

What is mucopolysaccharidosis type III?

Mucopolysaccharidosis type III is an inherited metabolic disease that affects the central nervous system. Individuals with mucopolysaccharidosis type III have defects in one of four different enzymes required for the breakdown of large sugars known as glycosaminoglycans or mucopolysaccharides.¹ The four enzymes, sulfamidase, alpha-N-acetylglucosaminidase, N-acetyltransferase, and N-acetylglucosamine-6-sulfatase, are associated with mucopolysaccharidosis types IIIA, IIIB, IIIC, and IIID, respectively.²⁻⁵ The signs and symptoms of all subtypes of mucopolysaccharidosis type III are similar and due to the build-up of the large sugar molecular heparan sulfate within lysosomes in cells. Mucopolysaccharidosis type III belongs to a group of diseases called lysosomal storage disorders and is also known as Sanfilippo syndrome.⁶

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

Symptoms of mucopolysaccharidosis type III vary in severity and age at onset and are progressive. Affected individuals typically show no symptoms at birth.⁶ Signs and symptoms are typically seen in early childhood and may include:⁷

- Developmental and speech delays
- Progressive cognitive deterioration and behavioral problems
- Sleep disturbances
- Frequent infections
- Cardiac valve disease
- Umbilical or groin hernias
- Mild hepatomegaly (enlarged liver)
- Decline in motor skills
- Hearing loss and vision problems
- Skeletal problems, including hip dysplasia and carpal tunnel syndrome
- Joint contractures
- Distinctive facial features

In the teenage years, symptoms may include:

- Severe dementia
- Lack of speech or communication
- Progressive difficulty swallowing
- Seizures

There is no cure or effective therapy for mucopolysaccharidosis type III. Treatment is supportive. Affected individuals usually survive until the end of the second or beginning of the third decade of life.⁷

How is mucopolysaccharidosis type III inherited?

Mucopolysaccharidosis type III is an autosomal recessive disease caused by mutations in one of four different genes, *SGSH*, *NAGLU*, *HGSNAT*, and *GNS*, which are associated with types IIIA, IIIB, IIIC, and IIID, respectively.⁶ An individual who has one mutation in any of these genes is a carrier and is not expected to have related health problems. An individual who has two mutations in the same gene, one from each parent, is expected to be affected with mucopolysaccharidosis type III. For example, a child with two *SGSH* mutations is expected to be affected with mucopolysaccharidosis type IIIA, and a child with one *SGSH* mutation and one *GNS* mutation is a carrier.

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 III?

Mucopolysaccharidosis type III can occur in individuals of all races and ethnicities. The estimated incidence worldwide is 1.73 in 100,000.^{8,9}

Select carrier frequency estimates

Type	Population	Carrier frequency
IIIA	Worldwide	1 in 170
IIIB	Dutch	1 in 244
IIIB	Worldwide	1 in 220

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-iii>

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

National Organization for Rare Disorders: <http://rarediseases.org/rare-diseases/mucopolysaccharidosis-type-iii/>

References

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