cells and the deposition of an aberrant matrix that increases the distance between the alveolar space and vascular structures, delaying and sometimes preventing gas exchange. This thickened interstitium accounts for poor oxygenation with exercise, increased lung stiffness exhibited as decreased compliance, small lung volumes, and increased work of breathing.

Because lung involvement by ILD may be sporadic, with areas of normal lung adjacent to areas of fibrosis, local differences in compliance may result in ventilation-perfusion mismatching, contributing to hypoxemia. The processes previously outlined account for the physiologic manifestations seen in disorders such as IPF and asbestosis.

In some ILDs, an obstructive rather than restrictive abnormality or mixed patterns are identified on pulmonary function testing, and lung volumes are relatively preserved on physiologic testing and imaging (Fig. 17-2). In diseases such as lymphangioleiomyomatosis, pulmonary LCH, and some cases of HP or sarcoidosis, obstructive or mixed patterns on pulmonary function testing occur with preservation of lung volumes. This pattern of disease is caused by proximal extension of the interstitial disease in the lung parenchyma with consequent involvement of the small airways. For example, in lymphangioleiomyomatosis, the small airways are narrowed by the proliferation of surrounding abnormal smooth muscle–like cells. This leads to increased airway resistance and airflow obstruction. Endobronchial disease with direct narrowing of the airways can occur in sarcoidosis, leading to similar effects. The finding of airflow obstruction does not rule out a diagnosis of ILD but may help to focus the differential diagnosis on particular diseases.

In ILD, a synthesis of clinical, functional, and imaging data, often in the context of a multidisciplinary approach, can determine the appropriate diagnosis. In many circumstances, however, clinical and imaging data are insufficiently specific, and lung biopsy must be undertaken. Surgical lung biopsy, typically using a thoracoscopic approach, is the preferred method of obtaining tissue for examination. Transbronchial lung biopsy through the bronchoscope yields small fragments of tissue, typically too small to allow appropriate examination of the lung architecture, and it is not recommended for the assessment of suspected IPF. However, transbronchial biopsies may be useful for certain ILDs, including sarcoidosis, cryptogenic organizing pneumonia, and HP.

The lung's response to injury is relatively stereotyped, and particular biopsy patterns of injury, such as usual interstitial pneumonia or granulomatous inflammation, are seen in a variety of disorders. Interpretation of lung biopsy results must be done in the appropriate context and with incorporation of clinical and imaging data. For example, a biopsy result of usual interstitial pneumonitis may carry a different prognosis in the setting of rheumatoid arthritis–associated ILD than in the setting of IPF. The typical manifestations of several ILDs are summarized in Table 17-1.

Management of ILD depends on the underlying cause, and treatments appropriate to specific entities are discussed later. Exposure avoidance is critical for HP, smoking-related ILD, and drug-induced ILD. Immunosuppressants are employed in a variety of the ILDs, with results depending on the specific disease. Supplemental oxygen and pulmonary rehabilitation may be helpful in advanced disease. Lung transplantation is performed in patients with limited life expectancy, and early referral is suggested for patients with a poor prognosis, as in IPF.

For a deeper discussion on this topic, please see Chapter 92, "Interstitial Lung Disease," in Goldman-Cecil Medicine, *25th Edition.*

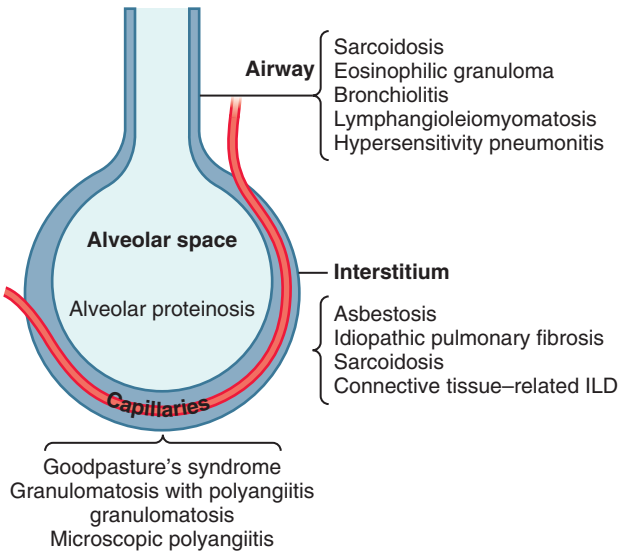

FIGURE 17-2 Interstitial lung disease (ILD) affects the interstitium of the lung at different locations. Depending on the site of disease activity, its consequences may vary. Diseases that affect the interstitium that surrounds the distal part of the alveoli lead to physiologic restrictions with reduced lung volumes. Diseases that preferentially affect the interstitium located near the more proximal parts of the acinus near the distal bronchioles may exhibit predominantly well-preserved lung volumes and physiologic obstruction.

IDIOPATHIC INTERSTITIAL PNEUMONIAS

The IIPs are a group of ILDs of unknown origins. In the 1970s, these conditions were considered to be different variations of IPF. However, the distinct clinical presentations, natural courses, and responses to treatment observed in these patients led to their reclassification as IIPs. The classification scheme suggested in a 2002 consensus statement by the American Thoracic and European Respiratory Societies was updated in 2013.

The major IIPs are IPF, idiopathic nonspecific interstitial pneumonia (NSIP), respiratory bronchiolitis–associated interstitial lung disease (RB-ILD), desquamative interstitial pneumonia (DIP), cryptogenic organizing pneumonia (COP), and acute interstitial pneumonia (AIP). Rare IIPs include lymphoid (or lymphocytic) interstitial pneumonia (LIP) and idiopathic pleuroparenchymal fibroelastosis. Some patients have idiopathic interstitial lung disease that does not meet criteria for any of these entities, and they are considered to have unclassifiable IIP.

Idiopathic Pulmonary Fibrosis

Definition and Epidemiology

Of the IIPs, IPF, formerly called *cryptogenic fibrosing alveolitis,* is the most common, affecting 85,000 to 100,000 individuals in the United States. IPF was defined in a consensus statement as a