Overview

Useful For
Screening patients suspected of having a lysosomal storage disorder

Genetics Test Information
This is a general urine screening test for a broad array of lysosomal storage (LSD) and related disorders. Not all LSDs are detectable by this method.

Highlights
Lysosomal storage disorders (LSD) are a group of genetic diseases characterized by the accumulation of substrates in the cells and tissues of affected individuals.

There is significant phenotypic overlap between LSDs making diagnosis a challenge.

In many cases, accumulating analytes spill out into bodily fluids and can be detected in urine; therefore, the first step in a diagnostic workup includes urine analyses for metabolites associated with specific LSDs.

The recognition of disease specific metabolites in the screening profile can help to secure a diagnosis.

Targeted follow-up testing can and should be performed using enzymatic or molecular assays.

Testing Algorithm
A combined analysis and interpretation is reported to the client.

Special Instructions
- Fabry Disease Testing Algorithm
- Biochemical Genetics Patient Information

Method Name
CTSNR, MQLNR: Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

MQNNR: Spectrophotometry (SP)

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

NY State Available
Yes

Specimen

Specimen Type
Urine

Necessary Information
Patient’s age is required.

Specimen Required
Supplies: Urine Tubes, 10 mL (T068)
Specimen Volume: 10 mL

Pediatric: 3 mL

Collection Instructions:
1. Collect a random urine specimen (early morning preferred).
2. 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
3 mL

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

Specimen Stability Information

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<th>Specimen Type</th>
<th>Temperature</th>
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<tr>
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Clinical and Interpretive

Clinical Information
Lysosomal storage disorders (LSD) are a diverse group of inherited diseases characterized by the intracellular accumulation of macromolecules leading to cell damage and organ dysfunction. Approximately 50 lysosomal storage disorders have been described with a wide phenotypic spectrum and ranging in severity from neonatal lethal to later onset milder variants.

Although classification is not always straightforward, LSDs are generally categorized according to the type of storage material that accumulates in the cells and tissues. Major categories include mucopolysaccharidoses, oligosaccharidoses, mucolipidoses, and sphingolipidoses. In many cases, accumulating analytes can be detected in urine. Screening for these disorders typically begins with an analysis to detect disease-specific metabolite patterns or profiles indicative of a LSD. The combined analysis of disease-specific markers for LSDs in multiple tests can allow for the identification of additional disorders that may not be picked up using any of the single tests alone.

Disorders detectable by this approach include the oligosaccharidoses alpha-mannosidosis, aspartylglucosaminuria, fucosidosis, Schindler disease, and sialidosis; the sphingolipidoses GM1 gangliosidosis, Sandhoff disease, galactosialidosis, saposin B deficiency, metachromatic leukodystrophy, multiple sulfatase deficiency, Fabry disease, Gaucher disease, and Krabbe disease; the mucopolysaccharidoses excluding MPS IX (hyaluronidase deficiency); the glycogen storage disorder Pompe disease and the mucolipidoses types II and III. Additionally, other disorders
such as CDG type IIb, and de-glycosylation disorders such as NGLY1-CDG may also be detected.

The mucopolysaccharidoses (MPS) are a subset of lysosomal storage disorders caused by the deficiency of any one of the enzymes involved in the stepwise degradation of dermatan sulfate, heparan sulfate, keratan sulfate, or chondroitin sulfate (glycosaminoglycans: GAGs). Undegraded or partially degraded GAGs (also called mucopolysaccharides) are stored in lysosomes and excreted in the urine. Accumulation of GAGs in lysosomes interferes with normal functioning of cells, tissues, and organs resulting in the clinical features observed in MPS disorders. There are 11 known enzyme deficiencies that result in MPS. In addition, abnormal GAG storage is observed in multiple sulfatase deficiency and in I-cell disease. Finally, an abnormal excretion of GAGs in urine is observed occasionally in other disorders including active bone diseases, connective tissue disease, hypothyroidism, urinary dysfunction, and oligosaccharidoses.

The oligosaccharidoses (glycoproteinoses) are a subset of lysosomal storage disorders 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 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 sphingolipidoses are a subset of lysosomal storage disorders caused by a defect in any one of the enzymes that degrade complex ceramide containing lipids. They are characterized by the excessive accumulation of sphingolipids in the tissues, particularly in the central nervous system resulting in progressive neurodegeneration and developmental regression. In 2 conditions, Fabry disease and Gaucher disease type I, there is only systemic involvement. In many cases, sphingolipidoses can be detected by through oligosaccharide analysis in urine.

Because of the similarity of features across disorders and their variability, clinical diagnosis of LSDs can be challenging; therefore, urine screening and the combined analysis of multiple urine screening tests is an important tool for the initial workup of an individual suspected of having a lysosomal storage disorder. Abnormal results can be followed up with the appropriate enzyme or molecular analysis.

Reference Values
An interpretive report will be provided.

Interpretation
Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. Follow-up testing is recommended to confirm a diagnosis.

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

Cautions
Specific enzymatic or molecular assays should be used to confirm positive results.

In rare instances, a normal excretion of ceramide trihexosides may be seen in individuals who are carriers of, or affected with, Fabry disease. If Fabry disease is clinically suspected, see Fabry Disease Testing Algorithm in Special Instructions for additional testing recommendations.

Occasionally, an abnormal value for total glycosaminoglycans (GAG) will be obtained on a specimen that yields a normal liquid chromatography-tandem mass spectrometry (LC-MS/MS) pattern. This situation can occur as an artifact when a patient is treated with low-molecular-weight heparin. Other known causes are sample contamination.
with acrylic polymers used in disposable diapers and several clinical situations associated with excessive connective tissue destruction, bladder disease, or bone disease.

Not all lysosomal storage disorders are detectable through urine screening.

**Clinical Reference**


**Method Description**

**Ceramide trihexosides and sulfatides** are determined by liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. LC-MS/MS is performed using a mobile phase to separate the ceramide trihexosides and sulfatides from the bulk of the specimen matrix. The MS/MS is operated in the multiple reaction monitoring (MRM) positive mode to follow the ceramide trihexosides and multiple reaction monitoring (MRM) negative mode to follow the sulfatides. (Unpublished Mayo method)


**Mucopolysaccharides (MPS) Qualitative, Urine:** Chondroitin sulfate, dermatan sulfate, heparan sulfate, and keratan sulfate are determined by LC-MS/MS analysis. Urine specimens are evaporated and the dry residue is subjected to methanalysis yielding the mucopolysaccharides for analysis as their unique repeating disaccharide units. LC-MS/MS is performed to separate the mucopolysaccharides from the bulk of the specimen matrix. (Auray-Blais C, Bherer P, Gagnon R, et al: Efficient analysis of urinary glycosaminoglycans by LC-MS/MS in mucopolysaccharidoses type I, II and VI. Mol Genet Metab 2011 Jan;102[1]:49-56)

**Oligosaccharide Screen, Urine:** Urine samples are extracted using Oasis HLB and carbograph columns and lyophilized overnight. Oligosaccharides are permethylated, the tubes centrifuged, and the supernatant removed. The supernatant is quenched with water, neutralized with acetic acid, extracted, eluted, and again lyophilized overnight. Specimens are resuspended, mixed 1:1 with a matrix solution, spotted onto a MALDI plate and allowed to air dry. The plate is then analyzed using a 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
14 days

Maximum Laboratory Time
18 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
82542x2-Ceramide Trihex and Sulfatide, U and Mucopolysaccharides, (MPS), QL, U
83864-Mucopolysaccharides (MPS), QN, U
84377-Oligosaccharide Screen, U

LOINC® Information

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