formation of pigmented lesions in the lung surrounded by emphysema, called *coal macules*. Progressive massive fibrosis may subsequently occur. Most patients have chronic cough, which is usually productive, resulting from bronchitis related to coal exposure or to tobacco. The chest radiograph shows diffuse, small, rounded opacities. As with silicosis, there is an association with rheumatoid arthritis. Caplan's syndrome is the occurrence of multiple, large, sometimes cavitary lung nodules in association with rheumatoid arthritis after coal dust exposure.

Asbestosis results from chronic exposure to asbestos, which is a fibrous silicate used for insulation, for friction-bearing surfaces, and to strengthen materials. The inhaled asbestos fibers are deposited in the lungs, where the small fibers may be phagocytosed and cleared through lymphatics to the pleural space, but the longer fibers are often retained. Asbestos exposure typically leads to pleural disease characterized by pleural plaques, effusion, and fibrosis, but it does not necessarily affect the lung parenchyma. If it does, it is called *asbestosis*, with interstitial lung fibrosis resulting from asbestos exposure.

Asbestosis is characterized by a gradual onset of dyspnea. As with other pneumoconioses, the risk and severity of disease are related to the extent and duration of exposure. Asbestosis is often diagnosed after exposure has ceased, and disease progression may continue in the absence of ongoing exposure because of the reaction to retained asbestos fibers in the lung.

The clinical presentation, pulmonary function tests, and imaging studies are similar to those for restrictive lung diseases such as IPF. However, the detection of significant pleural disease is useful in distinguishing this illness from other ILDs.

The diagnosis is made from the history of exposure and demonstration of concomitant pleural plaques and lower lobe–predominant fibrotic changes on the chest radiograph or CT scan. In uncertain cases, the demonstration of asbestos in tissue specimens may be necessary. Asbestos bodies are the characteristic finding and consist of asbestos fibers coated by iron-containing (ferruginous) material. Asbestos exposure increases the incidence of malignancy, including lung carcinoma and mesothelioma, especially among people who also smoke. It is uncertain whether asbestosis itself confers a heightened risk of malignancy independent of the effects of asbestos exposure alone. No specific treatment for asbestosis exists.

Berylliosis results from exposure to beryllium, a rare metal useful in modern, high-technology industries. Exposure to beryllium can lead to an acute chemical bronchitis and pneumonitis or chronic beryllium disease. Chronic beryllium disease is characterized by a multisystemic granulomatosis that is difficult to distinguish from sarcoidosis. The diagnosis is made by history of exposure, histologic examination, and laboratory confirmation using the beryllium lymphocyte proliferation test that is available at specialized centers. Corticosteroids may be useful in the treatment of berylliosis, but patients should avoid further exposure to beryllium.

Hypersensitivity Pneumonitis

Definition and Epidemiology

HP (formerly called *extrinsic allergic alveolitis)* is a relatively common ILD resulting from an exaggerated immune reaction in the alveoli and small airways to various small, inhaled organic antigens in sensitized individuals. Potential sensitizing antigens are diverse, ranging from bacterial, fungal, and animal proteins to low-molecular-weight chemicals (Table 17-5). Although evocative descriptions have been given to occupational forms of this disease (e.g., paprika splitter's lung resulting from sensitivity to inhaled paprika dust contaminated with *Mucor stolonifer),* more prosaic exposures may occur in everyday life, such as to contaminated hot tub water or to antigens from pet birds. The incidence and prevalence of HP are not well known, and underdiagnosis occurs.

Pathology

HP occurs as the result of an abnormally exuberant immune response in the alveoli and small airways to inhaled antigens, typically organic molecules, but also small chemical compounds such as isocyanates, which bind to haptens. This response occurs in a susceptible host; the underlying reasons for susceptibility are unclear but probably include genetic and environmental factors (e.g., pesticide exposure). Smokers are less likely than nonsmokers to develop HP, but they may have a more severe disease course if HP does occur. After exposure to an antigen, a susceptible individual develops an alveolitis with influx of neutrophils and lymphocytes. A T_H1-type immune response then leads to granuloma formation.

Typical lung biopsy findings include granulomatous inflammation with poorly formed granulomas containing foreign body giant cells, interstitial chronic inflammation with a bronchiolocentric component, and bronchiolitis. In chronic or end-stage disease, fibrosis occurs, and biopsies may feature areas with a UIP or NSIP pattern in addition to areas of granulomatous and airway-centered inflammation.

Clinical Presentation

The disease may manifest in an acute fashion (i.e., acute HP) several hours after intense exposure to a provocative antigen, with

TABLE 17-5 HYPERSENSITIVITY PNEUMONITIS

ANTIGEN	SOURCE	DISEASES
Thermophilic bacteria	Moldy hay, sugar cane, compost	Farmer's lung, bagassosis, mushroom worker's disease
Other bacteria, including atypical mycobacteria	Contaminated water, wood dust, fertilizer, paprika dust	Humidifier, detergent worker's disease, and familial hypersensitivity pneumonitis
Fungi	Moldy cork, contaminated wood dust, barley, maple logs	Suberosis, sequoiosis, and maple bark stripper's disease, malt worker's disease, and paprika splitter's lung
Animal protein	Bird droppings, animal urine, bovine and porcine pituitary powder	Pigeon breeder's lung, duck fever, turkey handler's disease, pituitary snuff-taker's disease, laboratory worker's hypersensitivity pneumonitis
Chemically altered human proteins (e.g., albumin)	Toluene diisocyanate, trimellitic anhydride, diphenylmethane diisocyanate	Hypersensitivity pneumonitis
Phthalic anhydride	Heated epoxy resin	Epoxy resin lung