315 Interstitial Lung Diseases

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Patients with interstitial lung diseases (ILDs) come to medical attention mainly because of the onset of progressive exertional dyspnea or a persistent nonproductive cough. Hemoptysis, wheezing, and chest pain may be present. Often, the identification of interstitial opacities on chest x-ray focuses the diagnostic approach on one of the ILDs.

ILDs represent a large number of conditions that involve the parenchyma of the lung—the alveoli, the alveolar epithelium, the capillary endothelium, and the spaces between those structures—as well as the perivascular and lymphatic tissues. The disorders in this heterogeneous group are classified together because of similar clinical, roentgenographic, physiologic, or pathologic manifestations. These disorders often are associated with considerable rates of morbidity and mortality, and there is little consensus regarding the best management of most of them.

ILDs have been difficult to classify because >200 known individual diseases are characterized by diffuse parenchymal lung involvement, either as the primary condition or as a significant part of a multiorgan process, as may occur in the connective tissue diseases (CTDs). One useful approach to classification is to separate the ILDs into two groups based on the major underlying histopathology: (1) those associated with predominant inflammation and fibrosis and (2) those with a predominantly granulomatous reaction in interstitial or vascular areas (Table 315-1). Each of these groups can be subdivided further according to whether the cause is known or unknown. For each ILD there may be an acute phase, and there is usually a chronic one as well. Rarely, some are recurrent, with intervals of subclinical disease.

Sarcoidosis (Chap. 390), idiopathic pulmonary fibrosis (IPF), and pulmonary fibrosis associated with CTDs (Chaps. 378, 382, 388, and 427) are the most common ILDs of unknown etiology. Among the ILDs of known cause, the largest group includes occupational and environmental exposures, especially the inhalation of inorganic dusts, organic dusts, and various fumes or gases (Chap. 311). A multidisciplinary approach—requiring close communication between clinician, radiologist, and when appropriate, pathologist—is often required to make the diagnosis. High-resolution computed tomography (HRCT) scanning improves the diagnostic accuracy and may eliminate the need for tissue examination in many cases, especially in IPF. For other forms, tissue examination, usually obtained by thoracoscopic lung biopsy, is critical to confirmation of the diagnosis.

TABLE 315-1 MAJOR CATEGORIES OF ALVEOLAR AND INTERSTITIAL INFLAMMATORY LUNG DISEASE

Lung Response: Alveolitis, Interstitial Inflammation, and Fibrosis	
Known Cause	
Asbestos	Residual of acute respiratory distress syndrome
Fumes, gases	Smoking-related
Drugs (antibiotics, amiodarone, gold) and chemotherapy drugs	Desquamative interstitial pneumonia
Radiation	Respiratory bronchiolitis–associated interstitial lung disease
Aspiration pneumonia	Pulmonary Langerhans cell granulomatosis
Unknown Cause	
Idiopathic interstitial pneumonias	Pulmonary alveolar proteinosis
Idiopathic pulmonary fibrosis (usual interstitial pneumonia)	Lymphocytic infiltrative disorders (lymphocytic interstitial pneumonitis associated with connective tissue disease)
Acute interstitial pneumonia (diffuse alveolar damage)	Eosinophilic pneumonias
Cryptogenic organizing pneumonia	Lymphangioleiomyomatosis
Nonspecific interstitial pneumonia	Inherited diseases
Idiopathic lymphocytic interstitial pneumonia	Tuberous sclerosis, neurofibromatosis, Niemann-Pick disease, Gaucher disease, Hermansky-Pudlak syndrome
Rare and ill-defined entities	
Idiopathic pleuroparenchymal fibroelastosis	
Acute fibrinous and organizing pneumonia	
Bronchiolocentric patterns of interstitial pneumonia	
Connective tissue diseases	Gastrointestinal or liver diseases (Crohn disease, primary biliary cirrhosis, chronic active hepatitis, ulcerative colitis)
Systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, systemic sclerosis, Sjögren syndrome, polymyositis-dermatomyositis	
Pulmonary hemorrhage syndromes	Graft-versus-host disease (bone marrow transplantation; solid organ transplantation)
Goodpasture syndrome, idiopathic pulmonary hemosiderosis, isolated pulmonary capillaritis	
Amyloidosis	
Lung Response: Granulomatous	
Known Cause	
Hypersensitivity pneumonitis (organic dusts)	Inorganic dusts: beryllium, silica
Unknown Cause	
Sarcoidosis	Bronchocentric granulomatosis
Granulomatous vasculitides	Lymphomatoid granulomatosis
Granulomatosis with polyangiitis (Wegener)	
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)	

PATHOGENESIS

The ILDs are nonmalignant disorders and are not caused by identified infectious agents. The precise pathway(s) leading from injury to fibrosis is not known. Although there are multiple initiating agent(s) of injury, the immunopathogenic responses of lung tissue are limited, and the mechanisms of repair have common features (Fig. 315-1).

As mentioned above, the two major histopathologic patterns are a granulomatous pattern and a pattern in which inflammation and fibrosis predominate.

Granulomatous Lung Disease This process is characterized by an accumulation of T lymphocytes, macrophages, and epithelioid cells organized into discrete structures (granulomas) in the lung parenchyma. The granulomatous lesions can progress to fibrosis. Many patients with granulomatous lung disease remain free of severe impairment of lung function or, when symptomatic, improve after treatment. The main differential diagnosis is between sarcoidosis (Chap. 390) and hypersensitivity pneumonitis (Chap. 310).

Inflammation and Fibrosis The initial insult is an injury to the epithelial surface that causes inflammation in the air spaces and alveolar walls. If the disease becomes chronic, inflammation spreads to adjacent portions of the interstitium and vasculature and eventually causes interstitial fibrosis. Important histopathologic patterns found in the ILDs include usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia, respiratory bronchiolitis/desquamative interstitial pneumonia, organizing pneumonia, diffuse alveolar damage (acute or organizing), and lymphocytic interstitial pneumonia. The development of irreversible scarring (fibrosis) of alveolar walls, airways, or vasculature is the most feared outcome in all of these conditions because it is often progressive and leads to significant derangement of ventilatory function and gas exchange.