TABLE 315-2 DIAGNOSTIC VALUE OF BRONCHOALVEOLAR LAVAGE IN INTERSTITIAL LUNG DISEASE

Condition	Bronchoalveolar Lavage Finding
Sarcoidosis	Lymphocytosis; CD4:CD8 ratio >3.5 most specific of diagnosis
Hypersensitivity pneumonitis	Marked lymphocytosis (>50%)
Organizing pneumonia	Foamy macrophages; mixed pattern of increased cells characteristic; decreased CD4:CD8 ratio
Eosinophilic lung disease	Eosinophils >25%
Diffuse alveolar bleeding	Hemosiderin-laden macrophages, red blood cells
Diffuse alveolar damage, drug toxicity	Atypical hyperplastic type II pneumocytes
Opportunistic infections	*Pneumocystis carinii*, fungi, cytomegalovirus-transformed cells
Lymphangitic carcinomatosis, alveolar cell carcinoma, pulmonary lymphoma	Malignant cells
Alveolar proteinosis	Milky effluent, foamy macrophages and lipoproteinaceous intraalveolar material (periodic acid–Schiff stain–positive)
Lipoid pneumonia	Fat globules in macrophages
Pulmonary Langerhans cell histiocytosis	Increased CD1+ Langerhans cells, electron microscopy demonstrating Birbeck granule in lavaged macrophage (expensive and difficult to perform)
Asbestos-related pulmonary disease	Dust particles, ferruginous bodies
Berylliosis	Positive lymphocyte transformation test to beryllium
Silicosis	Dust particles by polarized light microscopy
Lipoidosis	Accumulation of specific lipopigment in alveolar macrophages

indicated. Adequate-sized biopsies from multiple sites, usually from two lobes, should be obtained. Relative contraindications to lung biopsy include serious cardiovascular disease, honeycombing and other roentgenographic evidence of diffuse end-stage disease, severe pulmonary dysfunction, and other major operative risks, especially in the elderly.

TREATMENT INTERSTITIAL LUNG DISEASE

Although the course of ILD is variable, progression is common and often insidious. All treatable possibilities should be carefully considered. Because therapy does not reverse fibrosis, the major goals of treatment are permanent removal of the offending agent, when known, and early identification and aggressive suppression of the acute and chronic inflammatory process, thereby reducing further lung damage. Hypoxemia (Pao_2 <55 mmHg) at rest and/or with exercise should be managed with supplemental oxygen. Management of cor pulmonale may be required as the disease progresses **(Chaps. 280 and 304)**. Pulmonary rehabilitation has been shown to improve the quality of life in patients with ILD.

DRUG THERAPY

Glucocorticoids are the mainstay of therapy for suppression of the inflammation present in ILD, but the success rate is low. There have been no placebo-controlled trials of glucocorticoids in ILD, and so there is no direct evidence that steroids improve survival in many of the diseases for which they are commonly used. Glucocorticoid therapy is recommended for symptomatic ILD patients with eosinophilic pneumonias, COP, CTD, sarcoidosis, hypersensitivity pneumonitis, acute inorganic dust exposures, acute radiation pneumonitis, DAH, and drug-induced ILD. In organic dust disease, glucocorticoids are recommended for both the acute and chronic stages.

The optimal dose and proper length of therapy with glucocorticoids in the treatment of most ILDs are not known. A common starting dose is prednisone, 0.5–1 mg/kg in a once-daily oral dose (based on the patient's lean body weight). This dose is continued for 4–12 weeks, at which time the patient is reevaluated. If the patient is stable or improved, the dose is tapered to 0.25–0.5 mg/kg and is maintained at this level for an additional 4–12 weeks, depending on the course. Rapid tapering or a shortened course of glucocorticoid treatment can result in recurrence. If the patient's condition continues to decline on glucocorticoids, a second agent (see below) often is added and the prednisone dose is lowered to or maintained at 0.25 mg/kg per day.

Cyclophosphamide, azathioprine (1–2 mg/kg lean body weight per day), and mycophenolate mofetil, with or without glucocorticoids, have been tried with variable success in IPF, vasculitis, progressive systemic sclerosis, and other ILDs. An objective response usually requires at least 8–12 weeks to occur. In situations in which these drugs have failed or could not be tolerated, other agents, including methotrexate and cyclosporine, have been tried. However, their role in the treatment of ILDs remains to be determined.

Many cases of ILD are chronic and irreversible despite the therapy discussed above, and lung transplantation may then be considered **(Chap. 320e)**.

INDIVIDUAL FORMS OF INTERSTITIAL LUNG DISEASE

IDIOPATHIC PULMONARY FIBROSIS

IPF is the most common form of idiopathic interstitial pneumonia. Separating IPF from other forms of lung fibrosis is an important step in the evaluation of all patients presenting with ILD. IPF has a distinctly poor response to therapy and a bad prognosis.

Clinical Manifestations Exertional dyspnea, a nonproductive cough, and inspiratory crackles with or without digital clubbing may be present on physical examination. HRCT lung scans typically show patchy, predominantly basilar, subpleural reticular opacities, often associated with traction bronchiectasis and honeycombing (Fig. 315-2). A definite UIP pattern on HRCT is highly accurate for the presence of a UIP pattern on surgical lung biopsy. Atypical findings that should suggest an alternative diagnosis include extensive ground-glass abnormality, nodular opacities, upper or midzone predominance, and prominent hilar or mediastinal lymphadenopathy. Pulmonary function tests often reveal a restrictive pattern, a reduced D_{LCO}, and arterial hypoxemia that is exaggerated or elicited by exercise.

Histologic Findings Confirmation of the presence of the UIP pattern on histologic examination is essential to confirm this diagnosis. Transbronchial biopsies are not helpful in making the diagnosis of UIP, and surgical biopsy usually is required. The histologic hallmark and chief diagnostic criterion of UIP is a heterogeneous appearance at low magnification with alternating areas of normal lung, interstitial inflammation, foci of proliferating fibroblasts, dense collagen fibrosis, and honeycomb changes. These histologic changes affect the peripheral, subpleural parenchyma most severely. The interstitial inflammation is usually patchy and consists of a lymphoplasmacytic infiltrate in the alveolar septa, associated with hyperplasia of type 2 pneumocytes. The fibrotic zones are composed mainly of dense collagen, although scattered foci of proliferating fibroblasts are a consistent finding. The extent of fibroblastic proliferation is predictive of disease progression. Areas of honeycomb change are composed of cystic fibrotic air spaces that frequently are lined by bronchiolar epithelium and filled with mucin. Smooth-muscle hyperplasia is commonly seen in areas of fibrosis and honeycomb change. A fibrotic pattern with some features similar to UIP may be found in the chronic stage of several specific disorders, such as pneumoconioses (e.g., asbestosis), radiation injury, certain drug-induced lung diseases (e.g., nitrofurantoin), chronic aspiration, sarcoidosis, chronic hypersensitivity pneumonitis, organized chronic eosinophilic pneumonia, and PLCH. Commonly, other histopathologic features are present in these situations, thus allowing separation of these lesions from the UIP-like pattern. Consequently, the term *usual interstitial pneumonia* is used for patients in whom the lesion is idiopathic and not associated with another condition.