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American College of Medical Genetics and Genomics
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ACT Sheet

Newborn Screening ACT Sheet

[Elevated Immunoreactive Trypsinogen (IRT) + 1 DNA Variant]

Cystic Fibrosis (CF)

Differential Diagnosis: Cystic fibrosis carrier; 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 may be elevated due to CF, CF carrier status, or other reasons. Newborns with CF may or may not be symptomatic. A newborn with one *CFTR* variant may be a CF carrier or may have CF if the second variant is not identified by newborn screening. The majority of CF carriers are asymptomatic.

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

A newborn with one *CFTR* variant may be a CF carrier or may have CF if a second variant is present but was not identified by newborn screening. Sweat chloride testing will identify most but not all individuals with CF. 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. Due to improved medical treatments, the majority of individuals with CF survive well into adulthood.

Additional Information:

Alabama Newborn Screening Result:	Recommended Actions:
• IRT value in the top 4% of levels received each day • One or more DNA mutations identified	Diagnostic sweat test scheduled at an accredited CF Care Center*
*Accredited CF Care Centers are required to meet national accepted standards that have been developed by the Cystic Fibrosis Foundation and the Clinical and Laboratory Standards Institute. They offer a multidisciplinary approach to the management of CF.	

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Local Resources *(Insert Local Website Links)*

State Resource Site (Insert Website Information)

Name	Hector Gutierrez, M.D., Children's of Alabama Pediatric CF Care Center
Contact	1600 7th Avenue South, ACC 620, Birmingham, AL 35233
Comments	Staci Self, Clinic Coordinator, 205-638-5494

Local Resource Site (Insert Website Information)

Name	Okan Elidemir, M.D., Director, Pensacola Cystic Fibrosis Center
Contact	Nemours Children's Health, 8331 N. Davis Highway, Pensacola, FL 32514
Comments	Phone: (850) 505-4786 or (850) 473-4561 Fax: (850) 505-4787, ATTN: Kathy or Martina

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/