Mucopolysaccharidosis type I

Also known as:

- MPS I
- Hurler-Scheie syndrome
- Hurler syndrome
- IDUA deficiency
- MPS I H
- MPS I H-S
- MPS I S
- Scheie syndrome

Definition:

The *IDUA* gene provides instructions to produce the alpha-L-iduronidase (IDUA) enzyme that breaks down large sugar molecules in the body, which are called glycosaminoglycans. Mutations in the *IDUA* gene reduce or eliminate the function of the IDUA enzyme, which leads to a dangerous buildup of glycosaminoglycans within cells, specifically the lysosomes. The buildup of glycosaminoglycans increases the size of the lysosomes, which can lead to enlarged tissues/organs and cause a variety of symptoms. This buildup may also interfere with the function of some proteins inside the lysosomes, and disrupt the movement of molecules within the cell. There are two main types of MPS I, which are referred to as severe MPS I and attenuated MPS I.

Diagnosis:

Sequencing of the *IDUA* gene will be performed as part of the screening algorithm. Diagnostic confirmation, under the direction of a specialist, may include measurement of glycosaminoglycans in urine and IDUA enzyme activity in blood.

How is it inherited:

MPS I is inherited in an autosomal recessive pattern. Normally, a person has two functional copies of the *IDUA* gene. In people with MPS I, both copies of the gene have a mutation. Each parent of a newborn with MPS I typically has one functional gene and one mutated gene, and is considered a carrier. When both parents are carriers, the chance of a newborn inheriting two mutated genes is 25%.

Newborn Screening:

- **Incidence:** The estimated incidence of severe MPS I in the general population is 1 in 100,000, while the incidence of attenuated (less severe) MPS is 1 in 500,000.

- **New York State Method of Screening (First Tier):** Screening for MPS I disease is accomplished by analysis of IDUA enzyme activity by mass spectrometry. If concentrations are normal, the sample is deemed within acceptable limits. If abnormal, second tier screening is performed.
- **Second Tier Screening:** Sequencing of the *IDUA* gene.
- **Testing can be affected by:** IDUA enzyme activity may be low in healthy newborns, thus giving a false positive result. Within the *IDUA* gene, at least one pseudodeficiency allele has been identified which results in lower IDUA enzyme activity but no clinical symptoms of MPS I.
- **Interpretation/reporting of data:** Results are reported as screen negative, borderline or as a referral. A repeat specimen should be collected for a borderline result. Prompt consultation with a specialist is required for a referral.
- **Referral to Specialty Care Center:** Babies with an abnormal newborn screen for MPS I with an identified *IDUA* mutation are referred to an Inherited Metabolic Disease Specialty Care Center for a diagnostic evaluation.

Prognosis:

The prognosis is best for newborns who are diagnosed and treated quickly, prior to two years of age. There is no cure for this condition, but treatments can help to delay some symptoms, and manage others. Without treatment, babies with severe MPS I will experience a progressive decline in intellectual function, worsening of symptoms, and a shorter lifespan.

Symptoms:

There are many symptoms associated with MPS I, including enlarged head, lips, tongue, nose and vocal cords. Symptoms also include frequent upper respiratory infections, sleep apnea, hearing loss, recurrent ear infections, corneal clouding, narrowing of the spinal canal, joint deformities, and developmental delays and regressions. Because the symptoms of this disease vary from person to person, there may be additional symptoms in a person with MPS I that do not appear on this list. Usually, individuals with severe MPS I experience an earlier onset of symptoms than those with attenuated MPS I.

Symptoms in carriers:

Carriers do not typically have symptoms.

Treatment:

The two main treatment options for MPS I include hematopoietic stem cell transplant and enzyme replacement therapy. These treatments work by replacing the missing *IDUA* enzyme.

Educational materials:

More information:

https://rarediseases.info.nih.gov/diseases/10335/mucopolysaccharidosis-type-i

https://mpssociety.org/learn/

https://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-i