Definition

Cystic fibrosis is an inherited disease of the exocrine glands affecting lungs, skin, Gestrointestinal and hepatobiiliary systems.

- It leads to chronic exocrine pancreatic insufficiency, hepatobiliary disease, and abnormally high sweat electrolytes.

Etiology

CF is carried as an autosomal recessive trait.

The responsible gene has been localized on the long arm of chromosome 7. It encodes a membrane- associated protein called the cystic fibrosis transmembrane conductance regulator (CFTR).

Impairment of CFTR function causes reduced fluid production and enhanced sodium resorption through the epithelial Na chennels and basolateral Na/ATPase pumps of the airways epithelium.

Most common mutation is Delta 508

Epidemiology

- If both parents are heterozygote , there is 25% possibility of their children are homozygote and develop cystic fibrosis.
- White population > Black and Asian population.
- incidence is 1/2500. male to female is 1:1
- Females with cystic fibrosis have greater deterioration of pulmonary function with increasing age and younger mean age at death due to increase in hormone secretion during puberty.

Pathophysiology

Nearly all exocrine glands are affected in varying distribution and degree of severity. Glands may :

- Become obstructed by viscid or solid eosinophilic material in the lumen (pancreas, intestinal glands, intrahepatic bile ducts, gallbladder, and submaxillary glands).

- Appear histologically normal but secrete excessive Na and Cl (sweat, parotid, and small salivary glands).

Signs and symptoms

1. Gastrointestinal tract

- Meconium ileus
- Abdominal distention
- Intestinal obstruction
- Increased frequency of stools
- Failure to thrive (despite adequate appetite)
- Flatulence or foul-smelling flatus, steatorrhea
- Recurrent abdominal pain
- Jaundice
- GI bleeding

2. Respiratory system

- Cough
- Recurrent wheezing
- Recurrent pneumonia
- Atypical asthma
- Dyspnea on exertion
- Chest pain

3. Genitourinary tract

- Undescended testicles or hydrocele
- Delayed secondary sexual development
- Amenorrhea

Physical examination

Findings related to the pulmonary system may include the following:

- Tachypnea
- Respiratory distress with retractions
- Wheeze or crackles
- Cough (dry or productive of mucoid or purulent sputum)
- Increased anteroposterior diameter of chest
- Clubbing
- Cyanosis
- Hyperresonant chest upon percussion (crackles are heard acutely in associated pneumonitis or bronchitis and chronically with bronchiectasis)

Findings related to the GI tract include the following:

- Abdominal distention
- Hepatosplenomegaly (fatty liver and portal hypertension)
- Rectal prolapse
- Dry skin (vitamin A deficiency)
- Cheilosis (vitamin B complex deficiency)

Examination of other systems may reveal the following:

- Scoliosis
- Kyphosis
- Swelling of submandibular gland or parotid gland
- Aquagenic wrinkling of the palms (AWP)

Diagnosis

The diagnosis of cystic fibrosis (CF) is based on

- Typical pulmonary and GI tract manifestations
- Family history
- Universal newborn screening
- Prenatal screening test
- Sweat test results

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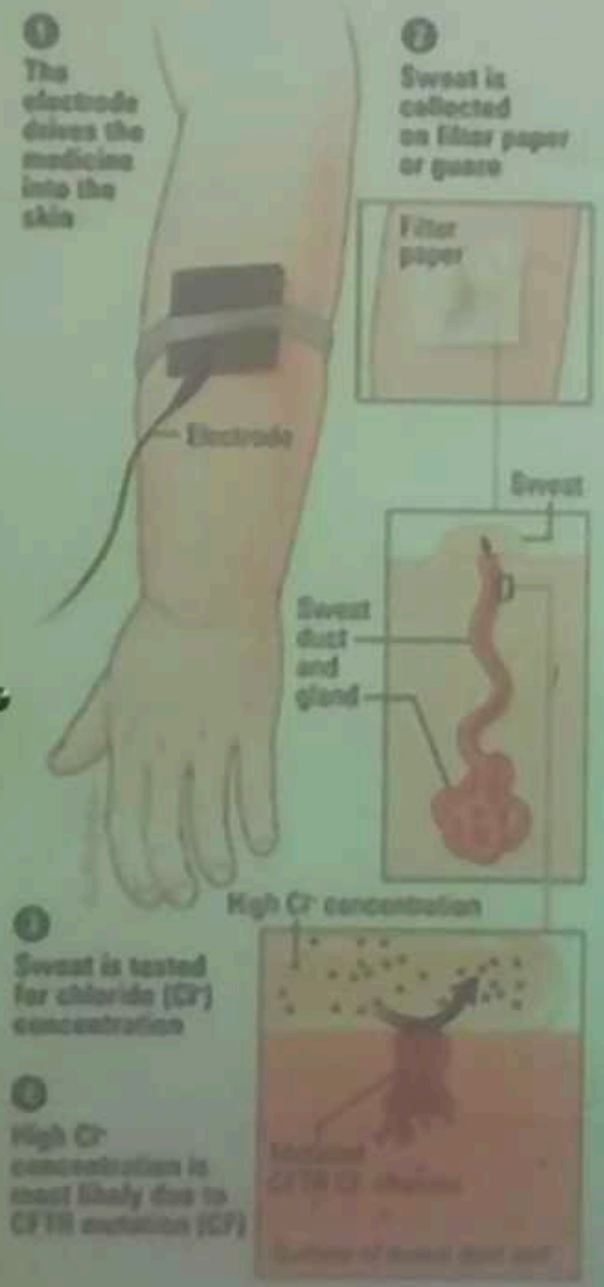
Requirements for a CF diagnosis include either

Positive genetic testing (two CF mutations) OR
two positive sweat chloride test findings (>60 mEq/L)
obtained on separate days.

And one of the following:

Typical chronic obstructive pulmonary disease
Documented exocrine pancreatic insufficiency
Positive family history (usually affected sibling)
A positive newborn screening



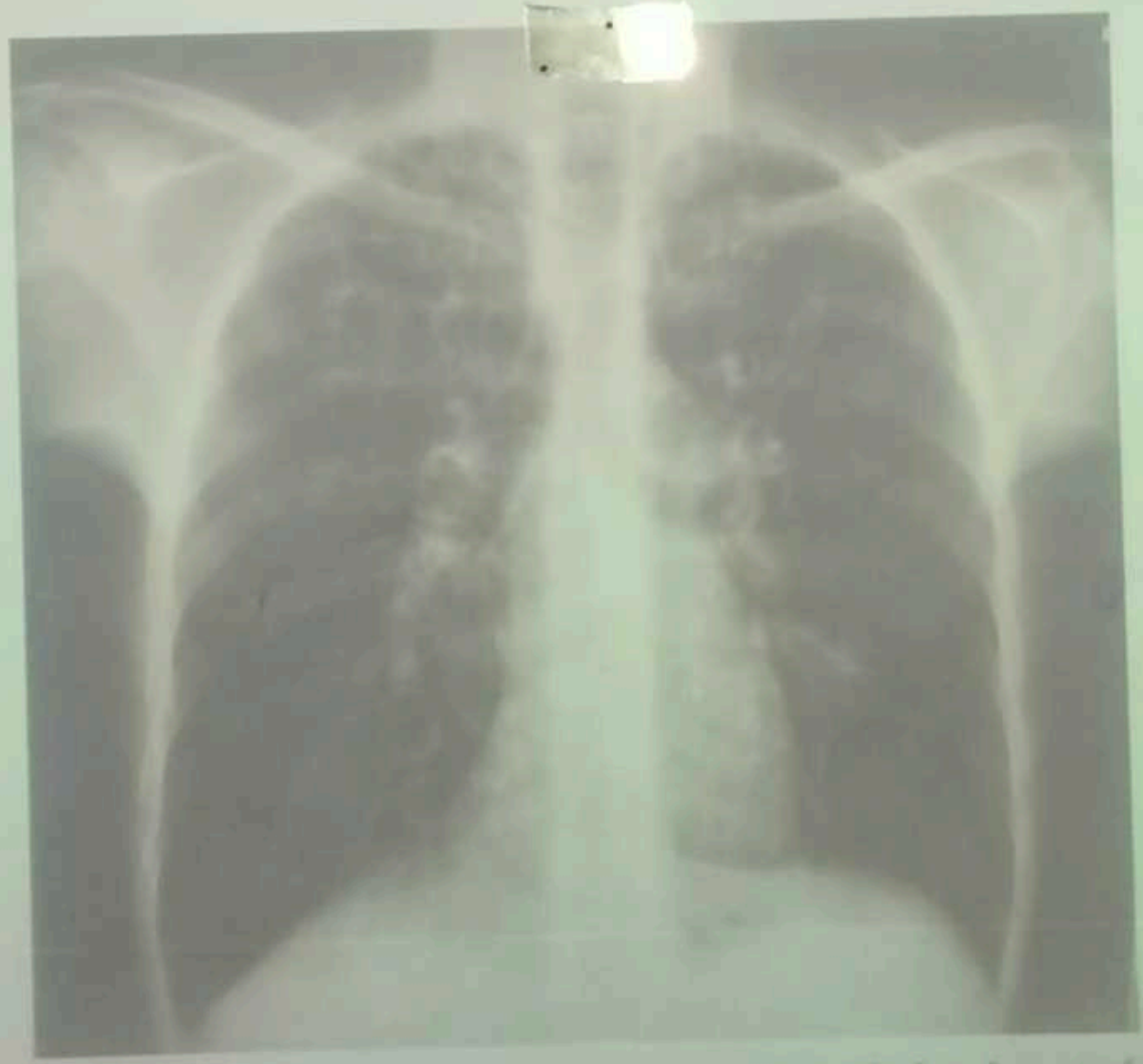
Cl concentration for infants (up to 6 months)	Result
0-29 mmol/L	CF is unlikely
30-59 mmol/L	intermediate
≥ 60 mmol/L	Indicative of CF

Cl concentration for infants older than 6 months, child and adult	Result
0-39 mmol/L	CF is unlikely
40-59 mmol/L	intermediate
≥ 60mmol/L	Indicative of CF

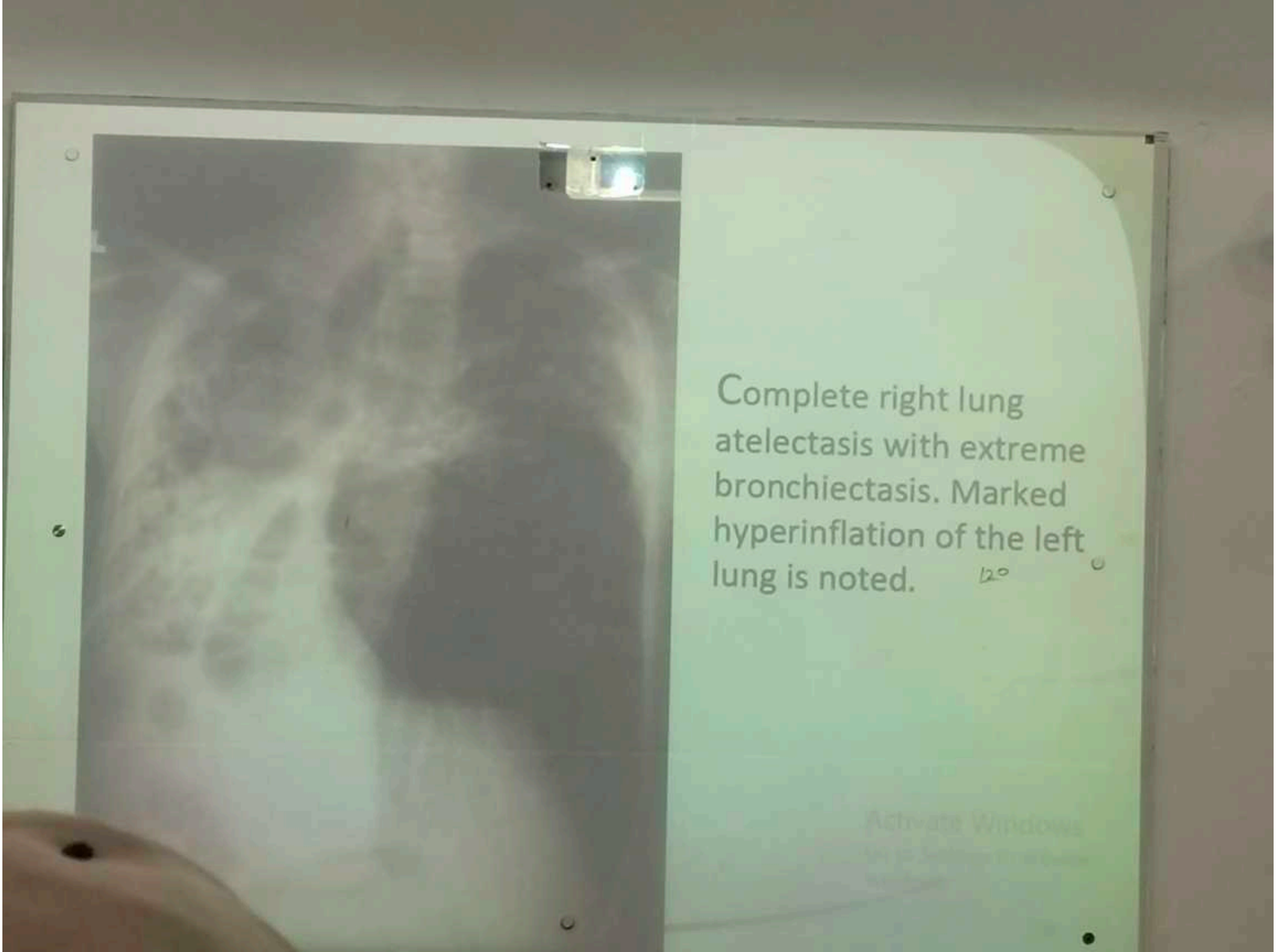
***The sweat test must be performed at least twice in each patient, preferably several weeks apart.**

Other examinations

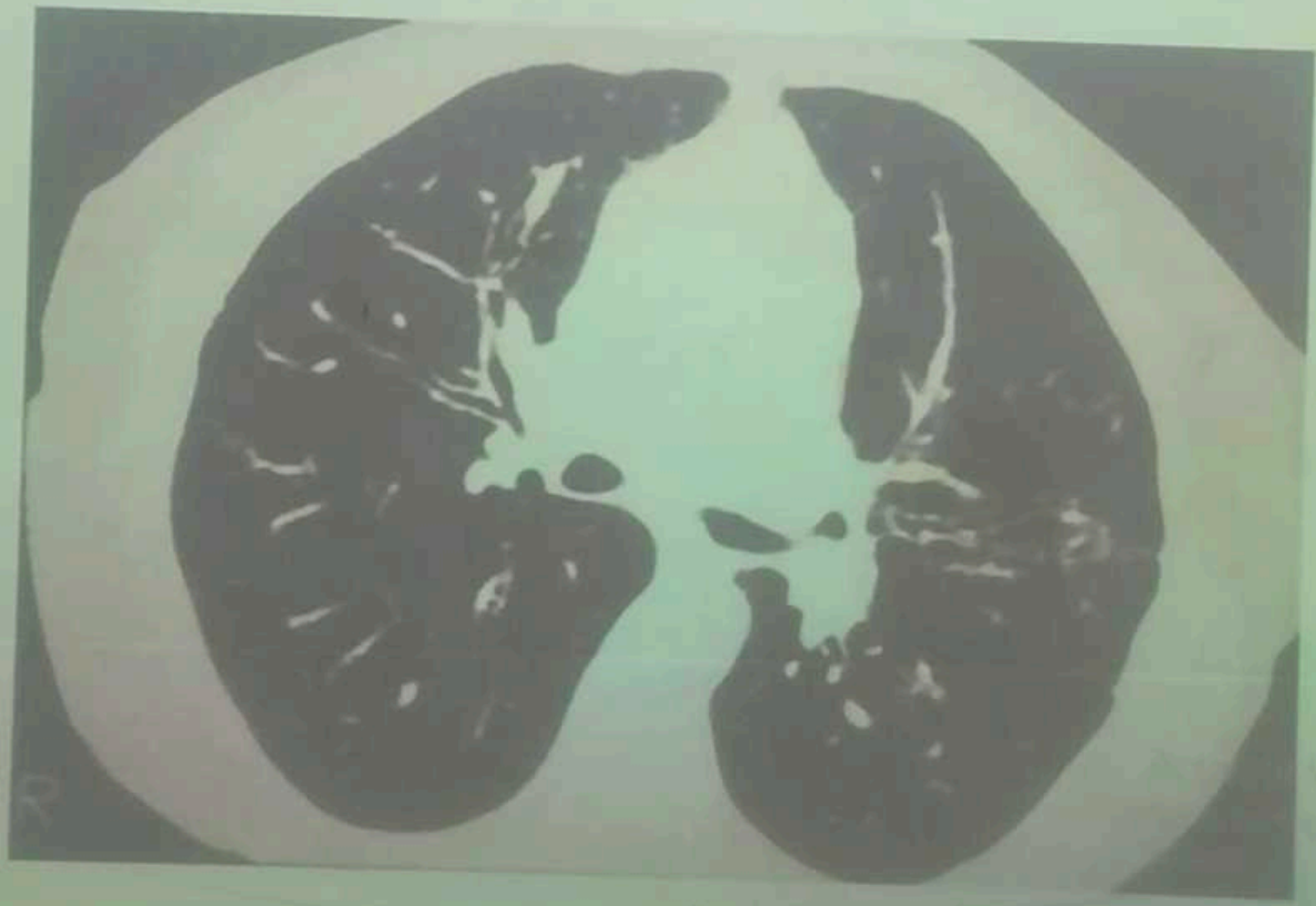
- Imaging test (X-ray, US, CT, MRI)
- Genotyping
- Pulmonary function test
- Bronchoalveolar lavage and sputum microbiology
- Immunoreactive trypsinogen
- Contrast barium enema

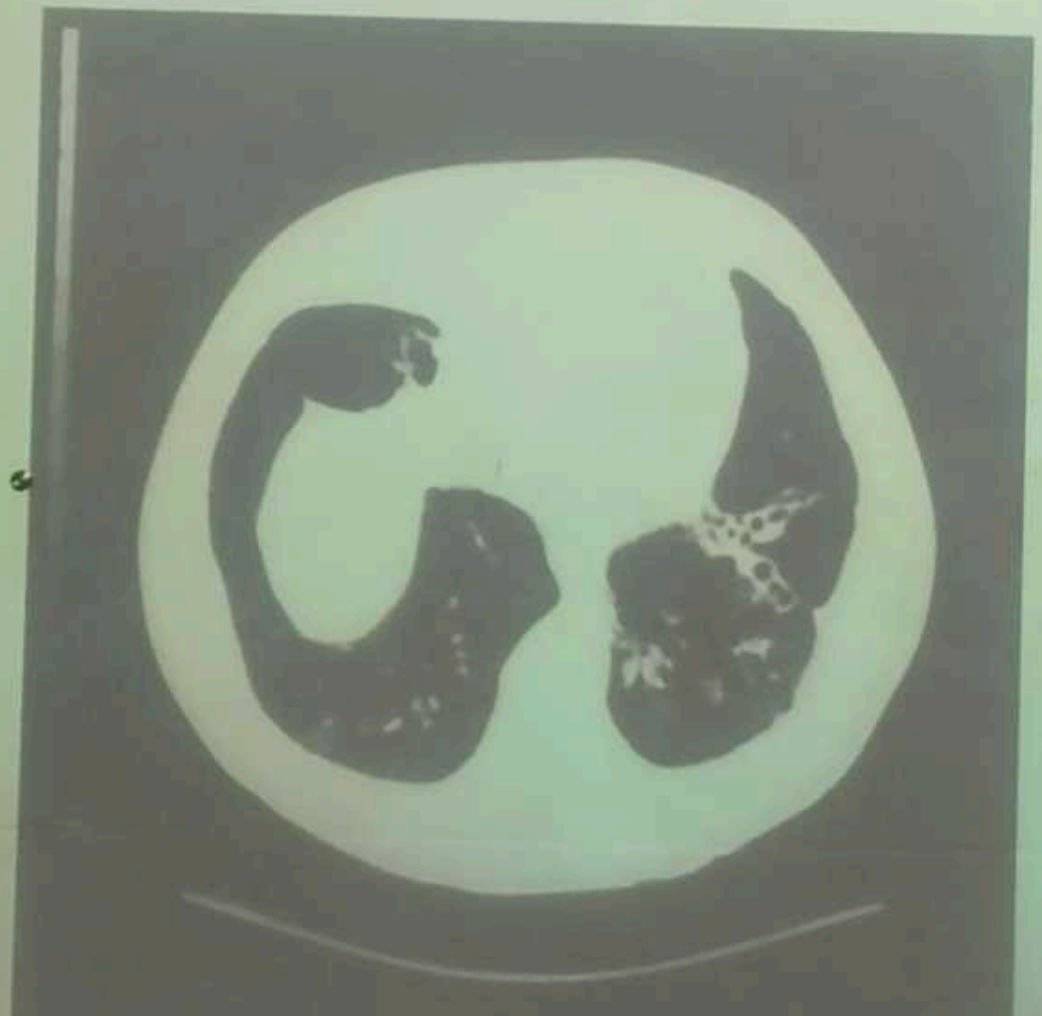


Hyperinflation and predominantly upper lobe bronchiectasis.

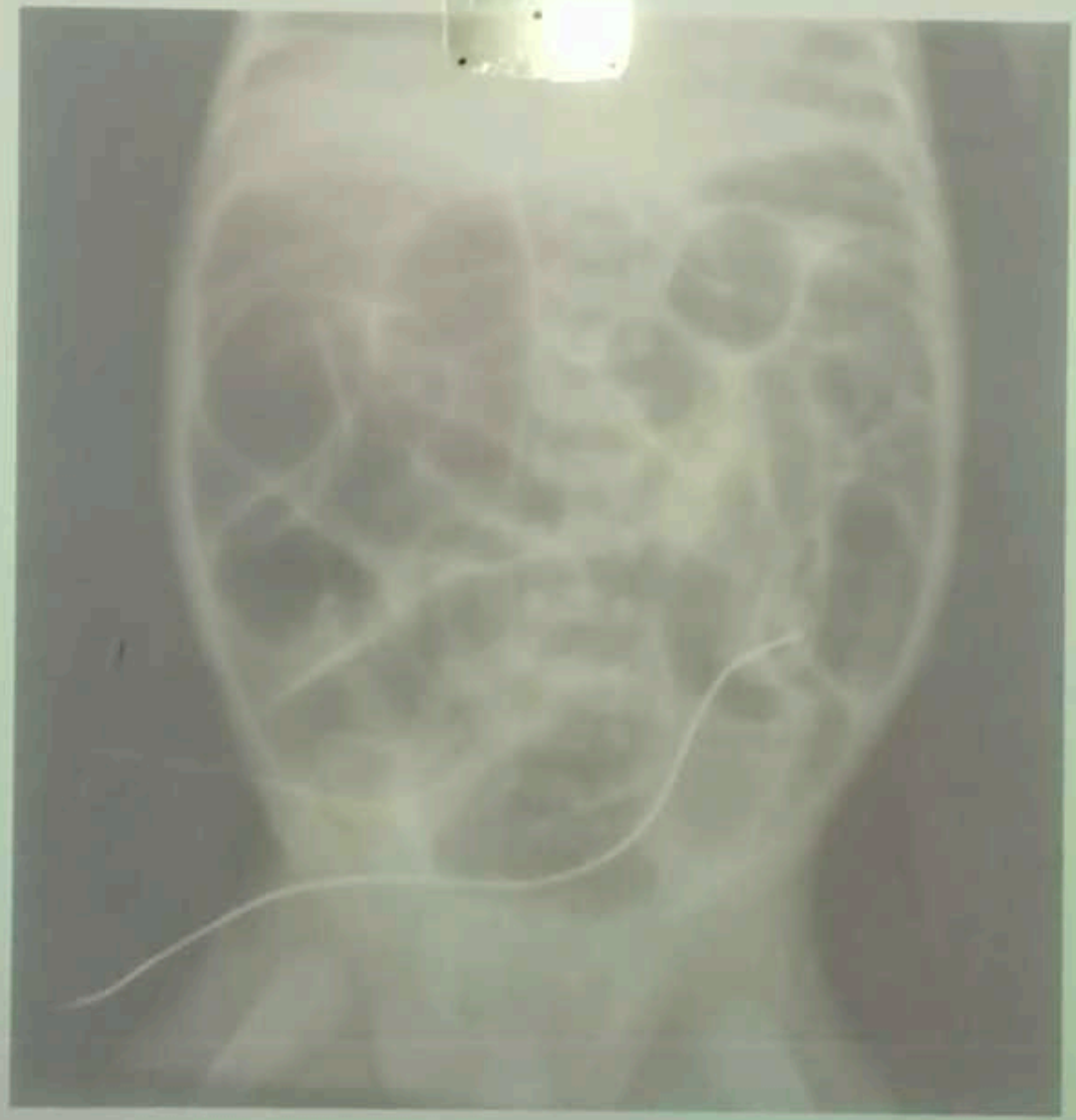

Complete right lung atelectasis with extreme bronchiectasis. Marked hyperinflation of the left lung is noted.
120

High-resolution CT image shows bronchial wall thickening (tram lines), predominantly in the upper lobes.

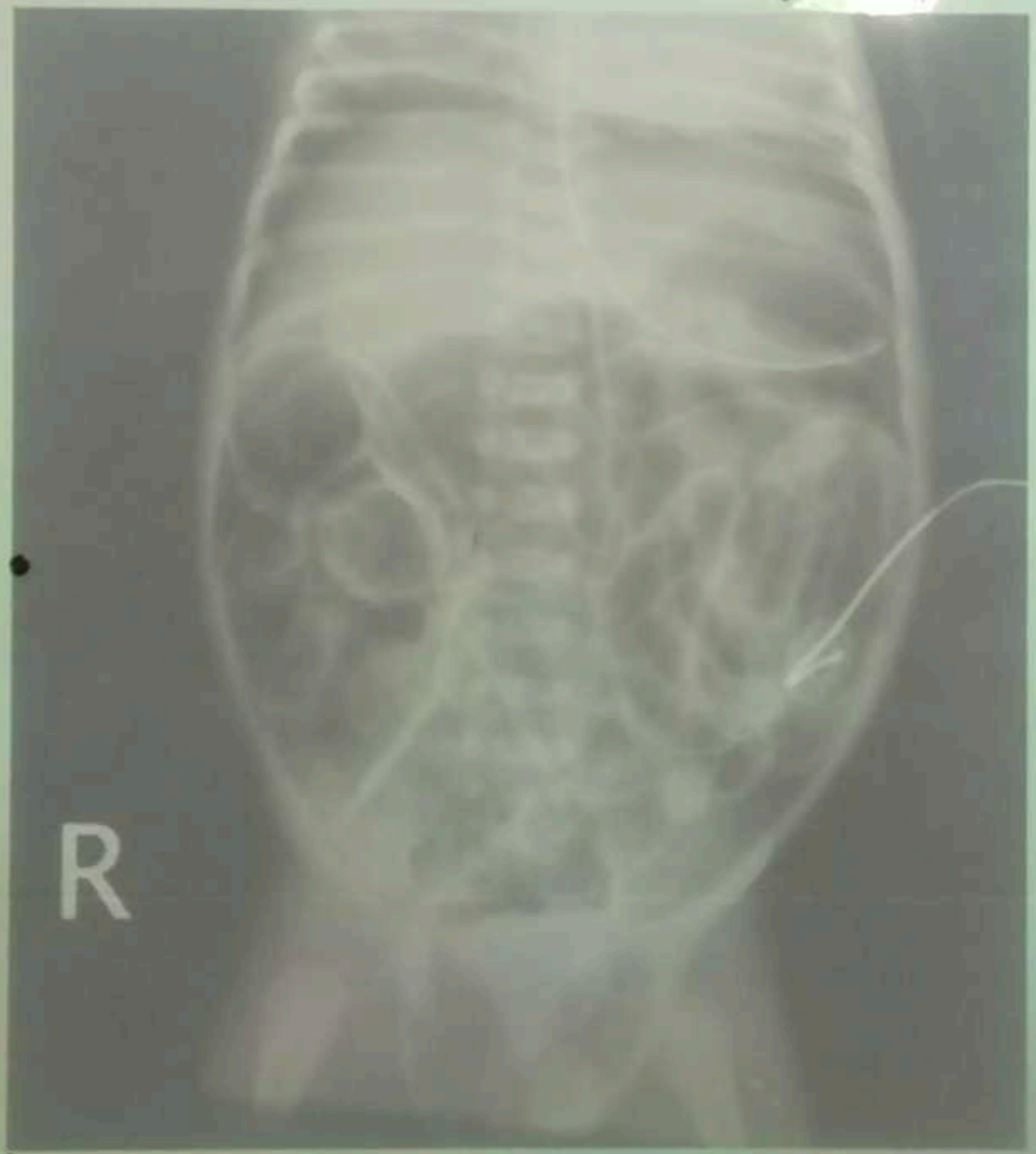




String-of-pearls sign in the left lower lobe in a patient with cystic fibrosis. The soft tissue surrounding each "pearl" indicates focal atelectatic, fibrotic lung.



Meconium ileus- Marked abdominal distension at 3 days of life. Dilation of bowel loops. No air is seen in the colon or rectum.



Progression to perforation, with overt free air under the diaphragm and a double air-contrast of bowel.

Sputum microbiology

The most common bacterial pathogens in the sputum of patients with cystic fibrosis are as follows:

- Haemophilus influenzae
- Staphylococcus aureus
- Pseudomonas aeruginosa
- Burkholderia cepacia
- Escherichia coli
- Klebsiella pneumoniae

Immunoreactive trypsinogen (IRT)

- is a pancreatic enzyme that can help with diagnosing CF in neonates with meconium ileus when IRT relative ratios are elevated greater than the 99th percentile.
- IRT plus sweat test was shown to increase sensitivity and specificity in screening.

Management

The primary goals of CF treatment include the following:

- Maintaining lung function as near to normal as possible by controlling respiratory infection and clearing airways of mucus
- Administering nutritional therapy (ie, enzyme supplements, multivitamin and mineral supplements) to maintain adequate growth
- Managing complications

Mild acute pulmonary exacerbations of cystic fibrosis can be treated successfully at home with the following measures:

- Increasing the frequency of airway clearance
- Inhaled bronchodilator treatment (especially if bronchial hyperresponsiveness is present or as part of airway clearance [inhaled bronchodilator followed by chest physical therapy and postural drainage)
- Chest physical therapy and postural drainage
- Increasing the dose of the mucolytic agent dornase alfa (Pulmozyme)
- Use of oral antibiotics (eg, oral fluoroquinolones)

Pancreatic enzyme supplements

- Pancrelipase (Creon, Pancreaze, Ultresa, Zenpep)

Mucolytics

- Dornase alpha (Pulmozyme)

Bronchodilators

- Inhaled beta2-agonist : Albuterol (AccuNeb, ProAir, Proventil HFA, VoSpire ER, Ventolin HFA)

Vaccination

- Vaccination against Pertussis, Haemophilus influenzae, Varicella, Streptococcus pneumoniae, and measles and annual influenza vaccination.

Airway clearance

- Postural drainage, percussion, vibration, and assisted coughing are recommended at the time of diagnosis and should be done on a regular basis

Antibiotics (oral, intravenous, or inhalation)

- Aerosolized form : gentamicin, aztreonam, colistin, and preservative-free high-dose tobramycin especially formulated for inhalation.
- First-generation to third-generation cephalosporins gives increasing gram-negative coverage and less gram-positive coverage, effective against Staphylococci and Haemophilus influenza
- Fluoroquinolones are effective against most gram-positive and gram-negative organisms, effective against P aeruginosa.
- Gentamicin is usually combined with one of the penicillins used to treat pseudomonad infections in patients with CF.
- Aztreonam is a monobactam antibiotic that elicits activity in vitro against gram-negative aerobic pathogens, including P aeruginosa.

- Vitamins
  - Fat soluble vitamins A, D, E, and K and water soluble biotin, folic acid, niacin, pantothenic acid, B vitamins (ie, B-1, B-2, B-6, B-12), and vitamin C.

CFTR Potentiators

- Cystic fibrosis transmembrane conductance regulator (CFTR) potentiators are the first available treatment that targets the defective CFTR protein.
- Ivacaftor (Kalydeco) - facilitates increased chloride transport by potentiating the channel-open probability (or gating) of certain CFTR gene mutations.

Surgical therapy may be required for the treatment of the following respiratory complications:

- Pneumothorax
- Massive recurrent or persistent hemoptysis
- Nasal polyps
- Persistent and chronic sinusitis

GI tract complications requiring surgical therapy are as follows:

- Meconium ileus
- Intussusception
- Gastrostomy tube placement for supplemental feeding
- Rectal prolapse

*Lung transplantation is indicated for the treatment of end-stage lung disease