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

ACT Sheet

Newborn Screening ACT Sheet

[Elevated Immunoreactive Trypsinogen (IRT); no DNA Variants identified]

Cystic Fibrosis (CF)

Differential Diagnosis: Cystic fibrosis; bowel or biliary atresia; trisomies; hypoglycemia; sepsis; neonatal stress; 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 that 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 is a nonspecific marker of pancreatic stress and may be due to CF, CF carrier status, or many other reasons.

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 contact 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).
- If symptomatic or if there is a family history of CF, refer promptly to CF Center for sweat testing and clinical evaluation, as recommended by specialist.
- 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 to confirm the diagnosis.

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, and include nasal polyps, growth delays, recurrent sinus and lung infections, diabetes, and malnutrition. Pancreatic insufficiency is found in 80 – 90% of cases.

Most neonates with elevated IRT levels without *CFTR* variants identified on newborn screening do not have cystic fibrosis. However, non-white individuals with CF are more likely to have rare *CFTR* variants not detected by newborn screening. Consistent symptoms, a family history of CF, or ancestry should guide the need for sweat testing. If affected, management may include antibiotics, CFTR modulators, pulmonary and nutritional support. Although affected males are generally infertile, assisted reproductive technology can be used to obtain sperm for fertilization. The majority of individuals with CF survive to adulthood with timely diagnosis and treatment.

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

 (Funded in part through MCHB/HRSA/HHS grant #U22MC03957; 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://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