Interstitial Lung Disease
Organization of Interstitial Lung Disease (ILD)

- Over 100 separate disorders under the auspices of ILD
  - Organized into subgroups of like disorders
Pathophysiology

- Primarily a disease of the interstium
- Repeated exposure to inflammatory agents or imperfect repair of damaged tissue leads to permanent damage.
  - Increased interstitial tissue replaces normal structures
  - Continuing injury or imperfect repair results in progressive damage and worsening impairment.

- Physiological impairment due to damage
  - V/Q mismatch, shunt, ↓DLCO
  - Increased WoB due to decreased CL
  - These all lead to exercise intolerance.
Characteristics of ILD

Clinical signs and symptoms of ILD

- Exertional dyspnea and nonproductive cough
  - Most common reason to seek medical care

- May see increased: sputum production, hemoptysis, or wheezing

- Nonrespiratory symptoms may help identify presence of connective tissue disorder.
Characteristics of ILD

Physical examination

- On auscultation
  - Most commonly, bibasilar fine inspiratory crackles
  - In some disorders, will only hear diminished air entry
    - i.e., sarcoidosis
  - Wheezing is uncommon and probably due to a comorbidity.

- Signs of right heart failure (late manifestation)
  - Pedal edema, JVD

- May see features of underlying connective tissue disease
Characteristics of ILD (cont.)

Chest radiographic features

- Considerable variability dependent on specific disorder

- Interstitial pulmonary fibrosis (IPF) has what is considered the classic ILD pattern.
  - Reduced volume
  - Bilateral, peripheral, basilar reticulonodular infiltrates
  - End-stage ILD presents with cystic honeycomb lung.

- IPF is the second most common ILD (sarcoidosis first), and a number of other ILDs present in a similar manner.
Physiological features

- Restrictive impairment is most common finding.
  - $\text{FEV}_1$ and FVC decreased while the $\text{FEV}_1$/FVC ratio is normal to increased
  - Lung volumes and DLCO are reduced.
  - $C_L$ resulting in small $V_T$ and increased WOB

- Less commonly, patients may have airflow obstruction.
  - May be sarcoidosis or some other mixed disease
  - Comorbidity with asthma or emphysema
  - May result in normal PFTs, but decreased DLCO
ILD: Exposure Related

Asbestos-related pulmonary disease following exposure to asbestos is associated with

- Pleural plaques, fibrosis, effusions, mesothelioma
- Atelectasis, parenchymal scarring, lung cancer

- Termed “asbestosis” if parenchymal fibrosis is present
- Presents with slowly evolving DOE, inspiratory crackles
- Shows typical PFTs, while chest radiograph often shows pleural change associated with asbestosis
- Only supportive therapy is available.
ILD: Exposure Related (cont.)

Chronic silicosis (inhaled silica particles)
- Exposure: mining, sandblasting, and foundries

- Chest radiograph shows apical nodular opacities
  - If these coalesce into large masses, it is called progressive massive fibrosis (PMF).

- If impaired, patients often have a mixed obstructive and restrictive picture with a low DLCO.

- Silicosis increases the odds of developing tuberculosis and lung cancer.
ILD: Exposure Related (cont.)

Coal worker’s pneumoconiosis (CWP)

- Used to think due to inhalation of silica, now understood that it is from a distinct exposure

- Simple CWP asymptomatic, small nodules on radiograph

- Cough and SoB if progresses to PMF similar to that seen in silicosis

- No treatment for silicosis or CWP except stop exposure
  - Steroids and $\beta_2$-agonists for significant airway obstruction
  - Exacerbations treated with steroids and antibiotics
Chapter 25

Interstitial Lung Diseases
Figure 25–1  A. Interstitial lung disease. Cross-sectional microscopic view of alveolar-capillary unit. N, Neutrophil; E, eosinophil; B, basophil; M, monocyte; MAC, macrophage; L, lymphocyte; FIB, fibroblast (fibrosis); TI, type I alveolar cell; TII, type II alveolar cell; RBC, red blood cell; PC, pulmonary capillary.  
B. Asbestosis (close-up of one alveolar unit). AF, Asbestos fiber; FIB, fibrosis; M, macrophage.
Introduction

- The term Interstitial lung disease (ILD) (also called diffuse interstitial lung disease, fibrotic interstitial lung disease, pulmonary fibrosis, or pneumoconiosis) refers to a broad group of inflammatory lung disorders.
- More than 180 disease entities are characterized by acute, sub-acute, or chronic inflammatory infiltration of alveolar walls by cells, fluid, and connective tissue.
If left untreated, the inflammatory process can progress to irreversible pulmonary fibrosis.

The ILD group comprises a wide-range of illnesses with varied causes, treatments, and prognoses.

However, because the ILD all reflect similar anatomic alterations of the lungs and, therefore, cardiopulmonary clinical manifestations, they are presented as a group in this chapter.
Anatomic Alterations of the Lungs

- Destruction of the alveoli and adjacent pulmonary capillaries
- Fibrotic thickening of the respiratory bronchioles, alveolar ducts, and alveoli
- Granulomas
- Honeycombing and cavity formation
- Fibrocalcific pleural plaques (particularly in asbestosis)
- Bronchospasm
- Excessive bronchial secretions (caused by inflammation of airways)
Because there are over 180 different pulmonary disorders classified as ILD, it is helpful to group them according to their occupational or environmental exposure, disease associations, and specific pathology.
### Table 25-1
**Overview of Interstitial Lung Diseases**

**Occupational, Environmental, and Therapeutic Exposures**

<table>
<thead>
<tr>
<th>Occupation/Environmental</th>
<th>Inorganic Exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asbestosis</td>
</tr>
<tr>
<td></td>
<td>Coal dust</td>
</tr>
<tr>
<td></td>
<td>Silica</td>
</tr>
<tr>
<td></td>
<td>Beryllium</td>
</tr>
<tr>
<td></td>
<td>Aluminum</td>
</tr>
<tr>
<td></td>
<td>Barium</td>
</tr>
<tr>
<td></td>
<td>Clay</td>
</tr>
<tr>
<td></td>
<td>Iron</td>
</tr>
<tr>
<td></td>
<td>Certain talcs</td>
</tr>
</tbody>
</table>
### Table 25-1
#### Overview of Interstitial Lung Diseases (Cont’d)

#### Occupational, Environmental, and Therapeutic Exposures

**Occupation/Environmental**

- **Organic Exposures**
  - Hypersensitivity pneumonitis
    - Moldy hay
    - Silage
    - Moldy sugar cane
    - Mushroom compost
    - Barly
    - Cheese
    - Wood pulp, bark, dust
    - Cork dust
    - Bird droppings
    - Paints
Occupational, Environmental, and Therapeutic Exposures

### Occupation/Environmental
- Medications and Illicit Drugs
  - Antibiotics
  - Antiinflammatory agents
  - Cardiovascular agents
  - Drug-induced systemic lupus erythematosus
  - Miscellaneous agents
- Radiation Therapy
- Irritant Gases
### Table 25-1
Overview of Interstitial Lung Diseases (Cont’d)

<table>
<thead>
<tr>
<th>Systemic Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Connective Tissue Disease</em></td>
</tr>
<tr>
<td>- Scleroderma</td>
</tr>
<tr>
<td>- Rheumatoid arthritis</td>
</tr>
<tr>
<td>- Sjögren’s syndrome</td>
</tr>
<tr>
<td>- Polymyositis or dermatomyositis</td>
</tr>
<tr>
<td>- Systemic lupus erythematosus</td>
</tr>
<tr>
<td><em>Sarcoidosis</em></td>
</tr>
<tr>
<td>Table 25-1</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td><strong>Idiopathic Interstitial Pneumonia</strong></td>
</tr>
<tr>
<td>● Idiopathic pulmonary fibrosis</td>
</tr>
<tr>
<td>● Nonspecific cryptogenic-organizing pneumonia</td>
</tr>
<tr>
<td>● Lymphocytic interstitial pneumonia</td>
</tr>
<tr>
<td>Specific Pathology</td>
</tr>
<tr>
<td>--------------------</td>
</tr>
<tr>
<td>Lymphangioleiomyomatosis</td>
</tr>
<tr>
<td>Pulmonary Langerhans cell histiocytosis</td>
</tr>
<tr>
<td>Pulmonary alveolar proteinosis</td>
</tr>
<tr>
<td>The pulmonary vasculitides</td>
</tr>
<tr>
<td>Wegener’s granulomatosis</td>
</tr>
<tr>
<td>Churg-Strauss syndrome</td>
</tr>
<tr>
<td>Lymphomatoid granulomatosis</td>
</tr>
<tr>
<td>Miscellaneous ILD</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Goodpasture’s syndrome</td>
</tr>
<tr>
<td>Idiopathic pulmonary hemosiderosis</td>
</tr>
<tr>
<td>Chronic eosinophilic pneumonia</td>
</tr>
</tbody>
</table>
**Box 25-1 Common Sources Associated with Asbestos Fibers**

- Acoustic products
- Automobile undercoating
- Brake lining
- Cements
- Clutch casings
- Floor tiles
- Firefighting suits
- Fireproof paints
- Insulation
- Roofing materials
- Ropes
- Steam pipe material
Box 25-2 Common Occupations Associated with Silica Exposure

- Tunneling
- Hard-rock mining
- Sandblasting
- Quarrying
- Stonecutting
- Foundry work
- Ceramics work
- Abrasives work
- Brick making
- Paint making
- Polishing
- Stone drilling
- Well drilling
Box 25-3 Additional Inorganic Causes of Interstitial Lung Disease

Aluminum
  • Ammunition workers
Baritosis (barium)
  • Barite millers and miners
  • Ceramics workers
Kaolinitosis (clay)
  • Brick makers and potters
  • Ceramics workers
Siderosis (iron)
  • Welders
Talcosis (certain talcs)
  • Ceramics workers
  • Papermakers
  • Plastics and rubber workers
<table>
<thead>
<tr>
<th><strong>Table 25-2</strong></th>
<th><strong>Causes of Hypersensitivity Pneumonia (Excerpts)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteria, Thermophilic</strong></td>
<td></td>
</tr>
<tr>
<td>- <em>Saccharopolyspora rectivirgula</em></td>
<td></td>
</tr>
<tr>
<td>- <em>Thermoactinomyces vulgaris</em></td>
<td></td>
</tr>
<tr>
<td>- <em>Thermoactinomyces sacchari</em></td>
<td></td>
</tr>
<tr>
<td>- <em>Thermoactinomyces candidus</em></td>
<td></td>
</tr>
<tr>
<td><strong>Bacteria, Nonthermophilic</strong></td>
<td></td>
</tr>
<tr>
<td>- <em>Baccillus subtilis, Bacillus cereus</em></td>
<td></td>
</tr>
</tbody>
</table>

Table 25-2
Causes of Hypersensitivity Pneumonia
(Excerpts) (Cont’d)

- **Fungi**
  - Aspergillus sp.
  - Aspergillus clavatus
  - Penicillium casiei, P. roqueforti
  - Alternaria sp.
  - Cryptostroma corticale
  - Graphium, Aureobasidium pullulans
  - Merulius lacrymans
  - Penicillium frequentans
  - Aureobasidium pullulans
  - Cladosporium sp.
  - Trichosporon cutaneum
**Table 25-2**  
**Causes of Hypersensitivity Pneumonia**  
(Excerpts) (Cont’d)

- **Amoebae**
  - *Naegleria gruberi*
  - *Acanthamoeba polyphaga*
  - *Acanthamoeba castellani*
Table 25-2
Causes of Hypersensitivity Pneumonia
(Excerpts) (Cont’d)

- **Animal Protein**
  - Avian proteins
  - Urine, serum, pelts
Table 25-2
Causes of Hypersensitivity Pneumonia
(Excerpts) (Cont’d)

*Chemicals*
- Isocyanates, trimellitic anhydride
- Copper sulfate
- Phthalic anhydride
- Sodium diazobenzene sulfate
- Pyrethrum
<table>
<thead>
<tr>
<th>Gas</th>
<th>Industrial Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorine</td>
<td>Chemical and plastic industries; water disinfection</td>
</tr>
<tr>
<td>Ammonia</td>
<td>Commercial refrigeration; smelting of sulfide ores</td>
</tr>
<tr>
<td>Ozone</td>
<td>Welding</td>
</tr>
<tr>
<td>Nitrogen dioxide</td>
<td>May be liberated after exposure of nitric acid to air</td>
</tr>
<tr>
<td>Phosgene</td>
<td>Used in the production of aniline dyes</td>
</tr>
</tbody>
</table>

Table 25-3. Common Irritant Gases Associated with Interstitial Lung Disease
**Box 25-4**
Medications and Illicit Drugs Associated with the Development of ILD

- Cardiovascular agents
  - Amiodarone
  - Tocainide
Chemotherapeutic agents

- Bleomycin
- Mitomycin-C
- Busulfan
- Cyclophosphamide
- Chlorambucil
- Melphalan
- Azathioprine
- Cytosine arabinoside
- Methotrexate
- Procarbazine
- Zinostatin
- Etoposide
- Vinblastine
- Imatinib
Drug-induced systemic lupus erythematosus
- Procainamide
- Isoniazid
- Hydralazine
- Hydantoins
- Penicillamine
Box 25-4
Medications and Illicit Drugs Associated with the Development of ILD (Cont’d)

- Illicit drugs
  - Heroin
  - Methadone
  - Propoxyphene
  - Penicillamine
Box 25-4
Medications and Illicit Drugs Associated with the Development of ILD (Cont’d)

- Miscellaneous agents
  - Oxygen
  - Drugs inducing pulmonary infiltrate and eosinophilia:
    - L-tryptophan
  - Hydrochlorothiazide
  - Radiation therapy
# TABLE 25-3 Common Irritant Gases Associated with Interstitial Lung Disease

<table>
<thead>
<tr>
<th>Gas</th>
<th>Industrial Setting</th>
</tr>
</thead>
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<tr>
<td>Phosgene</td>
<td>Used in the production of aniline dyes</td>
</tr>
</tbody>
</table>

Table 25-3. Common Irritant Gases Associated with Interstitial Lung Disease
Overview of the Cardiopulmonary Clinical Manifestations Associated with Interstitial Lung Diseases

The following clinical manifestations result from the pathophysiologic mechanisms caused (or activated) by

- Increased Alveolar-Capillary Membrane Thickness
- Excessive Bronchial Secretions
Fig. 9-10. Increased alveolar-capillary membrane thickness clinical scenario.
Fig. 9-12. Excessive bronchial secretions clinical scenario.
Clinical Data Obtained at the Patient’s Bedside
The Physical Examination

- Vital Signs
  - Increased
    - Respiratory rate (tachypnea)
    - Heart rate (pulse)
    - Blood pressure
The Physical Examination (Cont’d)

- Cyanosis
- Digital clubbing
- Peripheral edema and venous distension
  - Distended neck veins
  - Pitting edema
  - Enlarged and tender liver
Nonproductive cough

Chest Assessment Findings
- Increased tactile and vocal fremitus
- Dull percussion note
- Bronchial breath sounds
- Crackles, rhonchi
- Pleural friction rub
- Whispered pectoriloquy
Clinical Data Obtained from Laboratory Tests and Special Procedures
Pulmonary Function Test Findings
Moderate to Severe ILD
(Restrictive Lung Pathophysiology)

<table>
<thead>
<tr>
<th>Forced Expiratory Flow Rate Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>FEF$_{50%}$</td>
</tr>
<tr>
<td>N or ↓</td>
</tr>
</tbody>
</table>
# Pulmonary Function Test Findings

Moderate to Severe ILD  
( Restrictive Lung Pathophysiology)

<table>
<thead>
<tr>
<th>VT</th>
<th>IRV</th>
<th>ERV</th>
<th>RV</th>
<th>VC</th>
</tr>
</thead>
<tbody>
<tr>
<td>N or ↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IC</th>
<th>FRC</th>
<th>TLC</th>
<th>RV/TLC ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>N</td>
</tr>
</tbody>
</table>
There is an exception to the expected decreased diffusion capacity in the following two interstitial lung diseases:
- Goodpasture’s syndrome
- Idiopathic pulmonary hemosiderosis

The $\text{DL}_{\text{CO}}$ is often elevated in response to the increased amount of blood retained in the alveolar spaces that is associated with these two disorders.
### Arterial Blood Gases
**Mild to Moderate ILD**

**Acute Alveolar Hyperventilation with Hypoxemia**
*Acute Respiratory Alkalosis*

<table>
<thead>
<tr>
<th>pH</th>
<th>$\text{PaCO}_2$</th>
<th>$\text{HCO}_3$</th>
<th>$\text{PaO}_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑</td>
<td>↓</td>
<td>↓ (slightly)</td>
<td>↓</td>
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</tbody>
</table>
PaO\textsubscript{2} and PaCO\textsubscript{2} trends during acute alveolar hyperventilation.
Arterial Blood Gases
Severe chronic ILD

Chronic Ventilatory Failure with Hypoxemia
(Compensated Respiratory Acidosis)

<table>
<thead>
<tr>
<th>pH</th>
<th>PaCO₂</th>
<th>HCO₃⁻</th>
<th>PaO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>↑</td>
<td>↑(Significantly)</td>
<td>↓</td>
</tr>
</tbody>
</table>
PaO₂ and PaCO₂ trends during acute or chronic ventilatory failure.
## Arterial Blood Gases

### Acute Ventilatory Changes Superimposed On Chronic Ventilatory Failure

- Because acute ventilatory changes are frequently seen in patients with chronic ventilatory failure, the respiratory care practitioner must be familiar with and alert for the following:
  - Acute alveolar hyperventilation superimposed on chronic ventilatory failure
  - Acute ventilatory failure (acute hypoventilation) superimposed on chronic ventilatory failure
## Oxygenation Indices

**Moderate to Severe Stage ILD**

<table>
<thead>
<tr>
<th>(Q_S/Q_T)</th>
<th>(DO_2)</th>
<th>(VO_2)</th>
<th>(C(a-v)O_2)</th>
<th>(O_2ER)</th>
<th>(SvO_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑</td>
<td>↓</td>
<td>N</td>
<td>N</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Hemodynamic Indices</td>
<td>Severe ILD</td>
<td></td>
<td></td>
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<td></td>
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<td>---------------------</td>
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<td></td>
</tr>
<tr>
<td>CVP</td>
<td>↑</td>
<td>RAP</td>
<td>↑</td>
<td>PA</td>
<td>↑</td>
</tr>
<tr>
<td>SVI</td>
<td>N</td>
<td>CI</td>
<td>N</td>
<td>RVSWI</td>
<td>↑</td>
</tr>
<tr>
<td>Abnormal Laboratory Tests and Procedures</td>
<td></td>
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<td>------------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Hematology</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Increased hematocrit and hemoglobin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(polycythemia)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Radiologic Findings

- Chest Radiograph
  - Bilateral reticulonodular pattern
  - Irregularly shaped opacities
  - Granulomas
  - Cavity formation
  - Honeycombing
  - Pleural effusion
Figure 25-2. Reticulonodular pattern of interstitial pulmonary fibrosis in a patient with scleroderma.
Figure 25-3. Chest x-ray film of a patient with asbestosis.
Figure 25-4. Calcified pleural plaques on the superior border of the diaphragm (*arrows*) in a patient with asbestosis. Thickening of the pleural margins also is seen along the lower lateral borders of the chest. A, Anteroposterior view. B, Lateral view.
Figure 25-5. Acute farmer’s lung. Chest radiograph shows diffuse parenchymal ground-glass pattern with some areas of consolidation. The severity of parenchymal opacification in this case is unusual.
Figure 25-6. Honeycomb cysts in sarcoidosis. HRCT through the right midlung shows profuse clustered honeycomb cysts. The cysts are larger than the typical honeycomb cysts seen in usual interstitial pneumonia. Cysts are much less extensive in the left lung.
Figure 25-7. Wegener’s granulomatosis. Numerous nodules with a large (6-cm) cavitary lesion adjacent to the right hilus. Its walls are thick and irregular.
Figure 25-8. Pleural effusion in rheumatoid disease. Bilateral pleural effusions are present with mild changes of fibrosing alveolitis. The effusions were painless, and the one on the right had been present, more or less unchanged, for 5 months. Note the bilateral "meniscus signs."
General Management of ILD

- Oxygen Therapy Protocol
- Bronchopulmonary Hygiene Therapy Protocol
- Mechanical Ventilation Protocol
Plasmapheresis

Treatment of Goodpasture’s syndrome is directed at reducing the circulating anti-GBM antibodies that attack the patient’s glomerular basement membrane. Plasmapheresis, which directly removes the anti-GBM antibodies from the circulation, has been of some benefit.