**Mucopolysaccharidoses Type I (MPS-I)**

MPS-I is one of the lysosomal storage disorders. It is caused by the defect in the alpha-L-iduronidase (IDUA) gene. The enzyme IDUA breaks down mucopolysaccharides in the lysosome. If not broken down, mucopolysaccharides build up in the lysosomes causing them to swell, eventually burst and damage the cells. There are two main forms of MPS-I.

The most severe form is Hurler-Scheie in which there is little or no IDUA present. Newborns with this severe form can have:

* Umbilical or inguinal hernia
* Macrocephaly
* Macroglossia
* Hepatosplenomegaly
* Coarse facial features

Older children can have:

* Multiple organ involvement
* Developmental delay
* Corneal clouding
* Hearing loss
* Muscular weakness
* Stiff joints
* Obstructive airway disease

Symptoms usually appear before 1 year of age. Cardiac and respiratory symptoms are severe and usually lead to death before 10 years of age

The other common form is attenuated MPS-I. Individuals with this form may have some IDUA enzyme function. Symptoms usually occur between 3 and 10 years of age, and the child may have a normal lifespan.

Incidence: It is estimated that one in every 30,000 births worldwide is born with MPS-I; however, an exact rate of occurrence cannot be determined until more states are screening newborns for the disease

Diagnosis: Diagnosis is made by confirmatory testing conducted by or through consultation with an experienced metabolic geneticist.

Confirmatory Tests include:

* Quantitative IDUA level –if low, reflex to DNA
* Measuring GAGs (glycosaminoglycans) in urine – if high, reflex to DNA

Treatment: HSCT is considered standard of care for Hurler’s. If started early enough, can slow or halt cognitive decline. However, HSCT does not reduce need for hip, knee and cord compression surgeries, as well as cardiac valve surgery. There are complications to HSCT such as graft rejection, transplant related mortality and organ failure secondary to pre-transplant chemotherapy. Enzyme Replacement Therapy (ERT) for individuals with attenuated form of MPS-I can improve problems with breathing, growth, joints and the heart, but cannot treat cognitive problems.

False Positives: Low IDUA can be found in pseudodeficiencies, particularly in the African-American population.