



Genetic Fact Sheets for Parents Other Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – <http://www.newbornscreening.info>

Disorder name: Mucopolysaccharidosis Type I
Acronym: MPS I

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This fact sheet contains general information about MPS I. Every child is different and some of this information may not apply to your child specifically. Certain treatments may be recommended for some children but not others. If you have specific questions about MPS I and available treatments, you should contact your doctor.

What is MPS I?

MPS I is an inherited disorder that can affect many parts of the body. People with MPS I have problems breaking down substances in the body called glycosaminoglycans (GAGs). MPS I belongs to a group of disorders known as lysosomal storage disorders. There are two main types of MPS I: *severe* MPS I and *attenuated* MPS I.

Lysosomal Storage Disorders:

Lysosomal storage disorders (LSDs) are a group of inherited disorders. They are caused by enzymes that do not work properly.

Lysosomes are like recycling centers for cells. They are small sacs filled with enzymes. These enzymes help break down large molecules into smaller molecules that the body can re-use. People with LSDs are missing enzymes or have non-working enzymes. As a result, these people have problems breaking down certain large molecules into usable forms. This leads to a buildup of these molecules, which causes a variety of problems.

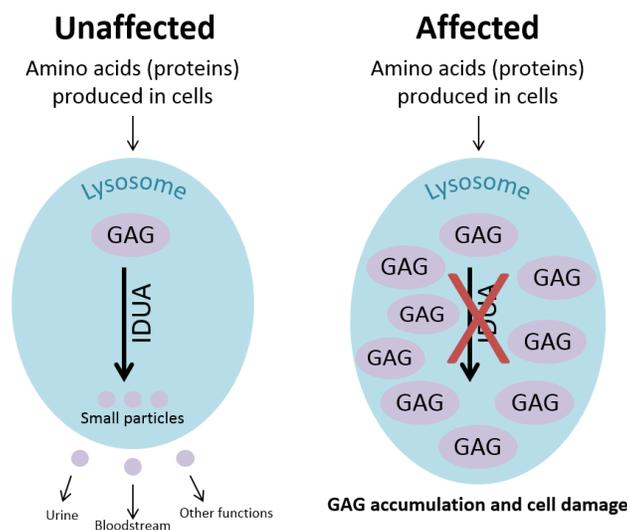
The symptoms and treatment vary between LSDs. They can also vary from person to person with the same LSD.

What causes MPS I?

MPS I occurs when an enzyme called alpha-L-iduronidase (IDUA) is missing or not working properly. Normally, IDUA helps cells break down GAGs into smaller particles that can enter the bloodstream and eventually be discarded or reused. When IDUA doesn't function properly, GAGs accumulate in cell lysosomes, leading to enlarged lysosomes and cell damage.

Individuals with the severe type of MPS I typically have no IDUA enzyme function. Individuals with the attenuated type of MPS I may have some IDUA enzyme function, which leads to less severe symptoms.

MPS I



What are the symptoms of MPS I?

The symptoms of MPS I are mainly a result of cells becoming enlarged due to the build-up of GAGs and the enlargement of the lysosomes.

People with the severe type of the disease tend to show symptoms before one year of age and are almost always diagnosed by 18 months old. They develop heart and breathing problems that become severe and usually lead to death before ten years of age.

The attenuated type of the disease is more variable. People with attenuated MPS I usually begin to show symptoms between the ages of three and ten. The severity of symptoms varies significantly between individuals. Symptoms are typically less severe than those seen in individuals with the severe type of the disease. Individuals with attenuated MPS I may or may not have a shortened lifespan.

Symptoms can include:

- Developmental delays and loss of skills (regression)
- Larger than normal liver and spleen (hepatosplenomegaly)
- Distinctive looking facial features with thickened lips, cheeks, tongue, and nose
- Generalized thickening of most long bones, particularly the ribs (dysostosis multiplex)
- Joint deformities that affect movement (contractures)
- Narrowing of the spinal canal (spinal stenosis)
- Heart valve abnormalities, which can lead to heart failure
- Frequent upper respiratory infections and ear infections
- Enlarged vocal cords, resulting in a deep voice
- Sleep apnea
- Excessive fluid buildup in the brain (hydrocephalus)
- Hearing loss
- Corneal clouding
- Carpal tunnel syndrome
- Short stature
- Umbilical hernia
- Inguinal hernia

What is the treatment for MPS I?

Because MPS I can affect many parts of the body, comprehensive treatment requires a team of many different specialists. All people with MPS I should be seen by a biochemical genetics doctor (or metabolic genetics specialist). The team may also include neurology (brain doctor), hematology (blood doctor), orthopedics (bone doctor), primary care, cardiology (heart doctor), pulmonology (lung doctor),

gastroenterology (liver doctor), audiology (hearing), ophthalmology (eye doctor), rehabilitation specialists (e.g., physical therapist), dental, and developmental specialists.

Children with MPS I are monitored closely for new or worsening issues. They are typically checked yearly for problems of the nerves, heart, bones, airway, sleep, eyes, and hearing. They are also assessed for learning and intellectual differences.

There are two main methods for treating both attenuated and severe MPS I. Both methods aim to replace missing IDUA enzyme activity: bone marrow transplant (also called hematopoietic stem cell transplant (HSCT) and enzyme replacement therapy (ERT).

1. Hematopoietic Stem Cell Transplant (HSCT)

Hematopoietic stem cell transplant is the best way to treat severe MPS I, and if it is successful, improvements are seen in survival, growth, facial features, liver and spleen size, hearing, heart disease, and lung disease. HSCT may help the neurologic-symptom individuals with mild disease. HSCT is not a cure but can significantly help some of the symptoms of severe MPS I. It is best if HSCT is done prior to age 2 years.

2. Enzyme Replacement Therapy (ERT)

MPS I is caused by not having enough of an enzyme called alpha-L-iduronidase (IDUA). Enzyme replacement therapy gives people a replacement form of that enzyme. This new enzyme replaces the IDUA in people with MPS I. This is a long-term treatment option, but it is not considered a cure. If enzyme replacement therapy is started prior to the onset of symptoms, it can often prevent or reduce the impact of some MPS I symptoms (except brain and central nervous system symptoms).

Supportive therapies can help treat the symptoms of MPS I:

- Physical therapy can help preserve joint function and increase range of motion.
- Wearing sunglasses can help reduce glare resulting from corneal clouding.
- Hearing aids may be considered in individuals experiencing hearing loss.
- Removal of the tonsils and adenoids can help decrease upper airway obstruction

What happens when MPS I is treated?

When HSCT is started early enough in those affected by severe MPS I (ideally before about 16 months - two years of age), cognitive decline may be slowed or even halted. This treatment can also improve other features such as cardiac, facial appearance, liver and spleen enlargement, joint symptoms, and hearing symptoms. However, significant bone, joint, and heart valve disease may still occur despite HSCT.

ERT can improve problems with breathing, growth, joints, and the heart, but cannot treat cognitive symptoms. If started early, it may improve bone problems.

ERT can improve liver size, linear growth, joint mobility, breathing, and sleep apnea in individuals with the attenuated type of MPS I.

MPS I

What causes the IDUA enzyme to be absent or not working correctly?

Genes tell the body how to make enzymes. The IDUA gene instructs the body to make the IDUA enzyme. Everyone has two copies of the IDUA gene. People with MPS I have changes, also called variants, in both copies of their IDUA genes. Because of the variants in the IDUA genes, the IDUA enzyme either does not work properly or is not made at all.

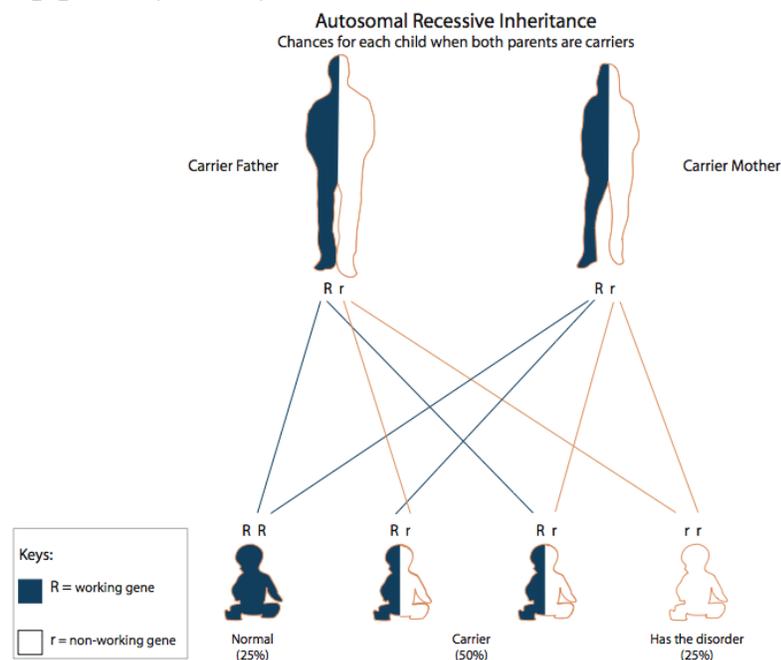
How is MPS I inherited?

MPS I is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has a pair of genes that make the IDUA enzyme. In people with MPS I, neither of the *IDUA* genes work correctly. These individuals inherit one non-working IDUA gene for the condition from each parent.

Parents of children with MPS I usually do not have the condition themselves. Instead, each parent has one non-working IDUA gene and one working IDUA gene. The parents are called carriers. Carriers do not have MPS I because one of their genes is working correctly. The working IDUA gene is able to make enough IDUA enzyme for the person to be healthy.

When both parents are carriers, each pregnancy has a 25% (1 in 4) chance of resulting in a child having MPS I (has the disorder). There is a 50% (1 in 2) chance for the child to be a carrier, just like the parents. There is a 25% (1 in 4) chance that the child will have two working genes (normal).



Genetic counseling is available to families who have children with MPS I. Genetic counselors can answer questions about how MPS I is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

Is genetic testing available?

A diagnosis of MPS I is usually made based on a doctor's evaluation and genetic testing. Genetic testing and enzyme testing for MPS I can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes (variants) in the IDUA genes that cause MPS I.

Because MPS I may be diagnosed by enzyme testing, DNA testing is not always necessary to diagnose your child. It is helpful to know the gene changes in a child with MPS I because it can help with testing in other family members and in prenatal testing of a future pregnancy.

What other testing is available?

Screening Tests

Newborn Screening

Newborn screening for MPS I is done in some states. A blood spot from the baby's heel is used to screen for many different conditions. Newborn screening detects MPS I by looking for IDUA enzyme activity. IDUA enzymes are active in every healthy newborn's blood. Since babies with MPS I have IDUA enzymes that are either missing or not working properly, they will have reduced enzyme activity.

If your child has had a positive screen for MPS I through a newborn screening program, it does not yet mean that he or she has MPS I. Other tests still need to be done in order to confirm the diagnosis.

Diagnostic Testing

When one or both parents are known to be carriers of the MPS I disease, newborn screening results are not enough to rule out MPS I disease in a newborn baby. In this case, more sensitive diagnostic testing should be done in addition to newborn screening, even if the newborn screening result is negative.

Confirmatory Testing

Confirmatory testing is needed for a diagnosis of MPS I. Each person may not need every one of the confirmatory tests.

Some of these special tests detect the amount of GAGs and IDUA enzymes in your baby's blood and urine. These blood or urine tests may be helpful to determine whether your child needs treatment, and then later to see whether treatment is working properly.

Genetic testing of the IDUA gene may be necessary after newborn screening.

Can you test for MPS I during a future pregnancy?

Once a genetic cause has been identified, DNA from the fetus can be tested. The sample for this testing is obtained by either chorionic villus sampling CVS or amniocentesis.

Parents may choose to have testing during pregnancy or wait until birth to have the baby tested. Parents may also choose to use assisted reproductive techniques to decrease the chance that their future children would have MPS I. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

Can other members of the family have MPS I or be carriers?

Having MPS I

Each full sibling (same mother and father) of a baby with MPS I has a 25% (1 in 4) chance of also having MPS I. Even older siblings who have not shown any symptoms of the disease could have attenuated MPS I that has not caused symptoms yet, but will in the future. All siblings of an individual with MPS I should be evaluated to see if they also have this disorder.

Not all states offer newborn screening for MPS I. Even if your baby's siblings have had normal newborn screening, they should be tested specifically for MPS I because early treatment can prevent more serious health problems. Talk to your doctor or genetic counselor about testing your other children for MPS I.

Carrier for MPS I

Each full sibling of a baby with MPS I has a 50% (1 in 2) chance of being a carrier. Full siblings who do *not* have MPS I have a 66% (2 in 3) chance of being a carrier. If you are a parent of a child with MPS I, your brothers and sisters have a 50% (1 in 2) chance of being a carrier. It is important for other family members to be told that they could be carriers. There is a small chance that they are also at risk to have children with MPS I.

Not all states offer newborn screening for MPS I. This makes it especially important to tell your family members if they are at risk for having a child with the disease.

Can other family members be tested?

Diagnostic testing

Siblings of a child with MPS I should be tested. Talk to your doctor or genetic counselor if you have questions about testing for MPS I.

Carrier testing

If both gene variants have been found in your child, other family members can have DNA testing to see if they are carriers. If you have questions about carrier testing, ask your genetic counselor or doctor.

How many people have MPS I?

MPS I is seen in all populations and about 1 in 100,000 people have the severe type and 1 in 500,000 have the attenuated type.

Does MPS I happen more often in a certain ethnic group?

MPS I occurs in people of all ethnic groups around the world.

Does MPS I go by any other names?

MPS I is also known as:

- Hurler syndrome
- Hurler-Scheie syndrome
- Scheie syndrome
- Alpha-L-Iduronidase deficiency
- IDUA deficiency
- Attenuated MPS I
- Severe MPS I

Where can I find more information?

National MPS Society

<http://www.mpssociety.org>

MedlinePlus

<https://medlineplus.gov/genetics/condition/mucopolysaccharidosis-type-i/>

Canadian Society for Mucopolysaccharide and Related Diseases Inc. (Canadian MPS Society):

<http://www.mpssociety.ca>

