MAYO CLINIC LABORATORIES

Test Definition: I2SB

Iduronate-2-Sulfatase, Blood Spot

Overview

Useful For

Supporting the biochemical diagnosis of mucopolysaccharidosis II (MPS II; Hunter syndrome)

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

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
MPSBS	Mucopolysaccharidosis, BS	Yes	No

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). If an enzyme deficiency is detected by this screening test, additional biochemical or molecular testing is required to confirm a diagnosis.

Testing Algorithm

If result interpretation is normal, testing is complete.

If result interpretation indicates mucopolysaccharidosis type II, quantitation of heparan sulfate, dermatan sulfate and keratan sulfate may be performed at an additional charge.

For more information see Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans

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)
- Blood Spot Collection Instructions
- Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type
Whole blood

Necessary Information
1. Patient's age is required.

2. Reason for testing is required.

Specimen Required
Submit only 1 of the following specimen types:

Preferred:

Specimen Type: Blood spot

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

Container/Tube:

Preferred: Blood spot collection card

Acceptable: Whatman Protein Saver 903 Paper, PerkinElmer 226 filter paper, Munktell filter paper, or blood collected in tubes containing ACD or EDTA and dried on filter paper.

Specimen Volume: 2 Blood spots

Collection Instructions:

1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Sample.
2. At least 2 spots should be complete (ie, unpunched).
3. Let blood dry on the filter paper at room temperature in a horizontal position for 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. Keep specimen dry.

Specimen Stability Information: Refrigerated (preferred) 60 days/Ambient 7 days/Frozen 60 days

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)

Acceptable:

Specimen Type: Whole Blood

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD)

Specimen Volume: 2 mL

Collection Instructions: Send whole blood specimen in original tube**. Do not aliquot.**

Specimen Stability Information: Refrigerate (preferred) 7 days/Ambient 48 hours

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

Blood spots: 1; Whole blood: 0.5 mL

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers	Reject
Insufficient specimen	Reject
Unapproved filter papers	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Varies		

Clinical & Interpretive

Clinical Information

Mucopolysaccharidosis II (MPS II; Hunter syndrome) is an X-linked lysosomal disorder caused by the deficiency of iduronate sulfatase enzyme due to disease-causing variants in the *IDS* gene. 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 female carriers 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 includes urine or blood glycosaminoglycans levels showing increased amounts of both dermatan and heparan sulfate (see MPSQU / Mucopolysaccharides Quantitative, Random, Urine and MPSBS / Mucopolysaccharidosis, Blood Spot). Reduced or absent activity of iduronate sulfatase 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 IDS / Mucopolysaccharidosis Type II, *IDS* Gene Sequencing with Deletion/Duplication, Varies).

Reference Values

>4.30 nmol/mL/hour

An interpretive report will be provided.

Interpretation

Abnormal results are not sufficient to establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on this assay, additional biochemical or molecular genetic analyses are required.

When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing, and in vitro, confirmatory studies (enzyme assay, molecular genetic analysis), and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

Cautions

Individuals with pseudodeficiency alleles can show reduced enzyme activity.

Carrier status (heterozygosity) for these conditions cannot be reliably detected.

Enzyme levels may be normal in individuals receiving enzyme replacement therapy or who have undergone hematopoietic stem cell transplant.

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

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; Accessed October 2, 2025. https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225544161
2. Hopwood JJ, Ballabio A. Multiple sulfatase deficiency and the nature of the sulfatase family. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; Accessed October 2, 2025. https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225546905

Performance

Method Description

One dried blood spot sample (DBS) is incubated with a mix of substrate and internal standard (IS) for iduronate 2-sulfatase, heparan N-sulfatase, alpha-N-acetylglucosaminidase, N-acetylgalactosamine-sulfate, beta-galactosidase, arylsulfatase B, beta-glucuronidase, and tripeptidyl peptidase 1. A second DBS sample is incubated with a mix of

substrate and IS for acetyl-CoA:alpha-glucosaminide N-acetyltransferase; and a third DBS sample with a mix of substrate and IS for palmitoyl-protein thioesterase 1. Following overnight incubation, the samples are combined, extracted by liquid-liquid extraction, and analyzed by tandem mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Thursday

Report Available
8 to 15 days

Specimen Retention Time
1 year

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
82657
83864 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
I2SB	Iduronate-2-sulfatase, BS	79462-8

Result ID	Test Result Name	Result LOINC® Value
BG749	Reason for Referral	42349-1
618290	Iduronate-2-sulfatase	79462-8
618417	Interpretation	59462-2
618416	Reviewed By	18771-6