

The New Jersey Department of Health and Senior Services

Cystic Fibrosis (CF)

Information for Health Professionals

Description

Cystic fibrosis (CF) is an autosomal recessive disease characterized primarily by progressive lung disease, pancreatic insufficiency, gastrointestinal obstruction and an excess of sodium and chloride in the sweat. The defective CF transmembrane conductance regulator (CFTR) gene results in thick mucus secretions, chronic obstructive lung disease, recurrent pulmonary infections, with eventual cardiopulmonary failure and death. Over 1000 mutations of the CFTR gene have been identified, with 70% of the mutations being Delta F508. Although life expectancy for people with cystic fibrosis has increased, most die by the time they are in their 30's.

Incidence

Cystic Fibrosis is the most common life-limiting, recessive genetic disorder in Caucasians with an incidence of 1 in 2,500 live births in the U.S. It is less common in African and Asian Americans.

Clinical Features

Common signs of CF include: recurrent or persistent respiratory problems; failure to thrive/malnutrition; steatorrhea/abnormal stools; meconium ileus/intestinal obstruction. Although the CF disease process commonly involves the sweat ducts, pancreas, and airways, other organs are also affected.

Many conditions prompt consideration of the diagnosis of CF. In infancy, these include meconium ileus (obstruction of the distal ileum or proximal colon with thickened, viscid meconium). It is theorized that the malnutrition and malabsorption that occurs in CF leads to hepatic steatosis and biliary obstruction, resulting in jaundice. Because of their high salt loss, infants may present with hypochloremic alkalosis. Because of their high ratio of surface area to volume, infants who have CF are prone to heat prostration. During infancy and beyond, failure to thrive is also a common presentation.

Involvement of the lung by the CF disease process accounts for much of the morbidity and almost all of the mortality from the disease. Although the lung tissue is normal at birth, patients soon acquire bacterial infection. In the first year of life, many types of bacteria, including enteric organisms, can be recovered from the CF infant's lung. Later in childhood, three organisms predominate: *Haemophilus influenzae*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. It should be noted that, early in life, patients may appear to be thriving and can be completely asymptomatic.

Screening

The screening tests for CF are done by the IEM Laboratory as part of the standard newborn screening. The test results are based on determination of heterogeneous circulating forms of immunoreactive trypsinogen (IRT) and the most common CF mutation that is usually associated with severe CF disease, $\Delta F508$. Newborn screening will not detect all forms of CF; IRT testing may miss patients with pancreatic sufficiency. Because IRT values decrease as a baby ages, IRT results are not reliable after 90 days, so prompt repeat screening is essential. The screening tests are an adjunct to clinical assessment, which is paramount. CF should be considered in infants with any of the signs and symptoms of the disease.

Confirmatory Testing

It is essential to confirm or exclude the diagnosis of CF in a timely fashion to avoid unnecessary testing, to provide appropriate interventions, prognostic and genetic counseling, and to ensure access to specialized medical services. In most cases the diagnosis of CF will be confirmed by measurement of chloride concentrations in pharmacologically-stimulated sweat. * Because newborns may not produce enough sweat for a reliable diagnosis in the first weeks of life, consultation with a pulmonary specialist is essential. Genetic testing may be performed.

Treatment

Treatment includes improving nutritional status with high calorie diets, parenteral and oral nutritional supplements and pancreatic enzymes. Besides antibiotic therapy to control pulmonary infections, improved patient outcomes have been seen with aggressive airway clearance techniques. Anti-inflammatory strategies are also logical for patients who have CF because the inflammatory response in the CF lung is excessive and deleterious. Evidence is mounting that early detection and early treatment will improve growth and slow down pulmonary deterioration.

Implications for Genetic Counseling

Genetic risk assessment and the use of family history and genetic testing can clarify carrier/disease status. Parents of a child diagnosed with CF are obligate carriers (heterozygotes) and have an alteration in one copy of the CFTR gene. Carriers are asymptomatic. Testing options for future pregnancies should be reviewed.

Siblings of a child diagnosed with CF have a 25% chance of being affected, a 50% chance of being an unaffected carrier, and a 25% chance of being unaffected and not being a carrier. It is recommended that all siblings of a child with Cystic Fibrosis be sweat tested.

Recommendations (please see algorithm on last page for clarification)

Initial Specimens

- **Expected Results:** < 90 ng/mL IRT is a negative screen
- **Positive Screen:** >130 ng/mL IRT and no copies of Δ F508 DNA mutation
Recommend: Repeat filter paper sample within 2 days and assess baby's health status.
- **Positive Screen:** \geq 90 ng/mL IRT and 1 or more copies of Δ F508 DNA mutation.
Recommend: Assess baby's health status and consult with a CF specialist.

Repeat Specimens

- **Positive Screen:** \geq 90 ng/mL IRT and no copies of Δ F508 DNA mutation.
- **Recommend:** Assess baby's health status and consult with a CF specialist.

Note: Newborn screening tests are an adjunct to clinical assessment, which is paramount. Cystic fibrosis should be considered in infants with any of the signs.

Bibliographic Reference

Davis, Pamela B. "Cystic Fibrosis." Pediatrics in Review 22.8 (2001)

Additional information:

Gene Tests/Gene Clinics

<http://www.genetests.org>

The Mayo Clinic

www.mayoclinic.com

National Heart, Lung and Blood Institute

<http://www.nhlbi.nih.gov/health/public/lung/other/cf.htm>

For questions, contact:

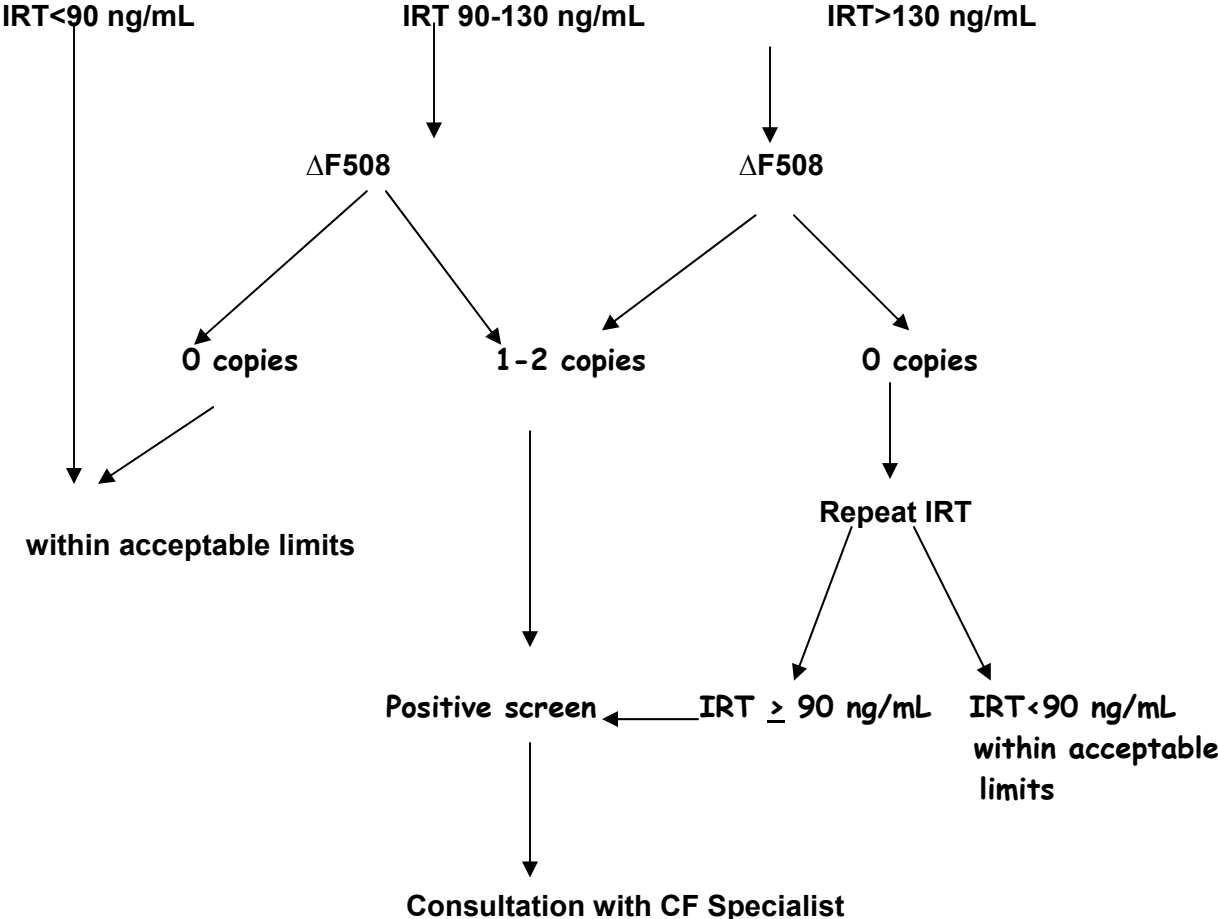
Inborn Errors of Metabolism Laboratory at (609) 292-3090

Newborn Screening and Genetic Services at (609) 292-1582

March 2005

Cystic Fibrosis Algorithm

Immunoreactive Trypsinogen (IRT) ng/mL and Genetic Mutation Δ F508



Modified by Dr. Roberto Nachajon, M.D.
Original algorithm courtesy of Steven Kanengiser, M.D.

