

the fibrotic process, either mildly, giving the appearance of a milky covering to the fibrosis, or with widespread fibrosis and symphysis (116, 140). The hilar lymph nodes are not usually enlarged or otherwise affected (10, 142).

Conglomerate lesions of massive fibrosis, comparable to the progressive massive fibrosis of coal workers, occur in the absence of tuberculosis (Gough, 5, p. 368), but are rare, unless the exposure has been to mixed dust including talc (10, 143) or silica (142, 144). In addition, these lesions appear to have a predilection for the lower lobes (142, 144), unlike other forms of progressive massive fibrosis. The occasional solitary fibrotic lesion is seen, for which the term asbestoma has been used (145). Necrobiotic nodules associated with rheumatoid disease (similar to those seen with Caplan's disease in coal workers) are seen (146-149), but only rarely (10).

Microscopic appearances. In animal studies, early dust reactions include a desquamative alveolar response (Webster, 9, p. 117), a reaction that may have its counterpart in man (144, 150). In addition, there is one case report of desquamative interstitial pneumonia with asbestos bodies in the lung (150), and the view has been expressed that this is one end of a spectrum that ends with fibrosing alveolitis (151). An idea of the abnormalities in the early stages of fibrosis comes from examination of biopsy material, usually sought to establish a diagnosis of asbestosis (131, 145). The early reaction in the interstitial tissue resembles that of other forms of interstitial pneumonia, with mixed leukocyte infiltration of the alveolar walls, moderate numbers of phagocytes in the alveoli, and varying degrees of organization with fibrosis (131, 145). In some cases, the early changes are concentrated at the level of the respiratory bronchiole, where reticulin fibers, macrophages, and dust particles collect (10, 116), leading subsequently to what has been termed the basic lesion of asbestosis, namely, a peribronchiolar fibrosis (116). From here, the process extends outward to involve the surrounding alveoli, leading to diffuse alveolar wall thickening, with peribronchiolar and perivascular fibrosis (116). In an occasional case, the fibrosis remains almost exclusively peribronchiolar (144, figure 5), but the more usual picture is that of a diffuse fibrosis, involving the interstitium, frequently associated with areas of solid fibrosis, where laminated collagen may replace the entire parenchyma. Such areas may also show alveolar cell hyperplasia and sclerosis of vessel

walls (116). The presence of ferruginous bodies is to be expected, and electron microscopy is likely to reveal very large numbers of uncoated and very fine particles and fibers (152). The pathologic findings in workers exposed to amosite and crocidolite have been shown to be essentially similar to those associated with chrysotile exposure (Wagner, 8, p. 373).

Pathogenesis

Reactions at the cell level have already been discussed, and at the organ level are presumed to relate to the number of cells reacting, which in turn is believed to relate to the retained "dose" of asbestos dust and/or fiber. This appears to be true for mild and moderate fibrosis, respectively, in animals (62) as well as in man, in whom the response has been related to "dose" retained, as reflected by concentration of coated and uncoated particles in the lung tissue at autopsy (49); however, there does not appear to be further progression from moderate to severe fibrosis associated with an increase in dose (49, 62). It is, therefore, postulated that the progression from moderate to severe fibrosis is due to other factors, e.g., nonspecific inflammation, as suggested by Ashcroft and Heppleston (49) or possibly to self-perpetuating host responses, as suggested by Turner-Warwick (144). Thus, based on her observations that non-organic-specific autoantibodies, especially antinuclear antibodies (ANA), occur with only slightly greater frequency in exposed, compared to nonexposed, persons in the general population, and within exposed populations, with greater frequency in those with clinical disease than those without (153-155), Turner-Warwick proposes that ANA acts as an accelerator once the fibrosis has been initiated by a separate agent (Turner-Warwick, 7, p. 258). Such an explanation would fit the clinical observation that asbestosis may appear for the first time and progress long after exposure to dust has ceased. The possibility that genetic factors influence the response to exposure is suggested in one study in which the HLA-B27 occurred with greater frequency in asbestosis cases compared to the general population (156). There is also a progressive decrease in the total lymphocyte count with advancing fibrosis, and the suggestion has been made that the cellular immune mechanism is disturbed in asbestosis (157).

The progression from diffuse interstitial fibrosis to conglomerate fibrosis may, in the past, have been associated with tuberculosis (125),

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