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FIBROGENIC DUSTS • 3

ASBESTOS

Disease related to inhalation of mineral dusts of asbestos appears to be the occupational illness of the 1960s, very like beryllium poisoning in the 1940s and 1950s. There is recorded evidence that the fire-resistant properties of the silicate asbestos were known to Plutarch (A.D. 70) who records its use in royal garments for burial rites. Charlemagne was said to own a tablecloth made of asbestos, cleaned by passage through fire (Hunter, 1969, p. 1009).

Industrial use of geologically different forms of asbestos are summarized in the following list:

Heat insulation	Air filtration
Brake linings	Paint filler
Electrical wire insulation	Shingles, asbestos boards
Pipe and furnace fitting	Pump packing
Asbestos textiles—clothing, blankets	Fireproofing steel beams in the construction industry
Vinyl asbestos tile	Laboratory hood construction

The exact composition of mineral dusts referred to as asbestos for commercial use and so inhaled by workers or city dwellers may be difficult to discover. The geologist's terminology is very different from that of industry and may change with new discovery. At present the industrially used forms of asbestos are named chrysotile, anthophyllite, amosite, and crocidolite. These chemically different silicates contain varying amounts of iron, chromium, calcium, sodium, magnesium, nickel, silicon dioxide, and water. Because asbestos occurs in the earth with other minerals and chemicals, the recorded disease may, in fact, be due to a mixture of inhaled material. Further, due to fluctuations in cost, demand, and disruption of supply by war, as well as the discovery of new uses, the precise character of the total asbestos dust exposure in an individual worker-patient, or a group thought to be similarly exposed, may be impossible to assess accurately in retrospect. For example, New England shipyard workers studied by HLH in the 1960s were found to have worked with three forms of commercially used asbestos in the course of removing old insulation from ships' boilers and pipes (an operation called lagging).

Another important problem far from settled is whether asbestos fibers acting as mechanical irritants deep in the lung are alone responsible for disease (Smith, Hubert, Badollet, 1972). Finely divided dust generated by any uncontrolled dry operation such as bagging, milling, or cutting asbestos insulation may, when inhaled, act as a chemical provoking fibrosis and/or neoplasia (Enter-

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line and Henderson, 1973). Evidence that this is true is supported by the finding that in one well-ventilated pipe covering shop a significant number of workers developed asbestosis and lung malignancy even though the asbestos fiber count in the air was below the then acceptable limit (Murphy et al., 1971).

There is a vast and increasing literature on the subject of asbestos-caused illness. The first case of asbestosis was reported in 1907 in England by Murray. This was followed by similar reports from a number of European countries and later reports in the United States, summarized in the Public Health Bulletin of 1938. Merewether (1956) in the 1930s first reported from England the risk of bronchiogenic carcinoma in men with asbestosis. The truly impressive increase in lung malignancy was confirmed by Lynch and Cannon in the United States (1948). Further publications from England in the 1950s established the carcinogenic behavior of asbestos (Gloyne, 1951; Doll, 1955). A single report from the United States (Isselbacher et al., 1953) suggested that, since the asbestos millworker whose case was presented was a heavy smoker, the malignancy was the result of two carcinogens—asbestos dust and tobacco. In 1960 Wagner et al. of South Africa published their now well-confirmed finding of malignant mesothelioma of pleura in workers and neighbors in asbestos mining communities. Kiviluoto (1960) published the remarkable x-ray finding of pleural plaques, confirmed by Muerman (1966) at autopsy in Finnish populations without associated illness. Fletcher (1972) found a significant increase in what he called lung deaths correlated with evidence in life of pleural plaques seen on chest x-ray.

Knowledge in all parts of the world of human illness due to asbestos and studies of the mineral dust, its character and biological behavior, are to be found in the published papers of an international symposium held in 1964 (Biological Effects of Asbestos, 1965). At this meeting, Gilson of the United Kingdom made a significant interpretation of accumulated experience (1965). He pointed out that a decrease in the amount of asbestos in workroom air acts to control the occurrence of pulmonary fibrosis and reveals a significant increase in asbestos-related lung cancer. At still lower doses, the malignant mesothelioma associated with certain asbestos exposures occurs. Several key facts are missing and great research effort is currently directed to their solution (Editorial: Harrington, 1971; Wagner et al., 1971; Gibson, 1973)— for example, it is not yet known which geologic forms of asbestos, from what natural source, cause malignancy and at what dose. Does asbestos cause malignancy without a second potentially active carcinogen—for example, cigarette smoking, chemicals such as nickel or the hy-

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drocarbons derived from the earth where asbestos is mined as suggested by Harrington (1965)? Do asbestos workers suffer a risk of gastrointestinal neoplasm, as Selikoff's group reports (1964)? The International Union Against Cancer is at work on the epidemiology, and a group under J. C. Gilson of the United Kingdom is at work on classification of x-ray abnormalities of asbestos workers for international use. Government sponsored groups in the United Kingdom and South Africa and industry and union supported groups in Canada and the United States are active in research. Unions and industry (Wegman, Theriault, Peters, 1973) involved with asbestos exposures are working on techniques for control of the risk (Brodeur, 1972; Selikoff, Churg, Hammond, 1965). Study of the literature to date is confusing, and it is difficult to present dependable consistent clinical, x-ray, pathologic, lung function findings of asbestos-related disease. This is due, in part, to the fact that recorded reports rarely supply the character and duration of the exposure to asbestos (Gibbs and Lachance, 1972).

clinical syndromes

The onset of asbestosis is usually gradual, characterized by the worker's awareness of dyspnea on exertion. Because this is so, and since the fibrogenic effect of asbestosis is progressive, there is an apparent delay in onset from last exposure, making the diagnosis more difficult. Dyspnea increases in severity with time and proves to be the chief cause of disability. Even in the absence of infection, a nonproductive cough may be troublesome. In some reported series, clubbing of the fingers is an early sign, presenting before shortness of breath. Pleuritic pain is common; hemoptysis, rare. On auscultation many cases of asbestosis are found to have persistent dry rales at both bases, referred to as asbestotic rales. As the disease progresses, such rales may be heard more widely, but rarely above the tip of the scapulae. These rales are thought due to bronchiectasis, caused by the local action of asbestos fibers. Such fibers are long, but small in diameter and act as local irritants in fine bronchioles, favoring continuing low-grade infection. It is not usual to hear a pleuritic rub. If, as is frequent, there is thickened pleura—or in late stages, emphysema—breath sounds are decreased. If pulmonary fibrosis exists alone, breath sounds are increased.

The patient may first visit the physician after the abrupt onset of severe dyspnea because of lung collapse due to an asbestos-induced tumor. Isselbacker et al. (1953) reported the case of an asbestos worker who complained chiefly of chronic backache, a symptom not unusual but not easily recognized as due to asbestosis. The patient, an asbestos textile worker, presented with

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marked clubbing, cyanosis, cough and dyspnea, all hardly noticed by the sick man because of their gradual onset and slow progression and thought by him to be due to heavy cigarette smoking. At autopsy, advanced pulmonary fibrosis in all lobes was found with a striking number of so-called asbestos bodies reflecting exposure, together with a bronchial malignancy with metastasis to the spine.

The variation in clinical findings is dependent on duration, intensity, and quality of exposure to asbestos (McDonald et al., 1972; Hardy, 1965). As in all chronic illness, the patient's reaction to his complaints has much to do with the clinical picture when he first decides to seek medical help. In occupational disease, loss of job, retirement age, and compensation claims process may influence the patient's action and hence the signs and symptoms a doctor has to deal with in making a correct diagnosis. As asbestosis progresses, all the signs of chronic lung illness appear, including anorexia, weight loss, secondary infection difficult to control, dyspnea severe enough to cause orthopnea, and right heart involvement. In cases of asbestos with malignancy, chest pain usually becomes intractable. Malignant pleural mesothelioma causes pleural effusion leading to collapse of lung and, if peritoneal mesothelioma is present, severe ascites and cachexia occur. In striking contrast are Finnish reports of plaques of parietal pleurae and diaphragm causing no symptoms or measurable disability (Muerman, 1966).

A number of groups of cases of asbestosis have been reported with tuberculosis as a complication of the disease. Such reports belong to past experience when acid fast infection was common. Secondary infection is so usual in asbestosis that it is likely that an occasional case will suffer tuberculous infection in areas where this disease is still common. Caplan's syndrome, an unusual way of handling dust in the lung of those suffering rheumatoid arthritis, was first reported in Welsh coal miners. Caplan's syndrome, considered a genetically determined pathologic response, has been reported in cases of asbestosis (Morgan, 1964; Solomon, et al., 1971).

Asbestos corn or warts are reported. These are increases in skin horny layer stimulated by the local action of asbestos fibers introduced traumatically. These warts carry no known pathological change leading to disability.

Reports in the literature do not agree on whether or not the pulmonary fibrosis of asbestosis progresses once exposure has stopped. On balance and judging from HLH's experience, if the dose of asbestos that reaches the lower respiratory tract is large enough to excite pathologic response and great enough to cause

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measurable lung function abnormality, the asbestosis becomes progressive (Murphy et al., 1972). It may be that infection, easily established in the lung of asbestosis, explains the progression to increasing fibrosis and varying degrees of emphysema, which in turn lead to right heart strain. Prior to control of asbestos dust in industry, the chief cause of death was cor pulmonale. Wyers' 1949 report and the 1966 publications of Kleinfeld et al. are helpful clinical reviews of asbestosis.

chest x-ray changes

Review of the many reports of roentgenologic findings due to excessive asbestos exposure underlines the wide variety of chest x-ray abnormalities (Lanza, 1938, pp. 166–190; Hurwitz, 1961; Rossiter et al., 1972). Such diversity is undoubtedly related to the character of the inhaled asbestos either alone or with another dust of fibrogenic potential, plus changes produced by complicating infection or emphysema in long-standing disease.

In individual cases there may be no evidence of asbestosis by x-ray even though clubbing is seen, lung function study shows measurable disability, and an experienced observer detects fine dry rales at the bases. In some reported series, thickened pleura is seen without visible parenchymal involvement. This is usually bilateral in contrast to the unilateral change due to emphysema, hemothorax, tuberculosis. The usually reported chest x-ray picture of asbestosis alone is of bilateral density involving the lower third of the lung initially, giving what is referred to as a "ground glass" appearance. As the disease progresses, especially if exposure continues, more and more of the lung is involved but apices are spared. The shadow of the right heart increases in size as the disease progresses. Experienced observers consider that blurring of the heart is an early sign of disease in parenchyma. Reports of x-ray findings include scattered nodular densities of varying size shadows consistent with Caplan's syndrome, emphysema, pleural effusion, infection, or the development of malignancy. Except in groups of asbestos workers whose exposures are well documented, x-ray findings can rarely be diagnostic. In contrast, the finding of pleural effusion (with or without pulmonary infiltrates associated with a history of asbestos exposure is practically pathognomonic of malignant mesothelioma. Gaensler and Kaplan (1971) report pleural effusion without malignancy as an early sign of asbestosis. Sluis-Cremer and Webster (1972) published nine cases of pleurisy with effusion—some with and some without asbestosis. Such pleural reactions may occur without asbestosis or malignancy. These authors report a high incidence of thickened visceral pleura at autopsy in asbestos-exposed persons. In sum-

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mary, pleural reaction may correlate with the kind of asbestos inhaled but does not at present offer prognostic significance.

lung function abnormalities

Dependable studies of lung function of asbestos workers complaining of dyspnea date from 1960 when a defect in gas diffusing capacity was reported (Williams and High-Jones, 1960). Since this date a number of studies have documented the changes due to the pulmonary fibrosis of asbestosis. Lung volume is reduced. If the pleural response is marked, expansion of the lung is severely limited, easily documented by measurement of vital capacity. Decrease in diffusing capacity and increase in alveolar-arterial oxygen difference have been so often discovered to be associated with disabling asbestos effect, even in the absence of x-ray changes, that they are considered an essential finding in the diagnosis. As the disease worsens, ventilation-perfusion abnormalities and decrease in pulmonary compliance are found as indices of pathologic changes of asbestosis and readily explain the patients' complaint of dyspnea on the slightest effort (Kleinfield et al., 1966a; Gandevia, 1967; Becklake et al., 1972).

pathologic changes

Pathologic changes due to inhalation of asbestos fibers and dust vary with quantity and kind of mineral. Benign pleural plaques first described in Finland by Meurman (1966) in parietal pleura are located at sites of greatest respiratory movement. These plaques are found to be collagenous connective tissue with secondary calcification without lung fibrosis, although asbestos bodies are present in the lung. The pathologic changes of asbestosis seen in workers is of itself a nonspecific pulmonary fibrosis, its severity correlated with exposure. Spencer (1962, pp. 341–345) describes a honeycombed effect in affected areas of the lung caused by emphysematous air sacs or greatly dilated bronchioles. According to Lynch and Cannon (1948), the initial reaction to asbestos particles forced into respiratory bronchioles and alveoli is edema, followed by chronic changes due to the action of phagocytes attacking the mineral dust. Ultimately, interstitial fibrosis leads to disruption of normal anatomy, leaving asbestos bodies, macrophages in the wall of involved alveoli. In all autopsy reports of chest disease due to asbestos, the parietal, and in severe cases the visceral, pleura are thickened. Similar involvement of diaphragm and pericardium are reported. While it has not as yet proved useful as a diagnostic tool, the finding of hyaluronic acid in asbestos-caused malignant mesotheliomas and in pleural fluid is of great interest (Wagner et al., 1960).

Epidemiologic knowledge has confirmed the fact that bronchiogenic carcinoma and malignant mesothelioma are significant

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risks in those exposed to unknown quantities of certain forms of asbestos (Wagner et al., 1971). In Canada, for example, where only chrysotile occurs, there is only a slight increase in bronchiogenic carcinoma associated with heavy exposure, but no cases of mesothelioma. Malignant mesothelioma has been reported to involve not only pleura but peritoneum. In individual asbestos workers, asbestosis and bronchial carcinoma or malignant mesothelioma may occur together. There are two reports from the United States of a significant increase in gastrointestinal malignancy in workers exposed to asbestos (Mancuso and Coulter, 1960; Selikoff et al., 1964; Smith, 1973). Newhouse and Thompson (1965) report the occurrence of mesothelioma in neighbors. This important and fascinating knowledge is to be found in the published report of an international meeting on the subject (Biological Effects of Asbestos, 1965). The report of Wright (1969) and the work of a Canadian group are evidence of the accumulating progress in the study of harmful effects of asbestos. Newhouse et al. (1972) studied the medical records of 900 female asbestos workers. They found an excess of deaths due to diseases of lung and pleura. Duration and intensity of exposure were of definite importance, but effect of cigarette smoking was not. Enterline and Henderson (1973) have shown that exposure to chrysotile and crocidolite asbestos in combination in the manufacture of asbestos cement pipe is a significantly greater cancer risk than exposure to chrysotile asbestos alone. Selikoff, Hammond, and Churg (1972) have published a report suggesting that amosite alone carries a significant hazard of malignancy. There is not general agreement that the workers studied by these authors were not exposed during some of their work with asbestos to one or more different types of asbestos dust or fibers. The point is currently (1973) important since fear of the cancer potential of crocidolite has made industry change to amosite. There is no doubt that amosite causes asbestosis since the fibers remain longer in the lung and are fragile, hence readily fractured to respirable size. In summary, with present knowledge it may be said that chrysotile can be mined and used safely with engineering control. Crocidolite is a serious hazard even in small doses, especially in combination with chrysotile and/or amosite. The threat of malignant mesothelioma from amosite exposure alone is at this date unknown (January, 1974), while the risk from crocidolite is definitely established.

asbestos bodies

Asbestos bodies, also called ferruginous or curious bodies in the past, and the presently increasing literature on the subject are of great importance in the diagnosis of asbestos disease.

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Asbestos bodies appear in various shapes. Some of these are as long as 75μ and are found in lung, sputum, and feces. Bodies of similar appearance are due to talc inhalation. These bodies appear brownish or black in color, often dumbbell in shape. The protein gel coating is twice as thick at the ends of the asbestos fiber as in its length, accounting for the dumbbell shape. Eventually the asbestos fiber disintegrates in tissue. Asbestos bodies are reportedly not found in diseased pleura. Activity of the macrophages in trying to engulf the asbestos fiber results in an iron-containing protein coating which is readily stained by Prussian blue or other stains with an affinity for iron. Discovery of asbestos bodies in the lungs of city dwellers, reported by Thomson (1965), led to the suggestion that rise in rates of lung malignancy in city dwellers might be related to asbestos from brake linings in street dirt. Further studies show that similar ferruginous bodies were present in lungs of those who died before the time of heavy motor traffic. The finding of asbestos bodies in sputum or lung biopsy proves exposure only.

treatment

There is no specific therapy for asbestosis. Control of respiratory infection may influence prognosis. Steroids have been tried without success. Because of the gas diffusion defect, the use of oxygen has proved helpful in control of symptoms. A single case of severe advanced asbestos-caused pleuritis was temporarily helped by surgical removal of thickened pleura.

Study of old and new reports of asbestosis makes it clear that engineering control must be strictly applied to workroom levels of both fiber and dust. The safe levels are constantly changing. While there are no entirely convincing studies to prove the point, a worker with recognized asbestosis should be urged to leave such exposure. This recommendation is based on the fact that clinical experience shows the pulmonary fibrosis of asbestosis to be a progressive disease. Because there are to date no reports of asbestos-related malignancy in nonsmokers, it is especially important for an asbestos worker to stop smoking.

control

The safe level of asbestos (so-called TLV) is continually being revised downward (Christensen, *Toxic Substances*, 1973). The most recent (1973) printed figures for all types of asbestos fibers, 5 fibers per ml greater than 5 microns in length of respirable size, were suggested by the British Hygiene Society in 1968 (Ann. Occup. Hyg. 11:47, 1968). The United States adopted this figure, and there is current agitation to reduce the safe figure to 2 fibers. The problems of sampling methods and counting are complex and not standardized as yet. Complete respiratory protection with outside air supply is essential for dusty asbestos operations. Substitution with less harmful fiberglass or magnesia with low asbestos content

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is the method of choice wherever possible. Wet methods and local exhaust ventilation may prove adequate for some less dusty operations.

SILICA (SILICON DIOXIDE)

Agricola, writing in the mid-sixteenth century, recorded his observation that women living in the Carpathian mountains might each have as many as seven husbands. The men working in local mines died of pulmonary disease at a young age. And in the years since, reports of mineral dust diseases of the chest have been published from all countries where mining is done. It is now known that such illness was in large part due to the fact that quartz, called silica (chemically silicon dioxide, SiO_2), which is abundant in the earth, has the unique property of acting synergistically with acid fast infection. There are few reliable data on the prevalence of silicosis in the United States, because of failure to recognize the disease. In addition there is no requirement for central reporting. Trasko in 1956 found records of 10,362 silicotics covering the period of 1950 through 1954 about which she writes, "obviously an underestimate of the real situation."

occupational exposure to silica

Because there is such a great amount of silica in the earth, all forms of tunnel construction and underground mining are associated with the risk of overexposure to silica, a risk very hard to control. Many silica-containing compounds are useful in industry, but it is those with free silica which carry a serious hazard because of the unique fibrogenic property of this mineral. Free forms of silica are used in industry because of their crystalline character. Those of importance industrially are quartzite, sandstone, flint, tripoli, and diatomaceous earth silica. Tables 11 and 12, adapted from Ladoo (1925), list the wide variety of industrial use of free quartz (silica). A number of operations here listed no longer carry a silica hazard since a nonfibrogenic material has been substituted; however, because of the great delay in onset of symptoms in some cases after the last exposure, they are included.

Table 11

Abrasive manufacturing	Refractory manufacturing
Ceramics manufacturing	Road construction
Foundry work	Sandpaper manufacturing
Furnace and kiln lining	Sandstone grinding
Granite cutting	Silver polishing
Mining	Street sweeping
Pottery making	Tunnel work

And to assist the physician in history taking, Table 12 identifies certain operations associated with the risk of silicosis.

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