

What is mucopolysaccharidosis type IVA?

Mucopolysaccharidosis type IVA is an inherited metabolic disease characterized by bone abnormalities.¹ Individuals with mucopolysaccharidosis type IVA have defects in the enzyme N-acetylgalactosamine 6-sulfatase, which breaks down large sugars called glycosaminoglycans or mucopolysaccharides.¹ The symptoms of mucopolysaccharidosis type IVA are due to the build-up of the large sugar molecule keratan sulfate within lysosomes in cells.¹ Mucopolysaccharidosis type IVA belongs to a group of diseases called lysosomal storage disorders and is also known as Morquio syndrome.^{1,2}

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

Symptoms of mucopolysaccharidosis type IVA vary in age at onset and severity and are progressive. Affected individuals typically do not show symptoms at birth and are not intellectually impaired.² Signs and symptoms of the severe, rapidly progressing, form of mucopolysaccharidosis type IVA typically appear between one and three years of age and may include:^{1,2,5,6}

- Skeletal abnormalities, including curvature of the spine, pectus carinatum (protrusion of the sternum), and short stature
- Spinal cord compression
- Progressive bone and joint problems, including Legg Perthes disease (osteonecrosis of the hip)
- Arthritis, often debilitating
- Narrowing of the airway, causing respiratory disease and sleep apnea
- Valvular heart disease
- Hearing impairment
- Corneal clouding, causing visual impairment
- Mild hepatomegaly (enlarged liver)
- Distinctive facial features

Later-onset forms of the disease may not be evident until late childhood or adolescence.² Symptoms are milder and progress more slowly than severe forms.²

There is no cure for mucopolysaccharidosis type IVA. Treatment is primarily supportive and may include surgical intervention, enzyme replacement, or hematopoietic stem cell therapy.^{5,6} Severely affected individuals often do not survive beyond the second or third decade of life.⁶

How is mucopolysaccharidosis type IVA inherited?

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

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.

Who is at risk for mucopolysaccharidosis type IVA?

Mucopolysaccharidosis type IVA can occur in individuals of all races and ethnicities. The prevalence in the general population is estimated to be between 1 in 200,000 and 1 in 300,000 individuals, with a calculated carrier frequency of approximately 1 in 250.¹

Having a relative who is a carrier or who is affected can increase an individual's risk to be 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?

Genetics Home Reference: <http://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-iv>

National MPS Society: <http://mpssociety.org/mps/mps-iv-morquio/>

National Organization for Rare Disorders (NORD): <http://rarediseases.org/rare-diseases/morquio-syndrome/>

References

1. Mucopolysaccharidosis type IVA. *Genetics Home Reference*. Available at <http://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-iv>. Accessed April 15, 2016
2. Regier DS *et al.* Mucopolysaccharidosis Type IVA. GeneReviews Available at <http://www.ncbi.nlm.nih.gov/books/NBK148668/> . Accessed January 18, 2016.
3. *GALNS*. *Genetics Home Reference*. Available at <http://ghr.nlm.nih.gov/gene/GALNS> . Accessed April 15, 2016.
4. *GLB1*. *Genetics Home Reference*. Available at <http://ghr.nlm.nih.gov/gene/GLB1>. Accessed April 15, 2015.
5. Morrone A *et al.* Morquio A Syndrome-Associated Mutations: A Review of Alterations in the GALNS Gene and a New Locus-Specific Database. *Hum Mutat*, 2014 35:1271–1279.
6. Tomatsu S *et al.* Mutation and Polymorphism Spectrum of the GALNS Gene in Mucopolysaccharidosis IVA(Morquio A) *Hum Mutat*, 2005 26:500-512,