Test Definition: MPSQU

Mucopolysaccharides Quantitative, Random, Urine

Overview

Useful For

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

Genetics Test Information

This test is used to aid in the diagnosis 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), keratan sulfate (KS) and chondroitin-6-sulfate (C6S) are markers for a subset of MPS.

In urine:
-DS and HS are markers for MPS types I, II, III, VI and VII.
-KS is a marker for MPS IVA and MPS IVB.
-C6S is a marker for MPS IVA and MPS VII.

Testing Algorithm

For more information see the following:
-Lysosomal Disorders Diagnostic Algorithm, Part 1
-Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans

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)

Special Instructions

- Biochemical Genetics Patient Information
- Lysosomal Disorders Diagnostic Algorithm, Part 1
- Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans

Highlights

Using liquid chromatography tandem mass spectrometry, this quantitative urine mucopolysaccharide screen provides analysis of the specific sulfates that are associated with at least 13 different disorders.

Method Name

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

NY State Available

Yes

Specimen

Specimen Type
Urine

Ordering Guidance
This test alone is not appropriate for the diagnosis of a specific mucopolysaccharidosis (MPS). Follow-up enzymatic or molecular genetic testing must be performed to confirm a diagnosis of an MPS.

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: For 6 hours before specimen collection, patient **should not** receive heparin.

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

Container/Tube: Plastic, 5-mL urine tube

Specimen Volume: 2 mL

Pediatric Volume: 1 mL

Collection Instructions: Collect a random urine specimen **(early morning preferred).**

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
1 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
Urine	Refrigerated (preferred)	90 days	
	Ambient	7 days	
	Frozen	365 days	

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-6-sulfate, which are 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. There are 11 known enzyme deficiencies that result in the accumulation of GAG. In addition, abnormal GAG storage is observed in multiple sulfatase deficiency and in I-cell disease. Finally, abnormal excretion of GAG in urine is observed occasionally in other disorders including active bone diseases, connective tissue disease, hypothyroidism, urinary dysfunction, and oligosaccharidoses.

Mucopolysaccharidoses are autosomal recessive disorders except for MPS II, which follows an X-linked inheritance pattern. Affected individuals typically experience a period of normal growth and development followed by progressive disease involvement encompassing multiple systems. The severity and features vary and may include facial coarsening, organomegaly, skeletal changes, cardiac abnormalities, and developmental delays. Moreover, disease presentation varies from as early as late infancy to adulthood.

A diagnostic workup for individuals with suspected MPS should begin with this test, which includes the quantitative liquid chromatography tandem mass spectrometry (LC-MS/MS) analysis of the specific sulfates or GAG. Interpretation is based upon pattern recognition of the specific sulfates detected by MS/MS and the quantitative analysis of their amounts of excretion. However, an abnormal mucopolysaccharide analysis is not sufficient to conclusively establish a specific diagnosis. It is strongly recommended to seek confirmation by an independent method, typically in vitro enzyme assay (available in either blood or cultured fibroblasts from a skin biopsy) or molecular analysis.

After a specific diagnosis has been established, this test can be appropriate for monitoring the effectiveness of treatment, such as a bone marrow transplant or enzyme replacement therapy (ERT). This test allows for monitoring of the excretion of specific sulfates, as these may change in patients with an MPS disorder undergoing treatment.

Table: Enzyme Defects and Excretion Products of Mucopolysaccharidoses

Disorder	Alias	Enzyme deficiency	Sulfates excreted
MPS I	Hurler/Scheie	Alpha-L-iduronidase	DS/HS
MPS II	Hunter	Iduronate 2-sulfatase	DS/HS
MPS III A	Sanfilippo A	Heparan N-sulfatase	HS
MPS III B	Sanfilippo B	N-acetyl-alpha-D-glucosaminidase	HS
MPS III C	Sanfilippo C	Acetyl-CoA:alpha-glucosaminide N-acetyltransferase	HS
MPS III D	Sanfilippo D	N-acetylglucosamine-6-sulfatase	HS
MPS IV A	Morquio A	Galactosamine-6-sulfatase	KS/C6S
MPS IV B	Morquio B	Beta-galactosidase	KS
MPS VI	Maroteaux-Lamy	Arylsulfatase B	DS

MPS VII	Sly	Beta-glucuronidase	DS, HS, C6S
MPS IX	Hyaluronidase deficiency	Hyaluronidase	None

KEY: C6S, chondroitin 6-sulfate; DS, dermatan sulfate; HS, heparan sulfate; KS, keratan sulfate

Mucopolysaccharidosis I is caused by a reduced or absent activity of the alpha-L-iduronidase enzyme due to disease-causing variant in the *IDUA* gene. MPS I can result in a wide range of phenotypes categorized into 3 syndromes: Hurler syndrome (MPS IH), Scheie syndrome (MPS IS), and Hurler-Scheie syndrome (MPS IH/S). Because these syndromes cannot be distinguished biochemically, they are also referred to as MPS I and attenuated MPS I. Clinical features and severity of symptoms of MPS I are variable, ranging from severe disease to an attenuated form that generally presents at a later onset with a milder clinical presentation. In general, symptoms may include coarse facies, progressive dysostosis multiplex, hepatosplenomegaly, corneal clouding, hearing loss, intellectual disabilities or learning difficulties, and cardiac valvular disease. Treatment options include hematopoietic stem cell transplantation and enzyme replacement therapy (ERT).

Mucopolysaccharidosis II (Hunter syndrome) is caused by a reduced or absent activity of the enzyme iduronate 2-sulfatase due to disease-causing variants in the *IDS* gene. The clinical features and severity of symptoms of MPS II 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, 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 in the lack of corneal clouding in MPS II. The inheritance pattern is X-linked and as such MPS II is observed almost exclusively in male patients, although symptomatic females have been reported. Treatment options include hematopoietic stem cell transplantation and ERT.

Mucopolysaccharidosis III (Sanfilippo syndrome) is caused by a reduced or absent activity of 1 of 4 enzymes (see Table above), resulting in a defect of 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. 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. Treatment options are limited to symptomatic management.

Mucopolysaccharidosis IVA (Morquio A syndrome) is caused by a reduced or absent N-acetylgalactosamine-6-sulfate sulfatase due to disease-causing variants in the *GALNS* gene. Clinical features and severity of symptoms of MPS IVA are variable and may include skeletal dysplasia, short stature, dental anomalies, corneal clouding, respiratory insufficiency, cardiac disease, and no neurologic involvement. Treatment with ERT is available.

Mucopolysaccharidosis IVB (Morquio B syndrome) is caused by a reduced or absent beta-galactosidase activity due to disease-causing variants in the *GLB1* gene. Clinical features and severity of symptoms of MPS IVB are 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. Treatment options are limited to symptomatic management.

Mucopolysaccharidosis VI (Maroteaux-Lamy syndrome) is caused by a deficiency of the enzyme arylsulfatase B due to disease-causing variants in the *ARSB* gene. Clinical features and severity of symptoms are variable and typically include short stature, dysostosis multiplex, facial dysmorphism, stiff joints, claw-hand deformities, carpal tunnel syndrome, hepatosplenomegaly, corneal clouding, cardiac defects, and no neurological involvement. Treatment options include hematopoietic stem cell transplantation and ERT.

Mucopolysaccharidosis VII (Sly syndrome) is caused by a deficiency of the enzyme beta-glucuronidase due to disease-causing variants in the *GUSB* gene. 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.

Mucopolysaccharidosis IX is a very rare disorder caused by a deficiency of the enzyme hyaluronidase due to disease-causing variants in the *HYAL1* gene. Patients present with short stature, flat nasal bridge, and joint findings. Urine GAG are normal in MPS IX.

Reference Values

Dermatan Sulfate
< or =1.00 mg/mmol creatinine

Heparan Sulfate
< or =4 years: < or =0.50 mg/mmol creatinine
> or =5 years: < or =0.25 mg/mmol creatinine

Chondroitin-6 Sulfate
< or =24 months: < or =10.00 mg/mmol creatinine
25 months-10 years: < or =2.50 mg/mmol creatinine
> or =11 years: < or =1.50 mg/mmol creatinine

Keratan Sulfate
< or =12 months: < or =2.00 mg/mmol creatinine
13-24 months: < or =1.50 mg/mmol creatinine
25 months-4 years: < or =1.00 mg/mmol creatinine
5-18 years: < or =0.50 mg/mmol creatinine
> or =19 years: < or =0.30 mg/mmol creatinine

Interpretation

Elevations of dermatan sulfate, heparan sulfate, keratan sulfate, and/or chondroitin-6-sulfate may be indicative of one of the mucopolysaccharidoses types I, II, III, IV, VI, or VII.

Elevations of any or all sulfate species may be indicative of multiple sulfatase deficiency or mucolipidosis II/III.

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

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 June 11, 2025. Available at www.acmg.net/PDFLibrary/MPSI-ACT-Sheet.pdf
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. 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 June 11, 2025 Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225544161
4. 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
5. Freeze HH, Steet R, Suzuki T, et al. Genetic Disorders of Glycan Degradation. In: Varki A, Cummings RD, Esko JD, et al, eds. Essentials of Glycobiology [Internet]. 4th edition. Cold Spring Harbor Laboratory Press; 2022. Accessed June 11, 2025. Available at: www.ncbi.nlm.nih.gov/books/NBK579991/

Performance

Method Description

Dermatan sulfate (DS), heparin sulfate (HS), keratan sulfate (KS) and chondroitin-6-sulfate (C6S) are enzymatically digested from urine. 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, KS and C6S to internal standard as determined by LC-MS/MS is used to calculate the concentration of DS, HS, KS and C6S in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday

Report Available

4 to 10 days

Specimen Retention Time

1 month

Test Definition: MPSQU

Mucopolysaccharides Quantitative, Random, Urine

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
82570

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MPSQU	Mucopolysaccharides Quant, U	94691-3

Result ID	Test Result Name	Result LOINC® Value
BG716	Reason for Referral	42349-1
605986	Dermatan Sulfate	94692-1
605987	Heparan Sulfate	94693-9
605988	Chondroitin-6 Sulfate	94690-5
605989	Keratan Sulfate	92806-9
605990	Interpretation	59462-2
605985	Reviewed By	18771-6