Diffuse Pulmonary Diseases

- **Obstructive**
  - Limitation of airflow
  - Increase in resistance due to partial or complete obstruction
- **Restrictive**
  - Reduced expansion of lung parenchyma

Obstructive vs. Restrictive

<table>
<thead>
<tr>
<th>Obstructive airway disease</th>
<th>Restrictive airway disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓FEV1</td>
<td>Normal FEV1, ↓TLC</td>
</tr>
<tr>
<td>Increase in resistance to airflow due to obstruction at any level</td>
<td>Reduced expansion of lung parenchyma with decrease in total lung capacity</td>
</tr>
</tbody>
</table>

- Emphysema
- Chronic bronchitis
- Bronchiectasis
- Asthma
- Tumor
- Foreign body

- Due to chest wall disorders (polio, obesity, pleural disease, kyphoscoliosis)
- Interstitial / infiltrative diseases (ARDS, dust diseases, interstitial fibrosis)
Pulmonary Function Tests
- Assess nature and severity of lung disease
- Quantify progression of disease and response to therapy.
- Assessment of pulmonary functions in people who are exposed to toxins including tobacco

http://www.youtube.com/watch?v=1rjN29hDXE&playnext=1&list=PLA12DC03CE96E32&feature=results_video

http://www.clevelandclinic.com
Obstructive Pulmonary Disease

Key players:

1. Asthma
2. Chronic Bronchitis
3. Emphysema
4. Bronchiectasis

Asthma

- Intermittent and reversible airway obstruction
- Increased responsiveness of the tracheobronchial tree to various stimuli
- Complex disorder in which multiple susceptibility genes interact with environmental factors to initiate pathologic reaction
- Chronic bronchial inflammation with eosinophils
- Bronchial smooth muscle hypertrophy hyper-reactivity
- Increased mucus production

“When I have an asthma attack
I feel like a fish with no water.”

-Jesse, age 5
**Asthma**

**Symptoms:** Wheezing, breathlessness, chest tightness, cough

**Incidence:** 5% of U.S. population
Increased incidence in the Western world in the past 4 decades

**Stimulus:** Infections, environmental irritants, cold air, stress, exercise

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**Asthma**

**Atopic:**

Immune Mediated. Type I hypersensitivity reaction. Involving Ig E bound to mast cells
- Begins in childhood, triggered by environmental allergens (dust, pollen etc.)
- Family history of asthma, atopy
- Tests: Skin reaction to allergen, Allergen sensitization test by serum radioallergosorbent tests showing IgE for various antigens

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**Asthma**

**Non-Atopic:**
- Non-immune triggering mechanisms (e.g., respiratory viruses, air pollutants like ozone)
- Hyperirritable bronchial tree: virus induced inflammation of the respiratory mucosa lowers the threshold of subepithelial vagal receptors to irritants
- Mechanisms not as well understood as atopic asthma, however, final pathways probably converge
- Tests: Skin and serum tests are negative
Drug induced Asthma
- Several drugs (aspirin most striking example)
- Patients with recurrent rhinitis and nasal polyps
- Drugs might induce skin reaction (urticaria) in addition to asthma

Occupational Asthma
- Fumes (epoxy resins, plastics), organic chemical dusts (wood, cotton, platinum), gases (toluene)
- Asthma develops after repeated exposure to incising agent

Pathogenesis of Asthma

Asthma Genetics
- Chromosome 5q has several susceptibility genes
  - IL 13 - genetic polymorphisms susceptibility for atopic asthma
  - CD 14 - SNP associated with occupational asthma
- ADAM 33 - 20q - member of the metalloproteinase family, polymorphisms accelerate bronchial smooth muscle proliferation
Pathology of Asthma

Status asthmaticus – Hyperinflated lungs

Mucus plug – Thick and tenaceous

Curschmann Spirals
Asthma

COMPLICATIONS

- Status asthmaticus (prolonged bout of asthma lasting for days, responding poorly to treatment)
- Emphysema
- Chronic bronchitis
- Pneumonia
- Bronchiectasis
- Cor pulmonale
Chronic Bronchitis

Clinical definition: Persistent productive cough for at least three consecutive months in at least two consecutive years

- Smokers
- Urban dwellers, smog-ridden cities
- Most common in middle aged men
- Complication: Cor pulmonale, heart failure
Chronic Bronchitis

Morphology:
Hypertrophy of mucus secreting glands
Goblet cell metaplasia
Inflammation
Fibrosis and obliterative changes in bronchioles
May lead to atypical metaplasia/dysplasia of the respiratory epithelium

Fig: Robbins and Cotran (old edition)

The Reid index measures the gland to wall ratio (normally glands are 40% of wall thickness as measured from epithelial basement membrane to cartilage)
Chronic Bronchitis

**COMPLICATIONS:**
- Cor pulmonale with cardiac failure
- Infections
- Bronchogenic carcinoma

Emphysema:

Destruction of walls of airspaces distal to terminal bronchioles, leading to permanent abnormal enlargement of air spaces.
Types of Emphysema

a) Centriacinar (centrilobular)
b) Panacinar (panlobular)
c) Distal acinar (paraseptal)
d) Irregular

Fig: Robbins and Cotran

Types of Emphysema

a) Centriacinar (Centrilobular) emphysema
   • Respiratory bronchioles
   • Upper lobes
   • Male smokers
   • Often associated with chronic bronchitis
   • Coal-workers pneumoconiosis
Types of Emphysema

b) Panacinar emphysema
   • Lower lobes
   • alpha1-antitrypsin deficiency
   • Whole acinus
Types of Emphysema

c) Distal acinar (Paraseptal) emphysema
  • Distal acinus
  • Along pleura and lobular septa
  • Adjacent to areas of fibrosis, scarring, atelectasis
    - can form multiple, contiguous, enlarged air spaces, can form cysts (bullae)
  • Could lead to spontaneous pneumothorax in young adults
**Types of Emphysema**

d) **Irregular emphysema**
   - Acini irregularly involved
   - Associated with scarring/healed inflammatory lesions
     - Mostly asymptomatic (probably most common)
Other Types of Emphysema

- Compensatory
- Senile
- Obstructive hyperinflation
- Bullous (> 1 cm in diameter)
- Interstitial

Pathogenesis of Emphysema

- Mild chronic inflammation, i.e. macrophages, CD8+ T lymphocytes, and neutrophils
- Protease-antiprotease theory
Hyperinflated lungs with formation of bullae

http://www.stritch.luc.edu/lumen/meded/radio/curriculum/medicine/emphysema.htm
Centrilobular Emphysema:
With marked upper lobe predominance

Destruction of alveolar walls;
Note: There is no fibrosis

**Alpha-1 Antitrypsin Deficiency**
- Genetic deficiency of alpha-1 antitrypsin
- Alpha-1 antitrypsin is the principle antielastase in serum and interstitial tissue
- Alpha-1 antitrypsin is encoded by codominantly expressed genes on the *Pi* locus of chromosome 14
- Normal phenotype of alpha 1 antitrypsin *PiMM*. Most common form in its deficiency is *PiZZ*.
- >80% of the *PiZZ* individuals develop emphysema.
### Bronchitis vs. emphysema

<table>
<thead>
<tr>
<th>Predominant Bronchitis</th>
<th>Predominant Emphysema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>40-45</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Mild; late</td>
</tr>
<tr>
<td>Cough</td>
<td>Early; copious sputum</td>
</tr>
<tr>
<td>Infections</td>
<td>Common</td>
</tr>
<tr>
<td>Respiratory insufficiency</td>
<td>Repeated</td>
</tr>
<tr>
<td>Cor pulmonale</td>
<td>Common</td>
</tr>
<tr>
<td>Airway resistance</td>
<td>Increased</td>
</tr>
<tr>
<td>Elastic recoil</td>
<td>Normal</td>
</tr>
<tr>
<td>Chest radiograph</td>
<td>Prominent vessels; large heart</td>
</tr>
<tr>
<td>Appearance</td>
<td>Blue bloater</td>
</tr>
</tbody>
</table>

Robbins Table 15-4

### Bronchiectasis

- Permanent dilatation of bronchi and bronchioles caused by destruction of the muscle and elastic tissue caused by chronic necrotizing inflammation.

### Bronchiectasis

Etiology and predisposing conditions:
- Obstruction (tumor, foreign bodies)
- Infection (TB, Aspergillus)
- Congenital/Hereditary
  - Cystic fibrosis
  - Kartagener’s syndrome
  - Immunodeficiency states
- Other (Rheumatoid arthritis, lupus, Graft versus Host Disease)
Bronchiectasis

Pathogenesis

Obstruction \rightarrow \text{Impaired clearing mechanisms} \rightarrow \text{Pooling of secretions distal to obstruction} \rightarrow \text{Inflammation of the airway with necrosis, fibrosis and eventual dilatation}

Cystic Fibrosis
- Severe bronchiectasis
- Primary defect in Chloride transport causing accumulation of viscous secretions obstructing the airways
- AR, chromosome 7
- Increased susceptibility to repeated infections, and widespread damage to the airway walls
Cystic Fibrosis

- Cystic fibrosis transmembrane conductance regulator
- Protein Function: CFTR protein product is a chloride channel protein found in membranes of cells that line passageways of the lungs, liver, pancreas, intestines, reproductive tract, and skin. CFTR is also involved in the regulation of other transport pathways.
- Associated Disorders: Defective versions of this protein, caused by CFTR gene mutations, can lead to CF and congenital bilateral aplasia of the vas deferens.
- About 70% of mutations observed in CF patients result from deletion of three base pairs in CFTR’s nucleotide sequence (delta F508).

Kartagener Syndrome

1. Sinusitis
2. Bronchiectasis
3. Situs inversus
4. Infertility

Caused by primary ciliary dyskinesia
Autosomal-recessive with variable penetrance
Absence/shortening of dynein arms
Complications of Bronchiectasis

- Respiratory insufficiency
- Cor pulmonale
- Brain abscesses
- Amyloidosis

Who has emphysema? Who has chronic bronchitis?

http://www.youtube.com/watch?v=LideJlY9cAk&feature=fvsr

Questions??
Summary of COPD

Emphysema
- Destruction and dilatation of acini
- Centriacinar: smoking
- Panacinar: alpha 1 antitrypsin deficiency
  - “Pink Puffers”

Chronic Bronchitis
- Cough
- Hypersecretion of mucus
- Smoking, pollutants
- Small airway disease
  - “Blue bloaters”

Bronchiectasis
- Damage to and dilatation of bronchial wall
- Permanent
- Infections, purulent mucus
Summary of COPD

Bronchial Asthma
- Episodes of bronchospasm
- Atopic or allergic
- Nonatopic (viruses and pollutants)
- Eosinophils, mucus plugs
  (Charcot-Leyden crystals and Curschmann's spirals)