TREATMENT Little data exist to support the management of ILD in RA. Initial treatment of rheumatoid ILD, if required, is typically with oral glucocorticoids, which should be tried for 1–3 months. The potential benefit of anti-tumor necrosis factor α (TNF-α) therapy has been clouded by concerns about the development of a rapid and occasionally fatal lung disease in patients with RA-associated ILD treated with anti-TNF-α therapy.

Systemic Lupus Erythematosus • *CLINICAL MANIFESTATIONS* (See also Chap. 378) Lung disease is a common complication in SLE. Pleuritis with or without effusion is the most common pulmonary manifestation. Other lung manifestations include the following: atelectasis, diaphragmatic dysfunction with loss of lung volumes, pulmonary vascular disease, pulmonary hemorrhage, uremic pulmonary edema, infectious pneumonia, and organized pneumonia. Acute lupus pneumonitis characterized by pulmonary capillaritis leading to alveolar hemorrhage is uncommon. Chronic, progressive ILD is uncommon (<10%). It is important to exclude pulmonary infection. Although pleuropulmonary involvement may not be evident clinically, pulmonary function testing, particularly D_{LCO}, reveals abnormalities in many patients with SLE.

HISTOLOGIC FINDINGS The most common pathologic patterns seen include NSIP, UIP, LIP, and, on occasion, organizing pneumonia and amyloidosis.

TREATMENT There have been no controlled trials of treatment for ILD in SLE. Treatment involves the use of a glucocorticoid, either alone or, more often, in combination with an additional immunomodulating agent.

Polymyositis and Dermatomyositis (PM/DM) • *CLINICAL MANIFESTATIONS* (See also Chap. 388) ILD occurs in ~10% of patients with PM/DM. Diffuse reticular or nodular opacities with or without an alveolar component occur radiographically, with a predilection for the lung bases (NSIP pattern). ILD occurs more commonly in the subgroup of patients with an anti-Jo-1 antibody that is directed to histidyl tRNA synthetase. Weakness of respiratory muscles contributing to aspiration pneumonia may be present. A rapidly progressive illness characterized by diffuse alveolar damage may cause respiratory failure.

HISTOLOGIC FINDINGS NSIP predominates over UIP, organizing pneumonia, or other patterns of interstitial pneumonia.

TREATMENT The optimal treatment is unknown. The most widely used initial treatment is oral glucocorticoids. Fulminant disease may require high-dose intravenous methylprednisolone (1.0 g/d) for 3–5 days.

Sjögren Syndrome • *CLINICAL MANIFESTATIONS* (See also Chap. 383) General dryness and lack of airway secretion cause the major problems of hoarseness, cough, and bronchitis.

HISTOLOGIC FINDINGS Lung biopsy is frequently required to establish a precise pulmonary diagnosis. Fibrotic NSIP is most common. Lymphocytic interstitial pneumonitis, lymphoma, pseudolymphoma, bronchiolitis, and bronchiolitis obliterans are associated with this condition.

TREATMENT Glucocorticoids have been used in the management of ILD associated with Sjögren syndrome with some degree of clinical success.

DRUG-INDUCED ILD

Clinical Manifestations Many classes of drugs have the potential to induce diffuse ILD, which is manifest most commonly as exertional dyspnea and nonproductive cough. A detailed history of the medications taken by the patient is needed to identify drug-induced disease, including over-the-counter medications, oily nose drops, and petroleum products (mineral oil). In most cases, the pathogenesis is unknown, although a combination of direct toxic effects of the drug (or its metabolite) and indirect inflammatory and immunologic events are likely. The onset of the illness may be abrupt and fulminant, or it may be insidious, extending over weeks to months. The drug may have been taken for several years before a reaction develops (e.g., amiodarone), or the lung disease may occur weeks to years after the drug has been discontinued (e.g., carmustine). The extent and severity of disease are usually dose-related.

Histologic Findings The patterns of lung injury vary widely and depend on the agent.

Treatment Treatment consists of discontinuation of any possible offending drug and supportive care.

EOSINOPHILIC PNEUMONIA

(See Chap. 310)

PULMONARY ALVEOLAR PROTEINOSIS (PAP)

Clinical Manifestations Although not strictly an ILD, PAP resembles and is therefore considered with these conditions. It has been proposed that a defect in macrophage function, more specifically an impaired ability to process surfactant, may play a role in the pathogenesis of PAP. PAP is an autoimmune disease with a neutralizing antibody of immunoglobulin G isotype against granulocyte-macrophage colony-stimulating factor (GM-CSF). These findings suggest that neutralization of GM-CSF bioactivity by the antibody causes dysfunction of alveolar macrophages, which results in reduced surfactant clearance. There are three distinct classes of PAP: acquired (>90% of all cases), congenital, and secondary. *Congenital PAP* is transmitted in an autosomal recessive manner and is caused by homozygosity for a frameshift mutation (121ins2) in the *SP-B* gene, which leads to an unstable SP-B mRNA, reduced protein levels, and secondary disturbances of SP-C processing. *Secondary PAP* is rare among adults and is caused by lysinuric protein intolerance, acute silicosis and other inhalational syndromes, immunodeficiency disorders, and malignancies (almost exclusively of hematopoietic origin) and hematopoietic disorders.

The typical age of presentation is 30–50 years, and males predominate. The clinical presentation is usually insidious and is manifested by progressive exertional dyspnea, fatigue, weight loss, and low-grade fever. A nonproductive cough is common, but occasionally expectoration of "chunky" gelatinous material may occur. Polycythemia, hypergammaglobulinemia, and increased LDH levels are common. Markedly elevated serum levels of lung surfactant proteins A and D have been found in PAP. In the absence of any known secondary cause of PAP, an elevated serum anti-GM-CSF titer is highly sensitive and specific for the diagnosis of acquired PAP. BAL fluid levels of anti-GM-CSF antibodies correlate better with the severity of PAP than do serum titers. Radiographically, bilateral symmetric alveolar opacities located centrally in middle and lower lung zones result in a "bat-wing" distribution. HRCT shows a ground-glass opacification and thickened intralobular structures and interlobular septa.

Histologic Findings This diffuse disease is characterized by the accumulation of an amorphous, periodic acid–Schiff–positive lipoproteinaceous material in the distal air spaces. There is little or no lung inflammation, and the underlying lung architecture is preserved.

Treatment Whole-lung lavage(s) through a double-lumen endotracheal tube provides relief to many patients with dyspnea or progressive hypoxemia and also may provide long-term benefit.

PULMONARY LYMPHANGIOLEIOMYOMATOSIS

Clinical Manifestations Pulmonary LAM is a rare condition that afflicts premenopausal women and should be suspected in young women with "emphysema," recurrent pneumothorax, or chylous pleural effusion. It is often misdiagnosed as asthma or chronic obstructive pulmonary disease. Whites are affected much more commonly than are members of other racial groups. The disease accelerates during pregnancy and abates after oophorectomy. Common complaints at presentation are dyspnea, cough, and chest pain. Hemoptysis may