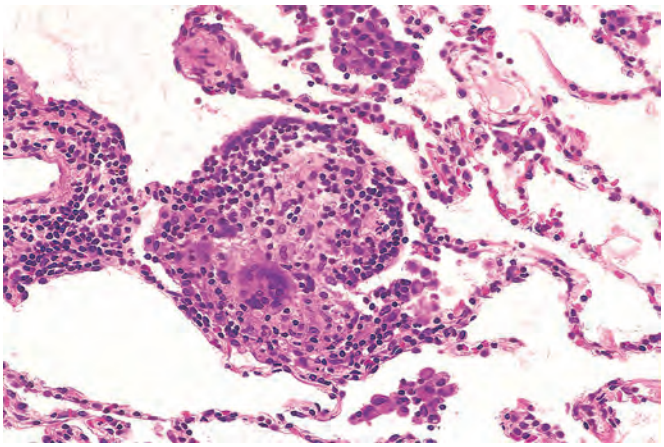

Figure 15-23 Hypersensitivity pneumonitis. Loosely formed interstitial granulomas and chronic inflammation are characteristic.

MORPHOLOGY

Histologic changes are characteristically centered on bronchioles. They include (1) interstitial pneumonitis, consisting primarily of lymphocytes, plasma cells, and macrophages (eosinophils are rare); (2) noncaseating granulomas in two thirds of patients (Fig. 15-23); and (3) interstitial fibrosis with fibroblastic foci, honeycombing, and obliterative bronchiolitis (in late stages). In more than half of patients, there is also evidence of an intra-alveolar infiltrate.

Clinical Features. The clinical manifestations are varied. Acute attacks, which follow inhalation of antigenic dust in sensitized patients, consist of recurring episodes of fever, dyspnea, cough, and leukocytosis. Micronodular interstitial infiltrates may appear in the chest radiograph, and pulmonary function tests show an acute restrictive disorder. Symptoms usually appear 4 to 6 hours after exposure and may last for 12 hours to several days. They recur with reexposure. If exposure is continuous and protracted, a chronic form of the disease supervenes, leading to progressive respiratory failure, dyspnea, and cyanosis and a decrease in total lung capacity and compliance—a picture similar to other forms of chronic interstitial disease.

Pulmonary Eosinophilia

Although relatively rare, there are several clinical and pathologic pulmonary entities that are characterized by an infiltration of eosinophils, recruited in part by elevated alveolar levels of eosinophil attractants such as IL-5.

Pulmonary eosinophilia is divided into the following categories:

- *Acute eosinophilic pneumonia with respiratory failure*. This is an acute illness of unknown cause. It has a rapid onset with fever, dyspnea, and hypoxemic respiratory failure. The chest radiograph shows diffuse infiltrates, and bronchoalveolar lavage fluid contains more than 25% eosinophils. Histology shows diffuse alveolar damage and many eosinophils. There is a prompt response to corticosteroids.
- *Secondary eosinophilia*, which occurs in a number of parasitic, fungal, and bacterial infections; in hypersensitivity pneumonitis; in drug allergies; and in association with asthma, allergic bronchopulmonary aspergillosis, or vasculitis (Churg-Strauss syndrome)
- *Idiopathic chronic eosinophilic pneumonia*, characterized by focal areas of cellular consolidation of the lung substance distributed chiefly in the periphery of the lung fields. Prominent in these lesions are heavy aggregates of lymphocytes and eosinophils within both the septal walls and the alveolar spaces. Interstitial fibrosis and organizing pneumonia are often present. These patients have cough, fever, night sweats, dyspnea, and weight loss, all of which respond to corticosteroid therapy. Chronic eosinophilic pneumonia is diagnosed when other causes of chronic pulmonary eosinophilia are excluded.

Smoking-Related Interstitial Diseases

Smoking-related diseases can be grouped into obstructive diseases (emphysema and chronic bronchitis, already discussed) and restrictive or interstitial diseases. A majority of individuals with idiopathic pulmonary fibrosis are smokers; however, the role of cigarette smoking in its pathogenesis has not been clarified yet. Desquamative interstitial pneumonia and respiratory bronchiolitis-associated interstitial lung disease are also smoking-associated interstitial lung diseases.

Desquamative Interstitial Pneumonia

Desquamative interstitial pneumonia is characterized by large collections of macrophages in the airspaces in a current or former smoker. The macrophages were originally thought to be desquamated pneumocytes, thus the misnomer "desquamative interstitial pneumonia."

MORPHOLOGY

The most striking finding is the accumulation of a large number of macrophages with abundant cytoplasm containing dusty brown pigment **(smokers' macrophages)** in the airspaces (Fig. 15-24). Finely granular iron may be seen in the macrophage cytoplasm. Some of the macrophages contain lamellar

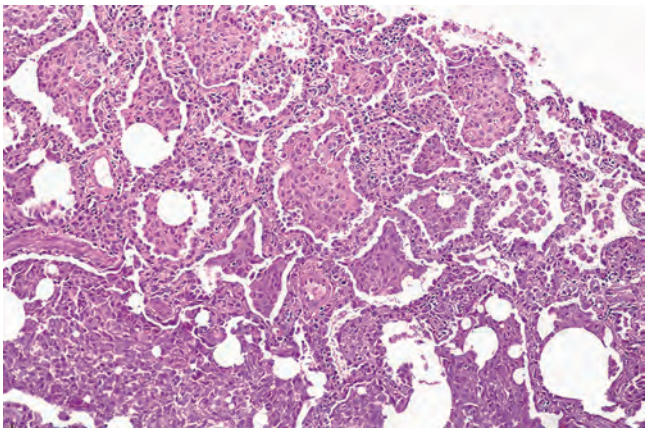

Figure 15-24 Desquamative interstitial pneumonia. Medium-power detail of lung demonstrates the accumulation of large numbers of macrophages within the alveolar spaces and only mild fibrous thickening of the alveolar walls.