

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.

Additional Information:

Alabama Newborn Screening Result:	Recommended Actions:
<ul style="list-style-type: none"> • 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*
<p>*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.</p>	

Disclaimer: This practice resource is designed primarily as an educational resource for medical geneticists and other clinicians to help them provide quality medical services. Adherence to this practice resource is completely voluntary and does not necessarily assure a successful medical outcome. This practice resource should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this practice resource. Clinicians also are advised to take notice of the date this practice resource was adopted, and to consider other medical and scientific information that becomes available after that date. It also would be prudent to consider whether intellectual property interests may restrict the performance of certain tests and other procedures.

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, Nemours Pensacola Cystic Fibrosis Center
Contact	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/>

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