MAYO CLINIC LABORATORIES

Test Definition: I2SBS

Iduronate-2-Sulfatase, Blood Spot

Overview

Useful For

Diagnosis of mucopolysaccharidosis II (MPS II, Hunter syndrome) using dried blood spot specimens

This test is **not useful** for determining carrier status for MPS II.

Genetics Test Information

This test provides diagnostic testing for individuals with positive newborn screen results or clinical signs and symptoms suspicious for mucopolysaccharidosis type II (MPS II, Hunter syndrome).

Testing Algorithm

The following algorithms are available:

-Lysosomal Storage Disorders Diagnostic Algorithm, Part 1

-Lysosomal Storage Disorders Diagnostic Algorithm, Part 2

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Storage Disorders Diagnostic Algorithm, Part 2
- Lysosomal Storage Disorders Diagnostic Algorithm, Part 1
- Blood Spot Collection Instructions

Method Name

Fluorometric Enzyme Assay

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Necessary Information

Provide a reason for testing with each specimen.

Specimen Required

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)

Container/Tube:
Preferred: Blood spot collection card
Acceptable: PerkinElmer 226 (formerly Ahlstrom 226) filter paper, Munktell TFN, and Whatman Protein Saver 903 paper
Specimen Volume: 2 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient 1 year of age or older is a fingerstick. See How to Collect Dried Blood Spot Samples via fingerstick.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.
Additional Information:
1. For collection instructions, see Blood Spot Collection Instructions
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

1 Blood spot

Reject Due To

Shows serum rings Multiple layers	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	90 days	FILTER PAPER
	Frozen	90 days	FILTER PAPER
	Refrigerated	90 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

The mucopolysaccharidoses are a group of 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 GAG in the lysosomes interferes with normal functioning of cells, tissues, and organs. Mucopolysaccharidosis II, (MPS II, Hunter syndrome) is an X-linked lysosomal storage disorder caused by the deficiency of iduronate sulfatase (IDS) enzyme and gives rise to the physical manifestations of the disease.

Clinical features and severity of symptoms are widely variable ranging from severe infantile onset disease to an attenuated form, which generally has a later onset with a milder clinical presentation. Symptoms may include coarse facies, short stature, enlarged liver and spleen, hoarse voice, stiff joints, cardiac disease, and profound neurologic involvement leading to developmental delays and regression. As an X-linked disorder, MPS II occurs primarily in male patients with an estimated incidence of 1 in 120,000 male births, although symptomatic carrier females have been reported. Treatment availability, including hematopoietic stem cell transplantation and enzyme replacement therapy, makes early diagnosis desirable, as early initiation of treatment has been shown to improve clinical outcomes. Newborn screening for MPS II has been implemented in some states.

A diagnostic workup in an individual with MPS II typically demonstrates elevated levels of urinary GAG and increased amounts of both dermatan and heparan sulfate (see MPSQU / Mucopolysaccharides Quantitative, Random, Urine and MPSBS / Mucopolysaccharides, Blood Spot). Reduced or absent activity of IDS can confirm a diagnosis of MPS II but may also be deficient in unaffected individuals with pseudodeficiency as well as individuals with multiple sulfatase deficiency. Enzymatic testing is not reliable to detect carriers. Molecular genetic testing of the IDS gene allows for detection of the disease-causing variant in affected patients and subsequent carrier detection in female relatives (see MPS2Z / Hunter Syndrome, Full Gene Analysis, Varies). Currently, no clear genotype-phenotype correlations have been established.(1)

Reference Values

> or =1.5 nmol/hour/mL

Interpretation

Results below 1.5 nmol/hour/mL in properly submitted specimens are consistent with iduronate-2-sulfatase deficiency (mucopolysaccharidosis II: MPS II, Hunter syndrome). If clinically indicated, consider further confirmation by molecular genetic analysis of the *IDS* gene. Note that this enzyme's activity can also be reduced in multiple sulfatase deficiency (MSD).(2) If clinically indicated, consider biochemical genetic testing of other sulfatases or molecular genetic testing of the *SUMF1* gene to exclude MSD.

Normal results (> or =1.5 nmol/hour/mL) are not consistent with iduronate-2-sulfatase deficiency.

Cautions

The presence of a pseudodeficiency allele may cause reduced activity of iduronate sulfatase in the artificial substrate used in this assay.

Enzyme levels may be normal in individuals receiving enzyme replacement therapy or who have undergone bone marrow transplant.

Iduronate-2-sulfatase can also be deficient in individuals with multiple sulfatase deficiency.

Clinical Reference

1. D'Avanzo F, Rigon L, Zanetti A, Tomanin R: Mucopolysaccharidosis type II: One hundred years of research, diagnosis,

and treatment. Int J Mol Sci. 2020 Feb 13;21(4):1258. doi: 10.3390/ijms21041258
2. Hopwood JJ, Ballabio A: Multiple sulfatase deficiency and the nature of the sulfatase family. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed January 13, 2022. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225546905
3. Neufeld EF, Muenzer J: The Mucopolysaccharidoses. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed January 13, 2022. Available at https://ommbid.mhmedical.com/content.aspx?bookId=2709&sectionId=225544161
4. Scarpa M: Mucopolysaccharidosis type II. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2007. Updated October 4, 2018. Accessed January 13, 2022. Available at www.ncbi.nlm.nih.gov/books/NBK1274/

Performance

Method Description

Whole blood is collected on a blood spot card. A 3-mm (one-eighth inch) disk is punched out of the dried blood spot into a microcentrifuge tube and inactivated bovine serum albumin is added. The extraction liquid is combined a substrate in a black 96-well plate. A blank is prepared using only preincubation extraction liquid, substrate, and filter paper punch containing no blood. All patients, controls, and blanks are set up in duplicate. After 2 incubations, a stop buffer is added to all wells. Calibrators are prepared and analyzed on every plate to calculate enzyme activity results based on fluorescence units in patient wells versus calibrators. The calibration is derived from 4-methylumbelliferone that is serially diluted manually in the plate, with the highest calibrator being equivalent to an enzyme activity of 3.125 nmol/hour/mL. The plate is then ready to be read using the spectrofluorometer. Fluorescence readings for duplicate wells are averaged, and the average fluorescence is used to calculate the enzyme activity result.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available

8 to 15 days

Specimen Retention Time

1 year

Performing Laboratory Location

Rochester

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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

82657

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
I2SBS	Iduronate-2-sulfatase, BS	79462-8

Result ID	Test Result Name	Result LOINC® Value
61901	Iduronate-2-sulfatase, BS	79462-8
35209	Reviewed By	18771-6
35210	Interpretation (I2SBS)	59462-2