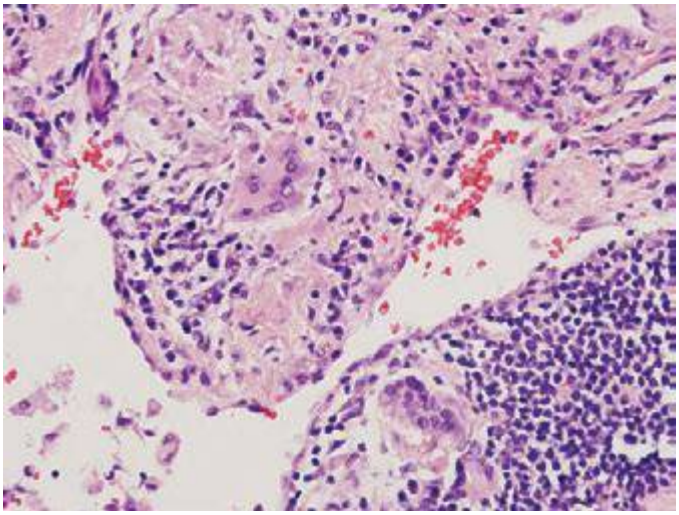

FIGURE 310-2 Open-lung biopsy from a patient with subacute hypersensitivity pneumonitis demonstrating a loose, nonnecrotizing granuloma made up of histiocytes and multinucleated giant cells. Peribronchial inflammatory infiltrate made up of lymphocytes and plasma cells is also seen. *(Courtesy of TJ Gross; with permission.)*

precipitins often provide false-negative results, because they represent an extremely limited proportion of the universe of potential offending environmental antigens.

Bronchoscopy Bronchoscopy with bronchoalveolar lavage (BAL) may be used in the evaluation of HP. Although not a specific finding, BAL lymphocytosis is characteristic of HP. However, in active smokers, a lower threshold should be used to establish BAL lymphocytosis, because smoking will result in lower lymphocyte percentages. Most cases of HP have a CD4+/CD8+ lymphocyte ratio of less than 1, but again, this is not a specific finding and has limited utility in the diagnosis of HP.

Lung Biopsy Tissue samples may be obtained by a bronchoscopic approach using transbronchial biopsy, or more architecturally preserved specimens may be obtained by a surgical approach (video-assisted thoracoscopy or open approach). As is the case with BAL, histologic specimens are not absolutely necessary to establish the diagnosis of HP, but they can be useful in the correct clinical context. A common histologic feature in HP is the presence of noncaseating granulomas in the vicinity of small airways (Fig. 310-2). As opposed to pulmonary sarcoidosis, in which noncaseating granulomas are well defined, the granulomas seen in HP are loose and poorly defined in nature. Within the alveolar spaces and in the interstitium, a mixed cellular infiltrate with a lymphocytic predominance is observed that is frequently patchy in distribution. Bronchiolitis with the presence of organizing exudate is also often observed. Fibrosis may be present as well, particularly as the disease progresses to its chronic form. Fibrotic changes may be focal but can be diffuse and severe with honeycombing in advanced cases, similar to findings in IPF.

Clinical Prediction Rule Although not meant as a set of validated diagnostic criteria, a clinical prediction rule for predicting the presence of HP has been published by the HP Study Group. They identified six statistically significant predictors for HP, the strongest of which was exposure to an antigen known to cause HP. Other predictive criteria were the presence of serum precipitins, recurrent symptoms, symptoms occurring 4–8 h after antigen exposure, crackles on inspiration, and weight loss.

DIFFERENTIAL DIAGNOSIS

Differentiating HP from other conditions that cause a similar constellation of respiratory and systemic symptoms requires an increased index of suspicion based on obtaining a history of possible exposure to an offending antigen. Presentations of acute or subacute HP can be mistaken for respiratory infection. In cases of chronic disease, HP must be differentiated from interstitial lung disease, such as IPF or nonspecific interstitial pneumonitis (NSIP); this can be a difficult task even with lung biopsy. Given the presence of pulmonary infiltrates and noncaseating granulomas on biopsy, sarcoidosis is also a consideration in the differential diagnosis of HP. Unlike in HP, however, hilar adenopathy may be prominent on chest x-ray, organs other than the lung may be involved, and noncaseating granulomas in pathologic specimens tend to be well formed. Other inhalational syndromes, such as organic toxic dust syndrome (OTDS), can be misdiagnosed as HP. OTDS occurs with exposure to organic dusts, including those produced by grains or mold silage, but neither requires prior antigen sensitization nor is characterized by positive serum precipitins.

TREATMENT HYPERSENSITIVITY PNEUMONITIS

The mainstay of treatment for HP is antigen avoidance. A careful exposure history must be obtained to attempt to identify the potential offending antigen and to identify the location where a patient is exposed. Once a potential antigen and location are identified, efforts should be made to modify the environment to minimize patient exposure. This may be accomplished with measures such as removal of birds, removal of molds, and improved ventilation. Personal protective equipment including respirators and ventilated helmets can be used but may not provide adequate protection for sensitized individuals. In some cases, fully avoiding specific environments may be necessary, although such a recommendation must be balanced against the effects to an individual's lifestyle or occupation. It is not uncommon for patients with HP due to exposure to household birds to be unwilling to remove them from the home.

Because acute HP is generally a self-limited disease after a discrete exposure to an offending antigen, pharmacologic therapy is generally not necessary. However, in so-called subacute and chronic forms of the disease, there is a role for glucocorticoid therapy. In patients with particularly severe symptoms as a result of subacute HP, antigen avoidance may be insufficient after establishing the diagnosis. Although glucocorticoids do not change the long-term outcome in these patients, they can accelerate the resolution of symptoms. While there is significant variability in the approach to glucocorticoid therapy by individual clinicians, prednisone therapy can be initiated at 0.5–1 mg/kg of ideal body weight per day (not to exceed 60 mg/d or alternative glucocorticoid equivalent) over a duration of 1–2 weeks, followed by a taper over the next 2–6 weeks. In chronic HP, a similar trial of corticosteroids may be used, although a variable component of fibrotic disease may be irreversible.

GLOBAL CONSIDERATIONS

As the ever-expanding list of antigens and exposures associated with the development of HP suggests, populations at risk for HP will vary globally based on specifics of local occupational, avocational, and environmental factors. Specific examples of geographically limited HP include summer-type pneumonitis seen in Japan and suberosis seen in cork workers in Portugal and Spain.

PULMONARY INFILTRATES WITH EOSINOPHILIA

Although eosinophils are normal constituents of the lungs, there are several pulmonary eosinophilic syndromes that are characterized by pulmonary infiltrates on imaging along with an increased number of eosinophils in lung tissue, in sputum, and/or in BAL fluid, with resultant increased respiratory symptoms and the potential for systemic manifestations. Because the eosinophil plays such an important role in each of these syndromes, it is often difficult to distinguish between them, but there are important clinical and pathologic differences as well as differences in prognosis and treatment paradigms.

CLASSIFYING PULMONARY INFILTRATES WITH EOSINOPHILIA AND GENERAL APPROACH

Because there are so many different diagnoses associated with pulmonary infiltrates with eosinophilia, the first step in classifying pulmonary