Test Definition: MPSWB

Mucopolysaccharidosis, Blood

Overview

Useful For

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

Quantification of heparan sulfate, dermatan sulfate, and keratan sulfate in whole blood specimens

Genetics Test Information

This test is recommended to aid in the diagnosis and monitoring of patients with mucopolysaccharidosis (MPS) types I, II, III, IV, and VI.

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

Dermatan sulfate, heparan sulfate, and keratan sulfate are markers for a subset of mucopolysaccharidoses.

Testing Algorithm

If the patient has abnormal newborn screening result for mucopolysaccharidosis type I, immediate action should be taken. Refer to the appropriate American College of Medical Genetics and Genomics Newborn Screening ACT Sheet.(1)

For more information, see the following:
-Newborn Screen Follow-up for Mucopolysaccharidosis Type I Decreased Alpha-L-Iduronidase Activity
-Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans

Special Instructions

- Biochemical Genetics Patient Information
- Newborn Screen Follow-up for Mucopolysaccharidosis Type I Decreased Alpha-L-Iduronidase Activity
- Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans

Highlights

Testing for ermatan sulfate, heparan sulfate, and keratan sulfate 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

Ordering Guidance

The preferred test to evaluate newborns with a positive newborn screen (reduced alpha-L-iduronidase or iduronate-2-sulfatase activity) for mucopolysaccharidosis type I or mucopolysaccharidosis type II, is MPS1B / Endogenous Mucopolysaccharidosis Type I (IDUA [Alpha-L-Iduronidase]) Biomarker, Blood Spot or MPS2B / Endogenous Mucopolysaccharidosis Type II (I2S [Iduronate-2-Sulfatase]) Biomarker, Blood Spot, respectively.

Specimen Required

Patient Preparation: For 6 hours before specimen collection, patient **should not** receive heparin.
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
Specimen Volume: 2 mL
Collection Instructions: Do not collect specimen from a line that may have been used to infuse heparin or has been flushed with heparin.

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

0.5 mL

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	7 days	
	Refrigerated	7 days	

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.

Mucopolysaccharidosis Type I (MPS I) is an autosomal recessive disorder caused by reduced or absent activity of the enzyme alpha-L-iduronidase due to disease-causing 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. 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. 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.

Mucopolysaccharidosis Type II (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.

Mucopolysaccharidosis Type III (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. MPS III 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 in a child who previously appeared normal. Severe neurologic degeneration occurs in most patients by 6 to 10 years, 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.

Mucopolysaccharidosis Type IVA (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.

Mucopolysaccharidosis Type IVB (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.

Mucopolysaccharidosis Type VI (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 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 =1900 nmol/L
6-10 years: < or =1750 nmol/L
11-15 years: < or =1500 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 types I, II, III, or VI.

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

Cautions

Administration of heparin before specimen collection may interfere with this assay and results should be interpreted with caution.

Clinical Reference

1. Newborn Screening ACT Sheet [alpha-L-iduronidase deficiency with or without glycosaminoglycan (GAG)

accumulation] Mucopolysaccharidosis Type I (MPS I). American College of Medical Genetics and Genomics; 2023. Updated November 2023. Accessed July 14, 2025. Available at www.acmg.net/PDFLibrary/MPSI-ACT-Sheet.pdf
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 15;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
Whole blood is spotted on filter paper and dried overnight. 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
Wednesday, Friday

Report Available
3 to 7 days

Specimen Retention Time
Residual whole blood: 7 days; Dried blood spot: 6 months

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

83864

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MPSWB	Mucopolysaccharidosis, B	94586-5

Result ID	Test Result Name	Result LOINC® Value
BA2870	Dermatan Sulfate	90233-8
BA2871	Heparan Sulfate	90235-3
BA2872	Total Keratan Sulfate	90236-1
BA2873	Interpretation (MPSWB)	59462-2
BA2874	Reviewed By	18771-6