TABLE 310-2 PULMONARY INFILTRATES WITH EOSINOPHILIA

Primary Pulmonary Eosinophilic Disorders
Acute eosinophilic pneumonia
Chronic eosinophilic pneumonia
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)
Hypereosinophilic syndrome
Pulmonary Disorders of Known Cause Associated with Eosinophilia
Asthma and eosinophilic bronchitis
Allergic bronchopulmonary aspergillosis
Bronchocentric granulomatosis
Drug/toxin reaction
Infection (Table 310-4)
Parasitic/helminthic disease
Nonparasitic infection
Lung Diseases Associated with Eosinophilia
Cryptogenic organizing pneumonia
Hypersensitivity pneumonitis
Idiopathic pulmonary fibrosis
Pulmonary Langerhans cell granulomatosis
Malignant Neoplasms Associated with Eosinophilia
Leukemia
Lymphoma
Lung cancer
Adenocarcinoma of various organs
Squamous cell carcinoma of various organs
Systemic Disease Associated with Eosinophilia
Postradiation pneumonitis
Rheumatoid arthritis
Sarcoidosis
Sjögren's syndrome

TABLE 310-3 DIAGNOSTIC CRITERIA OF ACUTE EOSINOPHILIC PNEUMONIA

Acute febrile illness with respiratory manifestations of <1 month in duration
Hypoxemic respiratory failure
Diffuse pulmonary infiltrates on chest x-ray
Bronchoalveolar lavage eosinophilia >25%
Absence of parasitic, fungal, or other infection
Absence of drugs known to cause pulmonary eosinophilia
Quick clinical response to corticosteroids
Failure to relapse after discontinuation of corticosteroids

eosinophilic syndromes is distinguishing between primary pulmonary eosinophilic lung disorders and those with eosinophilia that are secondary to a specific cause such as a drug reaction, an infection, a malignancy, or another pulmonary condition such as asthma. Table 310-2 lists primary and secondary pulmonary eosinophilic disorders.

For each patient, a detailed history is of utmost importance and can help elucidate what the underlying disease is. Details regarding onset, timing, and precipitants of specific symptoms can help discern one diagnosis from another. History regarding pharmacologic, occupational, and environmental exposures is instructive, and family and travel history are crucial. In addition to details about the sinuses and lungs, it is important to inquire about systemic manifestations and assess for physical findings of cardiac, gastrointestinal (GI), neurologic, dermatologic, and genitourinary involvement, all of which may give clues to specific diagnoses. Once the details from history and physical are teased out, laboratory testing (including measurements of blood eosinophils, cultures, and markers of inflammation), spirometry and radiographic imaging can help distinguish between different diseases. Often, however, BAL, transbronchial, or open lung biopsies are required. In many cases, biopsies or noninvasive diagnostic studies of other organs (e.g., echocardiogram, electromyogram, or bone marrow biopsy) can be helpful.

PATHOPHYSIOLOGY

Pathologically, the pulmonary eosinophilic syndromes are characterized by tissue infiltration by eosinophils (Fig. 310-2). In eosinophilic granulomatosis with polyangiitis (EGPA), extravascular granulomas and necrotizing vasculitis may occur in the lungs, as well as in the heart, skin, muscle, liver, spleen, and kidneys, and may be associated with fibrinoid necrosis and thrombosis.

The exact etiology of the various pulmonary eosinophilic syndromes is unknown; however, it is felt that these syndromes result from dysregulated eosinophilopoiesis or an autoimmune process because of the prominence of allergic features and the presence of immune complexes, heightened T cell immunity, and altered humoral immunity as evidenced by elevated IgE and rheumatoid factor. Because of its integral involvement in eosinophilopoiesis, interleukin 5 (IL-5) has been hypothesized to play an etiologic role, and efforts to block this cytokine are being investigated. Antineutrophil cytoplasmic antibodies (ANCAs) are present in about half of patents with EGPA; binding of ANCAs to vascular walls likely contributes to vascular inflammation and injury as well as chemotaxis of inflammatory cells.

ACUTE EOSINOPHILIC PNEUMONIA

Acute eosinophilic pneumonia is a syndrome characterized by fevers, acute respiratory failure that often requires mechanical ventilation, diffuse pulmonary infiltrates, and pulmonary eosinophilia in a previously healthy individual (Table 310-3).

Clinical Features and Etiology At presentation, acute eosinophilic pneumonia is often mistaken for acute lung injury or acute respiratory distress syndrome (ARDS), until a BAL is performed and reveals >25% eosinophils. Although the predominant symptoms of acute eosinophilic pneumonia are cough, dyspnea, malaise, myalgias, night sweats, and pleuritic chest pain, physical exam findings include high fevers, basilar rales, and rhonchi on forced expiration. Acute eosinophilic pneumonia most often affects males between age 20 and 40 with no history of asthma. Although no clear etiology has been identified, several case reports have linked acute eosinophilic pneumonia to recent initiation of tobacco smoking or exposure to other environmental stimuli including dust from indoor renovations.

In addition to a suggestive history, the key to establishing a diagnosis of acute eosinophilic pneumonia is the presence of >25% eosinophilia on BAL fluid. While lung biopsies show eosinophilic infiltration with acute and organizing diffuse alveolar damage, it is generally not necessary to proceed to biopsy to establish a diagnosis. Although patients present with an elevated white blood cell count, in contrast to other pulmonary eosinophilic syndromes, acute eosinophilic pneumonia is often not associated with peripheral eosinophilia upon presentation. However, between 7 and 30 days of disease onset, peripheral eosinophilia often occurs with mean eosinophil counts of 1700. Erythrocyte sedimentation rate (ESR), C-reactive protein, and IgE levels are high but nonspecific, whereas HRCT is always abnormal with bilateral random patchy ground-glass or reticular opacities, and small pleural effusions in as many as two-thirds of patients. Pleural fluid is characterized by a high pH with marked eosinophilia.

Clinical Course and Response to Therapy Although some patients improve spontaneously, most patients require admission to an intensive care unit and respiratory support with either invasive (intubation) or noninvasive mechanical ventilation. However, what distinguishes acute eosinophilic pneumonia from both other cases of acute lung injury as well as some of the other pulmonary eosinophilic syndromes is the absence of organ dysfunction or multisystem organ failure other than respiratory failure. One of the characteristic features of acute eosinophilic pneumonia is the high degree of corticosteroid responsiveness and the excellent prognosis. Another distinguishing feature of acute eosinophilic pneumonia is that complete clinical and radiographic recovery without recurrence or residual sequelae occurs in almost all patients within several weeks of initiation of therapy.