

Inherited Metabolic Storage Disorders: Hurler's Syndrome

Inherited metabolic storage disorders are a group of inherited diseases in which the lack of an enzyme affects various organs and tissues, including the brain. Enzymes are proteins that play many roles, including to metabolize (break down) substances in the body. In metabolic storage disorders, the body lacks an enzyme needed to metabolize a substance, such as a sugar. Instead, the substance builds up in the body, where it can damage the brain, nervous system, bones, organs and other tissues. Different metabolic disorders affect different enzymes and cause different types and levels of damage.

Metabolic storage disorders are caused by a mutation (mistake) in a gene that affects metabolism. Genes carry an inherited code of instructions that tells the body how to make every cell and substance in the body.

These disorders are rare. Many of them appear in childhood, although some can also appear in adults. A bone marrow or cord blood transplant (also called a BMT) is a treatment option for some of these disorders.

Mucopolysaccharidoses, also called MPS disorders, are a subgroup of metabolic disorders. Some MPS disorders have been treated with transplant:

- Hurler's syndrome (MPS I) – this is the form of MPS that doctors have the most experience treating with transplant, since 1980
- Maroteaux-Lamy syndrome (MPS VI)
- Sly syndrome (MPS VII)

Leukodystrophies are another subgroup of metabolic disorders, some of which have been treated with transplant:

- Cerebral X-linked adrenoleukodystrophy (ALD)
- Globoid-cell leukodystrophy (GLD) – also called Krabbe disease
- Metachromatic leukodystrophy (MLD)

If you or a family member has an inherited metabolic storage disorder, it is important to talk to a doctor who has experience treating the disorder. These disorders are rare and complex. Early diagnosis and prompt treatment are important. If your doctor has not treated other patients with your disorder, ask him or her to refer you to an expert for consultation. A doctor with experience treating the disorder can discuss whether transplant is a treatment option for you or your family member.

Hurler's Syndrome and Transplant

Hurler's syndrome is one of a group of inherited metabolic storage disorders in which the lack of an enzyme affects various organs and tissues, including the brain. Enzymes are proteins that play many roles, including to metabolize (break down) substances in the body. In metabolic storage disorders, the body lacks an enzyme needed to metabolize a substance, such as a sugar. Instead, the substance builds up in the body and causes damage.

An MPS Disorder

Hurler's syndrome is also called mucopolysaccharidosis I (MPS-I). It is one of a subgroup of metabolic disorders known as MPS disorders. MPS disorders are caused by a mutation (mistake) in a certain gene. A gene carries an inherited code of instructions that tell the body how to make every cell and substance in the body. The mutated gene in MPS disorders affects an enzyme called alpha-L-iduronidase (IDUA). This enzyme breaks down complex sugars called glycosaminoglycans (GAGs). The body needs GAGs to build bones and tissues, so a healthy body is always making and breaking down GAGs.

In people with MPS disorders, the body keeps making GAGs but does not have the enzyme to break them down. The GAGs are stored in cells throughout the body. As they build up, they damage organs and tissues.

Inheriting Hurler's Syndrome

Hurler's syndrome occurs in about one of every 100,000 babies born. A child inherits the syndrome when he or she gets two abnormal genes that affect the IDUA enzyme, one from each parent. If only one parent passes on the gene mutation, the child will not have the disease. Instead, the child will be a "carrier" and may pass the gene mutation to his or her own children.

Signs and Symptoms of Hurler's Syndrome

As GAGs build up in the body, signs and symptoms of the damage GAGs cause begin to appear. These may include:

- Problems with mental function (mental retardation)
- Heart problems, including changes in the valves
- Hearing problems and frequent ear infections
- Large head size, broad forehead and heavy eyebrows
- Deformed bones and stiff joints, especially the spine, hips, knees, wrists and fingers
- Short size
- Breathing problems

Signs and symptoms usually appear within the first year of life and grow worse over time. If the disease is not stopped, children with Hurler's syndrome usually die by 5 to 10 years of age.

Diagnosis

Tests doctors may use to diagnose Hurler's syndrome include:

- Urine tests for extra GAGs
- Tests of blood and/or skin samples to see if the body is making the IDUA enzyme
- Genetic tests for mutations to the gene for the IDUA enzyme
- X-rays to check for damage to the spine
- Electrocardiogram (EKG) or echocardiogram to check heart function and valve problems

Families affected by Hurler's syndrome may want to talk with a genetic counselor about family planning and the chances of having children with the disorder. Early diagnosis can enable early treatment of a child after birth, which can make a difference in outcomes.

Hurler's Syndrome Treatments

The goal of treatment for Hurler's syndrome is to give the body the missing enzyme so it can break down GAGs. The two main treatments for children with Hurler's syndrome are enzyme replacement therapy and a bone marrow or cord blood transplant.

Enzyme Replacement Therapy

For enzyme replacement therapy, a patient is given a drug that has the IDUA enzyme his or her body is missing. The drug is called laronidase, or Aldurazyme®. Treatment with laronidase can improve problems with breathing, growth, the bones, joints and heart. However, there is no evidence that it has any affect on mental development problems caused by Hurler's syndrome.

- Enzyme replacement therapy may be a good option for children who have a form of MPS I disorder that does not cause mental retardation (Scheie syndrome or Hurler's/Scheie syndrome).
- Some children with Hurler's syndrome may be treated with both enzyme therapy and a transplant. This approach is being studied in a clinical trial.

Bone Marrow or Cord Blood Transplant

A bone marrow or cord blood transplant (also called a BMT) is the only known treatment that can stop the progression of mental damage caused by Hurler's syndrome.

Transplant for Hurler's Syndrome

A transplant replaces the abnormal cells in the bone marrow (the cells with the mutated gene) with healthy cells from a family member or unrelated donor or cord blood unit. The healthy cells provide a source of the enzyme needed to break down GAGs and stop further damage to the body.

In general, a transplant has the best chance of success when it is done soon after diagnosis. Getting a transplant early is important to stop damage caused by the disorder before it becomes severe. Children who receive a transplant early enough can have normal or near-normal mental development. Damage to the organs is stopped and hearing may improve.

However, transplants for children who have already developed severe damage have had disappointing results. If the disorder has caused organ damage, a child has a higher risk of developing life-threatening complications from transplant. In addition, a transplant may not undo damage the disease has already done, especially to the nervous system. However, in some children, there have been improvements in some organs, such as the liver, airway and heart. The child must live with and be treated for the damage that already exists. For example, most children will need multiple surgeries to treat problems with bones, joints and other tissues.

Cord Blood Transplants

Recent studies have also shown good results for transplants using cord blood. Cord blood transplants may be an important option for children with Hurler's syndrome, because many do not have a suitable donor in their family and they need to have a transplant quickly. A suitable cord blood unit may be more quickly available than an unrelated adult donor.

Transplant Risks

A transplant is an intense treatment, and some possible side effects can be life-threatening. For children with Hurler's syndrome, three of the most serious risks of transplant are:

- Graft-versus-host disease (GVHD) – A common transplant complication that can range from mild to severe. For patients who receive a transplant to treat leukemia, GVHD may be linked with a beneficial graft-versus-leukemia effect. However, there is no benefit to GVHD for patients with Hurler's syndrome.
- Graft failure – Graft failure is when the donated cells (the graft) do not grow and make new blood cells for the body (engraft). Graft failure can be life-threatening. If the child's own cells return, he or she may survive, but the progress of the disease will not be stopped. Graft failure is a bigger risk for children being treated for Hurler's syndrome than for many other diseases.
- Bleeding in the lungs (pulmonary hemorrhage) – Children with Hurler's syndrome have an increased risk for this serious complication. Bleeding in the lungs can affect how well the child can breathe. In some cases, a child may need a breathing tube and a breathing machine (ventilator).

Making Treatment Decisions

If your child has Hurler's syndrome, it is important to see a doctor who is an expert in this disorder. If your doctor has not treated other patients with Hurler's syndrome, ask him or her to refer you to an expert for consultation. Since Hurler's syndrome gets worse quickly, it is important to see an expert as soon as possible. If transplant is a treatment option for your child, talk with your doctor about the risks, limits and possible benefits of transplant.

The NMDP's Office of Patient Advocacy (OPA) continually develops resources and materials to help patients, family members and doctors with questions about marrow or cord blood transplantation. In addition to print, audio and visual materials, OPA has bilingual (Spanish/English) case managers and LanguageLine interpreter services available for callers. All OPA materials and services are free and confidential. Call the OPA toll-free at 1 (888) 999-6743. Outside the United States call (612) 627-8140, or visit marrow.org/patient