CYSTIC FIBROSIS

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Cystic fibrosis (CF) is an inherited multisystem disorder of children and adults, characterized chiefly by obstruction and infection of airways and by maldigestion and its consequences. One of the commonest life-threatening autosomal recessive conditions (1:2000 live births) affecting Caucasians. The mutation occurs in a single gene that encodes the CF transmembrane conductance regulator (CFTR).
Autosomal recessive

Carrier father
Carrier mother

Unaffected
Affected
Carrier

Unaffected son
Carrier daughter
Carrier son
Affected daughter
Four long-standing observations are of fundamental pathophysiologic importance:
1-failure to clear mucous secretions.
2-a paucity of water in mucous secretions.
3-an elevated salt content of sweat and other serous secretions.
4-chronic infection limited to the respiratory tract.
A normal-functioning CFTR channel moves chloride ions to the outside of the cell while a mutant CFTR channel does not, causing sticky mucus to build up on the outside of the cell.
CLINICAL FEATURE

A. Organs affected by cystic fibrosis

- Sinuses: sinusitis (infection)
- Lungs: thick, sticky mucus buildup, bacterial infection, and widened airways
- Skin: sweat glands produce salty sweat
- Liver: blocked biliary ducts
- Pancreas: blocked pancreatic ducts
- Intestines: cannot fully absorb nutrients
- Reproductive organs: (male and female) complications

B. Normal airway

- Airway wall
- Airway lined with a thin layer of mucus

(Airway in cross-section)

C. Airway with cystic fibrosis

- Thick, sticky mucus blocks airway
- Widened airway
- Blood in mucus
- Bacterial infection
One of the first signs of cystic fibrosis (CF) that parents may notice is that their baby's skin tastes salty when kissed or the baby doesn't pass stool when first born.

Respiratory System Signs and Symptoms

1- frequent cough that brings up thick sputum (spit) or mucus that's sometimes bloody.
2- Lung infections caused by unusual germs that don't respond to standard antibiotics.
3- Sinusitis an infection of the air-filled spaces behind your eyes, nose, and forehead.
4- Bronchitis, pneumonia, pneumothorax, bronchiectasis, nasal polyp.
Mucus that blocks tubes, or ducts, in your pancreas and prevents enzymes from reaching your intestines causes most digestive system signs and symptoms.

1-Diarrhea.
2-Bulky or Foul Smelling, Greasy Stool.
3-Constipation.
4- Poor Weight Gain and Growth.
5-Pancreatist.
6-Liver disease.
7-Rectal Prolapse.
8-Gall Stone.
Men who have cystic fibrosis are infertile because they're born without a vas deferens. This is the tube that delivers sperm from the testicle to the penis.

A woman who has cystic fibrosis may have a hard time getting pregnant because of mucus blocking her cervix or other cystic fibrosis complications.
OTHER SIGNS, SYMPTOMS, AND COMPLICATIONS

1- Dehydration
2- increased heart rate
3- tiredness
4- weakness
5- decreased blood pressure
6- heat stroke
7- rarely, death.
8- clubbing
9- low bone density
The diagnosis of CF has been based on a positive quantitative sweat test (Cl- ≥ 60 mEq/L) in conjunction with 1 or more of the following:

1-typical chronic obstructive pulmonary disease,
2-documentated exocrine pancreatic insufficiency,
3-or a positive family history.
Diagnostic Criteria for Cystic Fibrosis (CF)

- Presence of typical clinical features (respiratory, gastrointestinal, or genitourinary)
- OR
- A history of CF in a sibling
- OR
- A positive newborn screening test
- PLUS
- Laboratory evidence for CFTR dysfunction:
  - Two elevated sweat chloride concentrations obtained on separate days
- OR
- Identification of two CF mutations
- OR
- An abnormal nasal potential difference measurement
The sweat test, using pilocarpine iontophoresis to collect sweat and chemical analysis of its chloride content, is the standard approach to diagnosis. A 3 mA electric current is used to carry pilocarpine into the skin of the forearm and locally stimulate the sweat glands. The amount of sweat collected should be measured and reported. For reliable results, at least 75 mg and preferably 100 mg of sweat should be collected. More than 60 mEq/L of chloride in sweat is diagnostic of CF when 1 or more other criteria are present.
A mild electrical current pushes medicine into skin to cause sweating.

Sweat is collected, and salt content is measured.
NON-CF CONDITIONS ASSOCIATED WITH ELEVATED CONCENTRATIONS OF SWEAT ELECTROLYTES INCLUDE

1-untreated adrenal insufficiency,
2- ectodermal dysplasia,
3- hereditary nephrogenic diabetes insipidus,
4-glucose-6-phosphatase deficiency,
5-hypothyroidism,
6-hypoparathyroidism,
7- familial cholestasis,
8-pancreatitis,
9-mucopolysaccharidoses,
10- fucosidosis,
11-malnutrition
DNA Testing. Several commercial laboratories test for 30–80 of the most common CFTR mutations. This testing identifies ≥90% individuals who carry 2 CF mutations.

Other Diagnostic Tests. The finding of increased potential differences across nasal epithelium, the loss of this difference with topical amiloride application, and the absence of a voltage response to a β-adrenergic agonist have been used to confirm the diagnosis in patients with equivocal or frankly normal sweat chloride values.
Exocrine pancreatic dysfunction is clinically apparent in many patients. Measurement of fat balances with a 3 day stool collection or direct documentation of enzyme secretion after duodenal intubation and pancreozymin-secretin stimulation provides a reliable measure, but these methods are cumbersome or invasive for children and are not routinely used.
Quantitation of elastase-1 activity in a fresh stool sample is a useful screening test. Measurement of immunoreactive trypsinogen in serum, used for newborn screening, also reliably distinguishes patients with CF, with and without pancreatic insufficiency... Many advocate yearly monitoring with a modified 2 hr oral glucose tolerance test (OGTT) after 10 yr of age. This approach is more sensitive than spot checks of blood and urine glucose levels and glycosylated hemoglobin levels.
1. Hyperinflation of lungs
2. Bronchial thickening and plugging
3. Ring shadows suggesting bronchiectasis
4. Nodular densities,
5. Patchy atelectasis
6. Hilar lymph nodes may be prominent
7. Confluent infiltrate follow
8. With advanced disease, impressive hyperinflation with markedly depressed diaphragms,
9. Anterior bowing of the sternum,
10. A narrow cardiac shadow are noted.
11. Cyst formation,
12. Extensive bronchiectasis,
13. Dilated pulmonary artery segments,
14. Segmental or lobar atelectasis are often apparent with advanced disease.
The finding of *S. aureus* or *P. aeruginosa* on culture of the lower airways (sputum) strongly suggests a diagnosis of CF. In particular, mucoid forms of *P. aeruginosa* are often recovered from CF lungs. *B. cepacia* recovery also suggests CF.

**Heterozygote Detection and Prenatal Diagnosis.**

**Mutation analysis should be fully informative when testing potential carriers or a fetus, provided that mutations within the family have been previously identified.**
Most newborns with CF can be identified by determination of immunoreactive trypsinogen and limited DNA testing on blood spots, coupled with confirmatory sweat analysis. This screening test is ≈95% sensitive. Newborn diagnoses can prevent early nutritional deficiencies and improve long-term growth, and may spare cognitive function. Early diagnosis also has the advantage of genetic counseling for the family and, in some cases, avoids protracted diagnostic efforts.
The core treatment of CF is
1-aggressive airway hygiene, 
2-nutritional support including pancreatic enzyme replacement, 
3-antibiotics, 
4-bronchodilators, 
5-aerosolized recombinant man DNase, which decreases sputum viscosity by digesting inflammatory cell DNA.
Common treatments for lung problems seen in cystic fibrosis may include:

1. Antibiotics for infections of the airways
2. Chest physical therapy
3. Exercise
4. Other methods.
5. Other treatments for lung problems may include:
6. Oxygen
7. Lung transplantation.
The type of antibiotic your doctor recommends will depend on:

- The strains of bacteria involved
- How serious your condition is
- Previous history of antibiotic use.
for relatively mild airway infections. The usual course of therapy is ≥2 wk, and maximal doses are recommended. Tetracycline should be avoided in children <9 yr of age. The quinolones are the only broadly effective oral antibiotics for Pseudomonas infection, but resistance emerges rapidly. Infection with mycoplasmal or chlamydial organisms has been documented, providing a rationale for the use of macrolides on an empirical basis for flare of symptoms. Macrolides may reduce the virulence properties of P. aeruginosa such as biofilm production and contribute anti-inflammatory effects. Long-term therapy with azithromycin times a week has been shown to improve lung function in patients with chronic P. aeruginosa infection.
Inhaled antibiotics can be effective for treating respiratory infections. Tobramycin, for example, can be used alone or with oral antibiotics. Inhaled tobramycin has been studied the most extensively. When given at a dose of 300 mg twice daily on alternate months for 6 months, it has been shown to be effective. Other antimicrobials such as colistin (75–150 mg) have been aerosolized 2 to 4 times a day.
Intravenous antibiotics for severe infections or when none of the oral antibiotics work. For the patient who has progressive or unrelenting symptoms and signs despite intensive home measures, intravenous antibiotic therapy is indicated. Although many patients improve within 7 days, it is usually advisable to extend the period of treatment to at least 14 days. Permanent intravenous access can be provided for long-term or frequent courses of therapy in the hospital or at home.

The aminoglycosides have a relatively short half-life in many patients with CF. The initial parenteral dose, , is generally given every 8 hr. After blood levels have been determined, the total daily dose should be adjusted.
Chest physical therapy for cystic fibrosis involves pounding your chest and back over and over again to dislodge the mucus from your lungs so that you can cough up the mucus. This therapy should be done three to four times each day.

Chest physical therapy is also often referred to as postural drainage because it requires you to be sitting or lying on your stomach with your head down while you do chest physical therapy. This allows gravity to help drain the mucus from your lungs.
Postural drainage is a technique for loosening mucus in the airway so that it may be coughed out.

Tapping is performed in certain areas with the patient in different positions.
Aerobic exercise may help to:
- Loosen the mucus
- Encourage coughing to clear the mucus
- Improve your overall physical condition.
Inhaled or, sometimes, oral steroids. Steroids are the most effective anti-inflammatory medicines.

Ibuprofen, a type of non-steroidal, anti-inflammatory medicine. It may slow the progress of cystic fibrosis in young children with mild symptoms.
Bronchodilators, which are inhaled drugs that relax the muscles around the airways so that the airways can open up. They should be taken just before chest physical therapy to help clear mucus. *Many CF patients may improve by only 5–10%, however.* *Cromolyn sodium or ipratropium hydrochlorides are alternative agents, but their efficacy has not been studied systematically.*
Treatment of obstructed airways sometimes includes tracheobronchial suctioning or lavage, especially if atelectasis or mucoid impaction is present. Bronchopulmonary lavage can be performed by the instillation of saline or a mucolytic agent through a fiberoptic bronchoscope. Antibiotics (usually gentamicin or tobramycin) can also be instilled directly at lavage.

Other Therapies.

Expectorants such as iodides and guaifusin do not effectively assist with the removal of secretions from the respiratory tract. Inspiratory muscle training can enhance maximum oxygen consumption during exercise as well as FEV$_1$. 

ENDOSCOPY AND LAVAGE
If the level of oxygen in your blood is too low, you may need oxygen therapy. Oxygen is usually given through nasal prongs or a mask.

**Lung Transplantation**

Lung transplantation requires surgery to replace one or both of your lungs with healthy lungs from a human donor. Factors that determine whether you can undergo lung transplantation include:

- The type of bacteria in your lungs
- Your age and weight
- The medications you are taking
- Whether you have other medical conditions, including osteoporosis
- How well your lungs are functioning.
Prescribe oral pancreatic enzymes to help you digest fats and proteins and absorb more vitamins. The enzymes should be taken in capsule form before every meal, including snacks.

Recommend supplements of vitamins A, D, E, and K to replace the fat-soluble vitamins that your intestines cannot absorb.

Recommend that you use a feeding tube, called a gastrostomy tube or T-tube, to add more calories at night while you are sleeping. The tube is placed in your stomach. Before you go to bed each night, you attach a bottle with a nutritional solution to the entrance of the tube and it feeds you while you sleep.
The most common complication is chronic respiratory infection. 

- Bowel problems, such as gallstones, intestinal obstruction, and rectal prolapse
- Coughing up blood
- Chronic respiratory failure
- Diabetes
- Infertility
- Liver disease or liver failure, pancreatitis, biliary cirrhosis
- Malnutrition
- Nasal polyps and sinusitis
- Osteoporosis and arthritis
- Pneumonia, recurrent
- Pneumothorax
- Right-sided heart failure (cor pulmonale)
CF remains a life-limiting disorder, although survival has improved dramatically in the past 30–40 yr. Male survival is somewhat better than female survival for reasons that are not readily apparent. Children in socioeconomically disadvantaged families have, on average, a poorer prognosis. Children with CF usually have good school attendance records and should not be restricted in their activity. With increasing life span, a new set of psychosocial considerations has emerged.
THANK YOU