fibrosis, carcinoma, mesothelioma, and other cancers. Use of asbestos is tightly restricted in many developed countries; however, there is little, if any, control in less developed parts of the world. Asbestos-related diseases include:

- Localized fibrous plaques or, rarely, diffuse pleural fibrosis
- Pleural effusions, recurrent
- Parenchymal interstitial fibrosis *(asbestosis)*
- Lung carcinoma
- Mesotheliomas
- Laryngeal, ovarian and perhaps other extrapulmonary neoplasms, including colon carcinomas; increased risk for systemic autoimmune diseases and cardiovascular disease has been proposed

An increased incidence of asbestos-related cancer in family members of asbestos workers has alerted the general public to the potential hazards of even low-level exposure to asbestos. However, the necessity of expensive asbestos abatement programs for environments such as schools with low, but measurable, airborne asbestos fiber counts remains a matter of contention.

Pathogenesis. **The disease-causing capabilities of the different forms of asbestos depend on concentration, size, shape, and solubility.** Asbestos occurs in two distinct geometric forms, *serpentine* and *amphibole*. The serpentine chrysotile form accounts for 90% of the asbestos used in industry. Amphiboles, even though less prevalent, are more pathogenic than chrysotiles, particularly with respect to induction of mesothelioma, a malignant tumor derived from the lining cells of pleural surfaces.

The greater pathogenicity of amphiboles is apparently related to their aerodynamic properties and solubility. Chrysotiles, with their more flexible, curled structure, are likely to become impacted in the upper respiratory passages and removed by the mucociliary elevator. Furthermore, once trapped in the lungs, chrysotiles are gradually leached from the tissues because they are more soluble than amphiboles. In contrast, the straight, stiff amphiboles may align themselves in the airstream and thus be delivered deeper into the lungs, where they can penetrate epithelial cells and reach the interstitium. Both amphiboles and serpentines are fibrogenic, and increasing doses are associated with a higher incidence of asbestos-related diseases.

In contrast to other inorganic dusts, asbestos can also act as a tumor initiator and promoter. Some of its oncogenic effects are mediated by reactive free radicals generated by asbestos fibers, which preferentially localize in the distal lung, close to the mesothelial layers. Toxic chemicals adsorbed onto the asbestos fibers also likely contribute to the oncogenicity of the fibers. For example, the adsorption of carcinogens in tobacco smoke onto asbestos fibers may be the basis for the remarkable synergy between tobacco smoking and the development of lung carcinoma in asbestos workers. Smoking also enhances the effect of asbestos by interfering with the mucociliary clearance of fibers. One study of asbestos workers found a fivefold increase of lung carcinoma with asbestos exposure alone, while asbestos exposure and smoking together led to a 55-fold increase in the risk.

As with silica crystals, **once phagocytosed by macrophages asbestos fibers activate the inflammasome and stimulate the release of proinflammatory factors and fibrogenic mediators.** The initial injury occurs at bifurcations of small airways and ducts, where asbestos fibers land, penetrate and are directly toxic to pulmonary parenchymal cells. Macrophages, both alveolar and interstitial, attempt to ingest and clear the fibers. Long-term deposition of fibers and persistent release of mediators (e.g., reactive oxygen species, proteases, cytokines, and growth factors) eventually lead to generalized interstitial pulmonary inflammation and interstitial fibrosis.

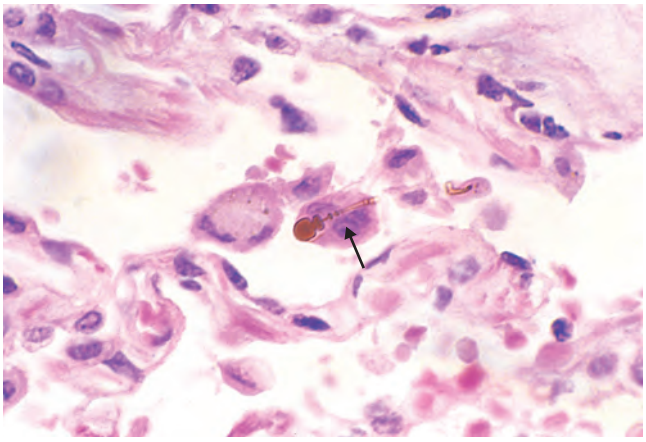

Figure 15-20 High-power detail of an asbestos body, revealing the typical beading and knobbed ends *(arrow)*.

MORPHOLOGY

Asbestosis is marked by **diffuse pulmonary interstitial fibrosis**, which is indistinguishable from diffuse interstitial fibrosis resulting from other causes, except for the presence of multiple **asbestos bodies**. Asbestos bodies are **golden brown, fusiform or beaded rods with a translucent center and consist of asbestos fibers coated with an iron-containing proteinaceous material** (Fig. 15-20). They arise when macrophages phagocytose asbestos fibers; the iron is presumably derived from phagocyte ferritin. Other inorganic particulates may become coated with similar iron-protein complexes and are called **ferruginous bodies**. Rare single asbestos bodies can be found in the lungs of normal people.

Asbestosis begins as fibrosis around respiratory bronchioles and alveolar ducts and extends to involve adjacent alveolar sacs and alveoli. The fibrous tissue distorts the architecture, creating enlarged airspaces enclosed within thick fibrous walls; eventually the affected regions become honeycombed. The pattern of fibrosis is similar to that seen in usual interstitial fibrosis, with fibroblastic foci and varying degrees of fibrosis, the only difference being the presence of numerous asbestos bodies. In contrast to coal workers' pneumoconiosis and silicosis, asbestosis begins in the lower lobes and subpleurally. The middle and upper lobes of the lungs become affected as fibrosis progresses. The scarring may trap and narrow pulmonary arteries and arterioles, causing pulmonary hypertension and cor pulmonale.

Pleural plaques, the most common manifestation of asbestos exposure, are well-circumscribed plaques of dense collagen (Fig. 15-21) that are often calcified. They develop most frequently on the anterior and posterolateral aspects of the **parietal pleura** and over the domes of the diaphragm. The size