• Genetics

- The most common life shortening autosomal recessive disease due to mutation on the long arm of chromosome 7.
- >1500 CFTR (CF transmembrane regulator protein) polymorphisms are associated with CF
- The most prevalent mutation is F 508 deletion
Cystic Fibrosis Gene

Sequence of nucleotides in CFTR gene

A
T
C
AT
C
TT
G
GT
GT

Amino acid sequence of CFTR protein

Isoleucine 506

Isoleucine 507

Phenylalanine 508

Deleted in many patients with cystic fibrosis

Glycine 509

Valine 510

Chromosome 7

Pathophysiology of CF

• The CFTR controls the Cl conductance in the apical epithelial cells (via the cAMP).
• The epithelial cells are unable to secrete salt and water on the airway surface.
• Thus, they can not hydrate secretions that in turn become **viscous and elastic** and difficult to be cleared by the mucociliary mechanisms.
• Similar events may take place in the pancreatic and biliary ducts as well as in the vas deferens.
• Because the sweat glands absorb chloride, salt is not retrieved from the primary sweat as it is transported to the skin surface and as a result its sodium and chloride levels are elevated.
The genetic defect underlying CF disrupts the functioning of several organs by causing ducts or other tubes to become clogged, usually by thick, sticky mucus or other secretions.

manifestations of CF:

1. Cough (productive)
2. Bulky, greasy stools with droplets of fat
3. Diabetes
4. Meconium ileus
5. Constipation
6. Azoospermia
7. Biliary cirrhosis
8. Pancreatitits
CYSTIC FIBROSIS

- Clinical Presentation
  - Pulmonary:
    - Cough
      - Its the most constant symptom
      - Dry at times, frequently productive
    - Increased anteroposterior diameter of the chest
    - Hyperresonance, scattered and localized crackles
    - Clubbing, cyanosis, acute sinusitis, nasal obstruction
CF: Newborn Screening

- Assessment of Immunoreactive trypsinogen (IRT)
- Confirmation of positive IRT by CF gene mutation analysis
- Confirmation of results with a sweat test
- Now present in all 50 states in the US
## Presenting Features of CF

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent respiratory symptoms</td>
<td>50%</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>43%</td>
</tr>
<tr>
<td>Abnormal stools</td>
<td>35%</td>
</tr>
<tr>
<td>Meconium Ileus, intestinal obstruction</td>
<td>19%</td>
</tr>
<tr>
<td>Family history</td>
<td>17%</td>
</tr>
<tr>
<td>Hyponatremia, acid-base abnormality</td>
<td>5%</td>
</tr>
<tr>
<td>Rectal prolapse</td>
<td>3%</td>
</tr>
<tr>
<td>Nasal polyps; chronic sinusitis</td>
<td>2%</td>
</tr>
<tr>
<td>Hepatobiliary disease</td>
<td>1%</td>
</tr>
</tbody>
</table>
CYSTIC FIBROSIS

- Clinical Presentation
  - Rhinorrhea and nasal polyps
  - As the lung disease progress; exercise intolerance, shortness of breath, growth failure, cor-pulmonale (rarely), respiratory failure, and death
  - Common pathogens
    - Staphylococcus aureus
    - Pseudomonas aeruginosa
Cystic Fibrosis

- Meconium ileus
  - 15-20% of newborn with CF the ileum is completely obstructed
  - Abdominal distension, emesis, failure to pass meconium in the first 24 and 48 hours
  - KUB will show air-fluid level with ground glass material in the central abdomen
CYSTIC FIBROSIS

• Meconium ileus
  – Gastrografin enema diagnostic and therapeutic
  – Hypertonic solution (electrolyte problem)
  – Surgery if medical management fails (to prevent rupture and peritonitis)
Cystic Fibrosis

- Pancreatic insufficiency
  - Malabsorption
    - Lack of endogenous digestive enzymes
    - Frequent foul bulky greasy stools, flatus, FTT

- Vitamin ADEK deficiency
  - Night blindness
  - Decreased bone density
  - Neurologic dysfunction (dementia, peripheral neuropathy) hemolytic anemia
  - Hypoprothrombinemia
CYSTIC FIBROSIS

• Clinical Presentation
  – Sexual development is typically delayed 2-3 years
  – Delayed time to conception
  – Azoospermia
  – Sexual function is unimpaired
CYSTIC FIBROSIS

- DIOS (Distal Intestinal Obstruction Syndrome)
  - Typical in teens and those with poor enzyme replacement adherence
- Rectal prolapse
- Nasal polyps
  - Are most prevalent in the 2nd decade of life
- Depression
  - Common in adults with CF
- Biliary cirrhosis 2-3% of cases
- IDDM: CFRDM (cystic fibrosis related diabetes mellitus)
CYSTIC FIBROSIS

• Diagnosis
  – Newborn screening
  – Sweat Chloride (Gold standard)
    • >40 less 6 months of age
    • >60 meq/L more 6 months old
  – Positive results should be confirmed
  – Negative results should be repeated if suspicion of diagnosis remain
  – False positive test
    • Eczema, or contaminated with cream or lotion
Cystic Fibrosis

- Diagnosis
  - Non-CF conditions associated with positive sweat chloride test
    - Untreated adrenal insufficiency
    - Ectodermal dysplasia
    - Hereditary nephrogenic diabetes insipidus
    - G6PD
    - Hypothyroidism
    - Malnutrition with hypoalbuminemia and edema
CYSTIC FIBROSIS

- Diagnosis
  - DNA testing
  - Pancreatic Function testing
    - Fecal elastase
    - 3 days stool fat measurement
CYSTIC FIBROSIS

- Treatments for CF may include the following:
  - Pancreatic enzyme supplements
  - Multivitamins (including fat-soluble vitamins)
  - Bronchodilators
  - Hydrating agents (7% hypertonic saline)
  - Mucolytics (DNase)
  - Nebulized, inhaled, oral, or intravenous antibiotics
SWEAT TEST

Normal under 6mos < 30 mmol/L
Normal over 6mos < 40 mmol/L
Borderline 40-60 mmol/L
Abnormal > 60 mmol/L

*In infants anything > 30 should be repeated and worked up
SWEAT TEST

Normal under 6mos<30 mmol/L
Normal over 6mos<40 mmol/L
Borderline 40-60 mmol/L
Abnormal >60 mmol/L

*In infants anything >30 should be repeated and worked up
 PRIMARY CILIARY DYSKINESIA (PCD)

- **Background**
  - Autosomal recessive
  - Abnormal ciliary motion and impaired mucociliary clearance.
  - Associated with partial or complete Situs Inversus (50%)
  - Male infertility
  - Some patients have asplenia or polysplenia with immune dysfunction
Chest X-Ray
Situs Inversus
Ciliary structure and function
Ciliary Ultrastructure Analysis
Ciliary structure and function

- Mucosal blanket covering cilia
- Goblet cell-produced glycoproteins give the gel layer of nasal mucus its viscosity and elasticity.
- Sol layer, less viscous, allowing ciliary movement, propelling the overlying gel and particles.
PRIMARY CILIARY DYSKINESIA (PCD)

- Clinical presentation
  - 100% of children has productive cough, sinusitis and otitis media
  - Chronic or recurring upper and lower respiratory infection
  - Lower lobe bronchiectasis
  - Frequent wheezing and may be diagnosed as asthma
PRIMARY CILIARY DYSKINESIA (PCD)

- **Diagnosis**
  - Abnormal ciliary ultrastructure on electron microscope
  - CT Scan
    - Involvement of paranasal sinuses
    - Bronchiectasis

- **Treatment**
  - Chest physical therapy
  - Antibiotics for infection
  - Surgery e.g. Tympanostomy, nasal polypectomy, rarely lobectomy
BRONCHOPULMONARY DYSPLASIA

• Background
  – Chronic lung disease of extreme prematurity
  – Prolonged ventilation
  – Volutrauma and barotrauma from positive pressure ventilation
ALTE/SUDDEN INFANT DEATH SYNDROME

- GERD most common association for awake ALTE
- Seizure 2nd most common association
- Respiratory from pertussis and RSV 3rd most common association
- High index of suspicion of child abuse important
- Observation, testing and treatment as supported by history and exam
ALTE/SUDDEN INFANT DEATH SYNDROME

- National recommendation on SIDS prevention
  - “Back to Sleep” supine position except few conditions
    - Marked decline in SIDS rate following this public policy education
  - Tummy time while awake
  - No smoking pre or post-natally
ALTE/SUDDEN INFANT DEATH SYNDROME

- Recognized risk factors:
  - Prematurity
  - Low birth weight
  - Co-sleeping
  - Prone sleeping
  - Overheating
  - Young maternal age
  - Smoking during pregnancy
  - Late or absent prenatal care
ALTE/SUDDEN INFANT DEATH SYNDROME

• National recommendation on Pacifiers:
  – Use pacifier once breast feeding has been established
  – Offer pacifier at bed time or nap time
• No correlation between pacifier use and length of breast feeding
• Apnea monitor do not reduce the risk of SIDS