

Overview

Useful For

Screening for selected oligosaccharidosis

Genetics Test Information

Oligosaccharidoses are characterized by the abnormal accumulation of incompletely degraded oligosaccharides in cells and tissues and the corresponding increase of related free oligosaccharides in the urine.

Clinical features of oligosaccharidoses often overlap; therefore, urine screening is an important tool in the initial workup for these disorders.

Enzyme or molecular analysis is required to make a definitive diagnosis.

Testing Algorithm

Oligosaccharide analysis may be considered in the workup of unexplained refractory epilepsy. For more information see [Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm](#) in Special Instructions.

Special Instructions

- [Biochemical Genetics Patient Information](#)
- [Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm](#)

Method Name

Matrix-Assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)

NY State Available

Yes

Specimen

Specimen Type

Urine

Advisory Information

This is the recommended test when clinical features are suggestive of, or when molecular testing results suggest, an oligosaccharidosis disorder identified by this test.

LSDS / Lysosomal Storage Disorders Screen, Random, Urine is the recommended screening test for the initial workup of a suspected lysosomal storage disorder particularly when clinical features are non-specific.

Necessary Information

1. **Patient's age is required.**

2. [Biochemical Genetics Patient Information](#) (T602, in Special Instructions) is recommended. This information aids in providing a more thorough interpretation of results. Send information with specimen.

Specimen Required

Supplies: Urine Tubes, 10 mL (T068)

Collection Container/Tube: Plastic, 10-mL urine tube

Specimen Volume: 8 mL

Pediatric Volume: 2 mL

Collection Instructions:

1. Collect a random urine specimen.
2. No preservative.
3. Immediately freeze specimen.

Forms

1. [Biochemical Genetics Patient Information](#) (T602) in Special Instructions
2. If not ordering electronically, complete, print, and send an [Inborn Errors of Metabolism Test Request](#) (T798) with the specimen.

Specimen Minimum Volume

2.5 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)	365 days	
	Refrigerated	15 days	
	Ambient	7 days	

Clinical and Interpretive

Clinical Information

The oligosaccharidoses (glycoproteinoses) are a subset of lysosomal storage disorders (LSD) caused by the deficiency of any one of the lysosomal enzymes involved in the degradation of complex oligosaccharide chains. They are characterized by the abnormal accumulation of incompletely degraded oligosaccharides in cells and tissues and the corresponding increase of related free oligosaccharides in the urine. Clinical diagnosis can be difficult due to the similarity of clinical features across disorders and their variable severity. Clinical features can include bone abnormalities, coarse facial features, corneal cloudiness, organomegaly, muscle weakness, hypotonia, developmental delay, and ataxia. Age of onset ranges from early infancy to adult and can even present prenatally.

The oligosaccharidoses and other storage disorders detected by this assay include alpha-mannosidosis, beta-



mannosidosis, aspartylglucosaminuria, fucosidosis, Schindler disease, GM1 gangliosidosis, Sandhoff disease, sialidosis, galactosialidosis, mucopolidoses types II and III, mucopolysaccharidosis IVA (Morquio A), mucopolysaccharidosis IVB (Morquio B), and Pompe disease (see table). Additional conditions that may be picked up by this test include other mucopolysaccharidoses, Gaucher disease, Krabbe disease, and some congenital disorders of glycosylation (*PMM2*, *NGLY1*, *MOGS*, *ALG1*, *MAN1B1*).

Conditions identifiable by method

Disorder	Onset	Gene	Enzyme deficiency	Worldwide incidence
Alpha-mannosidosis	Prenatal (type III) Infancy (type I) Juvenile/Adult (type II)	<i>MAN2B1</i>	Alpha-mannosidase	1:500,000
	Phenotype: continuum of clinical features ranging from severe and rapidly progressive disease to a milder and more slowly progressive course. Prenatal onset (type III) manifests as prenatal loss or early death from progressive neurodegeneration. Infantile onset (type I) is characterized by rapidly progressive mental retardation, hepatosplenomegaly, and severe dysostosis multiplex. Type II is milder and slower progressing with survival into adulthood.			
Beta-mannosidosis	Infancy to juvenile	<i>MANBA</i>	Beta-mannosidase	<100 patients described
	Phenotype: clinical features vary in severity and may include intellectual disability, respiratory infections, hearing loss, hypotonia, peripheral neuropathy, and behavioral issues.			
Aspartylglucosaminuria	Early childhood	<i>AGA</i>	Aspartylglucosaminidase	1:2,000,000 higher incidence in Finland approx 1:17,000
	Phenotype: normal appearing at birth followed by progressive neurodegeneration at 2-4 years, frequent respiratory infections, coarse features, thick calvarium, and osteoporosis. Slowly progressive mental decline into adulthood.			
Alpha-fucosidosis	Infancy to early childhood	<i>FUCA1</i>	Alpha-fucosidase	<100 patients described
	Phenotype: continuum within a wide spectrum of severity; clinical features include neurodegeneration, coarse facial features, growth delay, recurrent infections, dysostosis multiplex, angiokeratoma, and elevated sweat chloride.			
Schindler disease	Infancy (type I)	<i>NAGA</i>	Alpha-N-acetyl-galactosaminidase	<30 patients described
	Early childhood (type III)			
Adult (type II)				
Phenotype: continuum of clinical features ranging from severe and rapidly progressive disease to a milder and more slowly progressive course; infantile onset (type I) is characterized by rapidly progressive neurodegeneration. Type II is adult onset characterized by angiokeratoma and mild cognitive impairment, and type III is an intermediate and variable form ranging from seizures and psychomotor delay to milder autistic features.				



GM1 g angliosidosis	Infancy (type I)	<i>GLB1</i>	Beta-galactosidase (Beta-Gal)	1:200,000
	Late infantile/juvenile (type II)			
	Adult (type III)	<p>Phenotype: continuum of clinical features ranging from severe and rapidly progressive disease to a milder and more slowly progressive course; infantile onset (type I) is characterized by early developmental delay/arrest followed by progressive neurodegeneration, skeletal dysplasia, facial coarseness, hepatosplenomegaly, and macular cherry red spot. Later onset forms (types II and III) are milder and observed as progressive neurologic disease and vertebral dysplasia. Adult onset presents mainly with dystonia.</p>		
GM2 ga ngliosidosis variant 0 (Sandhoff disease)	Early infancy to juvenile or adult	<i>HEXB</i>	Beta-hexosaminidase A and B	1:400,000
	<p>Phenotype: infantile onset is characterized by rapidly progressive neurodegeneration, exaggerated startle reflex, "cherry red spot". Milder later-adult onset forms of the disease exist presenting with neurological problems such as ataxia, dystonia, spinocerebellar degeneration, and behavior changes.</p>			
Sialidosis (ML I)	Early adulthood (type I)	<i>NEU1</i>	Alpha-neuraminidase (Neu)	<30 patients described
	Earlier for congenital, infantile, and juvenile forms (type II)			
	<p>Phenotype: continuum of clinical features ranging from severe disease (type II) to a milder and more slowly progressive course (type I). Clinical features range from early developmental delay, coarse facial features, short stature, dysostosis multiplex, and hepatosplenomegaly to late onset cherry-red spot myoclonus syndrome. Seizures, hyperreflexia, and ataxia have been reported in more than 50% of later onset patients. A congenital form of the disease has been reported in which patients present with fetal hydrops or neonatal ascites.</p>			
Galactosialidosis	Early infancy, late infancy or early adult	<i>CTSA</i>	Cathepsin A causing secondary deficiencies in Beta-Gal and Neu	<30 patients described
	<p>Phenotype: continuum of clinical features ranging from severe and rapidly progressive disease to a milder and more slowly progressive course; clinical features of the early infantile type include fetal hydrops, edema, ascites, visceromegaly, dysostosis multiplex, coarse facies, and cherry red spot. The majority of patients have milder presentations, which include ataxia, myoclonus, angiokeratoma, cognitive and neurologic decline.</p>			



Mucopolysaccharidosis II -alpha-beta (I-cell)	Early infancy	<i>GNPTAB(alpha/beta)</i>	N-acetylglucosaminyl-1-phosphotransferase deficiency causing secondary intracellular deficiency of multiple enzyme activities	1:300,000
	Early childhood, may live well into adulthood	<i>GNPTG (gamma)</i>		
Mucopolysaccharidosis II I-alpha-beta and III-gamma (pseudo-Hurler polydystrophy)	Phenotype: I-cell resembles Hurler with short stature and skeletal anomalies, but presents earlier, is more severe, and can include cardiomyopathy and coronary artery disease. Pseudo-Hurler polydystrophy is milder and later presenting.			
Mucopolysaccharidosis IVB (Morquio B)	Infancy to adult	<i>GLB1</i>	Beta-Gal	1:75,000 N. Ireland 1:640,000 W. Australia
	Phenotype: progressive condition that largely affects the skeletal system. Features include short-trunk dwarfism, skeletal (spondyloepiphyseal) dysplasia, fine corneal deposits, and preservation of intelligence.			
Pompe disease (glycogen storage disease type II)	Early infancy	GAA	Alpha-glucosidase	1:40,000
	Late onset (childhood-adult)			
Phenotype: infantile onset is characterized by prominent cardiomegaly, hepatomegaly, hypotonia, and weakness. Later onset forms present with proximal muscle weakness and respiratory insufficiency.				

Reference Values

An interpretive report will be provided.

Interpretation

This is a screening test; not all oligosaccharidoses are detected. The resulting excretion profile may be characteristic of a specific disorder; however, abnormal results require confirmation by enzyme assay or molecular genetic testing.

When abnormal results are detected with characteristic patterns, a detailed interpretation is given, including an overview of results and significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional confirmatory studies (enzyme assay, molecular genetic analysis).

Cautions

This test may give false-negative results, especially in older patients with mild clinical presentations.

This test may give false-positive results for Pompe disease, especially in pediatric patients on infant formula.

Clinical Reference

1. Neufeld EF, Muenzer J. The mucopolysaccharidoses. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. *The Online Metabolic and Molecular Bases of Inherited Disease*. McGraw-Hill; 2020. Accessed May 01, 2020. Available at: <http://ommbid.mhmedical.com/content.aspx?bookid=2709§ionid=225544161>

2. Enns GM, Steiner RD, Cowan TM: Lysosomal disorders. In: Sarafoglou K, Hoffmann GF, Roth KS eds. *Pediatric Endocrinology and Inborn Errors of Metabolism*. McGraw Hill Medical; 2009

Performance**Method Description**

Urine samples are extracted using Oasis HLB and carbograph columns and lyophilized overnight. Oligosaccharides are permethylated, replacing all hydroxy groups (-OH) with methoxy groups (-OCH₃) and esterifies carboxyl groups (-COOH) to (-COOCH₃). After permethylation, the tubes are centrifuged and the supernatant taken off of the sodium hydroxide pellet. The supernatant is quenched, neutralized, extracted onto an Oasis HLB column, eluted and lyophilized again overnight. Specimens are resuspended, mixed with a matrix solution containing 2,5-dihydroxybenzoic acid, spotted onto a MALDI plate, and allowed to air dry. The plate is then analyzed using a matrix-assisted laser desorption/ionization tandem time-of-flight (MALDI TOF/TOF) 5800 Analyzer. (Xia B, Asif G, Arthur L, et al: Oligosaccharide analysis in urine by MALDI-TOF mass spectrometry for the diagnosis of lysosomal storage diseases. *Clin Chem*. 2013 Sep;59(9):1357-1368)

PDF Report

No

Day(s) and Time(s) Test Performed

Varies

Analytic Time

8 days

Maximum Laboratory Time

15 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

84377

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
OLIGU	Oligosaccharide Screen, U	49284-3

Result ID	Test Result Name	Result LOINC Value
64889	Oligosaccharide Screen, U	49284-3