in the case of other fibrogenic dusts, such as silica. This difference in clearance attributed to the greater cytotoxic effect of silica, which tends, therefore, to maintain an extracellular position (50), may explain why hilar node enlargement is a more consistent finding in association with silica exposure than in association with asbestos exposure (52).

Less is known about the penetration of ingested fibers through the wall of the gastrointestinal tract, although animal studies suggest that this does not occur (53), except in the face of a heavy load delivered directly into the stomach (40). What relevance this has to human disease, such as peritoneal mesothelioma, remains to be determined.

Once it has penetrated the lung, the dust appears to remain fixed, but may be remobilized, apparently even from dust macules or scars, the operative mechanism perhaps being episodes of pulmonary edema and/or infection (48). It is believed that such remobilization of dust may result in its excretion, a phenomenon that might explain the rare event of apparent regression of radiologic changes in the worker removed from exposure (Manfreda, Y.: Unpublished data). Alternatively, it may become resequestered and contribute to the extension of disease in the face of no further exposure.

Despite the fact that pleural reactions (effusion, fibrosis, and/or calcification and neoplasm) are common manifestations of asbestos exposure, there is little direct evidence as to how the asbestos gains access to the pleura, which presumably must happen to explain the pleural reactions. Asbestos bodies are rarely seen in the visceral pleura and have never been reported in plaques located in the parietal pleura of exposed persons, even though they may be readily found in the interstitial tissue of the same lung (54). By contrast, asbestos fragments have been found in mesotheliomas even without evidence of asbestosis or coated fibers in the lung (Hourihane, 5, p. 647). This has led to the suggestion that fibers that become coated in the lung are less mobile and less susceptible to lymphatic clearance than uncoated fibers. Thus, electron microscopic studies may reveal many more uncoated fibers in the pleura than anticipated from the scarcity of coated fibers. Alternatively, any fibers that are cleared to subpleural lymphatics may undergo dissolution more readily here than elsewhere in the lung. In any event, information that would shed light on this paradox might well lead to improved understanding of the factors underlying the pathogenesis of mesothelioma.

Coated Asbestos Fibers (Asbestos Bodies)

The coated asbestos fiber was recognized early in the 1900s, because of its characteristic appearance under light microscopy (55). It is usually a rod-shaped structure with clubbed ends, often beaded along its length, is yellow to brown in color, ranges in length from 10 to 30 μm and in thickness from 1 to 6 μm, and has a central, paler core. The coating, consisting of ferritin granules and an amorphous material, probably protein, varies in thickness from very thin to 5 μm (55–57).

On the basis of animal studies, coating is now believed to be an intracellular process and follows the engulfing of particles by macrophages to which they adhere (56). Several macrophages may fuse to engulf large fibers. It is while the fibers are surrounded by partially fused macrophages that coating begins (58). The fiber then becomes incorporated into intracytoplasmic vacuoles, and the first coating material appears to be some form of acid mucopolysaccharide (56). Iron in the form of hemosiderin then accumulates in the cytoplasm of the macrophage. Iron micelles, possibly derived from breakdown of hemoglobin, become subsequently incorporated into the phagosomes, and tend to concentrate around the fiber; eventually, there is clearing of ground substance (57). It is of interest that the process appears to be a progressive one, with the coating increasing with time and uncoated fibers becoming coated months or years after instillation (56); however, because the proportion of uncoated to coated fibers in human lungs appears to remain constant with time (49, 59), there must also be a parallel process of aging and dissolution of the coated fiber. There is some evidence that the coating of a fiber renders it nonfibrogenic. Why some particles become coated and others do not is not understood; however, size may be important, with the typical asbestos body developing only on large particles (greater than 5 μm) that cannot be completely engulfed by one macrophage (58).

It must also be emphasized that not all coated fibers seen in the lung have an asbestos core, and the process of coating is apparently used by the lung in response to a variety of other fibers encountered in the environment. These include glass and cotton fibers, diatomaceous earth, talc, graphite, and carborundum particles (10, 55).