Diffuse Pulmonary Diseases

1. Severe Obesity
2. Neuromuscular Disorder
3. Disease of the pleura

Diffuse Restrictive Pulmonary Diseases

Interstitial Pulmonary Diseases

Acute Respiratory Distress Syndrome

Occupational & Environmental Exposure

Drug & Treatment Related

Immune Related

Pneumoconiosis (Inorganic)

Hypersensitivity Pneumonitis (Organic)

Post ARDS

Idiopathic Pulmonary Fibrosis

Diffuse Obstructive Pulmonary Diseases

Emphysema

Chronic Bronchitis

Asthma

Bronchiectasis

Chronic Bronchitis

Centriacinar

Panacinar

Distal Acinar

Irregular

Idiopathic Pulmonary Fibrosis

Post ARDS

Idiopathic Pulmonary Fibrosis

Post ARDS
# Diffuse Obstructive Pulmonary Diseases

## Definition
- Limitation of airways
- Resistance caused by
  - Partial or complete obstruction of airways

## Diseases

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Emphysema</th>
<th>Chronic Bronchitis</th>
<th>Asthma</th>
<th>Bronchiectasis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>• Permanently distal of airspace distal to the terminal bronchiole</td>
<td>• Persistent productive cough for at least 3 consecutive months</td>
<td>• Chronic inflammatory disorder of airways</td>
<td>• Permanently distal of bronchi</td>
</tr>
<tr>
<td></td>
<td>• With destruction of the alveoli wall</td>
<td>• In at least 2 consecutive years</td>
<td>• Characterized by early morning and night</td>
<td>• Bronchiectasis due to hyperinflation</td>
</tr>
<tr>
<td></td>
<td>• Categorized into</td>
<td></td>
<td>• Wheeze, Difficulty in breathing</td>
<td>• Involved the LOWER LOBE of BILATERAL lungs</td>
</tr>
<tr>
<td></td>
<td>o Centriacinar</td>
<td></td>
<td>• Chest tightness, Cough</td>
<td>• Usually affect the more distal bronchi and bronchioles</td>
</tr>
<tr>
<td></td>
<td>o Panacinar</td>
<td></td>
<td></td>
<td>almost near to the pleura</td>
</tr>
<tr>
<td><strong>Macroscopic</strong></td>
<td>• Types</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>o Centriacinar</td>
<td>• Airways are</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>o Panacinar</td>
<td>o Swollen</td>
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<td></td>
<td></td>
<td>o Hyperemic</td>
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<td></td>
<td></td>
<td>• Covered by mucopurulent/mucinous secretion</td>
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<td></td>
<td></td>
<td>• Copious sputum</td>
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<tr>
<td><strong>Microscopic</strong></td>
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<tr>
<td></td>
<td>• Loss and thinning of alveolar walls</td>
<td>• Lungs were overdistended due to hyperinflation</td>
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<td></td>
<td>• Consequent enlargement of airspaces</td>
<td>• Small areas of Atelectasis</td>
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<td></td>
<td>• Extensive loss of pulmonary capillaries along the way</td>
<td>• Occlusion of Bronchi and Bronchioles by thick tenacious mucus plugs</td>
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<tr>
<td><strong>Morphology</strong></td>
<td>• Tracheal glands can be</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>o Hyperplasia</td>
<td>• Mucus plugs contain</td>
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<td></td>
<td>o Hypertrphy</td>
<td>o Curschmann Spirals</td>
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<td></td>
<td>o Goblet cells can be</td>
<td>o Whorls of shed epithelium</td>
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<tr>
<td></td>
<td>o Hyperplasia</td>
<td>o Charcoal-Leyden Crystals</td>
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<tr>
<td></td>
<td>o Metaplasia</td>
<td>o Cryoglobulins from Eosinophils</td>
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<tr>
<td></td>
<td>• Thickening of the submucosal gland</td>
<td>o Eosinophils</td>
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<td></td>
<td>compared to that of the bronchial wall</td>
<td>• Always remodeling, which include</td>
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<td></td>
<td>• Measured through Reid Index</td>
<td>o Thickening of basement membrane of the bronchial epithelium</td>
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<td></td>
<td>• Normal - 0.4</td>
<td>o Edematous with inflammatory cells infiltrate</td>
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<td></td>
<td>• Marked number of inflammatory cells, neutrophilia can also increased</td>
<td>o Prominence appearance of</td>
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<td></td>
<td>• Fibrosis may lead to a complete obstruction to the airways</td>
<td>Eosinophils</td>
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<td></td>
<td>o This is called Bronchiolitis Obliterans</td>
<td>• Mast cells</td>
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<td></td>
<td></td>
<td>• Increased size of Submucosal Glands</td>
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<td></td>
<td></td>
<td>• Hypertrophy of Bronchial smooth muscle cells</td>
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</table>

## Additional Infos

### Causes
- **Centriacinar**
  - Heavy smoker
- **Panacinar**
  - Congenital Alpha-1 Antitrypsin
- **Alopecic Asthma**
  - IgE and IgD mediated immunologic reaction to environmental allergens
- **Non-alopetic Asthma**
  - Viral infections, Inhaled pollutants

### Characteristics
- Normal FVC
- [FEV₁](#)
- [FEV₁/FVC](#)
- Septicemia
- Car Pulmonary
- Metastatic Cerebral Abscess
- Secondary Amyloidosis

## Complications
- Pneumonia
- Lung abscess
- Empyema
- Obstruction
- Tumors
- Foreign bodies
- Congenital Abnormalities
- Cystic Fibrosis
- Due to abnormal secretion of viscid mucus
- Immunoglobulin deficiencies
- Repeated bacterial infections
- Kartagener Syndrome
- Autosomal recessive
- Impaired function of cilia
<table>
<thead>
<tr>
<th>Differences Between Chronic Bronchitis and Emphysema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseases</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>Dyspnea</strong></td>
</tr>
<tr>
<td>• Mild</td>
</tr>
<tr>
<td>• Happens late</td>
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<tr>
<td><strong>Cough</strong></td>
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<tr>
<td>• Early onset</td>
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<tr>
<td>• Copious</td>
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<tr>
<td><strong>Infections</strong></td>
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<tr>
<td><strong>Respiratory Insufficiency</strong></td>
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<tr>
<td><strong>Cor-Pulmonale</strong></td>
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<tr>
<td><strong>Airway Resistance</strong></td>
</tr>
<tr>
<td><strong>Elastic Recoil</strong></td>
</tr>
<tr>
<td><strong>Chest Radiograph</strong></td>
</tr>
<tr>
<td><strong>Appearance</strong></td>
</tr>
<tr>
<td>• Due to hypersecretion of mucus, the airways tend to block, there is NO damage of blood vessels</td>
</tr>
<tr>
<td>• Due to obstruction, compensatory mechanism takes place</td>
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<tr>
<td>o Increased perfusion through increasing the Cardiac Output</td>
</tr>
<tr>
<td>o Reduced in Ventilation due to obstructed airways</td>
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<tr>
<td>o Leading to ↓V/P ratio</td>
</tr>
<tr>
<td>o Hence, reduce in ventilation make the compensatory mechanism less efficient</td>
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<tr>
<td>▪ Oxygen cant be pass to the body leads to Cyanosis (Blue)</td>
</tr>
<tr>
<td>• Other than tend to be obese, the lungs are hyperinflated, therefore patients appeared Bloated</td>
</tr>
</tbody>
</table>
### Diffuse Restrictive Pulmonary Diseases

**Definition**
- Expansion of lungs parenchyma
- Accompanied by ↓lung capacity
- Is one types of diffuse restrictive diseases
- It is an occupational lung diseases

**Factors Contributing to the Extent of Pneumoconiosis**

1. Amount of dust retain in the lung and airway
   - a. Degree of air pollution
   - b. Duration of exposure
2. Size and shape of particles
   - a. Minute particles may: i. Reach the terminal airways and alveoli
     ii. Settle in their lining to evoke inflammatory response
3. Additional effects of other irritants
   - a. Tobacco smoking magnifies the effect of Asbestos

**Types of Pneumoconiosis**

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Coal Worker's Pneumoconiosis (CWP)</th>
<th>Silicosis</th>
<th>Asbestosis</th>
</tr>
</thead>
</table>
| **Definition** | Type of Pneumoconiosis due to prolonged breathing in dust from
  a. Coal
  b. Graphite
  c. Man-made carbon
  d. Sputum
| - Coal dust: Asbestos fibers coated with iron oxides, or hydrogen disulfide
- Wool dust: More reactive due to the presence of wool surfactant
| - Type of Pneumoconiosis due to inhalation of
  o. Crystalline Silica Oxide (Silica)
  o. Usually present after decades of exposure
  o. Present as nodular fibrosis
  o. Pneumocystis
| - Type of Pneumoconiosis due to 20 years or more inhalation of
  o. Asbestos
  o. Asbestos exposure is linked with:
  - Asbestos (discussed here)
  - Localized fibrous plaques
  - Pleural effusions
  - Cancers
  - Lung carcinoma
  - Metastasolysis
  - Laryngeal carcinoma
  - Colon cancer

**Macroscopic**

| Simple CWP | Coal dust: Concentrated black deposits
- Coal macule
  - Coal dust: Black nodules
  - Coal dust: Black nodules
  - Coal dust: Black nodules
  - Coal dust: Black nodules
| - Silicotic nodule
  o. Early stage
    - The nodules are:
    - Tiny
    - Barely palpable
    - Discrete
    - Pale-to-black
    - Located at the UPPER LOBE
  o. Progressive stage
    - The nodules may:
    - Coalesce
    - Become hard
    - Collagenous scar
| - Massive fibrosis present
  o. Begins at the LOWER LOBE and SUBPLEURA
  o. Extends to the UPPER LOBE
  o. Contraction of the tissue distorts the normal tissue architecture of the lungs
  o. Visceral pleura may also become fibrotic
  o. The thickening stick with the anterior chest wall
  o. Lead to narrowing of arteries and arterioles, leading to:
    - Pulmonary hypertension
    - Co-Pulmonary

**Microscopic**

| Asymptomatic Anthracosis
  - Linear streak
  - Aggregate of black anthracotic pigments
  - Simple CWP
  - The nodules contain:
    - Dust-laden macrophages adjacent to respiratory bronchioles
    - Delicate collagenous networks
    - Panacinar emphysema may occur if the dilatation of alveoli is extensive
  - Complicated CWP
  - Center lesions often necrotic due to ischemia
  - The lesions are packed with:
    - Collagen
    - Pigment
| - Silicotic nodules are:
  o. Concentric layers of Hyalinized collagen
  o. Surrounded by dense capsule of condensed collagen
  o. With or without necrosis
  o. Under Polarized Microscope
    - Birefringent silica particles
| - Asbestos bodies
  o. Golden brown
  o. Fusiform/ beaded rods
  o. Translucent center
  o. Asbestos fibers coated with iron-containing proteinaceous materials
  o. Air spaces become capulated with fibrotic tissue leading to Honeycomb appearance

**Clinical Features**

| Complicated CWP with PMF may have increased
  o. Pulmonary dysfunction
    - Pulmonary hypertension
    - Pulmonary edema
    - Cor Pulmonale
| - Most workers are asymptomatic, accidental finding upon X-ray
  o. Shortness of breath becomes apparent when progressive massive fibrosis takes place
| - Dyspnea
  - Productive cough
  - Clubbing of fingers in the late stage

**Complications**

| Pulmonary dysfunction
| - COPD independent of smoking
  o. Silica may inhibit the activity of macrophages
| - Silicostuberculosis
  o. Silica may inhibit the activity of macrophages
| - Respiratory failure
  - Cor Pulmonale

**Characteristics**

- ↓FVC or Normal FVC
- Proportionate ↓FEV₁/FVC
- Normal FEV₁/FVC
<table>
<thead>
<tr>
<th>Disease</th>
<th>Definition and Epidemiology</th>
<th>Pathogenesis</th>
<th>Clinical Features</th>
<th>Morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sarcoidosis</strong></td>
<td><strong>Definition</strong> • Systemic granulomatous disease • Present with various clinical presentation o Bilateral Hilar Lymphadenopathy in 95% of cases o Followed by ▪ Lesion over Periorbital region ▪ Crops of numerous Papules on the skin</td>
<td>• Chronic inflammatory regulation is disorganized by which o ↑ intraalveolar and interstitial CD4+ T cells o ↑ Th1 cytokines ▪ IL-2 ▪ TNF • Increased release of other cytokines which favor recruitment of Monocytes • This has impinged injury on tissue</td>
<td>• 65-70% patient heal without complication, either o Spontaneously o With Steroid therapy • 10-15% patients succumb to o Pulmonary fibrosis o Cor-Pulmonale • Die due to ▪ Cardiac damage ▪ CNS damage</td>
<td>• Formation of multiple well-formed Non-caseating Granulomas • The granulomas can be o Schaumann Bodies ▪ Laminated concretions composed of ▪ Calcium ▪ Proteins o Asteroid Bodies ▪ Stellate inclusion within Giant Cells ** these inclusion bodies are NOT pathognomonic of Sarcoidosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Miscellaneous Diffuse Restrictive Pulmonary Disease</strong></th>
<th><strong>Definition and Epidemiology</strong></th>
<th><strong>Clinical Features</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Idiopathic Pulmonary Fibrosis (IPF)</strong> <strong>Usual Interstitial Pneumonia (UIP)</strong></td>
<td><strong>Definition</strong> • Clinicopathologic syndrome with characteristic o Radiological features o Pathological features o Clinical features</td>
<td><strong>Early symptoms</strong> • Increasing dypsnea on exertion • Dry cough <strong>Late symptoms</strong> • Hypoxemia • Cyanosis • Clubbing of fingers</td>
<td>It develops insidiously, the patients usually • Gradually deteriorate despite of treatment • Mean survival rate – 3years or less • Lungs transplant is the only definitive therapy</td>
</tr>
</tbody>
</table>
## Acute Diffuse Restrictive Pulmonary Disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Etiology</th>
<th>Pathogenesis</th>
<th>Morphology</th>
</tr>
</thead>
</table>
| **Acute Respiratory Distress Syndrome (ARDS)** | **Direct Lung Injury**<br>• Common causes<br>  ▪ Pneumonia<br>  ▪ Aspiration of gastric content<br>• Uncommon causes<br>  ▪ Pulmonary contusion<br>  ▪ Fat embolism<br>  ▪ Near drowning<br>  ▪ Inhalational injury | 1. Acute assault leads to increase production of<br>  a. IL-8<br>   i. Neutrophils<br>    1. Activation<br>    2. Chemotaxis<br>  b. IL-1 and TNF<br>   i. Neutrophils<br>    1. Activation<br>    2. Chemotaxis<br>   ii. Endothelial activation<br>  c. Pulmonary microvascular sequestration<br>2. These will subsequently lead to increase number of Neutrophils leading to increase secretion of<br>  a. Leukotriene<br>  b. Oxidants<br>  c. Proteases<br>3. Release of these chemical may lead to<br>  a. Damage to the epithelium<br>  b. Maintainance of inflammatory damage<br>4. Nevertheless, it is counteract by anti-inflammatory substances such as<br>  a. Anti-oxidant<br>  b. Anti-protease<br>  c. IL-10<br>5. Imbalance of this regulation may lead to an acute damage to the lung | **Macroscopic**<br>• Lungs appear<br>  ▪ Dark red<br>  ▪ Firm<br>  ▪ Airless<br>  ▪ Heavy<br>**Acute stage**<br>• Capillary congestion<br>• Necrosis of alveolar epithelial cells<br>• Interstitial and intraalveolar<br   ▪ Edema<br   ▪ Heamorrhage<br>• Present of Hyaline membrane lining the alveolar ducts<br>• Infiltration of inflammatory cells<br>**Organizing stage**<br>• Marked proliferation of Type 2 Pneumocytes<br>• Fibrinous exudation leads to alveolar fibrosis<br>• Marked thickening of alveolar wall<br   ▪ Due to proliferation of Interstitial cells<br>• Deposition of collagenous fibers | **Microscopic**

**Macroscopic**

- Dark red
- Firm
- Airless
- Heavy

**Microscopic**

- Capillary congestion
- Necrosis of alveolar epithelial cells
- Interstitial and intraalveolar
- Edema
- Heamorrhage
- Present of Hyaline membrane lining the alveolar ducts
- Infiltration of inflammatory cells

**Organizing stage**

- Marked proliferation of Type 2 Pneumocytes
- Fibrinous exudation leads to alveolar fibrosis
- Marked thickening of alveolar wall
- Due to proliferation of Interstitial cells
- Deposition of collagenous fibers

**Etiology**

- Direct Lung Injury
  - Common causes
    - Pneumonia
    - Aspiration of gastric content
  - Uncommon causes
    - Pulmonary contusion
    - Fat embolism
    - Near drowning
    - Inhalational injury

- Indirect Lung Injury
  - Common causes
    - Sepsis
    - Severe trauma with shock
  - Uncommon causes
    - Cardiopulmonary bypass
    - Acute pancreatitis
    - Drug overdosing
    - Transfusion of blood product

**Pathogenesis**

1. Acute assault leads to increase production of
   - IL-8
     i. Neutrophils
     1. Activation
     2. Chemotaxis
   - IL-1 and TNF
     i. Neutrophils
     1. Activation
     2. Chemotaxis
     ii. Endothelial activation
   - Pulmonary microvascular sequestration
2. These will subsequently lead to increase number of Neutrophils leading to increase secretion of
   - Leukotriene
   - Oxidants
   - Proteases
3. Release of these chemical may lead to
   - Damage to the epithelium
   - Maintainance of inflammatory damage
4. Nevertheless, it is counteract by anti-inflammatory substances such as
   - Anti-oxidant
   - Anti-protease
   - IL-10
5. Imbalance of this regulation may lead to an acute damage to the lung

**Morphology**

- Lungs appear
  - Dark red
  - Firm
  - Airless
  - Heavy
- Acute stage
  - Capillary congestion
  - Necrosis of alveolar epithelial cells
  - Interstitial and intraalveolar
    - Edema
    - Heamorrhage
  - Present of Hyaline membrane lining the alveolar ducts
  - Infiltration of inflammatory cells
- Organizing stage
  - Marked proliferation of Type 2 Pneumocytes
  - Fibrinous exudation leads to alveolar fibrosis
  - Marked thickening of alveolar wall
    - Due to proliferation of Interstitial cells
  - Deposition of collagenous fibers

**Macroscopic**

- Dark red
- Firm
- Airless
- Heavy

**Microscopic**

- Capillary congestion
- Necrosis of alveolar epithelial cells
- Interstitial and intraalveolar
- Edema
- Heamorrhage
- Present of Hyaline membrane lining the alveolar ducts
- Infiltration of inflammatory cells
- Marked thickening of alveolar wall
  - Due to proliferation of Interstitial cells
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