9

ASBESTOSIS

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Asbestos is the name given to a number of naturally occurring silicates with the common property of great resistance to destruction by physical or chemical means. They have a fibrous configuration which allow them to be woven into cloth. The most frequently used varieare chrysotile ($3MgO \cdot 2SiO_2 \cdot 2H_2O$), which has a serpentine form occurs in partly separated bundles, and certain of the amphiboles, which occur as straight, needle-like fibers. These include crocidolite ($NaFe(SiO_3)_2 \ FeSiO_2 \cdot H_2O$) or blue asbestos, amosite ($FeMgSiO_3$), anthophyllite ($(MgFe)_2Si_8O_{22}(OH)_2$), and tremolite ($Ca_2Mg_5Si_8O_{22}(OH)_2$).

HISTORICAL ASPECTS

Anthophyllite fibers have been found in the clay of pots made in Finland four thousand years ago, and were presumably added to give increased strength to the finished article. Asbestos was used in classical times for weaving into funeral shrouds and into wicks for lamps. Pliny in A.D. 50 mentioned that the weavers producing wicks for the lamps of the vestal virgins wore masks to avoid inhaling the dust.[1] However, widespread production of asbestos started about one hundred years ago in Canada and Russia. The initial report of a case of asbestosis was by Murray in 1907,[2] and Pancoast and co-workers described the radiographic changes in 1917.[3] The detailed description of the disease followed in 1927.[4,5] An increasing awareness of the hazards of asbestos in Great Britain culminated in the report of Merewether and Price[6] which resulted in the introduction of safety measures in asbestos factories and in medical supervision of the workers. Nevertheless, increasing use of asbestos in many industries has greatly increased the numbers of workers at risk of the disease and the number of cases certified continues to increase annually.

Asbestosis, from Occupational Lung Diseases (1975)
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An increased risk of lung cancer among asbestos workers was reported by Merewether in 1947[7] and by Doll in 1955,[8] and was confirmed in the United States by Selikoff in 1964.[9] Furthermore, Wagner and his colleagues[10] reported in 1960 the association between asbestos exposure and development of the rare pleural tumor, *mesothelioma*. These effects of asbestos are considered in detail in Chapter 18.

PRODUCTION AND USES OF ASBESTOS

The major producers of asbestos are Canada, South Africa, and the U.S.S.R. Small amounts are produced in Vermont but fewer than a thousand workers are employed in the mining and milling of asbestos in the United States. The Quebec mines are the Western World's most important producers of chrysotile, the type that constitutes about 70 per cent of all commercially produced asbestos. Large amounts of chrysotile are also produced in South Africa, where crocidolite and amosite are also mined, and in the U.S.S.R. Anthophyllite comes only from Finland.

Asbestos is obtained from both deep and surface mines, and the process, which may include the use of drilling and explosive charges, is liable to generate a considerable amount of dust. In general, however, at this stage much of the asbestos is bound into the parent rock in clumps and this, together with the use of effective dust suppression, has made asbestos mining less hazardous than might be anticipated. The raw asbestos is then crushed in mills, usually at the mine, to release the fibers which may then be carded to produce material containing parallel fibers suitable for spinning or incorporating into asbestos products. These processes generate large amounts of dust; this is also true of the cleaning and maintenance of the machinery. Subsequently the asbestos is transported in plastic bags (jute bags, being porous, have now largely been replaced) to the users, where it may be woven into cloth, incorporated into cement or plastics, or simply used as the free fibrous or powdered form for filling and insulation.

Approximately a million tons of asbestos are used annually in the United States. Three quarters of this is used, for its fireproofing and insulating properties, in the construction industry, almost all of it previously incorporated into cements, tiles, felts, and so on. These may need to be cut, drilled, or polished, giving rise to dust in the process, though a more obvious hazard arises from the use of free asbestos. In the construction industry, about 8 per cent of the asbestos used is in the free form, a particularly hazardous technique being the use of sprays of insulating paints which generate large amounts of airborne asbestos. With recognition of the hazard, this use is becoming less frequent. Insulation, or lagging, of hot water and steam pipes and electric lines in factories, houses, and ships is commonly performed by covering them

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with asbestos material. Originally the asbestos was used in a powder form, being mixed with water by the lagger and applied while wet. This reduced the dust hazard at the time, though workmen later requiring access to these pipes have to strip off the old and dry asbestos first, thus liberating the dust. Plumbers, demolition workers, and power station workers may therefore be at risk of asbestos exposure, as may those who work in or repair the engine rooms of ships. Most pipe insulation now is done by cutting and applying prefabricated material, dust being liberated in the cutting.

Outside the construction industry, asbestos is used in the production of fireproof textiles, paints, plastics, paper, brake and clutch linings, and the linings of some furnaces and kilns. Risks of exposure occur both in the production and in the repair and destruction of these materials. Furthermore, workmen using asbestos may conceivably transfer the hazard home on their clothing to their families. Some general atmospheric pollution with asbestos may occur in the region of mills and factories, a factor that has been suggested as a cause of mesothelioma though not of asbestosis. It has also been suggested that asbestos may reach the atmosphere as a result of the wear of roofing tiles and brake linings, though studies of the latter have shown that the heat of friction in braking causes asbestos to be converted into the nonfibrous inert silicate, forsterite. However, the potential dangers of asbestos, and particularly the risk of mesothelioma after only low exposures, should allow no complacency wherever asbestos is used.

MORBIDITY AND MORTALITY

The frequency with which asbestosis occurs in the exposed population is probably dependent on the length, pattern, and degree of exposure and possibly on the size and type of fiber. For Great Britain the numbers of workers newly certified as suffering from asbestosis, a diagnosis based on clinical, radiographic, and physiological abnormalities, has been increasing steadily from twenty in 1951 to fifty-three in 1961 and 145 in 1971. There is little doubt that these figures represent a real increase in the prevalence of the disease. On the other hand, in a nonoccupational setting, Selikoff and co-workers[11] have failed to demonstrate a greater frequency of the finding of asbestos bodies in the lungs of routine autopsies between 1934 and 1967, suggesting that the general public is not at any greater risk of asbestos exposure now than in 1934, at least in New York City. They found asbestos bodies in the lungs of 48 per cent of subjects examined. For the United States approximately forty thousand workers are exposed to asbestos in the insulation industry and about fifty thousand in the manufacture of asbestos products. Much larger, but unknown, numbers are secondarily exposed by these men in working alongside them or further manipulating their products. The numbers exposed

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in demolition work are large but unknown. This latter occupation may result in intermittent exposures to high dust levels of often unknown types of asbestos. Clearly it is desirable to know the risk of development of asbestosis in these trades, particularly in relation to total dust exposures. Unfortunately no completely satisfactory data are available, though Selikoff and colleagues[12] have shown in a detailed study that 10 per cent of insulation workers show signs of disease within ten years of starting in the trade, but within twenty years this has increased to 50 per cent and after more than twenty years almost all workers have evidence of the disease. There is thus good evidence of a relationship of the development of the disease to the length of exposure.

The picture is complicated somewhat by the excess of deaths among asbestos workers due to carcinoma.[8] Newhouse demonstrated an excess mortality from neoplasms of lung, pleura, and other sites after sixteen years of exposure in all male workers and after very short periods in those heavily exposed.[13] Excess mortality from other respiratory disease was observed only among workers heavily exposed over many years. Similar findings have been demonstrated in female asbestos workers.[14] The workers in these studies had been exposed to a mixture of asbestos types. McDonald and co-workers showed an excess mortality of 20 per cent in workers with high dust exposures in the chrysotile mining industry in Quebec, two thirds of this excess being due to asbestosis and one third to carcinoma, mainly of the respiratory tract.[15] In about one fifth of workers it appears, therefore, that the effects of asbestosis may be partly masked by the very serious complication of lung carcinoma.

The incidence of asbestosis is increasing as use of asbestos is becoming more widespread. There is however, inadequate information on the relationship between development of the disease and total dust exposure. There is evidence of a falling prevalence of asbestosis between 1929 and 1957 in one factory in Great Britain from 80 per cent to 3 per cent after twenty years' exposure,[16] and it is reasonable to suppose that where dust suppression is vigorously pursued similar decreases will be recorded. The chief cause for concern is in the construction and insulation industries, where dust control and education of workers and management have proved less easy to achieve.

An encouraging finding is that the average age of death from asbestosis has gradually risen, from around thirty at the time of the original report of the disease to forty-one in the 1930's and fifty-seven in 1965.[17] It is to be hoped that further improvements in industrial hygiene will allow asbestos workers to achieve their normal span.

CLINICAL FEATURES

The initial symptom of asbestosis is shortness of breath on exertion, often accompanied by a dry cough. This symptom develops only after

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several years of progressive pulmonary fibrosis. The dyspnea progresses even when the patient is removed from contact with asbestos, usually resulting in the development of cor pulmonale and death within fifteen years of the onset of the disease. In the later stages, cough, sputum, and loss of weight are frequently present and the patient is often subject to recurrent respiratory infections. Before the advent of chemotherapy, tuberculosis and bronchopneumonia were responsible for a high proportion of deaths among patients with asbestosis, but this is no longer the case. The complications of bronchogenic, gastrointestinal, and pleural neoplasms are frequent causes of death, the patient's pulmonary fibrosis making these tumors even less likely to be resectable than in otherwise well patients.

Though in many instances asbestosis will progress even after cessation of exposure, there is some evidence that very early detection may prevent progression to a serious stage of fibrosis.[18, 19] The early detection of the disease is therefore a matter of great importance. Among workers exposed regularly to asbestos, the disease might be expected to develop within fifteen to twenty years, though this clearly depends on dust levels, cases having been recorded as progressing from first exposure to death within ten years. In some occupations, such as spraying, an exposure of as little as three years may result in the development of asbestosis.[18] The cornerstones of early diagnosis are clinical examination, chest radiography, and lung function testing, and all three have at times been claimed to give the most consistent chance of early, presymptomatic diagnosis.

Clinical Examination

The first physical sign of asbestosis is the presence of repetitive end-inspiratory crackles in the dependent parts of the lungs.[20,21] These auscultatory findings are probably related to abnormal lung deflation[22] and are indistinguishable from those heard in other forms of pulmonary fibrosis or those occurring transiently in pneumonia and pulmonary edema. It is possible, though not proved, that the height of lung over which the crackles may be heard is an indication of the severity of the fibrosis. As the disease progresses, tachypnea, cyanosis, and frequently clubbing of the digits may be found.[23,24] Movements of the chest wall may become restricted and latterly signs of cor pulmonale, with tall jugular "a" waves, a right ventricular heave, and epigastric third and fourth heart sounds may be detected.

Radiographic Features

The inhalation of asbestos is associated with changes both in the lung parenchyma and in the pleura. There has been difficulty in the classification of the parenchymal changes because they are predominantly

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linear and irregular as opposed to the characteristically nodular changes found in silicosis and coal worker's pneumoconiosis. However, as a result of the suggestions of Bohlig[25] and Sluis-Cremer and Theron,[26] international agreement has been reached on an adaptation of the I.L.O. classification to include the irregular and pleural lesions of asbestos exposure in a general classification of radiological changes in pneumoconiosis. The resulting UICC/Cincinnati classification[27] is described in Chapter 10 and the symbols of this classification are used in the following description.

As in any diffuse lung disease, the earliest radiographic signs of asbestosis are undefinable and little interobserver agreement may be obtained on their presence or absence. Such fine, irregular, linear shadows are classified as 0/1 or 1/0 for profusion and as s for type. Larger irregular and linear opacities are classified as t and so-called coarse blotchy lesions as u. Whether there is any pathological significance attached to the differentiation of these opacities is not known, but this classification does provide a basis for further epidemiological and physiological studies.

Increasing profusion of the irregular shadows is indicated by an increased number up the scale from 1/0, 1/1, 1/2, 2/1, and so on up to 3/4. At the stages between 2/2 and 3/3 the normal pulmonary vascular markings become obscured by the opacities. This classification avoids the use of terms implying pathological processes, such as fibrosis or honeycombing, and simply grades the x-ray according to the size and profusion of the irregular opacities present. Standard films of the irregular opacities are available, and these are clearly necessary in order to achieve any form of international reproducibility.

Early evidence of asbestosis consists of linear shadows of varying thickness between less than 1 mm. and 3 mm., most marked in the lower zones (Fig. 9–1). Increasing profusion of these markings results in a gradual obscuring of the vascular pattern and of the cardiac and diaphragmatic borders (Fig. 9–2). To a lesser extent nodular shadows may be present and these may occasionally be the predominant opacity at an early stage. Ultimately there is a reduction in radiographic lung volume and the formation of cysts or honeycombing, combined with gradual increase in the cardiac size and dilatation of the proximal pulmonary arteries as cor pulmonale supervenes (Fig. 9–3). Throughout the course of the disease, with relatively few exceptions, the opacities are more profuse in the lower lung zones.

Only very occasionally do large masses, similar to those in complicated coal worker's pneumoconiosis, occur. In asbestosis, however, they have no particular predilection for the upper zones, being found in all parts of the lung.[28] The rare cases described in relation to rheumatoid disease have been basal in distribution.[29, 30]

Additional radiographic evidence of asbestos exposure, though not

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Figure 9-1 A. Chest radiograph of dock worker engaged for twenty years in repair work in ships' engine rooms, showing early changes of basal asbestosis and loss of volume shown by depressed horizontal fissure in right lower lobe. (Courtesy of Dr. J. Lyons.) B. Close-up view of left base of A, showing fine linear opacities of type S.



Figure 9–2 Development of asbestotic fibrosis in a shipyard demolition worker. A, Radiograph taken in 1967, showing only minimal linear and nodular changes at the bases. B, Radiograph taken in 1973, showing extensive basal fibrosis and honeycomb change. (Courtesy of Dr. J. Lyons.)

necessarily of asbestosis, may be obtained from the presence of pleural thickening[31] and pleural calcification[32] (Fig. 9–4). Most characteristically, bilateral obliteration of costophrenic angles and calcification on the diaphragm and in plaques overlying the posterior ribs may be found in asbestos-exposed subjects. In some investigations, conducted in areas where there is a known source of asbestos exposure, pleural plaques demonstrated at autopsy have been invariably associated with asbestos bodies in the lungs.[32] However, other investigations in areas where there is less of an asbestos hazard have failed to demonstrate a greater frequency of radiographic pleural lesions in asbestos-exposed subjects than in the control population.[33] Clearly there are other causes of pleural thickening and calcification, such as previous empyema, hemothorax, or pleurisy. If these conditions have been excluded, asbestos exposure is the most likely cause of pleural abnormalities and this is particularly so if the changes are bilateral.

The complications of bronchial carcinoma and pleural mesothelioma are described in Chapter 18. However, it has been recognized in shipyard workers exposed to asbestos that benign pleural effusions of a transient nature may occur in relation to the industrial exposure.[34]

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Figure 9–3 The final stages of asbestosis in a shipyard worker. Both lungs show diffuse fibrotic change, obscuring the cardiac border. The heart is dilated, and clinically this patient was in cardiac failure. (Courtesy of Dr. J. Lyons.)

Pulmonary Function

The characteristic functional abnormalities in asbestosis are progressive reduction in vital capacity and total lung capacity, a normal or sometimes slightly raised residual volume and reduction in diffusing capacity for carbon monoxide. As the disease advances, an increase in minute ventilation and arterial hypoxemia occur. Increased static recoil pressures and a decrease in lung compliance may be found. Exercise tests show hyperventilation and arterial desaturation. These changes do not differ from those found in other industrial and nonindustrial forms of pulmonary fibrosis.[20, 35]

More important than the functional definition of advanced disease is its detection at an early stage. Diffusing capacity seems to relate most closely to the degree of disability from asbestosis,[24] and attempts to detect the disease at a presymptomatic stage have concentrated on measurement of this and of vital capacity. Studies of lung function in relation to radiographic category[36, 37] have suggested that decrease in vital capac-

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Figure 9–4 A. Large, noncalcified plaques (arrowed) in a shipyard worker exposed to asbestos. In addition, scant parenchymal asbestotic lesions are present. (Courtesy of Dr. J. Lyons.) B. Close-up view of the right lower zone of chest film of another subject. A well delineated calcified pleural plaque is present on the right diaphragm.

ity and increase in exercise ventilation are the most sensitive tests. The above studies compared the steady state diffusing capacity with the vital capacity and found the former less sensitive, but since it is affected by hyperventilation, the steady state test may not be as useful as the single breath technique. In contrast, other workers have demonstrated a fall in diffusing capacity at an early stage of the disease.[19, 20] Fall in lung compliance parallels that in vital capacity.[37]

Detailed studies of lung mechanics[38] in asbestos miners with normal chest radiographs have shown a reduction in vital capacity and an increase in static lung recoil pressures in those subjects with the heaviest exposure to asbestos. These subjects still had normal single breath and steady state diffusing capacities. Moreover, the more heavily exposed miners in general had lower maximal expiratory flow rates at a given transpulmonary pressure than the less heavily exposed group, indicating an increased upstream airways resistance requiring a higher pressure to achieve an equal flow. This work is in line with pathological studies that show that the early lesions in asbestosis are around the respiratory bronchioles, where they might be expected to cause obstructive disease of the small airways of the lung.[39]

The subject exposed to asbestos may therefore be expected to show a slight reduction in vital capacity and diffusing capacity and an increase in the static transpulmonary pressures at a relatively early stage in the disease process. His subsequent clinical deterioration will then be accompanied by further changes in these measurements, increase in resting and exercise ventilation, and decrease in total lung capacity. Arterial hypoxemia, initially on exercise and subsequently at rest, will appear, leading to the development of the complete picture of progressive alveolar-capillary block and eventually cor pulmonale.

Studies of lung function in subjects with pleural calcification but no asbestosis have shown no significant abnormalities.[20] This might be expected, as the lesions are always on the parietal pleura and therefore unlikely to cause any restriction of lung expansion.

PATHOLOGY

The important pathological features of asbestos exposure are pulmonary fibrosis, the presence of asbestos bodies and fibers, and pleural plaques. In addition, massive fibrosis and chronic pleural thickening may be present, as may the complicating diseases, bronchial carcinoma or mesothelioma.

Asbestos Fibrosis

Macroscopically the appearance is of gray-white fibrosis, most extensive in the lower zones of the lungs (Fig. 9–5). Retraction of unin-

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Figure 9–5 Whole lung (Gough) section from patient with asbestosis, showing fibrotic changes and cyst formation in the lower lobe, with less marked changes in the lingula.

volved bronchi and bronchioles may cause an appearance of honeycombing and sometimes bronchiectasis. Occasionally areas of massive fibrosis occur, and sometimes these cause retraction of, and bullous formation in, surrounding lung. This may be present in any part of the lung. The rounded nodules of Caplan's syndrome have occasionally been described[29, 30, 40] and seem to occur in the lower zones. The distribution of the fibrosis predominantly in the lower parts of the lungs in asbestosis helps in the differential diagnosis,[41] most other forms of pulmonary fibrosis being either more generalized, as in fibrosing alveolitis, or predominantly in the upper zones, as in sarcoidosis, tubercle, and allergic alveolitis. Further help in the differentiation may come from associated pleural thickening and calcification. Occasionally, however, cases of mixed asbestosis and silicosis may be found, as in some South African miners, where the fibrosis may be misleadingly distributed mainly in the upper zones.

Microscopically, the earliest lesion in both human and experimental asbestosis appears to be an alveolitis in relation to asbestos fibers deposited in alveoli, principally around respiratory bronchioles. These alveoli fill with large cells which electron microscopic studies have shown to be the phagocytic lung macrophages.[42] These cells, some of which disintegrate, become organized, at first by deposition of fibrin and subsequently by collagen formation. Initially the more peripheral air spaces are uninvolved but eventually the fibrosis spreads out into distal air sacs and alveoli. Eventually intrabronchiolar spread results in a widespread network of fibrosis through the lungs, more marked at the bases, with dilatation of the uninvolved small airways.[43] Histologically, massive fibrosis differs from the more usual type only in being more confluent and extensive.

Asbestos Fibers and the Asbestos Body

The feature that most clearly differentiates asbestosis from other forms of lung fibrosis is the presence of asbestos bodies. These structures are yellow-brown in color and measure about 20 to 150 microns in length and 2 to 5 microns in width (Fig. 9–6). They have clubbed ends and a segmented or beaded appearance.[44] They appear to develop, at least initially, within lung macrophages, where there is an aggregation of small, 60 Å, granules around the phagocytosed asbestos fiber. These granules probably consist of ferritin.[42] In addition, under the electron microscope there appears to be deposition of a lighter and nongranular material on the asbestos fiber. The coating of ferritin forms clumps and may eventually produce a body up to 5 microns thick.

Such asbestos bodies may be found in the sputum of people exposed to asbestos, though they do not necessarily indicate asbestosis. They may also be demonstrated to be present in a high proportion of normal

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Figure 9–6 *A*, Two asbestos fibers, approximately 100 microns long, coated by iron-protein complex, from sputum of patient exposed to asbestos dust. *B*, Electron micrograph (×5000) showing asbestos bodies and fibers in lung tissue. Note the relative thinness of the fibers as compared to the bodies. Many fibers are seen to be uncoated, and their diameters would put them beyond the power of resolution of light microscopy.

lungs at routine autopsy,[45] by the use of ashed sections or special concentrating techniques, though routine hematoxylin and eosin staining reveals far fewer. There has been some dispute as to whether asbestos fibers invariably form the core of these bodies, as many other potentially respirable vegetable and mineral fibers may be found in the atmosphere.[46] However, electron microscopic studies are suggestive that amphiboles, though rarely chrysotile, are present in the center of these bodies.[47, 48] Studies of the frequency with which asbestos bodies may be found in the general autopsy population have shown no increase over thirty years in New York,[11] though there is evidence of an increase in relation to cumulative increase in asbestos usage in Britain.[47] These differences may be related to differences in the amount of bonded, as opposed to potentially free, asbestos constituting the increase in usage.

Histological studies in patients with asbestosis show asbestos bodies aggregated together in areas of fibrosis (Fig. 9–7) and elastic staining can demonstrate that these were originally intra-alveolar.[43] Moreover, in areas of fibrosis, naked asbestos needles are also found, and are most easily demonstrated by polarized light. These average around 0.5 micron in diameter and 15 microns in length. They are more numerous than was originally suspected on the basis of light microscopy and can be shown in regions of fibrosis where asbestos bodies are not demonstrable. It is likely that the coating of fibers to form asbestos bodies renders them less liable to provoke fibrosis.[49] Experimental studies on guinea pigs show that inhaled asbestos dust causes fibrosis whereas asbestos bodies do not.[50]

Pleural Plaques and Calcification

The pleural plaques associated with asbestos exposure have a characteristic distribution. They are found predominantly on the parietal pleura, though some fibrous pleurisy may be present on the visceral pleura. They tend to be more frequent in the posterolateral and basal parts of the pleura and on the central tendon of the diaphragm, and are distributed beneath the surface of the ribs, sometimes spreading from this site over the intercostal spaces (Fig. 9–8). They are associated with exposure to crocidolite, amosite, and anthophyllite but only with certain forms of Canadian chrysotile.

Histologically, these plaques consist of fibers of collagen arranged parallel to the surface. They are covered with an intact lining of mesothelial cells, though this cannot usually be demonstrated in postmortem specimens, and the deepest layers contain some fibroblasts and sometimes a few lymphocytes and plasma cells[51] (Fig. 9–9). Calcification, where present, occurs in the center of the plaque on degenerated collagen and is probably related to the age of the lesion. Asbestos bodies are not found in the plaques, though occasional asbestos fibers have been seen.

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Figure 9–7 A. Low power photomicrograph of lung of patient with severe asbestosis, showing masses of asbestos bodies and fibers situated in air spaces distorted by fibrosis. *B*. Medium power photomicrograph of lung from an early case of asbestosis, showing relatively few asbestos bodies in a focus of interstitial fibrosis.



Figure 9–8 Pleural plaques on the central tendon of the diaphragm of a subject who had died of myocardial infarction but who had a history of exposure to asbestos in the building trade.

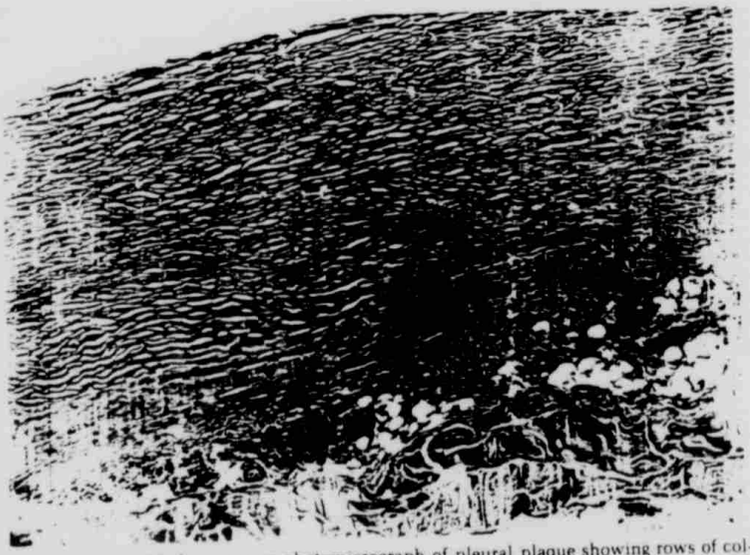


Figure 9–9 Medium power photomicrograph of pleural plaque showing rows of collagen fibers lying parallel to the surface. The deeper layers contain a few lymphocytes and plasma cells.

These observations have led Thomson[51] to conclude that pleural plaques are due to a hypersensitivity reaction to asbestos fibers which have reached the pleura by piercing lung tissue under the influence of gravity. It is likely that the aerodynamic properties of asbestos particles also play a role in determining whether they will reach the pleura and whereabouts in that tissue they are deposited. They become arrested only when they reach impenetrable tissue, such as bone or the diaphragmatic tendon, where they set up a mild chronic inflammatory reaction that leads to fibrosis.

Studies in Finland and South Africa have failed to show a definite relationship between pleural plaques and the development of mesothelioma. Indeed in some areas there seems to be an inverse relationship between them. It seems likely that these are two separate processes, though both associated with asbestos exposure.

PATHOGENESIS

Asbestos Inhalation

At first sight it seems surprising that fibers of 20 microns or so in length are found in the alveoli. However, it has been shown that the falling speed of a fiber is proportional to the square of its diameter, and length is less important. The falling speed of a particle is the factor of importance in determining whether the particle will be deposited in the larger airways by gravity or inertial impaction.[52] Only in the smallest airways does fiber length become important, resulting in interception of fibers at the level of the respiratory bronchioles.

Of the two major types of asbestos, the amphiboles (crocidolite, amosite, anthophyllite) are needle-like in shape, normally of less than 3 microns in diameter, and penetrate deeply into the lung (Fig. 9–10). More of these fibers are retained in the lungs of experimental animals than of chrysotile, which has a serpentine configuration and, usually occurring in partly joined bunches, a relatively higher effective fiber diameter. Timbrell,[52] using hollow lung casts sawn off at the respiratory bronchiole level, has confirmed that the amphiboles penetrate to this level in much larger amounts than chrysotile. This work has implications in regard to the relative toxicity of different forms of asbestos in humans and in particular to the development of mesothelioma (see Chapter 18).

Toxicity of Asbestos

The asbestos fiber, having reached the respiratory bronchiole and the alveoli at that level, appears to excite a lung macrophage response.

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Figure 9–10 Electron micrographs of U.I.C.C. standard samples of asbestos. ×3750. A. Crocidolite. B. Chrysotile.

Illustration continued on opposite page.



Figure 9–10 (*Continued*) C. Amosite. D. Anthophyllite. (Courtesy of Dr. V. Timbrell and Mr. M. Griffiths.)

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Fibers may be demonstrated engulfed in macrophages before the development of fibrosis, but the mechanisms provoking the fibrosis are still unclear. Three important mechanisms have been suggested.[53]

(1) The mechanical theory: This suggests that physical irritation by the sharp asbestos fiber causes alveolar inflammation and fibrosis. Failure to produce fibrotic lesions with similar but inert fibers such as fiberglass[54] is evidence against this theory.

(2) The chemical theory: This supposes that gradual solution of the asbestos fiber allows silicic acid and metallic ions to reach the tissues where they initiate a fibrogenic response. While asbestos is undoubtedly soluble, and, on the basis of studies of the amount of mineral in asbestos lung, more so than silica or coal, this theory has failed to gain general acceptance. It has been shown that chrysotile is more soluble yet less fibrogenic than other forms of asbestos and moreover that synthetic amorphous magnesium silicate, while chemically closely similar to chrysotile, fails to produce fibrosis when injected intratracheally into animals.[54]

(3) Autoimmune theories: These suggest that asbestos fibers when digested by lung macrophages cause the production of abnormal globulins or the liberation of tissue components not recognized as self. However, evidence for an immunological mechanism, in terms of the demonstration of antibodies of the rheumatoid type or of the type demonstrable by immunofluorescence, is not convincing.

On the whole it seems most likely that destruction of phagocytes by ingested asbestos fibers provides the initial stimulus to fibrosis. The initial stage may depend on one or a combination of chemical, physical, or immunological mechanisms, while the final stage may depend on the liberation of substances that stimulate fibrosis. Lipids and lipoproteins have been mentioned as possible agents.[53] Further experimental work is necessary before the answers will be known.

PREVENTION

The essential factor in preventing asbestosis is control of the amount of asbestos to which workers are exposed. There is evidence from epidemiological studies that both asbestosis and lung cancer are dose-related diseases, and the British Occupational Hygiene Society published hygiene standards for chrysotile asbestos exposure in 1968.[55] These were based on estimated dose-response curves relating to the development of basal crackles in response to exposure to chrysotile in the processing of asbestos. A standard of not greater than two fibers per cubic centimeter was estimated to be likely to produce early signs of asbestosis in fewer than 1 per cent of workers exposed over 50 years. It was

recommended that no worker be exposed to more than one hundred fiber-years per cubic centimeter and that additional precautions be taken in the case of necessary intermittent exposures to higher fiber levels. For counts over ten fibers per cubic centimeter, an approved and properly fitted mask should be worn, and for counts over forty fibers per cubic centimeter pressure-fed breathing apparatus should be provided. These dust standards have subsequently been recommended by the United States Public Health Service. A standard method for counting fibers, the membrane filter method, is recommended. This counts fibers of greater than 5 microns in length. If other methods are used they should be related to this one.

Control of dust levels in mining and processing of asbestos, as well as in its use, may also imply discharge of fibers into the outside atmosphere. Control of the effluent air is also therefore necessary, and similar dust monitoring should be applied here.

The clothing of asbestos workers should be carefully controlled. Overalls and caps should be provided, they should be dusted by vacuuming, and they should be collected in nonporous bags by the industry and laundered in a place where the hazard is known and controllable. All cleaning of floors and machinery should be by vacuum and not by sweeping.

The data on the effects of other forms of asbestos on humans are insufficient to produce separate standards,[34] except insofar as crocidolite is known to be associated with a higher risk of mesothelioma. This material therefore needs to be treated with greater caution and its use avoided as far as possible. Indeed, it would seem reasonable to continue a search for suitable inert substitutes for asbestos wherever they can be introduced.

DETECTION OF ASBESTOSIS

All workers regularly exposed to asbestos should have a preemployment examination including a respiratory history, chest radiograph, and lung function tests. These should include at least vital capacity and ideally also diffusing capacity for carbon monoxide. They should subsequently be reexamined at two year intervals and attention paid primarily to the development of basal crackles and changes in the radiograph. Changes in lung function must be related to the expected change with age. After ten years' employment the employee should be examined annually. All asbestos workers should be made aware of the potential hazard of the material, and, in view of the multiplicative dangers of cigarettes and asbestos, should be advised repeatedly not to smoke.

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MANAGEMENT

It is not established whether removal of a worker from exposure at the earliest signs of the disease will prevent progression. However, the chances of arresting the process must be greatest at an early stage and any person in whom the disease is detected should be removed from further exposure to asbestos. There is no evidence that steroids affect the course of the disease,[56] though no controlled trials of this treatment have been reported in early cases, and treatment must therefore be supportive. The patient should obtain industrial injury compensation and this should be reviewed regularly as his disability increases.

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