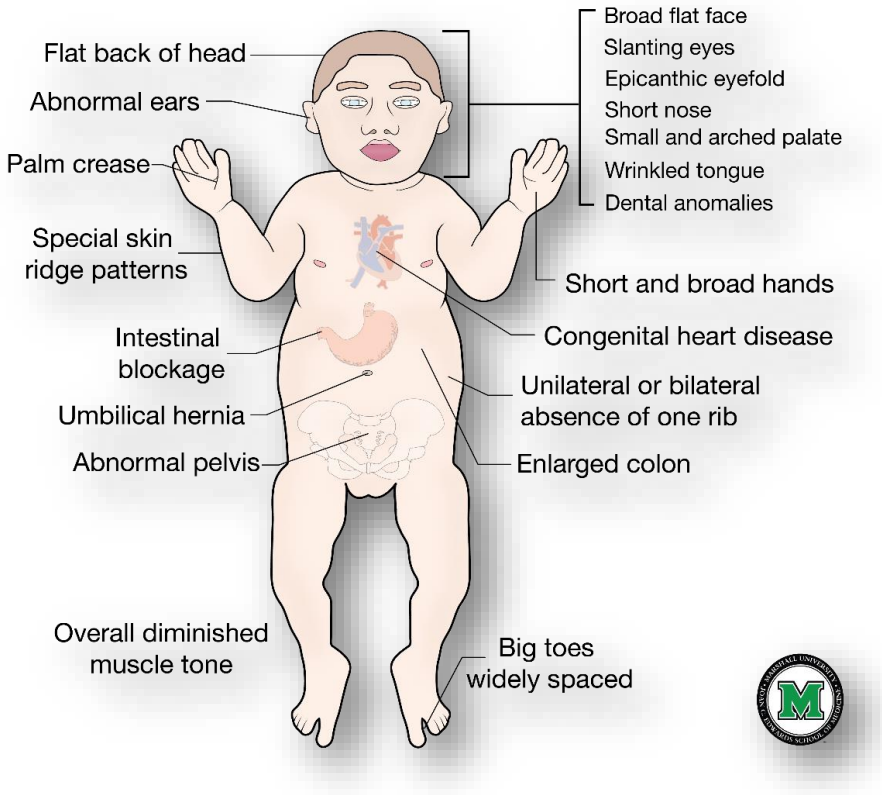
babycell™

The Life Saving Cord Blood Bank

A CLOSER LOOK AT
HURLER SYNDROME

What is Hurler Syndrome?

- Hurler Syndrome belongs to a group of inherited metabolic storage disorders in which a person cannot break down chains of sugar molecules called glycosaminoglycan. These complex sugars are necessary for the body to build bones and tissues.
- In Hurler syndrome, known as Mucopolysaccharidosis or MPS, critical body enzymes (alpha-L-iduronidase) is missing or deficient. Without this enzyme, the big molecules build up and progressively damage parts of the body.
- It is also known as Mucopolysaccharidosis type I or MPS I as well as Gargoylism.



Types of Hurler Syndrome?

- **Hurler syndrome**, also known as **Mucopolysaccharidosis type I** (**MPS I**). MPS I is divided into three subtypes based on severity of symptoms.

MPS I Or Hurler Syndrome

The most severe of the MPS I subtypes.

MPS I-S Or Scheie Syndrome

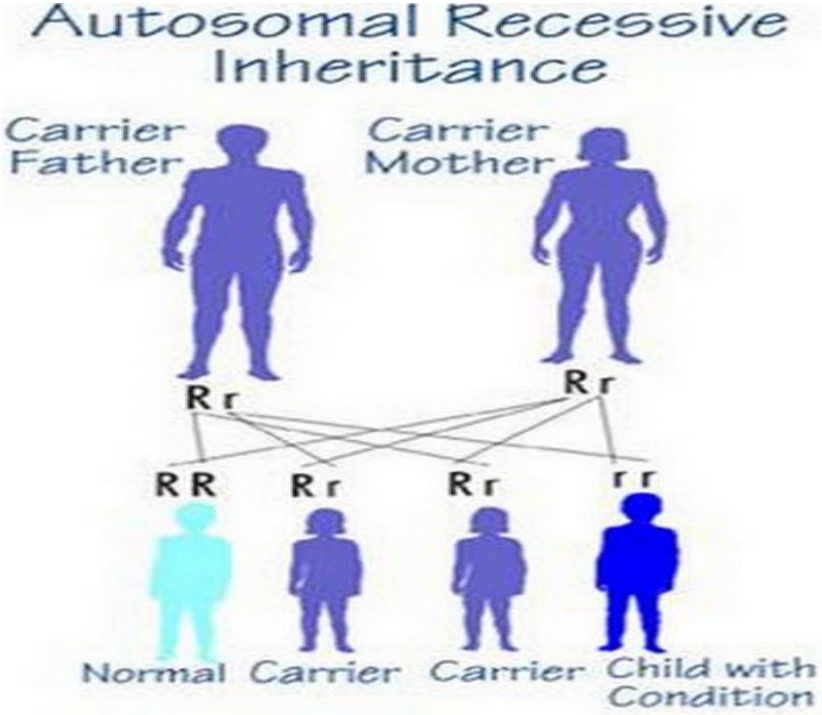
Is the less severe version of Hurler Syndrome. It is a condition characterized by corneal clouding, facial dysmorphism and normal lifespan.

MPS I H-S Or Hurler-Scheie Syndrome

It is also known as "Mucopolysaccharidosis type I H-S". It is a cutaneous condition, also characterized by mild mental retardation and corneal clouding.

What causes Hurler Syndrome?

- People with Hurler Syndrome usually have a deficiency in the enzyme alpha-L iduronidase, which helps break down long chains of sugar molecules called glycosaminoglycans and the deficient of this enzyme results in affecting various organs and tissues in the body. Without the enzyme, glycosaminoglycans build up and damage organs.
- The absence of alpha L-iduronidase would cause a buildup of heparin sulfate and dermatan sulfate causing damage to the organs, including the heart.
- Symptoms can range from mild to severe.



Epidemiology of Hurler Syndrome

International

Mucopolysaccharidosis type I (MPS I) has an estimated incidence of 1 case per 100,000 live births.

Mortality/Morbidity

Lifespan in mucopolysaccharidosis type I (MPS I) ranges from death in early childhood in the most severe form to adulthood in the least severe variant.

Race

Mucopolysaccharidosis type I (MPS I) is inherited in an autosomal recessive manner and affects both sexes.

Ref:

https://www.counsyl.com/services/family-prep-screen/diseases/hurler-syndrome/

https://recombine.com/diseases/hurler-syndrome

Symptoms of Hurler Syndrome

- Common symptoms of Hurler Syndrome include
  - having a short stature
  - mental retardation
  - difficulty in breathing
  - corneal clouding
  - chronic runny nose

- The symptoms would usually appear between 6 months to 2 years of age. Children affected with the condition usually live past the age of 5 but unfortunately do not survive beyond 10 years of age.

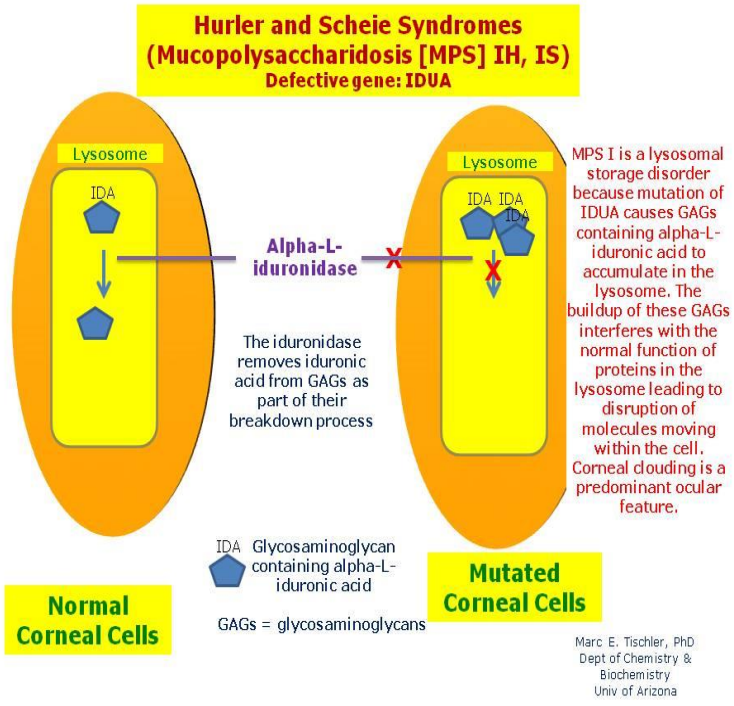
- It is usually marked by progressive deterioration. Enlargement of the liver and spleen are usually prevalent along with dwarfism and characteristic facial features like short nose, flat face and large head.

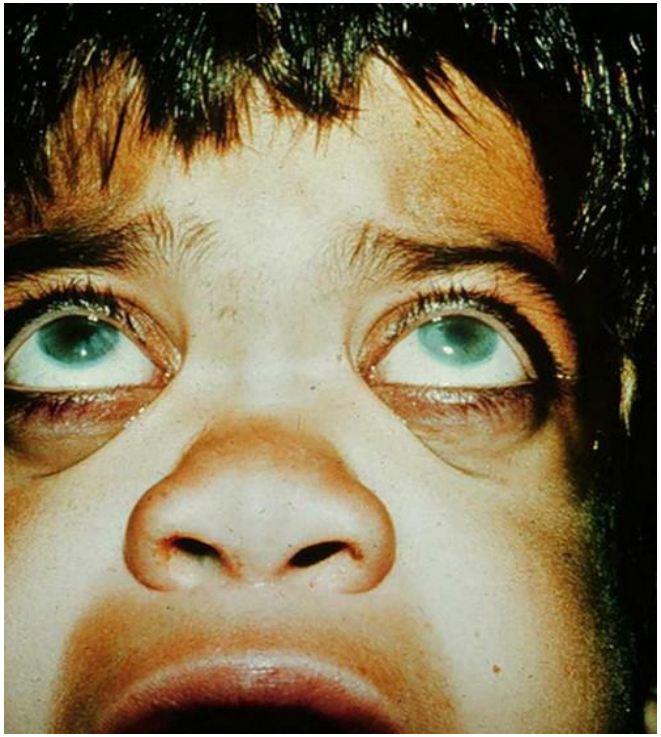
- Developmental delay is usually evident alongside mental retardation. By age 4, children would already stop developing. Physical skills would also deteriorate. Loss of hearing and enlargement of the tongue is possible. Carpal tunnel syndrome and limited range of movement in the joints are also highly likely.

- Children usually appear larger than normal at birth and may have inguinal or umbilical hernias. Height may increase faster in the first year but would stunt after reaching 3 years of age.

Symptoms of Hurler Syndrome

- Height of children suffering from Hurler Syndrome would usually reach around 4 feet and the body trunk would appear short with the ribs becoming wider and oar-shaped. Unique facial features would become more noticeable by 2 years of age.
- Feeding and bowel problems may be experienced by children.
- Obstructive airway disease, respiratory tract infections and cardiac problems would usually be the cause of death by children affected with Hurler syndrome.





How is Hurler Syndrome diagnosed

Hurler Syndrome can be diagnosed through clinical examination and a series of tests.

- Urine tests are undertaken to check excess mucopolysaccharides that may be excreted
- Blood tests and skin samples to check for the presence of alpha-L iduronidase
- Genetic tests for positive gene mutation
- Radiographic examination to check for damaged spine
- Electrocardiogram or echocardiogram to check heart function and valve problems
- Prenatal diagnosis through amniocentesis and chorionic villus sampling would determine if a foetus carries a mutated gene, which causes Hurler syndrome

Treatment of Hurler Syndrome

- Enzyme replacement therapy is usually undertaken to provide the alpha-L iduronidase, which the body lacks. This is done through medication like laronidase (Aldurazyme), which is commercially prepared by Genzyme. Laronidase has shown to be effective in improving problems associated with breathing, growth, heart, bones and joints. However, enzyme replacement therapy is not yet advised for those children who have MPS I with mental retardation like Scheie Syndrome and Hurler-Scheie Syndrome.

- Bone marrow transplantation (BMT) and umbilical cord transplantation (UCBT) are also used to treat MPS. Transplantation of the bone marrow or the umbilical cord have shown the capability to halt abnormal physical features and neurologic degeneration.

- Gene therapy is still under research.

Cord Blood transplant for treatment of Hurler Syndrome

- Haematopoietic stem cell transplants have become a valuable treatment for Hurler Syndrome, as transplanted cells can generate new, healthy, enzyme producing blood cells to replace the diseased cells.
- These donor cells will deliver enzymes to all organs, including the brain and can prevent disease progression.
- Cord blood has been proposed as an alternative stem cell source for children with HS since it has been suggested that cord blood may increase their levels of lysosomal alpha-L-iduronidase, which consequently may allow them to live longer with fewer complications.

REASONS TO CHOOSE CORD BLOOD STEM CELLS

A doctor might choose cord blood because of some of the ways it differs from marrow or peripheral blood.

More tolerant matching: A close match between the patient and the donor or cord blood unit can improve a patient's outcome after transplant. If you have an uncommon tissue type, you may not find a closely matched adult donor for you. However, a cord blood unit may be the best option.

More quickly available: Cord blood units are stored and ready to use. A cord blood unit can be selected and delivered to the transplant center in less than two weeks whereas it can take two months or more to find an unrelated marrow or peripheral blood donor.

Less GVHD: Graft-versus-host disease (GVHD) is a common complication after an allogeneic transplant (which uses cells unrelated donor). GVHD can range from mild to life-threatening. There is less chance of GVHD when the cord blood transplant is done using cells from a family member.

Case Studies

Cord-Blood Transplants from Unrelated Donors in Patients with Hurler's Syndrome

Susan L. Staba et al; N Engl J Med 2004; 350:1960-1969

- 20 children (10 boys and 10 girls) received cord-blood transplants from unrelated donors.
- Post transplantation, patients were evaluated every 6 to 12 months by multiple pediatric sub specialists in developmental pediatrics, ophthalmology, audiology, cardiology, pulmonology, and orthopedics.
- Eighty-five percent of the children survived with complete donor chimerism and normal peripheral-blood alpha-L-iduronidase activity.
- Haematopoietic stem-cell transplantation arrests the progression of Hurler's syndrome, averting death from cardiac causes and liver disease, improving growth and development, and prolonging survival

Case Studies

Hematopoietic stem cell transplantation improves the high incidence of neutralizing allo-antibodies observed in Hurler's syndrome after pharmacological enzyme replacement therapy.
Muhammad Ameer Saif et al; Haematologica September 2012 97: 1320-1328

- Development of an immunoglobulin G enzyme-linked immunosorbent assay as well as *in vitro* catalytic enzyme inhibition and cellular uptake inhibition assays and quantified enzyme inhibition by allo-antibodies.
- 8 patients were examined for the impact of these antibodies who received enzyme therapy before and during hematopoietic stem cell transplantation.
- High titer immune responses were seen in patients following exposure to alpha-L-iduronidase.
- Allogeneic haematopoietic stem cell transplantation was an effective and rapid immune tolerance induction strategy.

Cord Blood Transplantation

Step 1
- Collection, storage and cryopreservation of umbilical cord blood

Step 2
- Day -30 to -11: HLA typing and donor/recipient matching

Step 3
- Day -10: Patient admission and isolation in ICU room

Step 4
- Day -8: Pre-transplantation conditioning regimen for 8-10 day before transplantation

Step 5
- Day 0: Umbilical cord blood transplantation in patient

Step 6
- Day 1 to Day 25: Post transplantation follow up and monitoring

Cord Blood Transplantation

STEP 1: COLLECTION OF UMBILICAL CORD BLOOD

- Umbilical cord blood is collected by trained paramedic as per standard procedure and transported to the storage location.
- One can also plan second child and store umbilical cord blood for the treatment of their diseased first child.
- Collected cord blood sample is stored at GMP laboratory for future use.

STEP 2: HLA TYPING

- Before implantation, HLA typing (Cross matching) is need to do for checking donor- recipient compatibility.
- Also attention requires in the case of Blood Groups of both donor- recipient for ABO incompatibility.
- Assessment of medical history and reports.

STEP 3: HOSPITALIZATION

- Patient is admitted to the hospital before 8-10 days of transplantation date.
- Patient is completely isolated from the outside and keep in ICU unit to avoid contamination.
- Access is restricted to limited personnel only

Cord Blood Transplantation

STEP 4: PRE-OPERATIVE REGIMEN

- Preparative regimen is given to the patient to prepare for implantation.
- This includes medication, antibiotics and chemotherapy to ablate the patient's immune system and avoid GVHD after transplantation.

STEP 5: UMBILICAL CORD BLOOD TRANSPLANTATION

- Stored umbilical cord blood sample is procured from the lab before transplantation.
- Physician transplants the required quantity of umbilical cord blood cells intravenously into the patients body.
- The intravenous part of the transplant takes approximately 15 minutes.

STEP 6: POST TRANSPLANTATION FOLLOW UP

- After transplantation, patient will be under strict monitoring for 4-5 weeks for any side effects or complications.
- Haematological engraftments are checked using blood tests and analysis.
- It can takes months to recover full immune power for patient after transplantation.

Centers where UCB transplantations are done:

- AIIMS, New Delhi
- Apollo Specialty Hospitals, Chennai
- Global Hospitals, Hyderabad
- Tata Memorial Hospital, Mumbai
- KDA Hospital, Mumbai
- Jaslok Hospital, Mumbai
- Christian Medical College Hospital
- Sahyadri Speciality Hospital, Pune
- Ruby Hall Clinic, Pune

- Muhammad Ameer Saif, Brian W. Bigger, Karen E Brookes, Jean Mercer,Karen L. Tylee, Heather J. Church, Denise K. Bonney, Simon Jones, J. Ed Wraith,and Robert F. Wynn

  Haematologica September 2012 97: 1320-1328

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