Overview

Useful For
Diagnosing Pompe disease, when used in conjunction with acid alpha-glucosidase enzyme activity assays and molecular genetic analysis of the GAA gene

Monitoring Pompe patients on enzyme replacement therapy

May support the diagnosis and monitoring of other glycogen storage disorders; however, glucotetrasaccharide (Glc4) excretion appears to be less consistently elevated in glycogen storage disorders other than Pompe disease

This test is not useful for carrier screening

Highlights
Increased accumulation of glycogen in the lysosome is a typical finding due to lack of the lysosomal enzyme acid alpha-glucosidase (GAA). Excess glycogen is degraded to glucotetrasaccharide, which is excreted in urine.

Most individuals with glycogen storage disorder type II (GSD II, Pompe disease) and other glycogen storage disorders excrete glucotetrasaccharides in their urine.

Measuring glucotetrasaccharide in the urine can be helpful when employed in conjunction with GAA enzyme activity assay and molecular genetic analysis of the GAA gene.

Measuring glucotetrasaccharide in the urine of GSD II patients undergoing enzyme replacement therapy (ERT) has been reported as a useful tool for monitoring the effects of treatment.

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

Special Instructions
- Newborn Screen Follow-up for Pompe Disease

Method Name
Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Urine

Additional Testing Requirements
When requested for the diagnosis of Pompe disease (GSD II), glucotetrasaccharide concentrations in urine need to be interpreted in light of the clinical presentation and other laboratory tests, such as blood creatine kinase, alpha-glucosidase (GAA) activity, and GAA genotype.

Necessary Information
Patient's age and reason for referral are required.

**Specimen Required**

**Supplies:** Aliquot Tube, 5 mL (T465)

**Container/Tube:** Plastic, 5-mL urine tube

**Specimen Volume:** 3 mL

**Collection Instructions:**

1. Collect a random urine specimen.

2. No preservative.

**Forms**

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

**Specimen Minimum Volume**

1 mL

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

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**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). This leads to an accumulation of glycogen in the lysosome causing swelling, cell damage, and progressive organ dysfunction. In glycogen storage diseases, excess glycogen is degraded to glucotetrasaccharide (glucose tetrasaccharide: Glc4), which is excreted in urine. Measurement of Glc4 in urine is used for both initial diagnosis and monitoring of patients with Pompe disease.

Pompe disease is caused by deleterious variants in the *GAA* gene. The classic, early infantile onset form of the disease is characterized by progressive muscle hypotonia, weakness, hypertrophic cardiomyopathy, and death due to either cardiorespiratory or respiratory failure typically by the end of the first year of life. Juvenile and adult-onset forms of Pompe disease are characterized by later onset and longer survival. Primary symptoms of later-onset Pompe disease include muscle weakness and respiratory insufficiency, with cardiomyopathy only rarely developing. Based on data from newborn screening, the incidence is approximately 1 in 20,000 live births with most patients...
being affected with later onset forms of Pompe disease. The clinical phenotype depends on residual enzyme activity, with complete loss of activity causing onset in infancy.

Enzyme replacement therapy (ERT) improves outcome in many patients with either classic infantile onset or later onset Pompe disease. Early initiation of treatment improves the prognosis and makes early diagnosis of Pompe disease desirable. Because of this, newborn screening for Pompe disease has recently been added to the Recommended Uniform Screening Panel and already been implemented in some states.

Historically, diagnostic testing required a skin or muscle biopsy to measure GAA enzyme activity. Today, noninvasive enzyme assays and molecular genetic analysis of the GAA gene (GAAZ / Pompe Disease, Full Gene Analysis, Varies) are available for testing in blood and dried blood spots. In addition, Glc4 can be measured in urine to support a diagnosis of Pompe disease and other glycogen storage disorders.

Reference Values
< or =14 months: < or =14.9 mmol/mol Cr
> or =15 months: < or =4.0 mmol/mol Cr

Interpretation
An elevated excretion of glucotetrasaccharide is indicative of Pompe disease or other glycogen storage disorders.

Enzyme or molecular analysis is required to confirm suspected diagnosis.

Cautions
Elevated glucotetrasaccharide (Glc4) result may be due to dietary artifacts particularly ingestion of carbohydrates.

Clinical Reference

Performance
Method Description
A random urine sample is corrected per creatinine content. The creatinine-corrected urine is combined with ammonium hydroxide and internal standard in a 96-well filter plate. After centrifugation, an aliquot of the eluate is injected onto an amide column and analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) in negative mode. The ratio of the extracted peak area for glucotetrasaccharide to the internal standard is used to calculate the concentration of glucotetrasaccharide present.(Unpublished Mayo method)

PDF Report
No
Test Definition: HEX4
Glucotetrasaccharides, U

Day(s) and Time(s) Test Performed
Wednesday; 11 a.m.

Analytic Time
7 days (Not reported on Saturday or Sunday)

Maximum Laboratory Time
14 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
82542
82570

LOINC® Information

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