nervous system, and gastrointestinal involvement also can be seen.

Seventy percent of patients with microscopic polyangiitis are ANCA positive, and most have anti-MPO antibodies. Because anti-MPO and anti-PR3 antibodies can occur in microscopic polyangiitis and granulomatosis with polyangiitis, these diseases cannot be distinguished based on their ANCA pattern. However, they can be distinguished pathologically because microscopic polyangiitis is characterized by a focal, segmental necrotizing vasculitis affecting venules, capillaries, arterioles, and small arteries without clinical or pathologic evidence of necrotizing granulomatous inflammation. The absence or paucity of immunoglobulin localization in vessel walls distinguishes microscopic polyangiitis from immune complex–mediated small vessel vasculitis such as Henoch-Schönlein purpura and cryoglobulinemic vasculitis.

Treatments for granulomatosis with polyangiitis and microscopic polyangiitis are similar. Combination therapy with corticosteroids and cyclophosphamide is the standard of care to induce remission (level 1 evidence). Rituximab is also an option in this setting (level 1). Plasma exchange is added in cases of severe disease and provides better renal outcomes (level 1). Azathioprine (level 1) or methotrexate (level 1) can be substituted for cyclophosphamide if remission is achieved. Rituximab may be used for induction of remission in place of cyclophosphamide (level 1 evidence) or for relapsing disease (level 1). Novel therapies, including co-trimoxazole (sulfamethoxazole/trimethoprim) for remission maintenance (level 1) and TNF inhibitors for persistent disease, have been tried with some success.

Allergic granulomatosis or Churg-Strauss syndrome is characterized by the triad of asthma, hypereosinophilia, and necrotizing vasculitis. Many other organ systems, including the nervous system, skin, heart, and gastrointestinal tract, may be involved. The vasculitis can be associated with skin nodules and purpura. Although DAH and glomerulonephritis may occur, they are much less common than in the other small vessel vasculitides. Morbidity and mortality often result from cardiac or gastrointestinal complications or status asthmaticus and respiratory failure.

ANCAs are less helpful in the diagnosis of Churg-Strauss syndrome because only 50% of patients are ANCA positive. Anti-MPO antibodies are more commonly seen in these patients. Pathologically, a necrotizing small vessel vasculitis and an eosinophil-rich inflammatory infiltrate with necrotizing granulomas are seen. Most patients respond well to corticosteroids, but other immunosuppressants such as cyclophosphamide may be required for patients with refractory disorders.

Other well-known causes of pulmonary capillaritis include the collagen vascular disorders, anti–glomerular membrane antibody syndrome (i.e., Goodpasture's syndrome), and Henoch-Schönlein purpura. Goodpasture's syndrome causes DAH associated with glomerulonephritis due to anti–glomerular basement membrane antibodies to the α_3 chain of type IV collagen that is also found in the lung basement membrane. More than 90% of patients with Goodpasture's syndrome have anti–glomerular basement membrane antibodies detectable in the serum. For those without circulating antibodies, the diagnosis may be confirmed by lung biopsy, although the kidney is the preferred site. Up to 40% may also be ANCA positive, primarily with anti-MPO antibodies. Pathologically, linear deposition of antibody along the alveolar or glomerular basement membrane is visible by direct immunofluorescence.

The treatment of Goodpasture's syndrome is plasmapheresis and immunosuppression. The disease is fatal if left untreated.

ENVIRONMENTAL AND OCCUPATIONAL INTERSTITIAL LUNG DISEASES

Several environmental and occupational exposures may cause ILDs. They include the pneumoconioses, drug-induced ILD (discussed earlier), and HP. Pneumoconioses are lung diseases resulting from the inhalation of mineral dusts, including silica, coal dust, or asbestos. HP is caused by the inhalation of organic dusts.

For a deeper discussion on this topic, please see Chapter 93, "Occupational Pulmonary Disorders," in Goldman-Cecil Medicine, *25th Edition.*

Pneumoconiosis

The pneumoconioses result from the effects of accumulation of mineral dusts in the lungs; the typical reaction is fibrosis. The risk and extent of these diseases are related to the intensity and cumulative amount of exposure over time. Prevention of the pneumoconioses through occupational safeguards or, in the case of asbestos, legislative bans on use, is important because there are no effective treatments for these diseases.

Silicosis is a lung disease caused by exposure to crystalline-free silica, which results in an inflammatory and fibrotic reaction and the formation of the characteristic silicotic nodule. Occupations with a higher likelihood of exposure to silica include mining, stone cutting, carving, polishing, foundry work, and abrasive clearing (e.g., sandblasting). Although exposure is usually chronic (over years), accelerated and acute disease manifestations have been described in the setting of heavier short-term exposures.

Acute silicosis causes a pulmonary alveolar proteinosis and accumulation of surfactant in the alveolar spaces. Chronic silicosis results in simple nodular silicosis, which is usually asymptomatic unless the patient is also exposed to tobacco, and progressive massive fibrosis, which is characterized by extensive bilateral apical fibrosis resulting from the confluence of many silicotic nodules.

Patients with silicosis may have dyspnea or may be relatively asymptomatic but require further evaluation of an abnormal chest radiograph. Chest radiographs in uncomplicated silicosis show upper lobe nodular opacities, which may be subtle, whereas progressive massive fibrosis results in marked architectural distortion of the upper lobes (E-Fig 17-7). Hilar node enlargement may be accompanied by eggshell nodal calcification (E-Fig 17-8). Pulmonary function tests in simple nodular silicosis may be normal or show a mixed obstructive or restrictive pattern, whereas progressive massive fibrosis is typically associated with severe restriction and hypoxemia. Patients with silicosis are at elevated risk for tuberculosis and should be screened for latent tuberculosis infection; there is also an association between silicosis and rheumatoid arthritis.

Coal worker's pneumoconiosis is an uncommon cause of pulmonary fibrosis, occurring in workers exposed to coal dust and graphite. Usually, the patients are exposed while working in underground mines. Coal worker's pneumoconiosis results in the