### Interstitial Lung Diseases

**Characterized by:** • ↓ Expansion of the lung • ↓ TLC • FEV normal or proportionately reduced  
**Occurs in:** 1. Chest wall disorders  
2. Acute/chronic interstitial disease

#### Interstitial diseases

- Diffuse CT involvement  
- Restrictive Pulmonary changes  
- Tachypnea, dyspnea, crackles **NO WHEEZING**  
- Infiltrative X-ray changes  
- Progress to 2° Pulmonary hypertension → Cor Pulmonale → RHF  
- Syndromes can be distinguished early but late → all **HONEYCOMB LUNG**

- Inflammation and fibrosis of the pulmonary connective tissue, principally the most peripheral and delicate interstitium in the alveolar walls.  
- Physiological changes: Reductions in carbon monoxide diffusing capacity, lung volume, and compliance.  
- X-ray changes: bilateral infiltrative lesions in the form of small nodules, irregular lines, or ground-glass shadows, hence “infiltrative”

#### Incidence:

- Environmental: 25%  
- Sarcoidosis: 20%  
- Idiopathic pulmonary fibrosis: 15%  
- Collagen vascular disease: 10%  
- Remainder: 30%

#### Types

<table>
<thead>
<tr>
<th>Fibrosing diseases</th>
<th>Granulomatous diseases</th>
<th>Smoking-related Interstitial diseases</th>
</tr>
</thead>
</table>
| - Idiopathic pulmonary fibrosis  
- Cryptogenic Organizing Pneumonia  
- Pulmonary Involvement in Collagen Vascular Disease  
- Pneumoconioses (CWP, Silicosis, Asbestosis) | - Sarcoidosis  
- Hypersensitivity Pneumonitis | - Desquamative Interstitial Pneumonitis (DIP) |

#### Disease

<table>
<thead>
<tr>
<th>Alveolitis</th>
<th>Pathogenesis</th>
<th>Clinical</th>
<th>Labs/Histology</th>
</tr>
</thead>
</table>
| - Accumulation of inflammatory effector cells within the alveolar wall and within alveolar spaces | - Earliest manifestation of interstitial lung disease | - Distortion of normal alveolar structure  
- Chemokines injure parenchyma + fibrosis ↑ |

**Idiopathic Pulmonary Fibrosis**

- Diagnosis of exclusion

- Lung scarring from an unknown origin  
- Before: Perhaps chronic inflammation but anti-inflammatory drugs do not ameliorate symptoms  
- Now: Repetitive cycles of injury → healing → fibrosis

1. Begins by damage to type I pneumocytes  
2. Type II pneumocytes proliferate → alveolar spaces lined by cuboidal cells  
3. Fibroblastic proliferation: septa/intraalveolar exudate → intermixed normal & fibrotic lung  
4. Honeycomb lung

- Insidious onset  
- 40-70 years old  
- Unpredictable course, with most gradually deteriorating despite treatment  
- Mean survival: 3 years or less  
- Only definitive therapy: lung transplant

#### Cryptogenic Organizing Pneumonia (Bronchiolitis Obliterans Organizing Pneumonia) BOOP

- Either unknown etiology or 2° to infections and inflammatory lung injury (organism, drugs, etc)  
- Acute to sub-acute onset of fever, cough, dyspnea  
- Usually excellent prognosis  
- Supportive therapy, some require steroids

- Chest X-ray: Patchy bilateral infiltrates  
- Fibrous Tissue  
- Inflammatory Infiltrate
<table>
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<th>Pathogenesis</th>
<th>Clinical</th>
<th>Labs/Histology</th>
</tr>
</thead>
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| **Pulmonary Involvement in Collagen Vascular Disorders** | - SLE: Serositis  
- RA: Rheumatoid Nodules  
  o Necrosis in the middle, macrophages  
- Progressive Systemic Sclerosis (Scleroderma)  
  o Interstitial fibrosis $\rightarrow$ honeycomb  
- Dermatomyositis-polymyositis | - Pulmonary involvement in these diseases is usually a poor prognosis, but better than that of idiopathic pulmonary fibrosis | - |
| **Pneumoconioses** | - Organic/inorganic dusts, chemical fumes/vapors  
- Mostly occupational exposure  
- Air pollution in urban areas are also a risk  
1. Amount of dust retained in the lungs and airways  
  a. Dust concentration in the ambient air  
  b. Duration of exposure  
  c. Effectiveness of clearance mechanisms (smoking)  
2. Size and shape of particle  
  a. Most dangerous particles 1 – 5 $\mu$m in diameter $\rightarrow$ reach the terminal small airways and alveoli  
  b. Larger particles are less likely to dissolve and may persist in the lung parenchyma for years $\rightarrow$ chronic injury & fibrosis  
3. Particle solubility and cytotoxicity  
  a. Smaller particles tend to reach toxic levels rapidly $\rightarrow$ acute injury  
  b. Larger particles are less likely to dissolve and may persist in the lung parenchyma for years $\rightarrow$ chronic injury & fibrosis  
4. Additional effects of other irritants (ex. smoking) | - Slow, insidious onset  
- Appears years after exposure  
- Considerable morbidity/mortality  
- $\downarrow$ New cases due to safety | - |
| **Coal-workers Pneumoconiosis -CWP** | - Carbon dust alone or contaminated w/silica  
- $\uparrow$ incidence: TB, Chronic Bronchitis, emphysema | - Assymtomatic, Simple, Complicated  
- **Does NOT predispose to cancer** | - |
| **Asymptomatic Anthracosis** | - Carbon pigment engulfed by macrophages and then accumulates in the connective tissue along pulmonary lymphatics and in pulmonary lymph nodes | - Coal miners, urbanites, smokers | - |
| **Simple CWP** | - Coal macules (1-2 mm in diameter, carbon-laden macrophages) and coal nodules (also contain collagen) scattered in the lung, mostly upper lobes | - Little or no effect on pulmonary function | - Associated with centrilobular emphysema |
| **Complicated CWP** | - Multiple, irregular, intensely black scars (dense collagen & pigment)  
$\Rightarrow$ Progressive Massive Fibrosis (PMF)  
- PMF will continue to progress even when the person is no longer exposed to coal dust | - Worsening dyspnea, pulmonary hypertension and cor pulmonale  
- From simple CWP: many years  
- Only develops in <10% of CWP | - |
| **Caplan Syndrome** | - Pneumoconiosis w/Rheumatoid Arthritis  
- Nodular lesions similar to Rheumatoid nodules in the lung – fibroblasts, macrophages, collagen surround an area of central necrosis | - Occurs with CWP, asbestosis, silicosis | - |
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<th>Disease</th>
<th>Pathogenesis</th>
<th>Clinical</th>
<th>Labs/Histology</th>
</tr>
</thead>
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| **Silicosis** | - Inhalation of silicon dioxide  
- Slowly progressive nodular fibrosis  
- Crystalline forms (ex. Quartz) are most fibrogenic  
- Amorphous (non-crystalline, ex. Talc, mica) may produce damage if exposed in large amounts  
- Macrophages release fibrogenic cytokines and other mediators, such as TNF, IL-1, fibronectin, lipid mediators, oxygen radicals, and fibrogenic cytokines  

**Polarizing light demonstrates the presence of silica**<br>![Image](image1.png) | - Most prevalent chronic occupational disease  
- Mostly in sandblasters & miners  
- Generally asymptomatic  
- Detected by X-ray. **Fine nodularity in upper zones of the lungs**  
- Pulmonary function tests normal or moderately affected  
- Symptoms usually develop after PMF is present  
  - Disease progresses even when exposure to silica stops  
  - Associated with an increased susceptibility to tuberculosis because silica suppresses T-cell immunity + macrophage phagosome killing  
  - Possible carcinogen  | - Tiny collagenous nodules especially in **upper zones** of lungs, enlarge and coalesce to form readily visible hard collagenous scars  
- Lymph nodes can become calcified – seen radiographically as “**eggshell calcifications**”  
- Continues to progressive massive fibrosis  |
| **Asbestosis** | - **Asbestos** – general name applied to a group of crystalline hydrated silicates that form fibers  
- Begins in **lower lobes & subpleurally**, unlike CWP & silicosis,  
- Does not require chronic exposure – can be limited  
- Serpentine  
  - Less pathogenic  
  - More soluble  
  - More prevalent  
  - Curley, flexible  
- Amphibole  
  - More pathogenic  
  - Less soluble  
  - Less prevalent  
  - Straight, stiff, brittle  

**Don’t fragment**  
| Stays in **upper airway**  
| Goes deep into the lungs  

**BOTH** are fibroblastic (macrophage activation) & cause asbestosis related disease  

**Only amphiboles cause mesotheliomas**  | - Heaviest exposure occurs in **miners**, fabrication, installation and removal of asbestos containing products, such as **insulation**  
- Similar to other diffuse interstitial lung diseases  
- Sx appear 10-20 yrs after exposure  
- Can lead to cor pulmonale & death  
- Pleural plaques → usually no sx.  
- Poor prognosis w/cancer  | - Golden brown, fusiform or beaded rod with translucent center = asbestos fiber coated with iron-containing proteinaceous material  
- Formed when phages engulf the asbestos.  
- Coated iron & protein  
- Translucent center  

Distinguish from ferruginous body – inorganic fiber, other than asbestos, surrounded by iron/protein  |
| **Mesothelioma:**  | 1000x risk  | **Pleural Plaque:**  
| Size and # does not correlate w/exposure  |  |
| **Lung Cancer:**  | 5x risk  | - Most common of asbestos exposure  
- Well-circumscribed dense collagenous  
- Anterior and posterolateral aspects of parietal pleura, diaphragm  |
| w/smoking  | 55x risk  | - Complieations of Therapies  
- Cytotoxic Drugs (ex. Bleomycin) can cause pulmonary fibrosis by direct toxicity.  
- Amiodorone leads to pneumonitis by preferential concentration in the lung  |
| (b/c asbestos fibers absorb smoke carcinogens)  | - Acute Radiation Pneumonitis: Occurs in 10-20% of thorax-radiated patients 1-6 mo. post-radiation. Causes alveolitis or hypersensitivity pneumonitis → fibrosis  |
### Granulomatous Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogenesis</th>
<th>Clinical</th>
<th>Labs/Histology</th>
</tr>
</thead>
</table>
| **Sarcoidosis**       | - Multisystem disease of **unknown origin** characterized by non-caseating granulomas<br>- Possibly b/c of disordered immune regulation in genetically predisposed individuals exposed to agents<br>- Immunological abnormalities are present, suggesting cell-mediated response to unknown origin | - Variable, may be asymptomatic (dx incidentally by chest X-ray)<br>- Most patients present with insidious onset of respiratory symptoms or constitutional signs and symptoms<br>- Cough<br>- Erythema nodosum  
  o Skin lesion, often on shins, painful<br>- Dyspnea<br>- Neurologic manifestations | - Non-caseating granulomas found in<br  
  - Diffuse interstitial lung involvement > 90%<br>- Bilateral hilar lymph nodes >90%, but can occur in any node<br>- Tonsils, spleen, liver, bone marrow, skin, eye, salivary glands, and muscle<br>- Heart, kidneys, CNS and endocrine glands, occasionally<br>- Myelopthisic anemia ➔ BM replacement |
| **Hypersensitivity**  | - Spectrum of conditions<br  
  o Immunologically mediated<br  
  o Predominantly interstitial lung disorders<br  
  o Alveoli primarily affected (in contrast to asthma)<br>- Caused by intense and often prolonged exposure to inhaled organic dusts containing bacterial spores or products, fungi, or animal proteins | - Individuals have abnormal sensitivity and reactivity to the Ag<br>- May progress to chronic fibrotic lung disease<br>- **Early recognition and removal of precipitating cause, may prevent progression**<br>- Course<br  
  - Variable<br  
  - Acute – inhalation of dust in previously sensitized individual<br  
    o Fever, dyspnea, cough , 4-6 hours post-exposure<br  
    - Chronic – repeated exposure<br  
      o Chronic interstitial lung disease | - Evidence of both immune complex (type III) and T-cell mediated delayed (type IV) hypersensitivity<br>- Histologic changes occur in **bronchioles**: interstitial pneumonitis, noncaseating granulomas, interstitial fibrosis, intraalveolar infiltrate, and oblitative bronchiolitis (BOOP) |
| **Farmer’s Lung**     | - From spores of thermophilic *Actinomyces* in hay                                                                                              |                                                                                                   |                                                                                                     |
| **Pigeon Breeder’s Lung** | - Proteins from serum, excreta or feathers of birds                                                                                                |                                                                                                   |                                                                                                     |
| **Humidifier or Air conditioner Lung** | - Thermophilic bacteria in heated water reservoirs (ex. Hot tub)                                                                                   |                                                                                                   |                                                                                                     |
### Disease Pathogenesis

**Desquamative Interstitial Pneumonitis (DIP)**
- May be a smoking-related interstitial lung disease
- **Large collections of macrophages in the airspaces**
- *Misnomer* from previous belief that the macrophages were desquamated pneumocytes (LOL@idiots)

**Pulmonary Eosinophilia**
- Acute eosinophilic pneumonia with respiratory failure
- Simple pulmonary eosinophilia (Löffler syndrome)
- Tropical eosinophilia (Microfilaria)
- Secondary eosinophilia (infectious allergies)
- Idiopathic
- Churg Straus
  - Asthma in an adult
  - Vasculitis → skin, lungs, kidneys

**Pulmonary Alveolar Proteinosis**
- Bilateral opacification on x-ray
- Accumulation of acellular surfactant in alveoli and bronchioles
- Impaired surfactant clearance by pulmonary macrophages
  - Acquired: Auto-immune Anti-GM-CSF Antibodies
  - Secondary: Silicosis, tumors, immunodeficiency
  - Congenital: Genetic mutations of GM-CSF

### Clinical

**Desquamative Interstitial Pneumonitis (DIP)**
- **Minimal fibrosis** in most cases
- Insidious onset of dyspnea + cough
- Good prognosis with steroid therapy and smoking cessation (100% survival rate)

**Pulmonary Eosinophilia**
- **-**

**Pulmonary Alveolar Proteinosis**
- **-**

### Labs/Histology
- **-**

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**Need to know**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pulmonary Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleomycin</td>
<td>Pneumonia and fibrosis</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Hypersensitivity pneumonitis</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Pneumonitis and fibrosis</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Hypersensitivity pneumonitis</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Bronchospasm</td>
</tr>
<tr>
<td>β-Antagonists</td>
<td>Bronchospasm</td>
</tr>
</tbody>
</table>

**Restrictive Lung Summary**
- Lung injury → Alveolitis → Cellular and CT alterations → Fibrosis → End Stage (Honeycomb) Lung