Newborn Screening ACT Sheet

[alpha-L-iduronidase deficiency/ With or Without glycosaminoglycans (GAG)] Mucopolysaccharidosis Type 1 (MPS I)

Differential Diagnosis: Mucopolysaccharidosis Type 1 (MPS I), also historically known as Hurler syndrome, Hurler-Scheie syndrome, and Scheie syndrome. Pseudodeficiency can result in a positive screen but is not associated with disease.

Condition Description: MPS I is an autosomal recessive lysosomal storage disorder (LSD) caused by pathogenic variants in the *IDUA* gene leading to deficient alpha-L-iduronidase activity. It has an estimated incidence of less than 1 in 100,000 live births. This deficiency leads to the accumulation of glycosaminoglycans (also known as mucopolysaccharides) in the lysosome resulting in cellular dysfunction There is wide variability in severity and age of onset.

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Contact family to inform them of the newborn screening results and ascertain clinical status.
- Take a family history
- Consult with pediatric genetic or metabolic specialist
- Within one week:
  - Evaluate the newborn with attention to presence of umbilical hernia and hepatosplenomegaly (though the newborn exam is usually normal).
- Report findings to state newborn screening program.

Diagnostic Evaluation: Confirmatory alpha-L-iduronidase enzyme assay in leukocytes, urine /or blood glycosaminoglycans (GAGs, also called MPS). Patients with low alpha-L-iduronidase enzyme activity and elevated glycosaminoglycans in urine or blood will have *IDUA* gene analysis. This testing will also help determine if the child has a pseudodeficiency.

Clinical Considerations: The clinical presentation and severity of MPS I ranges from severe to attenuated. In general, clinical features may include coarse facies, progressive dysostosis multiplex, hepatosplenomegaly, cardiac valvular disease, umbilical hernia, corneal clouding, hearing loss, and developmental delay. Treatment options include hematopoietic stem cell transplantation, enzyme replacement therapy (ERT), and emerging therapies. Ongoing multi-specialty care is necessary. ERT administration should only be given under the guidance of a specialist with expertise in treatment of lysosomal storage disorders.

Additional Information:
Gene Reviews
Genetics Home Reference
OMIM
Clinicaltrials.gov

Referral (local, state, regional, and national):
Testing
Find Genetic Services

ACMG American College of Medical Genetics and Genomics Translating Genes Into Health®

LOCAL RESOURCES: Insert State newborn screening program web site links

State Resource site *(insert state newborn screening program website information)*

Name	
URL	
Comments	

Local Resource Site *(insert local and regional newborn screening website information)*

Name	
URL	
Comments	

APPENDIX: Resources with Full URL Addresses

Additional Information:

Gene Reviews
https://www.ncbi.nlm.nih.gov/books/NBK1162/

Genetics Home Reference
https://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-i

OMIM
https://www.omim.org/entry/607014?search=hurler&highlight=hurler

ClinicalTrials.gov
https://clinicaltrials.gov

Referral (local, state, regional and national):

Testing
https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=MPS+I

Find Genetic Services
https://clinics.acmg.net

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