associated with an increased risk of lung cancer death for both women and men.

Silicosis

Silicosis is a common lung disease caused by inhalation of proinflammatory crystalline silicon dioxide (silica) that usually presents after decades of exposure as slowly progressing, nodular, fibrosing pneumoconiosis. Currently, silicosis is the most prevalent chronic occupational disease in the world. Both dose and race are important in developing silicosis (African Americans are at higher risk than whites). As shown in Table 15-6, workers in a large number of occupations are at risk, including individuals involved with the repair, rehabilitation or demolition of concrete structures such as buildings and roads. Less commonly, the disease occurs in workers producing stressed denim by sandblasting, stone carvers, and jewelers using chalk molds. Occasionally, heavy exposure over months to a few years can result in acute silicosis, a disorder characterized by the accumulation of abundant lipoproteinaceous material within alveoli (identical morphologically to alveolar proteinosis, discussed later).

Pathogenesis. Silica occurs in both crystalline and amorphous forms, but crystalline forms (including quartz, cristobalite, and tridymite) are much more fibrogenic. Of these, quartz is most commonly implicated. After inhalation, the particles are phagocytosed by macrophages. The phagocytosed silica crystals activate the inflammasome, leading to the release of inflammatory mediators, particularly IL-1 and IL-18. The relatively benign response to silica in coal and hematite miners is thought to be due to coating of silica with other minerals, especially clay components, which render the silica less toxic. Although amorphous silicates are biologically less active than crystalline silica, heavy lung burdens of these minerals may also produce lesions.

MORPHOLOGY

Silicosis is characterized grossly in its early stages by tiny, barely palpable, discrete pale to blackened (if coal dust is also present) nodules in the hilar lymph nodes and upper zones of the lungs. As the disease progresses, these nodules coalesce into **hard, collagenous scars** (Fig. 15-18). Some nodules may undergo central softening and cavitation due to superimposed tuberculosis or to ischemia. Fibrotic lesions may also occur in the hilar lymph nodes and pleura. Sometimes, thin sheets of calcification occur in the lymph nodes and are seen radiographically as **eggshell calcification** (i.e., calcium surrounding a zone lacking calcification). If the disease continues to progress, expansion and coalescence of lesions may produce progressive massive fibrosis. Histologic examination reveals the hallmark lesion characterized by a central area of whorled collagen fibers with a more peripheral zone of dust-laden macrophages (Fig. 15-19). Examination of the nodules by polarized microscopy reveals the birefringent silicate particles (silica is weakly birefringent).

Clinical Course. Chest radiographs typically show a fine nodularity in the upper zones of the lung. Pulmonary functions are either normal or only moderately affected early in the course, and most patients do not develop shortness of breath until progressive massive fibrosis supervenes.

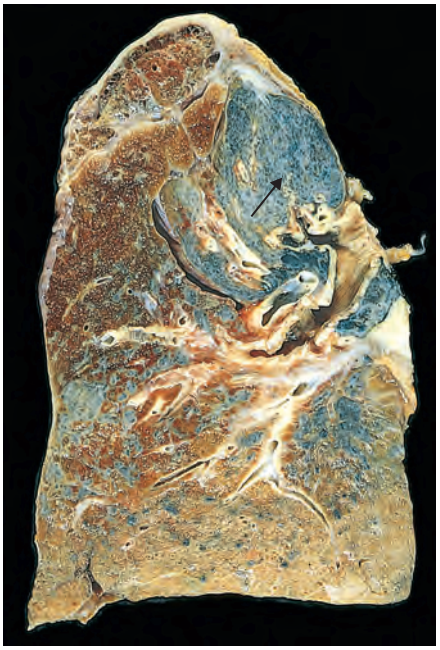

Figure 15-18 Advanced silicosis. Scarring has contracted the upper lobe into a small dark mass *(arrow)*. Note the dense pleural thickening. (Courtesy Dr. John Godleski, Brigham and Women's Hospital, Boston, Mass.)

The disease may continue to worsen even if the patient is no longer exposed. Silicosis is slow to kill, but impaired pulmonary function may severely limit activity. It is associated with an increased susceptibility to *tuberculosis*. This may be because crystalline silica inhibits the ability of pulmonary macrophages to kill phagocytosed mycobacteria. The onset of silicosis may be slow and insidious (10 to 30 years after exposure; most common), accelerated (within 10 years of exposure) or rapid (in weeks or months after intense exposure to fine dust high in silica; rare). Patients with silicosis have double the risk for developing lung cancer.

Asbestos-Related Diseases

Asbestos is a family of proinflammatory crystalline hydrated silicates that are associated with pulmonary

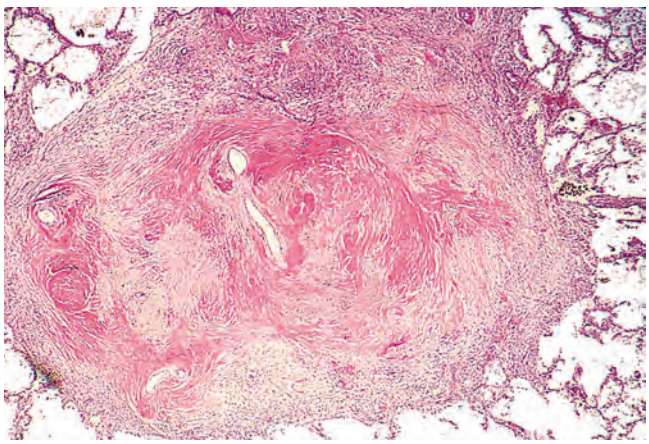

Figure 15-19 Several coalescent collagenous silicotic nodules. (Courtesy Dr. John Godleski, Brigham and Women's Hospital, Boston, Mass.)