Chapter 24

Interstitial Lung Disease
Objectives

- Describe how the entities grouped as the interstitial lung diseases (ILDs) are classified and organized.

- Describe the physiological changes in lung function seen in patients with ILD.

- List or identify the clinical signs and symptoms of ILD.

- Identify the radiographic abnormalities seen in the chest film of patients with ILD.

- List and describe the three most common types of occupational ILD.
Objectives (cont.)

- Identify the radiographic abnormalities seen in the chest film of patients with ILD.

- Describe the etiology, clinical features, and treatment for patients with hypersensitivity pneumonitis.

- State the incidence and typical clinical presentation for patients with sarcoidosis.

- Describe the risk factors and typical presentation of patients with idiopathic pulmonary fibrosis.
Objectives (cont.)

- List and describe examples of idiopathic interstitial pneumonias.

- Describe how to manage ILD in general and how some specific ILDs can be treated.
Organization of Interstitial Lung Disease (ILD)

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

![Diagram showing the organization of ILD disorders into known and unknown causes, subgroups of exposures, systemic diseases, genetic factors, specific IIPs, and specific pathologies.]

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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.
Characteristics of ILD (cont.)

Physiological features

- Restrictive impairment is most common finding.
  - FEV$_1$ and FVC decreased while the 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
Medications, Drugs, and Radiation

- Many drugs may cause ILD (see Box 24-1).
  - There is no specific pattern to drug-induced ILD
  - Diagnosis by known exposure to drug, subsequent development of ILD, and other causes are ruled out.
  - Treatment is avoidance of drug, possibly steroids

- Cancer radiation therapy may result in ILD.
  - Presentation within 6 months with ground-glass appearance on chest radiograph, often responds to short-course steroids
  - Dyspnea presenting after 6 months, have dense fibrotic tissue, can only offer supportive therapy
Hypersensitivity Pneumonitis (HP)

- A cell-mediated immune response to inhaled antigens
  - Patients must be sensitized by previous exposure.

- Acute HP: patient presents with acute SoB, chest pain, fever, chills, malaise, and cough (may be productive)

- Chronic HP: long-term antigen exposure leads to slow development over months to years
  - Presents with severe impairment that is difficult to distinguish from IPF
Hypersensitivity Pneumonitis (cont.)

- **Causative agents that can lead to HP**
  - Common organic antigens (bacteria and fungi) found in
    - Moldy hay (farmer’s lung)
    - Humidification systems (humidifier lung)
    - Bird feces (bird breeders lung)
  - Inorganic antigens from paints and plastics

- **Treatment**
  - Strict antigen identification and avoidance
  - Corticosteroids for symptomatic patients with acute HP
    - Improves recovery but not lung function
  - Chronic HP results in shorter survival and no known treatment
Systemic Disease Associated

- ILD is a complication of various connective tissue diseases, most commonly
  - Scleroderma, rheumatoid arthritis, Sjögren’s syndrome, and systemic lupus erythematosus (SLE)

- Significant pulmonary impairment prior to detection due to disease imposed sedentary lifestyle

- Poor correlation between severity and pulmonary and nonpulmonary aspects of these diseases
Clinical manifestations vary

- Dyspnea and cough are common.
- Crackles, wheezes, and pleural rubs may be heard.
- Typically restrictive disease
- Depending on disease location, may be obstructive
  - Sjögren’s disease in particular
- ↓DLCO
Systemic Disease Associated (cont.)

- HRCT results vary from normal to ground-glass appearance to noting reticular and fibrotic changes.
  - NSIP is associated with ground-glass appearance.
  - OP is associated with patchy consolidation with air bronchograms.
  - UIP is associated with reticular opacities, honeycomb

- Treatment of systemic inflammatory diseases varies.
  - Most common treatment for acute inflammation or rapid progression is prolonged immunosuppression.
  - Typical agents:
    - Cyclophosphamide, azathioprine
Sarcoidosis

- Most common ILD in United States.

- Idiopathic multisystem inflammatory disease that forms granulomas in lungs but often follows benign course

- Most common sign is asymptomatic hilar adenopathy.

- If symptomatic: cough, chest pain, dyspnea, wheezing

- Physiology may be normal, restrictive, obstructive, mixed

- Steroids may be used for sickest symptomatic patients.
Interstitial Lung Diseases of Unknown Cause

Idiopathic interstitial pneumonias (IIP)

- Most common is IPF, a progressive fibrotic lung disorder
  - Mostly in older patients (>60 years of age)
  - Present with chronic cough and DOE
  - HRCT: bibasilar, peripheral reticular pattern, with cysts
  - Lung biopsy shows UIP and is diagnostic.
  - Most die within 4 years of progressive lung fibrosis.
  - There is no effective treatment.
    - Oral steroids and azathioprine used but benefit few
    - Otherwise, supportive therapy
Idiopathic Interstitial Pneumonias

Nonspecific interstitial pneumonia (NSIP)

- An IIP with diffuse inflammation on surgical lung biopsy most commonly tied to fibrosis forming fibrotic NSIP
- On average occurs 7–10 years prior to IPF
- Presents with chronic cough and dyspnea
- HRCT shows ground glass (NSIP) or fibrotic changes and ground glass (fibrotic NSIP).
- Prognosis is 7–10 years with immunosuppression (steroids and cytotoxic agents).
Cryptogenic organizing pneumonia (COP)
- Patients are younger than those with IPF
- A third have an antecedent viral illness.
- Present with acute or subacute cough and dyspnea
- HRCT findings typical for acute pneumonia, but patient failed to respond to several courses of antibiotics
Idiopathic Interstitial Pneumonias (cont.)

Cryptogenic organizing pneumonia (COP) (cont.)

- Most improve with course of oral steroids
  - Number relapse when steroids stopped

- A few develop progressive fibrosis despite aggressive immunosuppression
  - Can offer lung transplantation
ILD With Distinct Pathology

Lymphangioleiomyomatosis (LAM)
- Rare, occurs mostly in women
- Proliferation of smooth muscle around small airways leading to severe obstruction and destruction of alveoli
  - Leads to formation of thin walled cysts
- Presents with DOE, obstructive impairment, ↓DLCO
- Progression from hardly noticeable in older women to steadily progressive for middle-aged women
ILD With Distinct Pathology (cont.)

Lymphangioleiomyomatosis (cont.)
- Pleurodesis is generally required for recurrent chylothorax

Treatment:
- Inhaled $\beta_2$-agonists and steroids
- Younger patients may at some point receive lung transplantation
ILD With Distinct Pathology (cont.)

Pulmonary Langerhans’ cell histiocytosis (PLCH)
- ILD associated with adult smokers
- Present with DOE, cough, diffuse inspiratory crackles, airway obstruction, and ↓DLCO
- HRCT: central mid-lung star-shaped nodules adjacent to thin-walled cysts
- Primary treatment: Stop ALL exposure to tobacco smoke
  - If smoke avoidance fails to halt progression, can try
    - Oral steroids: no proven benefit
  - May offer lung transplantation
Nonspecific Interstitial Lung Disease Therapies

- **Oxygen therapy**
  - Hypoxemia is common in ILD.
    - Should be evaluated at rest and on exertion
  - O$_2$ via nasal cannula may improve resting hypoxemia and allow greater exertion before desaturation
    - May improve quality of life and avoid cor pulmonale

- **Pulmonary rehabilitation and exercise therapy**
  - Not well studied
  - Encourage for all ILD patients to improve aerobic fitness, maintain activities, improve quality of life
Nonspecific Interstitial Lung Disease Therapies (cont.)

- Vaccinations and infection avoidance
  - CDC recommends annual pneumococcal and influenza vaccine.
  - Patient should frequently wash hands.
  - May need pneumocystis prophylaxis if immunocompromised.

- Transplantation
  - Only therapy shown to prolong life in end-stage ILD
  - Mortality is 10–25% at 1 year and 50–60% at 5 years.
  - Age (>65) and comorbidities often disqualify patients.