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

ACT Sheet

Newborn Screening ACT Sheet

[Iduronate 2-Sulfatase Deficiency]

Mucopolysaccharidosis Type II

Differential Diagnosis: Multiple sulfatase deficiency.

Condition Description: Mucopolysaccharidosis Type II (MPS II, also known as Hunter syndrome), and multiple sulfatase deficiency (MSD), are lysosomal disorders. MPS II is caused by an isolated deficiency of iduronate 2-sulfatase (I2S), an enzyme required to break down mucopolysaccharides known as glycosaminoglycans (GAGs). MSD is an extremely rare condition caused by deficiency of an enzyme affecting the posttranslational activation of I2S and other sulfatases (such as ARSA). In both MPS II and MSD, GAGs accumulate while in MSD sulfatides also accumulate. Infants with MPS II are asymptomatic and males are predominantly affected given the disease's X-linked inheritance. MSD is autosomal recessive and may present in neonates as intrauterine growth restriction,respiratory distress, corneal clouding and dysmorphic features.

You Should Take the Following Actions:

- Inform family of the newborn screening result.
- Ascertain clinical status (newborns are expected to be asymptomatic).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn (newborns with MPS II are expected to be asymptomatic).
- Initiate confirmatory/diagnostic testing and management, as recommended by the specialist.
- Provide the family with basic information about MPS II and MSD and their management.
- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Leukocyte I2S and arylsulfatase A (ARSA) enzyme activity and measurement of urine GAGs and sulfatides: Decreased I2S activity and normal ARSA activity are suggestive of MPS II, but these results do not exclude I2S pseudodeficiency which causes decreased enzyme activity without disease. Reduced I2S activity in isolation with elevated GAGs are consistent with MPS II. Reduced I2S and ARSA activities with elevated urine GAGs and sulfatides are consistent with MSD. Molecular genetic testing can confirm and differentiate these diagnoses.

Clinical Considerations: Although asymptomatic at birth, males with MPS II typically demonstrate progressive signs and symptoms beginning in the first year of life with short stature, coarse facial features, decreased joint mobility, macroglossia, inguinal hernias, hepatosplenomegaly, frequent upper respiratory tract infections; cognitive decline may present in childhood. Disease severity and progression are variable. Therapy should be initiated under the guidance of a specialist consisting of enzyme replacement therapy and symptomatic support. MSD is a neurodegenerative, multisystem disease of variable severity combining features of mucopolysaccharidoses and metachromatic leukodystrophy with onset usually in infancy. Treatment is supportive. (Rarity of MSD)

Additional Information:

How to Communicate Newborn Screening Results
Gene Reviews (MPS II | MSD)
Medline Plus (MPS II | MSD)
Condition Information for Families- HRSA Newborn Screening Clearinghouse

Referral (local, state, regional, and national):

Find a Genetics Clinic Directory
Genetic Testing Registry

Local Resources *(Insert Local Website Links)*

State Resource Site (Insert Website Information)

Name	
URL	
Comments	

Local Resource Site (Insert Website Information)

Name	
URL	
Comments	

Appendix *(Resources with Full URL Addresses)*

Additional Information

How to Communicate Newborn Screening Results

- https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/Resources/achdnc-communication-guide-newborn.pdf

Emergency Protocols (New England Consortium of Metabolic Programs)

Gene Reviews

- https://www.ncbi.nlm.nih.gov/books/NBK1274/
- https://www.ncbi.nlm.nih.gov/books/NBK538937/

Medline Plus

- https://medlineplus.gov/genetics/condition/mucopolysaccharidosis-type-ii/
- https://medlineplus.gov/genetics/condition/multiple-sulfatase-deficiency/

Condition Information for Families-HRSA Newborn Screening Clearinghouse

- https://newbornscreening.hrsa.gov/conditions/mucopolysaccharidosis-type-ii

Referral (local, state, regional and national)

Find a Genetics Clinic Directory

- https://clinics.acmg.net

Genetic Testing Registry

- https://www.ncbi.nlm.nih.gov/gtr/