NEBRASKA
Good Life. Great Mission.
DEPT. OF HEALTH AND HUMAN SERVICES

Cystic Fibrosis Information

Cystic Fibrosis, or CF, is one of the most common disorders detected by newborn blood spot screening. CF is an autosomal recessive genetic disorder. Persons with CF have mutations in the gene encoding for the CF transmembrane conductance regulator (CFTR) protein on both alleles of chromosome 7. Although greater than 1,000 mutations on the CFTR gene have been identified, the ΔF508 mutation occurs in approximately two thirds of all CF patients.

CFTR serves as a chloride channel. Its function is important to proper functioning of multiple organs and systems including the lungs, respiratory tract, pancreas, liver, gastrointestinal tract, genitourinary tract and sweat glands.

Clinical Features:

TEST RESULTS	LIKELY CAUSES	ACTIONS TO TAKE WHEN POSITIVE RESULT FOUND
IRT < 90	Normal	Keep report in med record
IRT> 90, 0 ΔF508 < 130	Normal	Keep report in med record
IRT> 90, 0 ΔF508 > 130	Inconclusive Possible Carrier Possible CF Possible false positive *	Repeat dried blood spot specimen @ 2 weeks of age

Patients with pancreatic insufficiency are the most severely affected. Pancreatic insufficiency causes fat and protein malabsorption. Associated gastrointestinal symptoms include loose, foul-smelling fatty stools and abdominal pain. Nutritional consequences include fat-soluble vitamin deficiencies and growth failure.

Deficient chloride transport in the lungs results in the production of abnormally thick mucus, which in turn leads to airway obstruction, neutrophil dominated inflammation and recurrent and progressive pulmonary infections. Acute viral respiratory infections are much more likely to develop into lower respiratory tract infections, leading to hospitalization and acquisition of chronic bacterial infections such as *Pseudomonas aeruginosa.*

Laboratory Tests:

Screening is done by an immunoassay measuring immunoreactive trypsinogen (IRT). Elevated IRT's reflex to check for the most common mutation associated with CF, ΔF508. If no copies of ΔF508 are found but the IRT is greater than 130, a repeat specimen will be requested. If one copy of the ΔF508 is present with an elevated IRT, a 36-mutation panel is done on the initial specimen, and if a second mutation is present the newborn is positive for CF. If two copies of ΔF508 are present the newborn is also positive for CF. When only one copy of ΔF508 is found (no others from the 36-mutation panel), sweat testing is recommended. A large percent of these newborns will be identified as carriers, not affected with cystic fibrosis.

IRT> 90, 1 ΔF508	Inconclusive Possible Carrier Possible CF	Sweat test
IRT> 90, 2 ΔF508	Positive for CF	Refer to CF Center
IRT > 90, 1 ΔF508 + other mutation	Positive for CF	Refer to CF Center

Meconium Ileus in infants with CF

Meconium ileus is an indicator often associated with CF diagnosis. However, patients with CF who have meconium ileus also are at risk of having a low IRT, and possibly being missed by the newborn screen. Therefore, the screening algorithm, to avoid missing one of these newborns, skips the IRT and goes directly to DNA if the presence of meconium ileus is communicated to the laboratory. This should be recorded on the filter paper collection form when known.

False Negatives

Despite improvements in screening techniques and the use of reflex testing to DNA on suspect specimens, there is still the risk that the newborn screen will not catch every newborn. If a patient exhibits signs or symptoms of CF, diagnostic testing should be initiated regardless of the screening result.

Confirmation and Treatment:

The diagnostic test for CF should be a sweat chloride by iontophoresis. Patients with two mutations may not need this if they are referred to an accredited CF center for comprehensive care with specialists familiar with the genotype-phenotype associations. Sweat testing is most efficient when infants are 4 weeks of age or older.

Screening Practice Considerations:

Detection of CF does not depend on nutritional factors. A blood transfusion may alter the values; therefore, **THE NEWBORN SCREENING SPECIMEN SHOULD ALWAYS BE COLLECTED PRIOR TO A BLOOD TRANSFUSION.** Some very premature or very sick newborns experience multiple transfusions, making it difficult to ever get a reliable and timely newborn screen. **Specimens collected on newborns older than 3 months of age will not be screened for cystic fibrosis, as the IRT is not sufficiently reliable as a screening test beyond this age.**

***** Other causes of elevated IRT's can include asphyxia, septicemia, CMV virus, hydronephrosis, trisomies (13, 18 & 21), obstructive liver disease and biliary atresia. The Nebraska Newborn Screening Program recommends repeat screening be collected when the infant is 2 weeks old (for newborns with inconclusive screen results) because in many cases the immunoreactive trypsinogen (IRT) will be normal on the repeat specimen by this age avoiding the more expensive tests.