Cystic Fibrosis (CF)

What is Cystic Fibrosis (CF)?

Cystic fibrosis is an inherited, chronic, and progressive disease of the body's mucus glands. CF primarily affects the respiratory and digestive systems (including the exocrine pancreas, intestine, and hepatobiliary system) in children and young adults. The exocrine sweat glands and the reproductive system are also usually involved.

INCIDENCE

Occurs in 1:2,500-3,000 Caucasian newborns, no data in the Filipino population.

In the NBS data for 111,127 Filipino newborns born and screened in California, USA between 7 July 2005 and 6 July 2011, five newborns were confirmed to have CF.

CLINICAL MANIFESTATION

Clinical manifestations, onset of disease, and severity of CF is variable. Respiratory disease is the most frequent cause of morbidity and mortality in patients with CF, but gastrointestinal, pancreatic, and hepatobiliary disease are commonly encountered during the first year of life.

Early clinical manifestations seen in newborn and infancy period include:

- **Respiratory disease:** constant coughing or wheezing, thick mucus and phlegm, frequent pneumonia and bronchitis, nasal polyps
- **Gastrointestinal and nutritional problems:** meconium ileus, intestinal obstruction, neonatal cholestasis, failure to thrive, steatorrhea, diarrhea, rectal prolapse
- **Others:** salty sweat, anemia

Chronic health issues that affect various organ systems in patients with CF include the following:

- **Respiratory system:** Repeated bouts of bronchitis or pneumonia leading to bronchiectasis, collapsed lung, bleeding from the lungs, or lung failure, pulmonary hypertension, sinus disease
- **Digestive system:** Gastroesophageal reflux disease, small intestinal problems (bacterial overgrowth, inflammation, and dysmotility), chronic abdominal pain, disorders of the large intestines (distal intestinal obstruction syndrome, constipation, chronic diarrhea, rectal prolapse, and colorectal cancer), liver disease (elevated AST/ALT, elevated GGT, hepatic steatosis, portal hypertension, cirrhosis, cholangiopathy), gallbladder and bile duct disease (small or absent gallbladder, gallbladder dysfunction, symptomatic cholelithiasis, and malignancy), pancreatic disease (pancreatic insufficiency, pancreatitis, pancreatic cystosis, and diabetes mellitus)
- **Others:** Poor growth and poor weight gain, electrolyte abnormalities (acute or chronic hypovolemia with hyponatremia, hypochloremia, hypokalemia and metabolic alkalosis), fatigue, anemia, infertility due to blocked or absent vas deferens in males, musculoskeletal disorders (reduced bone mineral content and increased rates of fractures and kyphoscoliosis, hypertrophic osteoarthropathy), recurrent venous thrombosis, nephrolithiasis and nephrocalcinosis, aquagenic wrinkling

PATHOPHYSIOLOGY

Mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene lead to decreased chloride transport across the apical membrane of secretory epithelial cells, elevated intracellular sodium, and decreased extracellular water, resulting in thickened secretions in the affected structures. The manifestations are secondary to the resulting inflammation, obstruction, and dysfunction of the various organs.

Inheritance: autosomal recessive

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SCREENING

Early detection of CF through newborn screening is important since it allows prompt diagnosis, timely intervention, and improved outcomes. The Philippine Newborn Screening employs an assay to detect **increased serum Immunoreactive trypsinogen (IRT) on fluoroimmunoassay.**

CONFIRMATORY TESTING

Diagnosis of CF is confirmed by any of the following tests: **(1) sweat chloride test (>60 mEq/L); (2) identification of biallelic pathogenic or likely pathogenic variants in CFTR; or (3) transepithelial nasal potential difference measurements characteristic of CF.**

Diagnostic Criteria of CF

At least one of the following:
One or more typical phenotypic features of CF:
- Chronic Pulmonary Disease
- Chronic Sinusitis
- Characteristic gastrointestinal and nutritional abnormalities
- Salt loss syndromes
- Obstructive azoospermia

History of CF in a sibling
Positive newborn screening test

PLUS at least one of the following:
Elevated sweat chloride concentration
Two CFTR gene mutations to cause CF on separate alleles*
Abnormalities in NPD testing that are typical for CF**

*using mutation classifications identified in the CFTR2 project
**NPD testing measures abnormalities in ion transport across the nasal epithelium

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Overview of Disease Management

The main goal of treatment is to keep the lungs clear of thick mucus and to provide the correct amount of calories and nutrients to keep the patient healthy. Certain treatments may be advised for some children but not others. When necessary, treatment is usually needed throughout life.

- **Respiratory** – antibiotics for infections, bronchodilators, mucolytics, CFTR modulators, chest physiotherapy, steroids, heart/lung transplantation
- **Gastrointestinal** – nutritional therapy, oral pancreatic enzymes, mucolytics, enemas
- **Prevention of complications** – exercise, immunization, appropriate diet

Diet

- **Vitamin supplements:** People with CF have trouble absorbing some vitamins, especially fat-soluble vitamins such as vitamin A, D, E and K. Thus, supplementation may be needed.
- **Well-balanced, higher-calorie diet, low in fat and high in protein:** Many babies and children with CF need more food than typical in order to stay healthy. Some children with CF need up to twice the normal number of calories to grow appropriately. A dietitian who has experience with CF can help come up with a good nutrition plan for the patient. Pancreatic enzymes (which help in digestion) are often prescribed.
- **Extra fluid:** The patient may need to drink more water and liquids in order to help loosen the thick mucus and to prevent dehydration. Children with CF lose more salt than others, especially during exercise or in hot weather.

Other important considerations

- Children with CF should be given all the usual childhood vaccinations according to the regular schedule. It is especially important to have the measles vaccine, annual vaccinations against influenza, the 13-valent pneumococcal conjugate vaccine series, and the 23-valent pneumococcal polysaccharide vaccine administered after 2 years of age. All patients with CF should be vaccinated against COVID-19 as soon as they are eligible.
- They should be kept away from smoke exposure, especially from cigarette smoke as this can add to lung damage.
- Frequent hand washing is encouraged for patients and caregivers to prevent the spread of infection.
- Incorporate regular physical activity and exercise into daily activities to maintain the child's lung function and improve overall health.
- Enemas and mucolytic agents are used to treat intestinal obstructions.
- During illnesses or acute exacerbations of CF, the child may need to be seen in the hospital for treatment.

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