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CARRIER SCREEN

Mucopolysaccharidosis type I

What is mucopolysaccharidosis type I?

Mucopolysaccharidosis type I is an inherited metabolic disease characterized by developmental delays, distinctive facial features, enlarged organs, and skeletal and joint abnormalities.[1] Individuals with mucopolysaccharidosis type I have defects in the enzyme α-L-iduronidase, which breaks down large sugars known as glycosaminoglycans or mucopolysaccharides.[1,2] The symptoms of mucopolysaccharidosis type I are due to the build-up of the large sugar molecules heparan sulfate and dermatan sulfate within lysosomes in cells. Mucopolysaccharidosis type I belongs to a group of diseases called lysosomal storage disorders and is also known as Hurler syndrome, Hurler-Scheie syndrome, or Scheie syndrome.[1]

What are the symptoms of mucopolysaccharidosis type I and what treatment is available?

Symptoms of mucopolysaccharidosis type I vary in severity and age at onset and are progressive. Affected individuals often do not show symptoms at birth. Symptoms of the severe form of the disease are typically seen in infancy and may include: [3]

- Distinctive facial features (usually after age one)
- Umbilical or groin hernias
- Frequent infections
- Hepatosplenomegaly (enlarged liver and spleen)
- Progressive intellectual disability
- Hypertrichosis (excess body hair)
- Spinal and joint deformity and stiffness, causing short stature
- Corneal clouding, causing vision loss
- Heart problems, especially valve disease
- Hearing loss
- Hydrocephalus (fluid build-up in the brain)
- Death usually by late childhood without treatment

The less severe form of the disease, known as attenuated mucopolysaccharidosis type I, is characterized by onset after two years of age and a slower progression of symptoms. Hearing loss and heart valve disease are common, and learning disabilities or developmental delay may also occur. Without treatment, life expectancy ranges from the 20s or 30s to a usual lifespan.[3]

There is no cure for mucopolysaccharidosis type I. Treatment includes supportive care for symptoms. For individuals who meet specific criteria, hematopoietic stem cell transplantation and/or enzyme replacement therapy may be available and can improve some of the physical symptoms. While neither will reverse intellectual disability, hematopoietic stem cell transplantation may prevent further intellectual impairment.[3]

Mucopolysaccharidosis type I is included in newborn screening panels in some states in the United States.[4]

How is mucopolysaccharidosis type I inherited?

Mucopolysaccharidosis type I is an autosomal recessive disease caused by mutations in the *IDUA* gene.[1] An individual who inherits one copy of an *IDUA* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *IDA* mutations, one from each parent, is expected to be affected with mucopolysaccharidosis type I.

If both members of a couple are carriers of a mutation in the same gene, the risk of having an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

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Who is at risk for mucopolysaccharidosis type I?

Mucopolysaccharidosis type I can occur in individuals of all races and ethnicities. Worldwide, the estimated incidence is 1 in 100,000,[3] with a calculated carrier frequency of 1 in 158.

Having a relative who is a carrier or is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

National MPS society: http://www.mpssociety.org/mps/mps-i

MPS I: http://mps1disease.com

References

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4. National Newborn Screening Status Report. November 2, 2014. Available at http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/nbsdisorders.pdf . Accessed January 6, 2016.