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

ACT Sheet

Newborn Screening ACT Sheet

[Elevated Immunoreactive Trypsinogen (IRT) + 2 DNA Variants]

Cystic Fibrosis (CF)

Differential Diagnosis: Cystic fibrosis; CRMS (CFTR-Related Metabolic Syndrome).

Condition Description: Cystic fibrosis is a multisystem disorder affecting all races and ethnicities. It is caused by pathogenic variants in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene, an epithelial ion channel protein which maintains salt and water balance within cells. In individuals with CF, pathogenic variants in the *CFTR* gene cause thickened mucus, blocking the pulmonary and gastrointestinal systems. An elevated IRT level is a nonspecific marker of pancreatic stress and is often elevated in infants with CF. Newborns with CF may or may not be symptomatic. A newborn with two or more *CFTR* variants is likely affected with CF. Findings range from asymptomatic to respiratory and/or gastrointestinal signs and symptoms. The majority of affected individuals survive to adulthood. A small number of newborns may be classified as CF carriers or may have an indeterminate diagnosis (CRMS). Individuals with CRMS are asymptomatic but a small percentage eventually develop CF.

You Should Take the Following Actions:

- Inform the family of the newborn screening result.
- Ascertain clinical status (cough, abdominal pain, dehydration, frequent or oily stools) and inquire about family history of CF.
- Consult with CF specialist and/or reach out to newborn screening program for assistance within 48 hours.
- Evaluate the newborn (poor weight gain, dehydration, cough, respiratory distress, meconium ileus, abdominal pain, jaundice, abnormal stools).
- Refer promptly to CF Center for sweat testing, clinical evaluation and genetic counseling.
- Provide family with basic information about CF.

- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Sweat Chloride Testing performed at a *CF Care Center accredited by the CF Foundation* : may confirm the diagnosis. Additional Molecular Genetic Testing: may be required.

Clinical Considerations: Cystic fibrosis is a progressive disorder affecting all races and ethnicities in which abnormal salt regulation causes the accumulation of thickened mucus within the body. The symptoms are variable, ranging from nasal polyps, growth delays, recurrent sinus and lung infections, diabetes, and malnutrition. Pancreatic insufficiency is found in 80 – 90% of cases. Although males are generally infertile, assisted reproductive technology can be used to obtain sperm for fertilization. Management may include antibiotics, CFTR modulators, and pulmonary and nutritional support. Due to improved medical treatments, the majority of individuals with CF survive well into adulthood.

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Additional Information:

How to Communicate Newborn Screening Results
Gene Reviews
Medline Plus
Condition Information for Families- HRSA Newborn Screening Clearinghouse
Cystic Fibrosis Foundation
Clinicaltrials.gov

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

Find a Genetics Clinic Directory
Genetic Testing Registry
Find a CF Care Center

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://bit.ly/NBSResultsHRSA

Gene Reviews
- https://www.ncbi.nlm.nih.gov/books/NBK1250/

Medline Plus
- https://medlineplus.gov/genetics/condition/cystic-fibrosis/

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

Cystic Fibrosis Foundation
- https://www.cff.org/

Clinicaltrials.gov
- https://clinicaltrials.gov/

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/

Find a CF Care Center
- https://apps.cff.org/ccd?_ga=2.114810501.381175015.1706627402-180508355.1696535979