MAYO CLINIC LABORATORIES

Test Definition: MPSBS

Mucopolysaccharidosis, Blood Spot

Overview

Useful For

Supporting the biochemical diagnosis of mucopolysaccharidoses types I, II, III, IV, or VI

Quantification of heparan sulfate, dermatan sulfate, and keratan sulfate in dried blood spot specimens

Genetics Test Information

This test is used as a second-tier newborn screen for mucopolysaccharidosis (MPS) types I and II and to aid in the diagnosis and monitoring of patients with MPS types I, II, III, IV, and VI.

Testing Algorithm

If the patient has abnormal newborn screening result for mucopolysaccharidosis type 1, immediate action should be taken. Refer to the appropriate ACMG Newborn Screening ACT Sheet.(1)

For more information, see the following:
-Newborn Screen Follow-up for Mucopolysaccharidosis Type I.
-Newborn Screening Follow up for Mucopolysaccharidosis type II

Special Instructions

- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screen Follow-up for Mucopolysaccharidosis Type I
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions
- Newborn Screening Follow-up for Mucopolysaccharidosis type II

Highlights

Accumulation of undegraded glycosaminoglycans (GAGs) leads to progressive cellular dysfunction and results in the typical clinical features seen with this group of disorders.

Dermatan sulfate (DS), heparan sulfate (HS), and keratan sulfate (KS) are markers for a subset of mucopolysaccharidoses (MPS).

Testing for DS, HS, and KS in dried blood spots can aid in the diagnosis of MPS types I, II, III, IV, and VI.

Method Name

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

NY State Available

Yes

Specimen

Specimen Type
Whole blood

Specimen Required
Patient Preparation: Do not administer low-molecular-weight heparin prior to collection
Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Collection Container:
Preferred: Blood Spot Collection Card
Acceptable: Whatman Protein Saver 903 paper, PerkinElmer 226 filter paper, Munktell filter paper, local newborn screening card, postmortem screening card, 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 of age is a fingerstick. See How to Collect Dried Blood Spot Samples via fingerstick.
2. Completely fill at least 2 circles on the filter paper card (approximately 100 microliters blood per circle).
3. Let blood dry on filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. 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. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume
See Specimen Required

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers/applications	Reject
Insufficient	Reject

specimen	

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	100 days	FILTER PAPER
	Frozen	100 days	FILTER PAPER
	Refrigerated	100 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

The mucopolysaccharidoses (MPS) are a group of disorders caused by a deficiency of any of the enzymes involved in the stepwise degradation of dermatan sulfate, heparan sulfate, keratan sulfate, or chondroitin sulfate (glycosaminoglycans: GAG, also called mucopolysaccharides). Undegraded or partially degraded GAG are stored in lysosomes and excreted in the urine. Accumulation of GAG in lysosomes interferes with normal functioning of cells, tissues, and organs resulting in the clinical features observed in MPS disorders. Depending on the extent of the enzyme deficiency and type of accumulating storage material, MPS patients may present with a variety of clinical findings, including coarse facial features, cardiac abnormalities, organomegaly, intellectual disabilities, short stature, and skeletal abnormalities.

MPS I is an autosomal recessive disorder caused by reduced or absent activity of the enzyme alpha-L-iduronidase due to variants in the *IDUA* gene. This enzyme deficiency results in a wide range of clinical phenotypes, which cannot be distinguished via biochemical methods and are further categorized as MPS IH (Hurler syndrome), MPS IS (Scheie syndrome), and MPS IH/S (Hurler-Scheie syndrome). Clinically, they are also referred to as MPS I and attenuated MPS I. MPS IH is the most severe and has an early onset consisting of skeletal deformities, coarse facial features, hepatosplenomegaly, macrocephaly, cardiomyopathy, hearing loss, macroglossia, and respiratory tract infections. Developmental delay is noticed as early as 12 months, and without treatment, death usually occurs before 10 years of age. MPS IH/S has an intermediate clinical presentation characterized by progressive skeletal symptoms called dysostosis multiplex. Individuals typically have little or no intellectual dysfunction. Corneal clouding, joint stiffness, deafness, and valvular heart disease can develop by early to mid-teens. Survival into adulthood is common. Comparatively, MPS IS presents with the mildest phenotype. The onset occurs after 5 years of age. It is characterized by normal intelligence and stature; however, affected individuals do experience joint involvement, visual impairment, and obstructive airway 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.

MPS II, Hunter syndrome, is an X-linked lysosomal storage disorder caused by a reduced or absent activity of the enzyme iduronate 2-sulfatase. The clinical features and severity of symptoms of MPS II are widely variable ranging from severe disease to an attenuated form, which generally presents later in life with a milder clinical presentation. In general, symptoms may include coarse facial features, short stature, enlarged liver and spleen, hoarse voice, stiff joints, cardiac disease, and profound neurologic involvement leading to developmental delays and regression. The clinical presentation of MPS II is similar to that of MPS I with the notable difference of the lack of corneal clouding in MPS II. Due to the X-linked inheritance pattern, MPS II is observed almost exclusively in male patients with an estimated incidence of 1 in 170,000 male births. Symptomatic female carriers have been reported but are very rare. Treatment options include hematopoietic stem cell transplantation and enzyme replacement therapy.

MPS-III, Sanfilippo syndrome, is caused by a reduced or absent activity of 1 of 4 enzymes involved in heparan sulfate degradation. Patients with MPS III uniformly excrete heparan sulfate resulting in similar clinical phenotypes and are further classified as type A, B, C, or D based upon the specific enzyme deficiency. Sanfilippo syndrome is characterized by severe central nervous system (CNS) degeneration but only mild physical disease. Such disproportionate involvement of the CNS is unique among the MPS. Onset of clinical features, most commonly behavioral problems and delayed development, usually occurs between 2 and 6 years of age in a child who previously appeared normal. Severe neurologic degeneration occurs in most patients by 6 to 10 years of age, accompanied by a rapid deterioration of social and adaptive skills with death generally occurring by their 20s. The occurrence of MPS III varies by subtype with types A and B being the most common and types C and D being very rare. The collective incidence is approximately 1 in 58,000 live births.

MPS IVA, Morquio A syndrome, is caused by a reduced or absent N-acetylgalactosamine-6-sulfate sulfatase activity. Clinical features and severity of symptoms of MPS IVA are widely variable but may include skeletal dysplasia, short stature, dental anomalies, corneal clouding, respiratory insufficiency, and cardiac disease. Intelligence is usually normal. Estimates of the incidence of MPS IVA syndrome range from 1 in 200,000 to 1 in 300,000 live births. Treatment with enzyme replacement therapy is available.

MPS IVB, Morquio B syndrome, is caused by a reduced or absent beta-galactosidase activity, which gives rise to the physical manifestations of the disease. Clinical features and severity of symptoms of MPS IVB are widely variable, ranging from severe disease to an attenuated form, which generally presents at a later onset with a milder clinical presentation. In general, symptoms may include coarse facies, short stature, enlarged liver and spleen, hoarse voice, stiff joints, cardiac disease, but no neurological involvement. The incidence of MPS IVB is estimated to be about 1 in 250,000 live births. Treatment options are limited to symptomatic management.

MPS VI, Maroteaux-Lamy syndrome, is an autosomal recessive lysosomal storage disorder caused by the deficiency of the enzyme arylsulfatase B. Clinical features and severity of symptoms are widely variable but typically include short stature, dysostosis multiplex, facial dysmorphism, stiff joints, claw-hand deformities, carpal tunnel syndrome, hepatosplenomegaly, corneal clouding, and cardiac defects. Intelligence is usually normal. Rapidly progressing forms have an early onset of symptoms, significantly elevated GAG (especially dermatan sulfate), and can lead to death before the second or third decade. A more slowly progressing form has a later onset, milder skeletal manifestations, smaller elevations of GAG, and typically a longer lifespan. Estimates of the incidence of MPS VI range from 1 in 250,000 to 1 in 300,000. Treatment options include hematopoietic stem cell transplantation and enzyme replacement therapy.

Elevations of dermatan and/or heparan sulfate are seen in MPS types I, II, III, and VI.

Elevations of keratan sulfate are seen in MPS IV.

Reference Values

DERMATAN SULFATE (DS)
Newborn-< or =2 weeks: < or =200 nmol/L
>2 weeks: < or =130 nmol/L

HEPARAN SULFATE (HS)
Newborn-< or =2 weeks: < or =96 nmol/L

>2 weeks: < or =95 nmol/L

TOTAL KERATAN SULFATE (KS)
< or =5 years: < or =1,900 nmol/L
6-10 years: < or =1,750 nmol/L
11-15 years: < or =1,500 nmol/L
>15 years: < or =750 nmol/L

Interpretation

Elevations of dermatan sulfate and/or heparan sulfate may be indicative of one of the mucopolysaccharidoses: type I, II, III, or VI.

Elevations of keratan sulfate may be indicative of mucopolysaccharidoses type IV.

Cautions

No significant cautionary statements

Clinical Reference

1. ACMG Newborn Screening ACT Sheets. Accessed August 30, 2023. Available at www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx?hkey=9d6bce5a-182e-42a6-84a5-b2d88240c508
2. de Ruijter J, de Ru MH, Wagemans T, et al. Heparan sulfate and dermatan sulfate derived disaccharides are sensitive markers for newborn screening for mucopolysaccharidoses types I, II and III. Mol Genet Metab. 2012;107(4):705-710
3. de Ru MH, van der Tol L, van Vlies N, et al. Plasma and urinary levels of dermatan sulfate and heparan sulfate derived disaccharides after long-term enzyme replacement (ERT) in MPS I: correlation with the timing of ERT and with total urinary excretion of glycosaminoglycans. J Inherit Metab Dis. 2013;36(2):247-255
4. Osago H, Shibata T, Hara N, et al. Quantitative analysis of glycosaminoglycans, chondroitin/dermatan sulfate, hyaluronic acid, heparan sulfate, and keratan sulfate by liquid chromatography-electrospray ionization-tandem mass spectrometry. Anal Biochem. 2014;467:62-74
5. Peck DS, Lacey JM, White AL, et al. Incorporation of second-tier biomarker testing improves the specificity of newborn screening for mucopolysaccharidosis type I. Int J Neonatal Screen. 2020;6(1):10. doi:10.3390/ijns6010010
6. Clarke LA, Dickson P, Ellinwood NM, Klein TL. Newborn screening for mucopolysaccharidosis I: Moving forward learning from experience. Int J Neonatal Screen. 2020;6(4):91. doi:10.3390/ijns6040091

Performance

Method Description

Blood spot specimens are eluted and sonicated. Dermatan sulfate (DS), heparin sulfate (HS), and keratan sulfate (KS) are enzymatically digested. The reaction mixture is centrifuged and analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). The ratio of the extracted peak area of DS, HS, and KS to internal standard as determined by LC-MS/MS is used to calculate the concentration of DS, HS, and KS in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed
Monday, Wednesday, Friday

Report Available
3 to 5 days

Specimen Retention Time
6 months

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

CPT Code Information
83864

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MPSBS	Mucopolysaccharidosis, BS	94586-5

Result ID	Test Result Name	Result LOINC® Value
43693	Dermatan Sulfate	90233-8
43694	Heparan Sulfate	90235-3
43695	Interpretation (MPSBS)	59462-2
43696	Reviewed By	18771-6
BA2869	Total Keratan Sulfate	90236-1