MAYO CLINIC LABORATORIES

Test Definition: MPSER

Mucopolysaccharides Quantitative, Serum

Overview

Useful For

Quantification of dermatan sulfate, heparan sulfate, and keratan sulfate in serum to support the biochemical diagnosis of mucopolysaccharidoses types I, II, III, IV, VI, or VII

Genetics Test Information

This test provides diagnostic testing and monitoring of patients with mucopolysaccharidoses (MPS) types I, II, III, IV, VI, and VII.

Accumulation of undegraded glycosaminoglycans (GAG; also known as mucopolysaccharides) 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 MPS.

Testing for DS and HS in serum can aid in the diagnosis of MPS types I, II, III, VI, and VII.

Testing for KS in serum can aid in the diagnosis of MPS IVA and MPS IVB.

Testing Algorithm

For more information see Newborn Screening Follow up for Mucopolysaccharidosis type II

Special Instructions

- Biochemical Genetics Patient Information
- Newborn Screening Follow-up for Mucopolysaccharidosis type II

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Ordering Guidance

This test alone is not diagnostic for a specific mucopolysaccharidosis. Follow-up testing must be performed to confirm a diagnosis.

Necessary Information

1. Patient's age is required.

2. Reason for testing is required.

3. Biochemical Genetics Patient Information (T602) is recommended. This information aids in providing a more thorough interpretation of results. Send information with specimen.

Specimen Required

Patient Preparation: Do not administer low-molecular weight heparin prior to collection.

Collection Container/Tube: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Pediatric: 0.2 mL

Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

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

0.2 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	90 days	
	Frozen	90 days	
	Ambient	14 days	

Clinical & Interpretive

Clinical Information

The mucopolysaccharidoses 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-6- sulfate, collectively called glycosaminoglycans (GAG). 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 mucopolysaccharidosis (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 that can include 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 that are further categorized as MPS IH (Hurler syndrome), MPS IS (Scheie syndrome), and MPS IH/S (Hurler-Scheie syndrome), which are not typically distinguishable via biochemical methods. 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 of age, and death usually occurs before 10 years of age when left untreated. 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-adolescence. 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 (ERT).

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. Female patients who are symptomatic carriers are very rare but have been reported. Treatment options include hematopoietic stem cell transplantation and ERT.

MPS III (Sanfilippo syndrome) is caused by a reduced or absent activity of any 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 of age accompanied by a rapid deterioration of social and adaptive skills. Death generally occurs by the third decade of life (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. Treatment is limited to symptomatic management.

MPS IVA (Morquio A syndrome) is caused by a reduced or absent N-acetylgalactosamine-6-sulfate sulfatase. 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 ERT 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 of life. 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 ERT.

MPS VII (Sly syndrome) is caused by a deficiency of the enzyme beta-glucuronidase and is extremely rare. The phenotype varies significantly from mild to severe presentations and may include macrocephaly, short stature, dysostosis multiplex, hepatomegaly, coarse facies, and impairment of cognitive function. Likewise, the age of onset is variable ranging from prenatal to adulthood. Treatment options include hematopoietic stem cell transplantation and ERT.

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

Elevations of keratan sulfate are seen in MPS types IVA and IVB.

Reference Values

DERMATAN SULFATE
< or =300.00 ng/mL

HEPARAN SULFATE
< or =55.00 ng/mL

TOTAL KERATAN SULFATE
< or =5 years: < or =1800.00 ng/mL
6-18 years: < or =1500.00 ng/mL
> or =19 years: < or =1200.00 ng/mL

Interpretation

Elevations of dermatan sulfate, heparan sulfate, and/or keratan sulfate may be indicative of one of the mucopolysaccharidoses types I, II, III, IV, VI, or VII.

Elevations of all three sulfate species may be indicative of multiple sulfatase deficiency.

Rarely, an elevation of keratan sulfate may be indicative of alpha-fucosidosis.

Cautions

A normal total keratan sulfate result does not exclude a diagnosis of mucopolysaccharidoses IVA.

Clinical Reference

1. 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
2. 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
3. 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
4. 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; 2019. Accessed November 29, 2023. https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225544161
5. Puckett Y, Mallorga-Hernandez A, Montano AM. Epidemiology of mucopolysaccharidoses (MPS) in the United States: challenges and opportunities. Orphanet J Rare Dis. 2021;16(1):241

Performance

Method Description

Serum specimens are diluted and dermatan sulfate (DS), heparan 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 and HS in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Twice per month

Report Available

9 to 15 days

Specimen Retention Time

1 month

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
MPSER	Mucopolysaccharides Quant, S	93726-8

Result ID	Test Result Name	Result LOINC® Value
BG714	Reason for Referral	42349-1
604908	Dermatan Sulfate	2203-8
604909	Heparan Sulfate	93725-0
604910	Total Keratan Sulfate	93724-3
604911	Interpretation (MPSER)	59462-2
604907	Reviewed By	18771-6