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

ACT Sheet

Newborn Screening ACT Sheet

[Decreased α-galactosidase A]

Fabry Disease

Differential Diagnosis: Fabry disease; α-galactosidase A pseudodeficiency.

Condition Description: Fabry disease is a lysosomal storage disorder caused by a deficiency of α-galactosidase A, disrupting the normal processing of glycosphingolipids and resulting in the progressive accumulation of globotriaosylceramide (GL-3) throughout the body. Although Fabry disease is an X-linked disorder, females can also develop significant morbidity and mortality. Newborns and infants are asymptomatic.

You Should Take the Following Actions:

- Inform family of the newborn screening result.
- Newborns are expected to be asymptomatic. Elicit family history of kidney disease, heart disease, stroke, or paraesthesias.
- Consult with metabolic specialist.
- Evaluate the newborn.
- Initiate confirmatory/diagnostic testing, as recommended by the specialist.
- Provide the family with basic information about Fabry disease and its management.

- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Leukocyte α-galactosidase A enzyme assay in males: Decreased enzyme activity in males is suggestive of Fabry disease, but this result does not exclude pseudodeficiency. Enzyme testing is not informative in females. Pseudodeficient α-galactosidase A activity does not cause clinical disease and is considered a false positive screen result. Molecular genetic testing is required to confirm the diagnosis in both males and females.

Clinical Considerations: Males with Fabry disease typically present in childhood or adolescence with acroparesthesias of the hands and feet when febrile or when exposed to excessive heat or cold. They may also present with gastrointestinal issues, multiple angiokeratomas, sweating abnormalities (reduced or increased), corneal opacity, and proteinuria leading to renal insufficiency in adulthood. Males with residual α-galactosidase A activity may present later in life with either a renal or cardiac form of Fabry disease. Unless treated, there is progressive involvement of the kidneys, heart and nervous system. Females may present in adulthood with acroparesthesias and other organ involvement. Therapy, such as enzyme replacement therapy, should be initiated at the first sign of symptoms under the guidance of a specialist.

Additional Information:

How to Communicate Newborn Screening Results
Gene Reviews
Medline Plus
Condition Information for Families- HRSA Newborn Screening Clearinghouse
ClinGen Actionability Report

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

Find a Genetics Clinic Directory
Genetic Testing Registry

 (Funded in part through MCHB/HRSA/HHS grant #U22MC03957;#UH9MC30770 National Coordinating Center for the Regional Genetics Networks)

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

Gene Reviews
- https://www.ncbi.nlm.nih.gov/books/NBK1292/

Medline Plus
- https://medlineplus.gov/genetics/condition/fabry-disease/

Condition Information for Families-HRSA Newborn Screening Clearinghouse
- https://newbornscreening.hrsa.gov/conditions/fabry-disease

ClinGen Actionability Report
- https://actionability.clinicalgenome.org/ac/Pediatric/ui/stg2SummaryRpt?doc=AC047

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/