Overview

Useful For
Diagnosis of mucopolysaccharidosis I, Hurler, Scheie, and Hurler-Scheie syndromes in whole blood specimens

Testing Algorithm
See Newborn Screen Follow-up for Mucopolysaccharidosis Type I in Special Instructions.

For more information, see Newborn Screening Act Sheet Mucopolysaccharidosis Type I: Decreased Alpha-L-Iduronidase in Special Instructions.

Special Instructions
- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Newborn Screening Act Sheet Mucopolysaccharidoses Type I: Decreased Alpha-L-Iduronidase
- Newborn Screen Follow-up for Mucopolysaccharidosis Type I
- Informed Consent for Genetic Testing (Spanish)

Method Name
Fluorometric Enzyme Assay

NY State Available
Yes

Specimen

Specimen Type
Whole blood

Necessary Information
Provide a reason for referral with each specimen.

Specimen Required

Container/Tube:
- Preferred: Lavender top (EDTA)
- Acceptable: Yellow top (ACD)

Specimen Volume: 2 mL

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 in Special Instructions:
   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602) in Special Instructions.

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

**Specimen Minimum Volume**

0.5 mL

**Reject Due To**

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**Specimen Stability Information**

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<tr>
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**Clinical and Interpretive**

**Clinical Information**

The mucopolysaccharidoses (MPS) are a group of lysosomal storage disorders caused by the deficiency of any of the enzymes involved in the stepwise degradation of dermatan sulfate, heparan sulfate, keratan sulfate, or chondroitin sulfate, also known as glycosaminoglycans (GAG). Accumulation of GAGs in lysosomes interferes with normal functioning of cells, tissues, and organs. There are 11 known disorders that involve the accumulation of GAGs. MPS disorders involve multiple organ systems characterized by coarse facial features, cardiac abnormalities, organomegaly, intellectual disabilities, short stature, and skeletal abnormalities.

Mucopolysaccharidosis I (MPS I) is an autosomal recessive disorder caused by a reduced or absent activity of the enzyme alpha-L-iduronidase due to mutations in the IDUA gene. More than 100 mutations have been reported in individuals with MPS I. Deficiency of alpha-L-iduronidase can result in a wide range of phenotypes categorized into 3 syndromes: Hurler syndrome (MPS IH), Scheie syndrome (MPS IS), and Hurler-Scheie syndrome (MPS IH/S). Because these syndromes cannot be distinguished biochemically, they are also referred to as MPS I and attenuated MPS I.

Clinical features and severity of symptoms of MPS I are variable, ranging from severe disease to an attenuated form that generally presents at a later onset with a milder clinical presentation. In general, symptoms may include coarse facies, progressive dysostosis multiplex, hepatosplenomegaly, corneal clouding, hearing loss, intellectual disabilities or learning difficulties, and cardiac valvular disease. The incidence of MPS I is approximately 1 in 100,000 live births. Treatment options include hematopoietic stem cell transplantation and enzyme replacement therapy.

A diagnostic workup in an individual with MPS I typically demonstrates elevated levels of urinary GAG (MPSQN / Mucopolysaccharides [MPS], Quantitative, Urine) and increased amounts of both dermatan and heparan sulfate being detected (MPSSC / Mucopolysaccharides [MPS] Screen, Urine). Reduced or absent activity of alpha L-
iduronidase can confirm a diagnosis of MPS I; however, enzymatic testing is not reliable for carrier detection. Molecular sequence analysis of the \textit{IDUA} gene allows for detection of the disease-causing mutation in affected patients and subsequent carrier detection in relatives. To date, a clear genotype-phenotype correlation has not been established.

\textbf{Reference Values}

$\geq 1.0$ nmol/hour/mL

An interpretive report will be provided.

\textbf{Interpretation}

Specimens with results below 1.0 nmol/hour/mL in properly submitted specimens are consistent with alpha-L-iduronidase deficiency (mucopolysaccharidosis I). Further differentiation between Hurler, Scheie, and Hurler-Scheie is dependent upon the clinical findings.

Normal results ($\geq 1.0$ nmol/h/mL) are not consistent with alpha-L-iduronidase deficiency.

\textbf{Cautions}

The presence of a pseudodeficiency allele may cause reduced activity of alpha-L-iduronidase in the artificial substrate used in this assay. This can result in values below the normal reference range, but will typically be greater than levels found in patients with mucopolysaccharidosis I (MPS I).

This test cannot reliably determine carrier status for MPS I.

This test does not differentiate between Hurler and Scheie syndromes.

\textbf{Clinical Reference}


\textbf{Performance}

\textbf{Method Description}

Whole blood is spotted onto filter paper. A one-eighth inch (3-mm) disk is punched out of the dried blood spot (DBS) into a 96-well, round-bottom plate. Forty microliters of 50 mM formate buffer with 0.3 micrograms D-saccharic acid-1,4-lactone is added as elution liquid and 20 microliters of 2 mM 4-methylumbelliferyl-alpha-L-iduronide in water
as the substrate (60 microliters total volume + DBS). A blank is prepared using only elution liquid, substrate, and filter paper punches containing no blood (60 microliters total volume + blank punches). All patients, controls, and blank are set up in duplicate (2 punches total, 1 punch per well). After the incubation period (20 hours at 37 degrees C), all of the liquid from the plate is manually transferred to a 96-well, flat-bottom black plate. A calibration curve is prepared and analyzed on every plate to calculate enzyme activity results, based on fluorescence units in patient wells vs. calibrators. The calibration is derived from 4-methylumbelliferone (4-MU) that is serially diluted manually in the plate with the highest calibrator being equivalent to an enzyme activity of 10.4 nmol/hour/mL. Two hundred microliters of stop buffer (150 mM EDTA, pH 11.4) is added to all wells (patients, controls, blanks, calibrators). The plate is then read on the spectrofluorometer. Fluorescence readings for duplicate wells are averaged, and the average fluorescence is used to calculate the enzyme activity result. (Civallero G, Michelin K, de Mari J, et al: Twelve different enzyme assays on dried-blood filter paper samples for detection of patients with selected inherited lysosomal storage diseases. Clin Chim Acta 2006;372:98-102)

PDF Report
No

Day(s) and Time(s) Test Performed
Varies

Analytic Time
8 days

Maximum Laboratory Time
15 days

Specimen Retention Time
1 year

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
82657

LOINC® Information

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