of a defined CTD. A raised lactate dehydrogenase (LDH) level is a nonspecific finding common to ILDs. Elevation of the serum level of angiotensin-converting enzyme is common in ILDs, especially sarcoidosis. Serum precipitins confirm exposure when hypersensitivity pneumonitis is suspected, although they are not diagnostic of the process. Antineutrophil cytoplasmic or anti-basement membrane antibodies are useful if vasculitis is suspected. The electrocardiogram is usually normal unless pulmonary hypertension is present; then it demonstrates right-axis deviation, right ventricular hypertrophy, or right atrial enlargement or hypertrophy. Echocardiography also reveals right ventricular dilation and/or hypertrophy in the presence of pulmonary hypertension.

CHEST IMAGING STUDIES

Chest X-Ray ILD may be first suspected on the basis of an abnormal chest radiograph, which most commonly reveals a bibasilar reticular pattern. A nodular or mixed pattern of alveolar filling and increased reticular markings also may be present. Subgroups of ILDs exhibit nodular opacities with a predilection for the upper lung zones (sarcoidosis, PLCH, chronic hypersensitivity pneumonitis, silicosis, berylliosis, RA [necrobiotic nodular form], ankylosing spondylitis). The chest x-ray correlates poorly with the clinical or histopathologic stage of the disease. The radiographic finding of honeycombing correlates with pathologic findings of small cystic spaces and progressive fibrosis; when present, it portends a poor prognosis. In most cases, the chest radiograph is nonspecific and usually does not allow a specific diagnosis.

Computed Tomography HRCT is superior to the plain chest x-ray for early detection and confirmation of suspected ILD (Fig. 315-2). In addition, HRCT allows better assessment of the extent and distribution of disease, and it is especially useful in the investigation of patients with a normal chest radiograph. Coexisting disease is often best recognized on HRCT scanning, e.g., mediastinal adenopathy, carcinoma, or emphysema. In the appropriate clinical setting, HRCT may be sufficiently characteristic to preclude the need for lung biopsy in IPF, sarcoidosis, hypersensitivity pneumonitis, asbestosis, lymphangitic carcinoma, and PLCH. When a lung biopsy is required, HRCT scanning is useful for determining the most appropriate area from which biopsy samples should be taken.

PULMONARY FUNCTION TESTING

Spirometry and Lung Volumes Measurement of lung function is important in assessing the extent of pulmonary involvement in patients with ILD. Most forms of ILD produce a restrictive defect with reduced total lung capacity (TLC), functional residual capacity, and residual volume (Chap. 306e). Forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) are reduced, but these changes are related to the decreased TLC. The FEV_1/FVC ratio is usually normal or increased. Lung volumes decrease as lung stiffness worsens with disease progression. A few disorders produce interstitial opacities on chest x-ray and obstructive airflow limitation on lung function testing (uncommon in sarcoidosis and hypersensitivity pneumonitis but common in tuberous sclerosis and LAM). Pulmonary function studies have been proved to have prognostic value in patients with idiopathic interstitial pneumonias, particularly IPF and nonspecific interstitial pneumonia (NSIP).

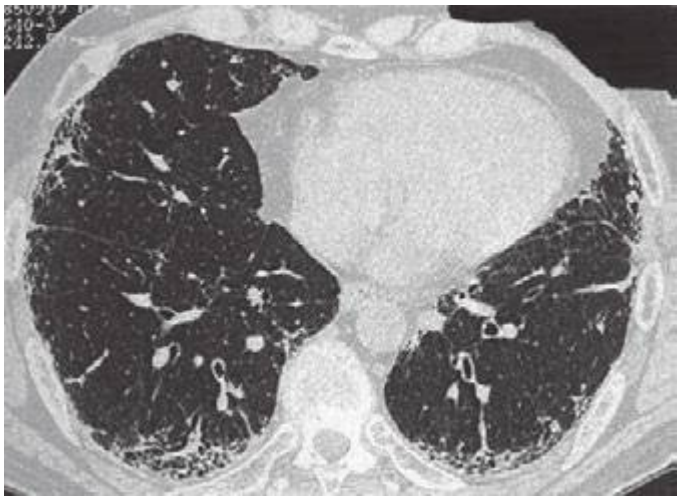

FIGURE 315-2 Idiopathic pulmonary fibrosis. High-resolution computed tomography image shows bibasal, peripheral predominant reticular abnormality with traction bronchiectasis and honeycombing. The lung biopsy showed the typical features of usual interstitial pneumonia.

Diffusing Capacity A reduction in the diffusing capacity of the lung for carbon monoxide (D_{LCO}) is a common but nonspecific finding in most ILDs. This decrease is due in part to effacement of the alveolar capillary units but, more important, to mismatching of ventilation and perfusion ($\dot{V}/\dot{Q}$). Lung regions with reduced compliance due to either fibrosis or cellular infiltration may be poorly ventilated but may still maintain adequate blood flow, and the ventilation-perfusion mismatch in these regions acts like true venous admixture. The severity of the reduction in D_{LCO} does not correlate with disease stage.

Arterial Blood Gas The resting arterial blood gas may be normal or reveal hypoxemia (secondary to a mismatching of ventilation to perfusion) and respiratory alkalosis. A normal arterial O_2 tension (or saturation by oximetry) at rest does not rule out significant hypoxemia during exercise or sleep. Carbon dioxide (CO_2) retention is rare and is usually a manifestation of end-stage disease.

CARDIOPULMONARY EXERCISE TESTING

Because hypoxemia at rest is not always present and because severe exercise-induced hypoxemia may go undetected, it is useful to perform exercise testing with measurement of arterial blood gases to detect abnormalities of gas exchange. Arterial oxygen desaturation, a failure to decrease dead space appropriately with exercise (i.e., a high V_D/V_T [dead space/tidal volume] ratio [Chap. 306e]), and an excessive increase in respiratory rate with a lower than expected recruitment of tidal volume provide useful information about physiologic abnormalities and extent of disease. Serial assessment of resting and exercise gas exchange is an excellent method for following disease activity and responsiveness to treatment, especially in patients with IPF. Increasingly, the 6-min walk test is used to obtain a global evaluation of submaximal exercise capacity in patients with ILD. The walk distance and level of oxygen desaturation tend to correlate with the patient's baseline lung function and mirror the patient's clinical course.

FIBEROPTIC BRONCHOSCOPY AND BRONCHOALVEOLAR LAVAGE (BAL)

In selected diseases (e.g., sarcoidosis, hypersensitivity pneumonitis, DAH syndrome, cancer, pulmonary alveolar proteinosis), cellular analysis of BAL fluid may be useful in narrowing the differential diagnostic possibilities among various types of ILD (Table 315-2). The role of BAL in defining the stage of disease and assessment of disease progression or response to therapy remains poorly understood, and the usefulness of BAL in the clinical assessment and management remains to be established.

TISSUE AND CELLULAR EXAMINATION

Lung biopsy is the most effective method for confirming the diagnosis and assessing disease activity. The findings may identify a more treatable process than originally suspected, particularly chronic hypersensitivity pneumonitis, COP, respiratory bronchiolitis–associated ILD, or sarcoidosis. Biopsy should be obtained before the initiation of treatment. A definitive diagnosis avoids confusion and anxiety later in the clinical course if the patient does not respond to therapy or experiences serious side effects from it.

Fiberoptic bronchoscopy with multiple transbronchial lung biopsies (four to eight biopsy samples) is often the initial procedure of choice, especially when sarcoidosis, lymphangitic carcinomatosis, eosinophilic pneumonia, Goodpasture syndrome, or infection is suspected. If a specific diagnosis is not made by transbronchial biopsy, surgical lung biopsy by video-assisted thoracic surgery or open thoracotomy is