

Mucopolysaccharidosis Type II

Subjects: Genetics

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Definition

Mucopolysaccharidosis type II (MPS II), also known as Hunter syndrome, is a condition that affects many different parts of the body and occurs almost exclusively in males. It is a progressively debilitating disorder; however, the rate of progression varies among affected individuals.

1. Introduction

At birth, individuals with MPS II do not display any features of the condition. Between ages 2 and 4, they develop full lips, large rounded cheeks, a broad nose, and an enlarged tongue (macroglossia). The vocal cords also enlarge, which results in a deep, hoarse voice. Narrowing of the airway causes frequent upper respiratory infections and short pauses in breathing during sleep (sleep apnea). As the disorder progresses, individuals need medical assistance to keep their airway open.

Many other organs and tissues are affected in MPS II. Individuals with this disorder often have a large head (macrocephaly), a buildup of fluid in the brain (hydrocephalus), an enlarged liver and spleen (hepatosplenomegaly), and a soft out-pouching around the belly-button (umbilical hernia) or lower abdomen (inguinal hernia). People with MPS II usually have thick skin that is not very stretchy. Some affected individuals also have distinctive white skin growths that look like pebbles. Most people with this disorder develop hearing loss and have recurrent ear infections. Some individuals with MPS II develop problems with the light-sensitive tissue in the back of the eye (retina) and have reduced vision. Carpal tunnel syndrome commonly occurs in children with this disorder and is characterized by numbness, tingling, and weakness in the hand and fingers. Narrowing of the spinal canal (spinal stenosis) in the neck can compress and damage the spinal cord. The heart is also significantly affected by MPS II, and many individuals develop heart valve problems. Heart valve abnormalities can cause the heart to become enlarged (ventricular hypertrophy) and can eventually lead to heart failure.

Children with MPS II grow steadily until about age 5, and then their growth slows and they develop short stature. Individuals with this condition have joint deformities (contractures) that significantly affect mobility. Most people with MPS II also have dysostosis multiplex, which refers to multiple skeletal abnormalities seen on x-ray. Dysostosis multiplex includes a generalized thickening of most long bones, particularly the ribs.

There are two types of MPS II, called the severe and mild types. While both types affect many different organs and tissues as described above, people with severe MPS II also experience a decline in intellectual function and a more rapid disease progression. Individuals with the severe form begin to lose basic functional skills (developmentally regress) between the ages of 6 and 8. The life expectancy of these individuals is 10 to 20 years. Individuals with mild MPS II also have a shortened lifespan, but they typically live into adulthood and their intelligence is not affected. Heart disease and airway obstruction are major causes of death in people with both types of MPS II.

2. Frequency

MPS II occurs in approximately 1 in 100,000 to 1 in 170,000 males.

3. Causes

Mutations in the *IDS* gene cause MPS II. The *IDS* gene provides instructions for producing the I2S enzyme, which is involved in the breakdown of large sugar molecules called glycosaminoglycans (GAGs). GAGs were originally called mucopolysaccharides, which is where this condition gets its name. Mutations in the *IDS* gene reduce or completely eliminate the function of the I2S enzyme. Lack of I2S enzyme activity leads to the accumulation of GAGs within cells, specifically inside the lysosomes. Lysosomes are compartments in the cell that digest and recycle different types of molecules. Conditions that cause molecules to build up inside the lysosomes, including MPS II, are called lysosomal

storage disorders. The accumulation of GAGs increases the size of the lysosomes, which is why many tissues and organs are enlarged in this disorder. Researchers believe that the GAGs may also interfere with the functions of other proteins inside the lysosomes and disrupt the movement of molecules inside the cell.

3.1. The Gene Associated with Mucopolysaccharidosis Type II

- IDS

4. Inheritance

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

5. Other Names for This Condition

- Hunter Syndrome
- I2S deficiency
- Iduronate 2-sulfatase deficiency
- MPS II

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Keywords

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