Test Definition: HEX4

Glucotetrasaccharides, Random, Urine

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 patients with Pompe disease 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.

Testing Algorithm

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

Special Instructions

- Newborn Screen Follow-up for Pompe Disease

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 Pompe disease (glycogen storage disorder type II: GSD II,) 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 patients with GSD II undergoing enzyme replacement therapy (ERT) has been reported as a useful tool for monitoring the effects of treatment.

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 (glycogen storage disorder type II), urine glucotetrasaccharide concentrations need to be interpreted in light of the clinical presentation and other laboratory test results, such as blood creatine kinase, alpha-glucosidase (GAA) activity, and GAA genotype.

Necessary Information

1. Patient's age is required.

2. Reason for testing is required.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

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 a Biochemical Genetics 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

Specimen Type	Temperature	Time	Special Container
Urine	Frozen (preferred)	87 days	
	Ambient	14 days	
	Refrigerated	28 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). 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 and may also be elevated in other glycogen storage disorders.

Pompe disease is caused by disease-causing variants in the *GAA* gene. The 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. The clinical phenotype depends on residual enzyme activity, with complete loss of activity causing onset in infancy.

Enzyme replacement therapy (ERT) improves outcomes in many patients with either classic infantile-onset or later-onset Pompe disease. Early initiation of treatment improves 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 (GAAW / Acid Alpha-Glucosidase, Leukocytes) and molecular genetic analysis of the *GAA* gene (GAAN / Pompe Disease, *GAA* Gene Sequencing with Deletion/Duplication, 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

An elevated glucotetrasaccharide (Glc4) result may be due to dietary artifacts, particularly ingestion of carbohydrates.

Normal glucotetrasaccharide (Glc4) levels may be seen in patients with late-onset Pompe disease.

Clinical Reference

1. Sluiter W, van den Bosch JC, Goudriann DA, et al. Rapid ultraperformance liquid chromatography-tandem mass spectrometry assay for a characteristic glycogen-derived tetrasaccharide in Pompe disease and other glycogen storage diseases. Clin Chem. 2012;58(7):1139-1147
2. Young S, Stevens RD, An Y, et al. Analysis of a glucose tetrasaccharide elevated in Pompe disease by stable isotope dilution–electrospray ionization tandem mass spectrometry. Anal Biochem. 2003;316(2):175-180
3. Chien YH, Goldstein JL, Hwu WL, et al. Baseline urinary glucose tetrasaccharide concentrations in patients with infantile- and late-onset Pompe disease identified by newborn screening. JIMD Rep. 2015;19:67-73
4. Young SP, Piraud M, Goldstein, JL, et al. Assessing disease severity in Pompe disease: the roles of a urinary glucose tetrasaccharide biomarker and imaging techniques. Am J Med Genet C Semin Med Genet. 2012;160C(1):50-58
5. Morales-Vila A, Corbalan-Rivas A, Carnero-Gregorio M, et al. Biomarkers in glycogen storage diseases: an update. Int. J Mol Sci. 2021;22(9):4381. doi:10.3390/ijms22094381

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 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

Day(s) Performed
Wednesday

Report Available
4 to 10 days

Specimen Retention Time
1 month

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
82542
82570

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HEX4	Glucotetrasaccharides, U	53868-6

Test Definition: HEX4

Glucotetrasaccharides, Random, Urine

Result ID	Test Result Name	Result LOINC® Value
64174	Glucotetrasaccharides, U	53868-6
BG710	Reason for Referral	42349-1
BA2896	Intepretation (HEX4)	59462-2
BA2897	Reviewed By	18771-6