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 spots

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.

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.

Testing Algorithm
See [Newborn Screen Follow-up for Mucopolysaccharidosis Type I](#) in Special Instructions.

For more information, see [Newborn Screening Act Sheet Mucopolysaccharidosis Type I: Decreased Alpha-L-Iduronidase](#) in Special Instructions.

Special Instructions
- [Biochemical Genetics Patient Information](#)
- [Blood Spot Collection Card-Spanish Instructions](#)
- [Newborn Screening Act Sheet Mucopolysaccharidoses Type I: Decreased Alpha-L-Iduronidase](#)
- [Newborn Screen Follow-up for Mucopolysaccharidosis Type I](#)
- [Blood Spot Collection Card-Chinese Instructions](#)
- [Blood Spot Collection Instructions](#)

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:** Card-Blood Spot Collection (Filter Paper)

**Acceptable:** Whatman Protein Saver 903 paper, Ahlstrom 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 dried blood spots

**Collection Instructions**

1. Completely fill at least 2 circles on the filter paper card (approximately 100 microliters blood per circle).
2. Let blood dry on filter paper at room temperature in a horizontal position for 3 or more hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.

**Additional Information:**

1. For collection instructions, see Blood Spot Collection Instructions in Special Instructions.
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

**Forms**

1. Biochemical Genetics Patient Information (T602) in Special Instructions.
2. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

**Specimen Minimum Volume**

See Specimen Required

**Reject Due To**

| Blood spot | Shows serum rings Insufficient specimen |

**Specimen Stability Information**

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Clinical and 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: GAGs, also called mucopolysaccharides). Undegraded or partially degraded GAGs are stored in lysosomes and excreted in the urine. Accumulation of GAGs 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 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 mutations 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 cannot be distinguished 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, 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 males with an estimated incidence of 1 in 170,000 male births. Symptomatic carrier females 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 MPSs. Onset of clinical features, most commonly behavioral problems and delayed development, usually occurs between 2 and 6 years of age in a child who

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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. 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<=2 weeks: < or =200 nmol/L

>2 weeks: < or =130 nmol/L

**HEPARAN SULFATE (HS)**

Newborn<=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
Test Definition: MPSBS
Mucopolysaccharidosis, BS

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 1 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**


**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) and Time(s) Test Performed**
Monday, Wednesday, Friday; 9 a.m.

**Analytic Time**
2 days

**Maximum Laboratory Time**
7 days

**Specimen Retention Time**
1 year

**Performing Laboratory Location**
Test Definition: MPSBS
Mucopolysaccharidosis, BS

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
83864

LOINC® Information

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