information see Newborn Screen Follow-up for Pompe Disease.

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

Highlights

This test is used to diagnose Pompe disease. It is based upon a ratio calculated between the creatine and creatinine 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.

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

Due to reference range differences, this 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: Blood Spot Collection Card
Acceptable: PerkinElmer 226 filter paper, Munktell filter paper, Whatman Protein Saver 903 paper, local newborn screening card, or blood collected in tubes containing ACD or EDTA, and dried on filter paper
Specimen Volume: 3 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Sample.
2. Completely fill at least 3 circles on the filter paper card (approximately 100 microliters blood per circle).
3. Let blood dry completely on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. 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

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

1 Blood spot

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers	Reject
Insufficient specimen	Reject
Specimens known to have been exposed to elevated temperatures	Reject

above ambient	

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated (preferred)	90 days	
	Ambient	28 days	
	Frozen	90 days	

Clinical & 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 variants 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 elevated 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 using the creatine:creatinine 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 guidance in the decision to submit samples for additional confirmatory testing by molecular genetic analysis (GAAN / Pompe disease, *GAA* Gene Sequencing with Deletion/Duplication, Varies).

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) will be 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 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 by Mayo Clinic Laboratories. 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: beyond muscle glycogen accumulation. 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. 2018;20(8):840-846. doi:10.1038/gim.2017.190
3. Leslie N, Bailey L. Pompe Disease. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 1993-2025. Updated August 21, 2025. Accessed October 2, 2025. Available at: www.ncbi.nlm.nih.gov/books/NBK1261/

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 containing known concentrations of isotopically labeled amino acids and acylcarnitines, which are used as internal standards. The extract is derivatized by the addition of 3M hydrochloric acid in n-butanol. From the residual blood spot, a second extraction and derivatization are performed and analyzed concurrently by flow injection tandem mass spectrometry for creatine and creatinine.(Turgeon C, Magera MJ, 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:
Three 1/8-inch dried blood spots (DBS) are excised from a single specimen. The enzymes are extracted from 2 DBS by incubating the specimens with a mix of substrate and internal standard for acid sphingomyelinase, beta-glucocerebrosidase, alpha-glucosidase, alpha-galactosidase, galactocerebrosidase, alpha-L-iduronidase, and iduronate 2-sulfatase. The sample is then purified by liquid-liquid extraction. The third DBS is extracted with methanol containing d4-C26 lysophosphatidylcholines. The resulting extracts are then combined, evaporated, and reconstituted before analysis by tandem mass spectrometry.(Tortorelli S, Turgeon C, Gavrilov D, et al. Simultaneous testing for 6

lysosomal disorders and X-adrenoleukodystrophy in dried blood spots by tandem mass spectrometry. Clin Chem. 2016;62[9]:1248-1254)

PDF Report
No

Day(s) Performed
Monday through Sunday

Report Available
2 to 3 days

Specimen Retention Time
6 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US 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