

### What are GM1 gangliosidosis and mucopolysaccharidosis type IVB?

GM1 gangliosidosis and mucopolysaccharidosis type IVB (MPS IVB) are two distinct inherited metabolic disorders with variable severity and age at onset caused by mutations in the *GLB1* gene.<sup>1</sup> Mutations in the *GLB1* gene cause abnormalities in the enzyme beta-galactosidase, which is required for the breakdown of a phospholipid (GM1 ganglioside) and a large sugar molecule (keratin sulfate).<sup>2</sup> Mutations in the *GLB1* gene also cause abnormalities in elastin-binding protein, which is a component of the body's connective tissue.<sup>2</sup> Symptoms of MPS IVB are due to a toxic buildup of keratin sulfate.<sup>2</sup> Symptoms of GM1 gangliosidosis are due to a toxic buildup of keratin sulfate and GM1 ganglioside and/or from defects in elastin-binding protein.<sup>2</sup> GM1 gangliosidosis and MPS IVB belong to a group of disorders called lysosomal storage disorders.<sup>1</sup> MPS IVB is also known as Morquio syndrome type B.<sup>1</sup>

### What are the symptoms of GM1 gangliosidosis and mucopolysaccharidosis type IVB and what treatment is available?

GM1 gangliosidosis is a disease with progressive central nervous system dysfunction. Three clinically overlapping forms have been described, based primarily on the age of onset: type I (infantile), type II (late infantile/ juvenile), and type III (adult or chronic).<sup>3</sup>

Signs and symptoms of the severe infantile form of GM1 gangliosidosis typically appear by six months of age and may include:<sup>3</sup>

- Slowed development with subsequent regression
- Weakened muscles
- Hepatosplenomegaly (enlarged liver and spleen)
- Skeletal abnormalities
- Seizures
- Profound intellectual disability
- Corneal clouding
- Retinal deterioration with cherry-red spot and resulting loss of vision
- Distinctive facial features
- Cardiomyopathy
- Death in early childhood

Signs and symptoms of the late-infantile form and juvenile forms of GM1 gangliosidosis typically appear by 18 months and five years of age, respectively, and may include a developmental plateau with subsequent regression, skeletal dysplasia, and shortened life expectancy.<sup>1,3</sup>

Signs and symptoms of the adult or chronic form of GM1 gangliosidosis typically begin in the second to third decade of life and may include dystonia (involuntary muscle contractions) and vertebral abnormalities.<sup>1</sup> Life expectancy is variable.<sup>3</sup>

MPS IVB is a progressive disease with multiple skeletal abnormalities, joint hypermobility, corneal clouding, and involvement of multiple organ systems.<sup>1,4</sup> Affected individuals appear normal at birth and symptoms appear in early to late childhood or adolescence.<sup>1</sup> Intelligence is not affected unless the central nervous system is impacted by spinal cord compression.<sup>1</sup> Signs and symptoms typically include:<sup>1,4</sup>

- Skeletal abnormalities, including short stature
- Hypermobile and/or restricted movement in joints
- Underdevelopment of the odontoid process in the neck

- Increased risk for spinal cord compression
- Corneal clouding, causing visual impairment
- Hearing impairment
- Respiratory disease
- Sleep apnea
- Hepatomegaly (enlarged liver)
- Distinctive facial features
- Umbilical or inguinal hernia
- Variable life expectancy, depending on disease course

There are no cures for GM1 gangliosidosis or MPS IVB. Treatment is primarily supportive, with a focus on managing symptoms and improving quality of life.<sup>1</sup>

### **How are GM1 gangliosidosis and mucopolysaccharidosis type IVB inherited?**

GM1 gangliosidosis and mucopolysaccharidosis type IVB are autosomal recessive diseases caused by mutations in the *GLB1* gene.<sup>1</sup> An individual who inherits one copy of a *GLB1* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *GLB1* mutations, one from each parent, is expected to be affected with a *GLB1*-related disorder.

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 GM1 gangliosidosis and mucopolysaccharidosis type IVB?**

GM1 gangliosidosis and mucopolysaccharidosis type IVB are rare conditions that can occur in individuals of all races and ethnicities. The worldwide incidence of GM1 gangliosidosis is estimated to be 1 in 100,000 with a carrier frequency of about 1 in 160.<sup>1,3</sup> The prevalence of mucopolysaccharidosis type IVB is estimated to be about 1 in 250,000 with an estimated carrier frequency of about 1 in 250.<sup>1,4</sup>

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?**

Cure GM1 Foundation: <http://www.curegm1.org>

Genetics Home Reference:

For GM1 gangliosidosis: <http://ghr.nlm.nih.gov/condition/gm1-gangliosidosis>

For MPS IV: <http://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-iv>

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

**References**

1. Regier DS and Tiftt CJ. *GLB1*-Related Disorders. GeneReviews Available at <http://www.ncbi.nlm.nih.gov/books/NBK164500/>. Accessed January 19, 2016.
2. *GLB1* gene. *Genetics Home Reference*. Available at <http://ghr.nlm.nih.gov/gene/GLB1>. Accessed May 4, 2016.
3. GM1 gangliosidosis. *Genetics Home Reference*. Available at <http://ghr.nlm.nih.gov/condition/gm1-gangliosidosis>. Accessed May 4, 2016.
4. Mucopolysaccharidosis type IV. *Genetics Home Reference*. Available at <http://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-iv>. Accessed May 4, 2016.