Cystic Fibrosis (CF)

Cystic fibrosis (CF) is a disorder characterized by pulmonary obstruction often accompanied by exocrine pancreatic dysfunction. A defect in the cystic fibrosis transmembrane conductance regulator (CFTR) gene leads to obstruction of exocrine pancreatic ducts. This causes an increase in the pancreatic enzyme immunoreactive trypsinogen (IRT) in blood. Elevated IRT can also occur in premature/stressed infants.

CF usually affects the lungs, pancreas, intestines, liver and sweat glands, causing failure to thrive, steatorrhea, intestinal obstruction, salt loss, and progressive obstructive lung disease.

Inheritance:	Autosomal recessive
Estimated Incidence:	1:3,500 (varies by ethnic group)
1st tier screening result:	Elevated IRT
Abnormal 2nd tier result:	1 or more CF mutations found
Method of Notification:	All abnormal 1st tier screening results are sent to the provider of record and reflexed to CF 2nd tier confirmatory testing. Abnormal lab reports may also be faxed to a regional pediatric pulmonologist, upon written request.
Next Steps if Abnormal:	A portion of the initial sample will be tested by 2nd tier molecular method. If initial IRT is elevated and no mutations are found on CF 2nd tier test, see infant to ascertain health status. **If IRT was < 170, no further bloodspots are needed**.

All infants with an elevated IRT >170 ng/ml should still be referred for sweat chloride testing, even if no mutations are detected on 2nd tier testing.

Neonatal Presentation:	Usually none. **Meconium ileus** or volvulus may occur in 5-10% of affected infants. Prolonged jaundice without other cause is more common than very early lung disease.

All infants with meconium ileus should be thoroughly evaluated for CF, regardless of the IRT screen. A normal IRT value does not rule out CF in these infants.

Diagnosis:	Sweat chloride testing at a CF Foundation accredited care center is necessary for final diagnosis. Initiate treatment as recommended by specialist. **Please report all diagnostic information to the SC Newborn Screening Program**.

Standard Treatment: Chest physiotherapy to aid in airway clearance. Antibiotics or other medications to treat lung infections as needed. Pancreatic enzymes if indicated; vitamins; NaCl supplements. Close monitoring of growth parameters and use of nutritional supplements as needed to enhance/maintain appropriate growth/development.

Suggested Follow-up for Cystic Fibrosis

If one or more mutations are found on the CF 2nd tier test, perform sweat chloride testing. Also see chart below for further follow-up recommendations:

Likely Interpretation of Abnormal Results			
# of mutations	*Sweat test result*	*Counseling*	*Probable Diagnosis/ Next Step*
0	No sweat test needed	None	*R/O* CF*
1	Normal	Basic counseling by CF center staff	Carrier
1	Abnormal	Genetic counseling by Certified Genetic Counselor	CF
2	Normal	Basic counseling by CF center staff	Further tests to be done at CF center
2	Abnormal	Genetic counseling by Certified Genetic Counselor	CF

Advice for Family: Provide basic information about CF. The handout, "*When Baby Needs a Second Test for Cystic Fibrosis"* may be used for this purpose.

Special Considerations:

Premature/Sick Infants - The stress of prematurity and/or illness can lead to falsely elevated IRT test results.

Prenatal Screening and confirmatory testing - For general population CF carrier screening, the American College of Medical Genetics (ACMG) and American College of Obstetricians and Gynecologists (ACOG) recommend a core panel of 23 mutations that will identify 49–98% of carriers, depending on ethnic background.

The SC DHEC Public Health Laboratory will perform an extended confirmatory panel of 60+ mutations for screen positive infants. The extended panel includes the recommended core panel of 23 mutations, as well as some of the world's most common and North American-prevalent mutations.

***Note**: Negative CF 2nd tier testing in an infant or parents does not definitively rule out the possibility of CF. Infants may have other rare mutations that are not included in a standard CF 2nd tier test screening panel.

False Negative Test Results: Some infants with CF may have a false negative IRT/CF screen. Physicians must remain alert to clinical signs of CF in older babies, despite normal initial screening results.

Internet Resources:

http://www.acmg.net/PDFLibrary/Cystic-Fibrosis-ACT-Sheet.pdf
https://www.acmg.net/PDFLibrary/CF-Mutation-not-R117H.pdf

https://www.acmg.net/PDFLibrary/CF-No-Mutation.pdf

https://ghr.nlm.nih.gov/condition/cystic-fibrosis

http://www.cff.org