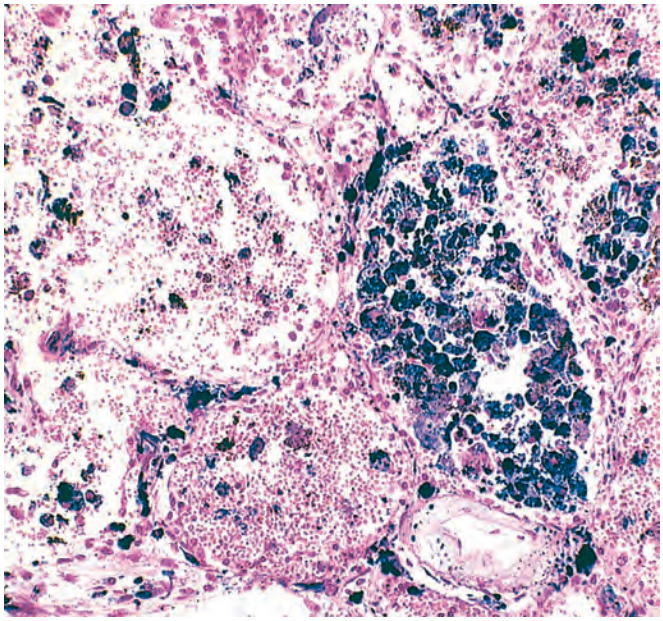

Figure 15-31 Diffuse pulmonary hemorrhage syndrome. There is acute intra-alveolar hemorrhage and hemosiderin-laden macrophages, reflecting previous hemorrhage (Prussian blue iron stain).

Diffuse Pulmonary Hemorrhage Syndromes

Pulmonary hemorrhage is a dramatic complication of some interstitial lung disorders. Among these so-called *pulmonary hemorrhage syndromes* (Fig. 15-31) are (1) Goodpasture syndrome, (2) idiopathic pulmonary hemosiderosis, and (3) vasculitis-associated hemorrhage, which is found in conditions such as hypersensitivity angiitis, Wegener granulomatosis, and systemic lupus erythematosus (Chapter 11).

Goodpasture Syndrome

Goodpasture syndrome is an uncommon autoimmune disease in which kidney and lung injury are caused by circulating autoantibodies against the noncollagenous domain of the α3 chain of collagen IV. When only renal disease is caused by this antibody, it is called anti-glomerular basement membrane disease. The term *Goodpasture syndrome* designates the 40% to 60% of patients who develop pulmonary hemorrhage in addition to renal disease. The antibodies initiate inflammatory destruction of the basement membrane in renal glomeruli and pulmonary alveoli, giving rise to *rapidly progressive glomerulonephritis* and a *necrotizing hemorrhagic interstitial pneumonitis.* Although any age can be affected, most cases occur in the teens or 20s, and in contrast to many other autoimmune diseases, there is a male preponderance. The majority of patients are active smokers.

Pathogenesis. The immunopathogenesis of the syndrome and the nature of the Goodpasture antigens are described in Chapter 20. The trigger that initiates the production of anti-basement membrane antibodies is still unknown. Because the epitopes that evoke anticollagen antibodies are normally hidden within the molecule, it is presumed that some environmental insult such as viral infection, exposure to hydrocarbon solvents (used in the dry cleaning industry), or smoking is required to unmask the cryptic epitopes. As in other autoimmune disorders, a genetic predisposition is indicated by association with certain HLA subtypes (e.g., HLA-DRB1*1501 and *1502).

MORPHOLOGY

In the classic case, the lungs are heavy, with areas of red-brown consolidation. Histologically, there is focal necrosis of alveolar walls associated with intra-alveolar hemorrhages. Often the alveoli contain hemosiderin-laden macrophages (Fig. 15-31). In later stages there may be fibrous thickening of the septae, hypertrophy of type II pneumocytes, and organization of blood in alveolar spaces. In many cases immunofluorescence studies reveal linear deposits of immunoglobulins along the basement membranes of the septal walls. The kidneys have the characteristic findings of focal proliferative glomerulonephritis in early cases or crescentic glomerulonephritis in patients with rapidly progressive glomerulonephritis. Diagnostic linear deposits of immunoglobulins and complement are seen by immunofluorescence studies along the glomerular basement membranes even in the few patients without renal disease.

Clinical Features. Most cases begin clinically with respiratory symptoms, principally hemoptysis, and radiographic evidence of focal pulmonary consolidations. Soon, manifestations of glomerulonephritis appear, leading to rapidly progressive renal failure. The most common cause of death is uremia. The once dismal prognosis for this disease has been markedly improved by intensive *plasmapheresis*. This procedure is thought to be beneficial by removing circulating antibasement membrane antibodies as well as chemical mediators of immunologic injury. Simultaneous immunosuppressive therapy inhibits further antibody production, ameliorating both lung hemorrhage and glomerulonephritis.

Idiopathic Pulmonary Hemosiderosis

Idiopathic pulmonary hemosiderosis is a rare disorder characterized by intermittent, diffuse alveolar hemorrhage. Most cases occur in young children, although the disease has been reported in adults as well. It usually presents with an insidious onset of productive cough, hemoptysis, and anemia associated with diffuse pulmonary infiltrations similar to Goodpasture syndrome.

The cause and pathogenesis are unknown, and no antibasement membrane antibodies are detectable in serum or tissues. However, favorable response to long-term immunosuppression with prednisone and/or azathioprine indicates that an immunologic mechanism could be involved in the pulmonary capillary damage underlying alveolar bleeding. In addition, long-term follow-up of patients shows that some of them develop other immune disorders.

Polyangiitis With Granulomatosis

Previously called Wegener granulomatosis, this autoimmune disease most often involves the upper respiratory tract and/or the lungs, with hemoptysis being the common presenting symptom. Its features are discussed in Chapter