Cystic Fibrosis:

“Cystic fibrosis is an inherited multisystem disorder characterized by obstruction & infection of airways & maldigestion & its consequences”.
Genetics:

AR – 1/3500 live births

Gene locus on long arm of chromosome 7

CF gene - CF transmembrane regulator (CFTR)

CFTR - cAMP - regulated chloride channel

Expressed on epithelial cells

>1500 mutations - most prevalent ΔF508
The net ion flow across normal and cystic fibrosis cell
Pathophysiology (cont...)

1- Paucity of water in mucus secretions

2- Failure to clear mucous secretions

3- Ch. infection limited to respiratory tract

4- Elevated salt content of sweat & other serous secretions
Pathology:

Lungs:

Bronchiolitis – Bronchitis- Bronchiectasis
Bronchiectatic cysts
Pneumothorax
Hemoptysis
Secondary pulmonary HTN
Paranasal sinuses:

Epithelial lining hyperplastic & hypertrophied

Polypoid lesions, mucopyocele & erosion of bone may occur

Multiple polyps
Pancreas:

Small & cystic

In 85-90% of cases replacement with fibrous tissue & fat

Foci of calcification may occur

Islets of langerhans – architectural disruption
Intestinal Tract:

Minimal changes

Esophageal & duodenal glands are distended with mucous secretions

Crypts of appendix & rectum are distended with secretions
Biliary System:

- Occasional prolonged NNJ
- Focal biliary cirrhosis in 25% cases
- Fatty infiltration in 30%
- Symptomatic multilobular biliary cirrhosis
- Gallbladder-hypoplastic
- Atresia of cystic duct & stenosis of distal common bile duct
Genitourinary system:

Endocervicitis

In >95% males epididymis, vas deferens & seminal vesicles are obliterated

Generalized amyloidosis rare
Clinical Manifestations:

Respiratory Tract:

Symptoms
- Cough, Wheezing, Shortness of breath
- Exercise intolerance
- Rhinorhea, Nasal obstruction

Signs
- Cyanosis, Digital clubbing,
- Increased AP diameter of chest
- Gen. hyper resonance, Coarse crackles,
- Expiratory wheeze
- Acute sinusitis, Nasal polyps
Intestinal Tract:

Meconium Ileus:
In 15-20% Newborn

Meconium Plug Syndrome:
Less specific than meconium ileus
Distal intestinal obstruction
with fecal material in older pts
Intestinal Tract:

- Symptoms
  - Greasy stool, Excessive flatus
  - Acid or bile reflux
  - Vit. Deficiencies- ADEK

- Signs
  - Protuberant abdomen
  - Intussusception
  - Fecal impaction of cecum
  - Subacute appendicitis,
  - Anasarca
Biliary Tract:

- Biliary cirrhosis 2-3% pts
- Biliary colic
- Icterus,
- Ascites
- Hematemesis
- Hypersplenism
- Neonatal Hepatitis like picture
- Hepatomegaly
Pancreas:

Exocrine pancreatic insufficiency

Hyperglycemia,
Glycosuria
Polyuria
Weight loss

after 10 yrs of age
when 8 % acquire diabetes

Recurrent acute pancreatitis
Genitourinary system:

An average of 2 yrs delay in sexual development

**Males**

>95% azoospermic
Sexual function unimpaired

**Female**

Cervicitis
Secondary amenorrhea
Decrease fertility
Pregnancy well tolerated
Sweat Glands:

- Excessive loss of salt in sweat
- During gastroenteritis & warm weather
- Hypochloremic alklosis
Diagnostic Criteria for Cystic Fibrosis

Presence of typical clinical features
  OR
History of CF in a sibling
  OR
Positive newborn screening test

PLUS

Lab evidence for CFTR dysfunction

  Two elevated sweat Chloride tests
  OR
Identification of 2 CF mutations
  OR
An abnormal nasal potential difference measurement
Diagnosis:

Sweat Testing

> 60mEq/L of chloride in sweat

Threshold levels of 40mEq/L have been suggested

Values b/w 40-60mEq/L suggest CF at all ages
Radiology

Pulmonary
Hyperinflation of lung,
Atelactasis & Bronchiectasis
Dilated pulmonary artery segment

Paranasal Sinuses
Pan opacification
Failure of frontal sinus to develop

Fetal USG
Ileal obstruction with meconium in 2nd trimester
Pulmonary Function

Not obtained till 5-6 yrs of age
RV & FRC are increased (early)
Declining total lung capacity & VC(late)

Microbiological Studies
Staph aureus,
pseudomonas aeruginosa, B. cepacia
Newborn Screening
   Immunoreactive trypsinogen in blood spots
   Confirmatory sweat & DNA testing

Other Investigations as Indicated
   Cardiac: ECG, Echocardiography
   GIT: S. proteins, LFTs, coagulation studies, x-ray abdomen, USG abdomen, hepatobiliary Tc-99 Scintigraphy, PTC, ERCP, pancreatic function tests
   Other: urea & electrolytes
Management of CF:

Aims:

1. Ensure optimal growth & development
2. Delaying progress of pulmonary disease
3. Preventing & treating complications
4. Normal life style
5. Patient & family education
6. Recognition & treatment of psychological complications

Multidisciplinary approach
Treatment:

1- Treatment of Lung disease

2- Treatment of Gastrointestinal disease

3- Nutritional therapy

4- Treatment of Complications
Treatment of lung disease:

1. Antibiotics
2. Chest physiotherapy
3. Nebulized treatment
4. Bronchodilators
5. Anti inflammatory treatment
6. Mucolytic treatment
8. Hemoptysis
9. Pneumothorax
10. Cor- Pulmonale
11. Immunization- influenza
Antibiotic therapy:
Staph aureus, H. influenzae, P. aeruginos, Burkholderia cepacia

Intermittent oral Antibiotic Therapy
Continuous oral Antibiotic Therapy
I/V antibiotic therapy

Important points to remember are-
Sputum cultures do reflect lung flora
Double dose
Adult dose from 7yrs
Chest Physio Therapy

Postural drainage
Percussion & vibration
10-20 min, One to 4 time a day
Routine aerobic exercises
Nebulized Treatment:

- Hypertonic saline
- Bronchodilators
- Mucolytics
- Antibiotics
- Cromolyn
- Corticosteroids
- Dornase Alpha
- Nebulized amiloride (Na+ channel blocker)
Bronchodilator Treatment:

Increased bronchial activity in 40-75 % pts
Standard asthma treatment

Anti- Inflammatory treatment:

Long term corticosteroids & Ibuoprofen –
Slow the progression of CF
Hemoptysis:

Minor hemoptysis - No specific treatment

Hemoptysis > 15-20ml

Admit in Ward
O₂ Inhalation
Vit. K
Blood transfusion
Antibiotics
Stop chest physiotherapy
Treatment of GIT disease:

1. PERT
2. Salt
3. Management of meconium ileus
4. DIOS
5. Rectal prolapse
6. Liver & biliary tract disease
7. Fibrosing Colonopathy
8. Abd. Pain
PERT: (Lipase, Amylase, Proteases)

Fat absorption improves from 60% without therapy to 85-90% with therapy

An upper limit of 10,000 units lipase/kg/day

PERT for infants 500-1000 U lipase/g of dietary fat

PERT for children 500-4000 U lipase/g of dietary fat

Fibrosing colonopathy
Nutritional Therapy:

*CF pts require 120% of normal energy requirement

*Liberal diet containing

  Fats, Sugar
  Milk products, Protein foods

*Salt

  < 6m  0.5g/d
  6-12m 1.0g/d
  1-5yrs 2.0g/d
  >5yrs 3.0g/d
Treatment of other Complications:

1. Diabetes Mellitus-
   DKA rare

2. Musculoskeletal problems-
   Pulmonary care & NSAID

3. Lung transplantation-
   Life expectancy <2yrs
   Quality of life impaired
   Frequent life threatening hemoptysis
Prognosis:

Median survival 40 yrs

> 90 % mortality is due to lung disease

Cirrhosis is second life threatening complication

Poor prognosis factors include

- Female sex
- Multiple organ involvement
- Abnormal chest x-ray 12m after diagnosis
- Poor growth
- Recurrent hemoptysis
- Pneumothorax
- Corpulmonale
Thank You
Pulmonary Treatment (Cont...)
Bronchodilator Treatment
- Inhaled B2 agonists
- Anticholinergics, Oral theophylline
Anti Inflammatory Treatment
- Long term use of oral corticosteroids & ibuprofen
Mucolytic Treatment:
- Dornase Alpha (Recombinant Human Deoxyribonuclease 1)
  - Cleaves extracellular DNA & decreases viscoelasticity of purulent secretions
  - Used in chronic suppurative disease or obstructive disease
- Dose: 2.5 mg OD
Pulmonary Treatment (Cont…)

Aerosolized Antibiotic Therapy

Inhaled tobramycin, 300mg twice daily on alternate months for 6 months
Ticarcillin, 0.5g, BD OR QID
Colistin, 20-40mg, BD OR QID
Intravenous Antibiotic Therapy

Indicated in pts. Who have progressive or unrelenting symptoms or signs despite intensive home measures

Period of treatment is 14 days

Pseudomonas requires 2 drug therapy
The net ion flow across normal and cystic fibrosis
Other Diagnostic Tests

↑ potential difference across nasal epithelium

Loss of this difference with topical amiloride application

Absence of voltage response to B–adrenergic agonist

Failure to sweat when a combination of isoproterenol and atropine is injected in skin
Pathophysiology

**CFTR mutation**

In airways cells can’t excrete Cl- from cells into the lumen through cAMP mediated CFTR channels

Cl- is trapped inside the cells

sodium follows chloride & water follows sodium

secretions in the lumen become viscous & elastic & are harder to clear

Secretions are Retained & obstruct airway

In sweat glands cAMP mediated conductance of Cl- in to the cells is defective

so Cl- can’t be absorbed from the sweat

sodium follows chloride

salt is lost in sweat
CFTR: A cAMP-Regulated Chloride Channel

Airway Lumen

NORMAL

Submucosa

CYSTIC FIBROSIS