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

ACT Sheet

Newborn Screening ACT Sheet

[alpha-L-iduronidase deficiency with or without glycosaminoglycan (GAG) accumulation]

Mucopolysaccharidosis Type I (MPS I)

Differential Diagnosis: Mucopolysaccharidosis Type I (MPS I; Hurler syndrome), MPS I attenuated (Hurler-Scheie syndrome; Scheie syndrome).

Condition Description: Mucopolysaccharidosis Type I (MPS I) is an autosomal recessive lysosomal disorder. It is caused by a deficiency of alpha-L-iduronidase resulting in the accumulation of glycosaminoglycans (mucopolysaccharides) in lysosomes and subsequent cellular dysfunction. There is wide variability in severity and in age of onset.

You Should Take the Following Actions:

- Inform family of newborn screening result.
- Ascertain clinical status (newborns are expected to be asymptomatic).
- Consult with pediatric metabolic specialist within the first week of life.
- Evaluate the newborn (umbilical/inguinal hernia).
- Initiate confirmatory/diagnostic testing and management, as recommended by the specialist.
- Provide the family with basic information about MPS I.

- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: **Alpha-L-iduronidase enzyme assay in leukocytes, urine /or blood glycosaminoglycans (dermatan/heparan sulfates):** low alpha-L-iduronidase enzyme activity and elevated glycosaminoglycans in urine or blood confirm MPS I. **Molecular genetic testing:** may confirm the diagnosis and help to distinguish MPS I from pseudodeficient alpha-L-iduronidase activity.

Clinical Considerations: Although asymptomatic at birth, individuals with MPS I generally develop clinical findings within the first year of life, including coarse facies, progressive dysostosis multiplex, hepatosplenomegaly, cardiac valvular disease, umbilical hernia, sleep apnea, corneal clouding, hearing loss, and developmental delay. Disease progression and life expectancy depend upon the severity of the disease: untreated infants with the severe form often do not survive childhood, while those with the attenuated form may develop learning disabilities, progressive joint limitations, and may have a normal lifespan. Treatment includes hematopoietic stem cell transplant and enzyme replacement therapy with supportive care. Individuals with pseudodeficient alpha-L-iduronidase activity are unaffected.

Local Referral Site:

UAB Genetics
Alicia Roberts,RD - UAB Genetics
VHL108B
1670 University Blvd
Birmingham, AL 35233
Phone: 205-996-6983
Fax: 205-975-6389

Alabama Newborn Screening Program
1-866-928-6755

Additional Information:

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

Medline Plus
https://medlineplus.gov/genetics/condition/mucopolysaccharidosis-type-i/

Condition Information for Families- HRSA Newborn Screening Clearinghouse
https://newbornscreening.hrsa.gov/conditions/mucopolysaccharidosis-type-i

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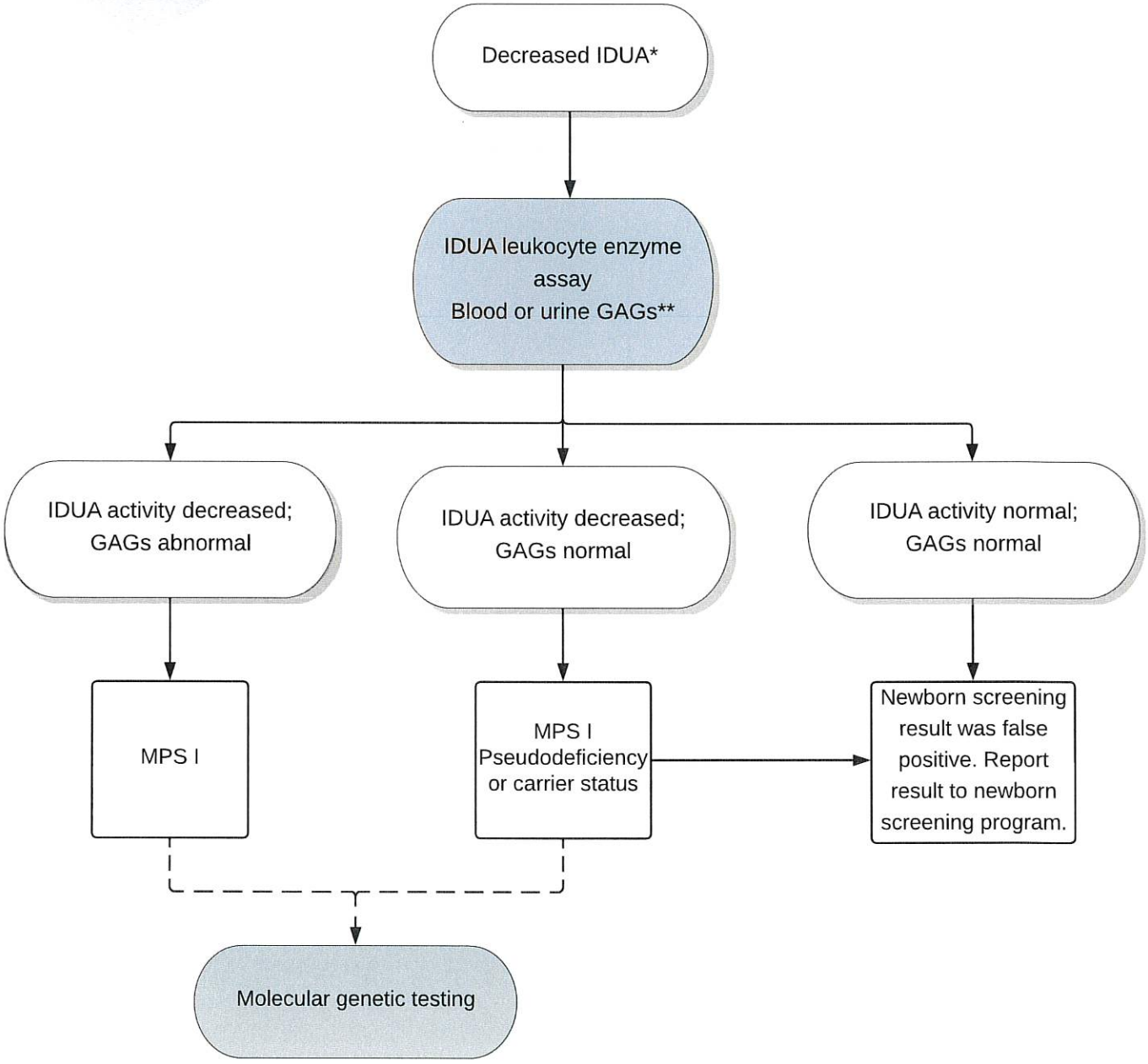
MPS I: Decreased Alpha-L-Iduronidase; Elevated Dermatan and Heparan Sulfates*



Key

- Actions are shown in shaded ovals; results are in the unshaded ovals. Diagnostic outcomes are shown in boxes.
- Dashed line reflects an optional test.
- *Heparan and dermatan sulfates (GAGs) not measured by all screening programs.
- **Serum, urine, or dried bloodspots.

Abbreviations:
IDUA = alpha-L-Iduronidase
GAGS = glycosaminoglycans
MPS I = Mucopolysaccharidosis Type I

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