NBS Info Sheet

Mucopolysaccharidosis Type-I (MPS I)

Mucopolysaccharidosis type I (MPS I or Hurler Syndrome) is an inherited condition that affects many different parts of the body. It is considered a lysosomal storage disorder because people with MPS I have lysosomes (the recycling center of each cell) that cannot break down certain types of complex sugars. This causes undigested sugar molecules and other harmful substances to build up in cells throughout the body, resulting in a variety of symptoms.

Clinical Symptoms

There are two types of MPS I – severe and attenuated – that differ in signs, symptoms, and age of onset. The severity of the condition depends on how much IDUA activity is present. IDUA activity shows how well your baby can break down GAGs.

High levels of GAGs can damage many parts of the body.

The timing and type of problems caused by MPS I vary between different people. For the severe form of the condition, outward signs appear by age 2. For the milder form, signs or symptoms may not appear under later in childhood.

Signs of the condition may include the following:

- Soft out-pouching around their belly button or lower stomach (umbilical or inguinal hernia)
- A bony lump on their back (curvature of the spine)
- Large head (macrocephaly)
- Facial features that are different from their parents
- Delays in development or problems with learning
- Swollen abdomen
- Cloudy eyes
- Hearing loss
- Frequent runny noses
- Noisy breathing, or snoring

Incidence

The severe form of mucopolysaccharidosis type I occurs in about 1 in 100,000 newborns. The attenuated form is less common and occurs in approximately 1 in 500,000 newborns.

Genetics and Inheritance

Your body uses complicated sugars called glycosaminoglycans (GAGs) in several important processes. An enzyme called alpha-L-iduronidase (IDUA) breaks down GAGs so that the body can use them. This process occurs in special compartments inside your cells called lysosomes.

MPS I is a condition that occurs when IDUA is absent or present at low levels. The lysosomes then have trouble breaking down GAGs. This causes a buildup of GAGs in the tissues that can result in problems throughout the body. GAGs used to be called mucopolysaccharides, which is where the condition got its name.

MPS I is an autosomal recessive condition. Babies inherit the condition when each parent passes down a nonworking *IDUA* gene to their baby. Only babies with two nonworking *IDUA* genes—one from the mom and one from the dad—have this condition.

- People with one working copy and one nonworking copy of the *IDUA* gene are called carriers.
- Carriers do not have or develop the condition. However, they may pass down a nonworking copy of the gene to their children.
- If two parents are carriers of a nonworking copy of the *IDUA* gene, they have a 1 in 4 chance of having a child with MPS I.
- Carriers for MPS I often do not know they are carriers before having a child with the condition. In most cases, families have no history of the condition until the birth of a child with MPS I.
- Parents who already have a child with MPS I still have a 1 in 4 chance of having another child with MPS I. This 1 in 4 chance stays the same for all future children.

Treatment

Physical Therapy

Physical therapy is a very important part of treating the signs and symptoms of MPS I. Consistent physical therapy early on can help preserve mobility and lessen pain and joint stiffness.

Surgeries

Removal of the tonsils and adenoids and insertion of ventilating (ear) tubes can prevent some upper respiratory infections and may reduce hearing loss. Hearing aids may be recommended for some individuals. Children with mild to severe MPS I may develop a buildup of fluid in the brain (hydrocephaly), a surgery to relieve the pressure inside the skull may be recommended.

Diet

A dietician can help you create a nutrition plan to help control diarrhea and constipation, which may occur in those with severe MPS I. There is no diet that can prevent the storage of GAGs because they are actually created by the body.

Medications

If baby has periods of constipation, health care providers may recommend laxatives to be used very conservatively to relieve discomfort.

Enzyme Replacement Therapy (ERT)

Enzyme replacement therapy (ERT) can be an effective treatment for symptoms of MPS I that do not involve the central nervous system. This treatment aims to supplement the enzymes that are present at low levels in your baby's lysosomes. ERT may improve growth, joint movement, sleep apnea, respiratory function, pain levels, vision, and liver/spleen enlargement.

Hematopoietic Stem Cell Transplantation (HSCT)

Hematopoietic stem cell transplantation (HSCT) to improve the signs and symptoms of MPS I. Hematopoietic stem cells can be found in bone marrow, the bloodstream, or the umbilical cord blood of newborn babies. Transplanted hematopoietic stem cells are administered through an intravenous (IV) line. This therapy may reduce facial coarseness and liver/spleen enlargement, improve hearing, stabilize heart function, and slow the decline of cognitive function.

Screening Methodology

The testing methodology for MPS I in Kansas is Digital microfluidics (DMF). Digital microfluidics is a paradigm in which complex bioassay protocols are executed using a simple toolkit of droplet operations such as, dispensing, transporting, mixing, and disposal. Droplets are manipulated through electrical control of surface tension (electrowetting). Tiny droplets are transported omnidirectionally on a printed circuit board substrate with utmost versatility allowing complex droplet operations. Any assay can be developed by leveraging this versatility of droplet operations, enabling rapid implementation of multifunctional diagnostic testing.

The development of fluorometric enzymatic assays including alpha-L-iduronidase (IDUA), the enzyme deficient in MPS I, allows for a quantitative measurement of the enzyme.

A low IUDA level indicates the possibility of MPS-I. *Kansas will send out for 2nd tier testing with Mayo Clinic. Patient should still be evaluated while waiting for 2nd tier testing results.*

https://baebies.com/technology/

https://pmc.ncbi.nlm.nih.gov/articles/PMC7711648/

https://newbornscreening.hrsa.gov/conditions/mucopolysaccharidosis-type-i

What to do after Presumptive Positive

1) The clinician should immediately check on the clinical status of the baby. *Kansas will send out for 2nd tier testing with Mayo Clinic. Patient should still be evaluated while waiting for 2nd tier testing results.*

2) Consultation with a metabolic specialist is essential.

3) The specialist may request urine organic acid analysis and other labs on the baby.

4) Call KS Newborn Screening Program at 785-291-3363 with questions about results.

5) Report clinical findings to the Newborn Screening Program at 785-291-3363.

6) Same birth siblings (twins, triplets) of infants diagnosed with MPS I should be re-screened; additional testing of these siblings also may be indicated.

7) Consider testing older siblings. Some individuals may be affected, but show no symptoms of the condition.

Confirmation of Diagnosis

Enzyme Testing:

MPS I is characterized by a deficiency in the alpha-L-iduronidase enzyme, which is responsible for breaking down GAGs. Enzyme activity can be measured in blood samples or skin cells.

Urine GAG Analysis:

Elevated levels of GAGs, particularly dermatan sulfate and heparan sulfate, can be detected in the urine.

DNA testing:

The alterations to the *IDUA* gene that cause MPS I can be detected via a DNA test. DNA testing can confirm the MPS I diagnosis.

Communication of Results to Parents

If a baby is diagnosed with MPS I, the following points should be conveyed to parents:

• Parents should understand that treatment for MPS I will be lifelong.

• Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and includes pediatrics and a metabolic specialist. Other providers may include cardiology, physical therapy, and nutritionist.

• Genetic counseling may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.

Patient Resources

National MPS Society

https://mpssociety.org/

For consultation, contact:

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