ABOUT MPS I Mucopolysaccharidosis I

Disease Overview[1]

MPS I disease is a rare, inherited lysosomal storage disorder caused by the deficiency of the lysosomal enzyme α-L-iduronidase. Deficiency of this enzyme results in the progressive accumulation of non-degraded material (called glycosaminoglycans, or GAGs) in cells throughout the body.

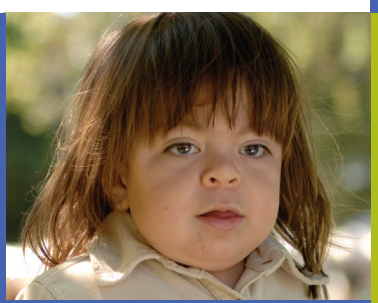
Historically known as Hurler, Hurler-Scheie, and Scheie syndromes, MPS I includes a highly heterogeneous spectrum of severity, signs, symptoms and affected organ systems. Clinical manifestations of MPS I are chronic, progressive, and multisystemic in nature, including: organomegaly (enlarged liver and spleen), dysostosis multiplex (abnormally shaped bones), coarse facial features and severe arthropathy. Hearing, vision, respiratory and cardiovascular functions are affected and joint mobility is typically severely reduced.

Ben, MPS I Hurler-Scheie

MPS I Disease Spectrum[1]

Symptom Presentation	Severe Patients	Attenuated Patients
Stiffened Joints	+++	++
Skeletal Abnormalities	+++	++
Carpal Tunnel Syndrome	+++	++
Cardiac (Valvular) Disease	+++	++
Recurrent Ear, Nose and Throat Infections	+++	+
Obstructive Airway Disease/ Sleep Apnea	+++	+
Corneal Clouding	+++	++
Spinal Cord Compression	+++	+
Hepatomegaly/ Splenomegaly	+++	+
Inguinal or Umbilical Hernia	+++	+
Hearing Loss	+++	+
Cognitive Impairment	+++	+
Growth Deficiencies	+++	+
Coarse Facial Features	+++	+
Communicating Hydrocephalus	+++	-
Abnormally Shaped Teeth	+++	-

Scale of severity: +++ most severe to - not present



Ximena, MPS I Hurler

Anisa, MPS I Hurler-Scheie

Kali, MPS I Hurler-Scheie

Diagnosis[1-3]

Accurate early diagnosis is important to help facilitate disease management.

Definitive diagnosis is confirmed by enzyme assay indicating low or absent α-L-iduronidase in leukocytes, plasma or cultured skin fibroblasts.

Major Signs and Symptoms[1]

- Coarse facial features
- Corneal clouding
- Recurrent ear, nose and throat infections
- Noisy breathing/snoring
- Obstructive airway disease
- Joint stiffness without inflammation
- Hernia
- Short stature
- Skeletal deformities
- Enlarged liver and spleen

If you suspect MPS I Disease, please consult a Metabolic Specialist or Geneticist immediately.

For more information, call Sanofi Genzyme Medical Information at 800-745-4447 (option 2).

Photos used with patient permission

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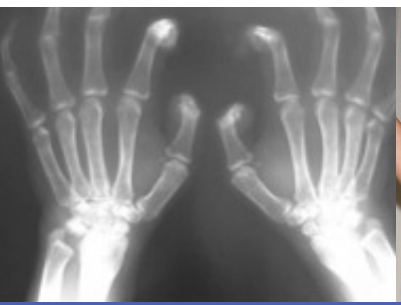
Differential Diagnosis[1,2,4]

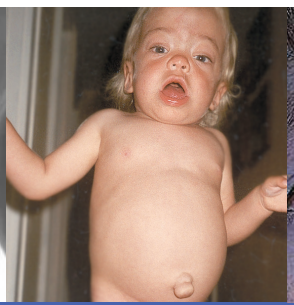
Diagnosis is often delayed since signs and symptoms may be shared with other disorders.

Some common differential diagnoses include:

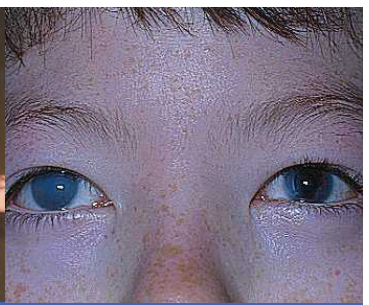
- Juvenile rheumatoid arthritis
- Rheumatoid arthritis
- Idiopathic rheumatoid arthritis
- Other mucopolysaccharidoses
- Multiple sulfatase deficiency
- Arthogryposis



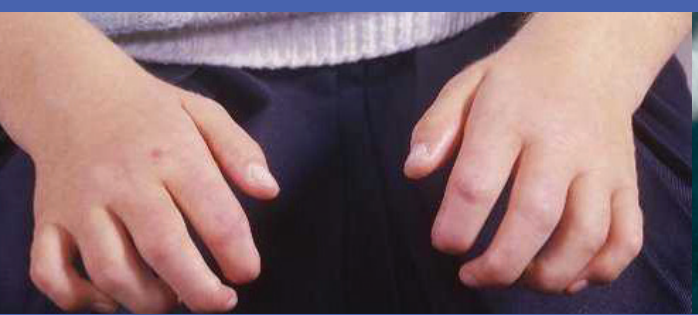
Joint contractures
(Courtesy of Dr. Rassi)



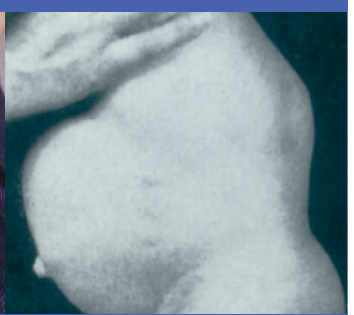
Organomegaly/hernia
(Courtesy of National MPS Society, Inc.)



Corneal clouding in patient's right eye and corneal transplant in left eye
(Courtesy of Dr. E. Wraith)



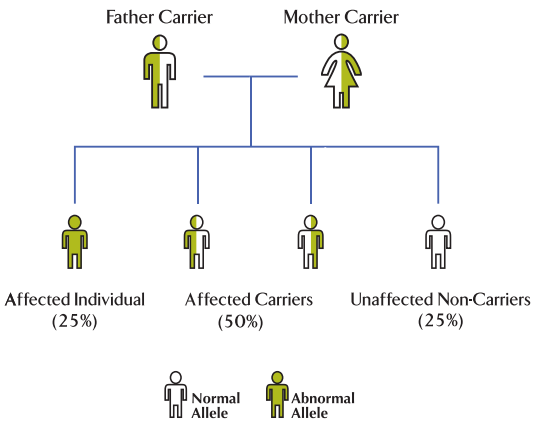
Joint contractures without inflammation
(Courtesy of Dr. E. Wraith)



Gibbus deformity
(Courtesy of Emil Kakkis, MD)

Genetics[1]

- Autosomal recessive
- Panethnic
- Estimated worldwide incidence 1:100,000



MPS I Disease Inheritance[1]

MPS I is autosomal recessive and affects males and females equally.

When both parents are carriers of the disease-causing genetic mutation, there is a 25% chance with each pregnancy of having a child affected with MPS I, a 50% chance of having a child who carries the gene mutation, and a 25% chance of having a child who does not carry the mutation.

For more information, including additional resources:
visit mps1disease.com

Diagnosis may be based on a unique combination of symptoms rather than on a single presenting symptom. Symptom recognition and early diagnosis lead to earlier disease management.

References

1. Neufeld EF, Muenzer J. The Mucopolysaccharidoses. In: Valle D, Beaudet AL, Vogelstein B, Kinzler KW, Antonarakis SE, Ballabio A, Gibson K, Mitchell G. eds. New York, NY: McGraw-Hill; 2014. http://ommbid.mhmedical.com/content.aspx?bookid=971&Sectionid=62642135. Accessed March 03, 2016.
2. Cobos P, Steglich C, Santer R, Lukacs Z, Gal A. Dried blood spots allow targeted screening to diagnose mucopolysaccharidosis and mucolipidosis. In: JIMD Rep. Springer Berlin Heidelberg; 2014.
3. Cobos, PN, Steglich, C, Santer, R, Lukacs, Z, Gal, A. Dried blood spots allow targeted screening to diagnose mucopolysaccharidosis and mucolipidosis. JIMD Rep. 2192-8304.
4. Cimaz R, Vijay S, Haase C, Coppa G, Bruni S, Wraith E, et al. Attenuated type I mucopolysaccharidosis in the differential diagnosis of juvenile idiopathic arthritis: a series of 13 patients with Scheie syndrome. Clin Exp Rheumatol 2006;24:196-202.

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