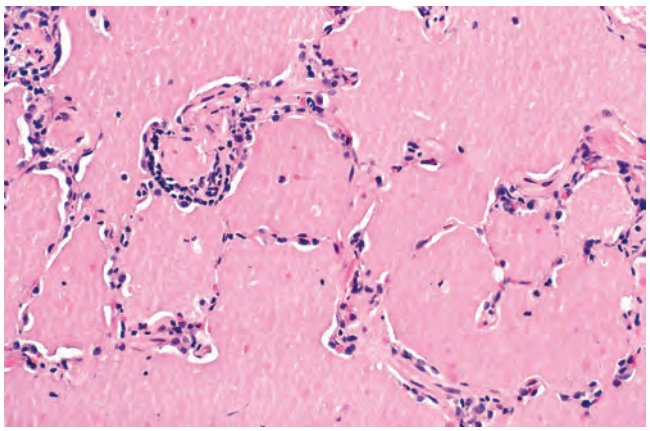

Figure 15-25 Pulmonary alveolar proteinosis. The alveoli are filled with a dense, amorphous, protein-lipid granular precipitate, while the alveolar walls are normal.

Adult patients, for the most part, present with cough and abundant sputum that often contains chunks of gelatinous material. Some have symptoms lasting for years, often with febrile illnesses. These patients are at risk for developing secondary infections with a variety of organisms. Progressive dyspnea, cyanosis, and respiratory insufficiency may occur, but other patients follow a benign course, with eventual resolution of the lesions. Whole-lung lavage is the standard of care and provides benefit regardless of the underlying defect. GM-CSF therapy is safe and effective in more than half of the patients with autoimmune PAP while therapy directed at the underlying disorder may be helpful in secondary PAP.

Surfactant Dysfunction Disorders

Surfactant dysfunction disorders are diseases caused by mutations in genes encoding proteins involved in surfactant trafficking or secretion. The mutated genes include the following:

- *ATP-binding cassette protein member 3* (*ABCA3*) is the most frequently mutated gene in sufactant dysfunction disorders. It is an autosomal recessive disorder and usually presents in the first few months of life with rapidly progressive respiratory failure followed by death. Less commonly it comes to attention in older children and in adults with chronic interstitial lung disease.
- *Surfactant protein C* is the second most commonly mutated gene in sufactant dysfunction disorders. It is autosomal dominant with variable penetrance and severity in 45% and sporadic in 55%. It has a highly variable course.
- *Surfactant protein B* is the least commonly mutated gene and is associated with an autosomal recessive form of sufactant dysfunction disorder. Typically, the infant is full term and rapidly develops progressive respiratory distress shortly after birth. Death ensues between 3 and 6 months of age.

MORPHOLOGY

There is variable amount of intra-alveolar pink granular material, type II pneumocyte hyperplasia, interstitial fibrosis and alveolar simplification. Immunohistochemical stains show the lack of surfactant proteins C and B in their respective deficiencies. Ultrastructurally, abnormalities in lamellar bodies in type II pneumocytes can be seen in all three; small lamellar bodies with electron dense cores are diagnostic for *ABCA3* mutation (Fig 15-26).

Diseases of Vascular Origin

Pulmonary Embolism and Infarction

Pulmonary embolism is an important cause of morbidity and mortality, particularly in patients who are bedridden, but also in a wide range of conditions that are associated with hypercoagulability. Blood clots that occlude the large pulmonary arteries are almost always embolic in origin. The usual source—thrombi in the deep veins of the leg (>95% of cases)—and the magnitude of the clinical problem were discussed in Chapter 4. Pulmonary embolism causes more than 50,000 deaths in the United States each year. Its incidence at autopsy has varied from 1% in the general population of hospital patients to 30% in patients dying after severe burns, trauma, or fractures. It is the sole or a major contributing cause of death in about 10% of adults who die acutely in hospitals. By contrast, large-vessel pulmonary thromboses are rare and develop only in the presence of pulmonary hypertension, pulmonary atherosclerosis, and heart failure.

Pathogenesis. **Pulmonary embolism usually occurs in patients with a predisposing condition that produces an increased tendency to clot (thrombophilia).** Patients often have cardiac disease or cancer, or have been immobilized for several days or weeks prior to the appearance of a

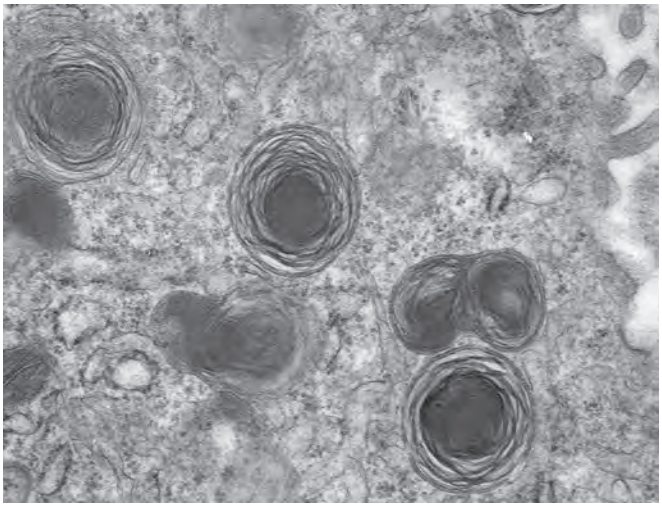

Figure 15-26 Pulmonary alveolar proteinosis associated with mutation of the *ABC3* gene. An electron micrograph shows type 2 pneumocytes containing small surfactant lamellae with electron dense cores, an appearance that is characteristic of cases associated with *ABCA3* mutations.

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