USEFUL FOR

Quantification of heparan sulfate and dermatan sulfate in dried blood spots can support the biochemical diagnosis of one of the mucopolysaccharidoses types I, II, III, or VI.

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, and VI.

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), and 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.

REFERENCE VALUES

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<td>Dermatan sulfate (DS)</td>
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<tr>
<td>Heparan sulfate (HS)</td>
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ANALYTIC TIME

2 days
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 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 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 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 GAGs 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 GAGs, 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/or enzyme replacement therapy.

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

**INTERPRETATION**

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