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The Spectrum of Asbestos-Related Diseases

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Diseases caused by exposure to asbestos are prime examples of environmentally-related illnesses. Asbestos produces asbestosis from large exposures over short latent periods; it acts as a carcinogen from small exposures over long latent periods; and it induces mesothelioma with minute exposures. Its presence as the magic mineral is ubiquitous in our modern society.

Asbestos, An Environmental Contaminant

Man has used asbestos for centuries. The wicks of the oil lamps of the vestal virgins were asbestos. It was used in Finland as a pottery cement 4,500 years ago. It was used in 28 B.C. by a Greek doctor for acoustic insulation. It is almost inevitable that that remarkable traveler Marco Polo came upon asbestos mines in Siberia. It is equally unsurprising that it was regarded as a curiosity and the subject of witchcraft until the end of the 17th Century.[1] Its commercial use began when serpentine asbestos was discovered in Canada and used in the conservation of heat. Its use can thus be traced throughout all history, but in the last 100 years it has increased a thousand times, and in the last 15 years its use has probably increased geometrically.[2]

Asbestos has been aptly called "the lethal dust"[1] because of its ability to cause crippling respiratory disease and because of its association with malignant disease of the lungs, the pleura, the peritoneum and the alimentary tract. Editorials on its dangers abound and grim warnings of its hazards are found in the medical journal of every specialty in every language throughout the world. And yet man continues to use it, and many doctors are only dimly aware of its potential for causing disease.

Asbestos is everywhere.[3] This fact was first sharply focused by a series of consecutive autopsy studies carried out first in Cape Town, South Africa, and then in Miami, Florida. It was shown that asbestos could be found in the lungs of 30 percent of all men and 20 percent of all women

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who died in these cities.[4] Subsequently, asbestos was found in 41 percent of an autopsy series in Pittsburgh. Similar statistics resulted from autopsy series in New York, Montreal, Belfast and London.[5-9] Asbestos should be considered almost a normal postmortem finding in the lungs of urban dwellers. It has become such a "normal" finding that one wonders why the citizens of Perugia in Italy manage to escape? For there, only 1 percent of the population harbors asbestos when they die.[10]

There are 400 factories making asbestos in America. They employ 31,000 people directly in the manufacture of more than 3,000 different articles. But these are not the only workers at risk. Another five million, mainly in the construction industry,[11-13] are exposed in their work to significant levels of asbestos.

Moreover, asbestos fibers have been found in beer, sherry, soft drinks and tap water.[14] Fibrils were found in six out of seventeen samples tested of commercially available parenteral medications, presumably a result of asbestos filtration.[15] Asbestos is found in the antifreeze used in our cars, is a hazard for dental nurses, is used in plastics and for manufacturing brake linings. It has been used in the construction of homes and commercial buildings, as well as in ships, in every type of insulation and refrigeration, and for the production of papers and textiles.[13,16] It is contained in sewer pipes, used in surfacing roads and is found in many types of paint sprays. Furthermore, it is not necessary to work in contact with this material to be at risk, for someone in your household may bring it into your atmosphere. Merely washing clothes that are heavily contaminated with asbestos may bring the danger of malignant disease.[17]

We are surrounded by asbestos in the course of our normal lives. Not only do we inhale it or rub talc containing asbestos onto our skin, but occasionally we even swallow it. In Japan, for instance, rice is often treated with a substance containing tremolite and anthophyllite asbestos to enhance the flavor. It has been suggested that there may be a link between this custom and the high rate of cancer of the stomach in Japan.[18] Of course, there are so many factors involved in this condition that such a relationship must remain pure speculation.

Animals have not escaped: one would expect to find asbestos in donkeys or mules that work in an asbestos mine, but it has also been found in baboons and rats living in the hills surrounding the mills in the northwest part of the Cape Province of South Africa.[19] (A full description of the contamination of the atmosphere by asbestos has been provided by Paul Brodeur in *Asbestos and Enzymes.*[20,21])

Characteristics of the Mineral

Asbestos is a commercial term covering some 30 silicate compounds occurring in serpentine and amphibole rocks. Only six have economic significance. One of these, chrysotile, is fibrous and when examined through an electron microscope is seen to have hollow fibers rolled in sheets of varying length.[22] Chemically, chrysotile is hydrated magnesium silicate containing some iron oxide, magnesium and aluminum. The other five commercially significant asbestos compounds all come from amphibole rocks. Crocidolite, one of the five, differs from chrysotile because it has solid fibers arranged in bundles, which are more than twice the diameter of the fine, hollow chrysotile fibers.[22] These five other products differ mainly in the quantity of calcium or iron which each may or may not contain.[23]

Commercial asbestos is almost always mixed, and chrysotile provides 95 percent of industrial asbestos. It is a very flexible product with high tensile strength and heat resistance. It is resistant to moisture, to the corrosive action of acids, and is of course incombustible.[24]

It seems probable that the characteristics of the fibers as well as the chemical nature of compounds may have significance in causing disease. The particle size is also important, but perhaps the ratio of volume to mass (some fibers are hollow whereas others are solid) is more important. This ratio may vary as much as a factor of three. This will affect not only the airborne concentration, but the behavior of dust in the air, the pattern of its inhalation, and quite possibly its subsequent behavior in the body. This significance may be dramatically shown by noting that one pound of asbestos from the northern part of the Cape Province in South Africa may contain as much as 30 times the number of fibers as the same weight of asbestos from the geographically nearby Transvaal.[25] There is a great geographical difference in the pattern of disease resulting from asbestos inhalation and one may postulate that this results from physical and chemical variations, as well as from other factors such as smoking and intercurrent disease.[26] To enable research to progress, the International League Against Cancer (UICC) has

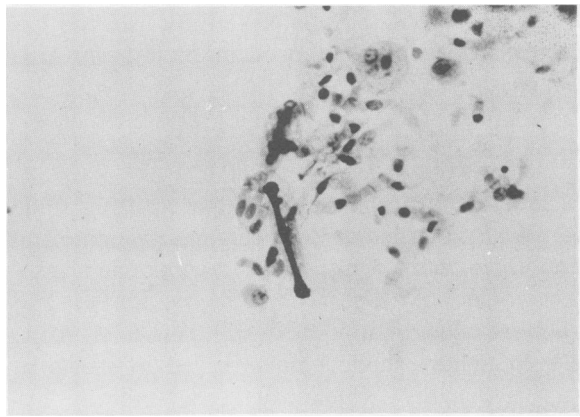

Figure 1.—Asbestos or ferruginous body in cytologic examination of sputum of asbestos worker. (Oil immersion, reduced 50 percent from ×1500)

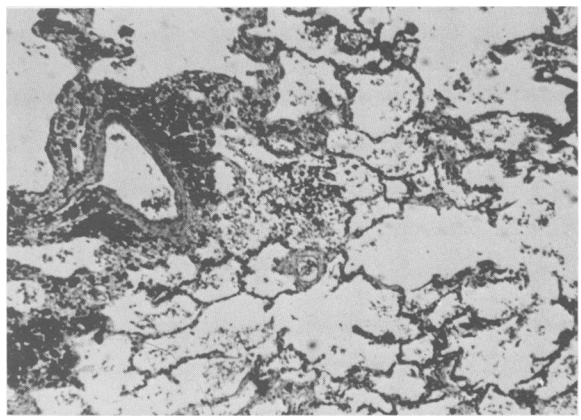

Figure 2.—Lung from autopsy specimen showing thickening and edema of the interlobular and alveolar septa, occasional asbestos bodies and many alveolar spaces filled with macrophages. (Hematoxylin and eosin, reduced 50 percent from ×400)

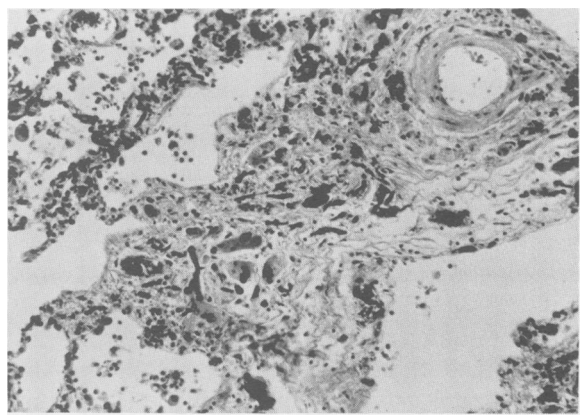

Figure 3.—Lung from autopsy specimen showing clubbed asbestos bodies, dense fibrosis and extensive collagenisation. (Hematoxylin and eosin, reduced 50 percent from ×700)

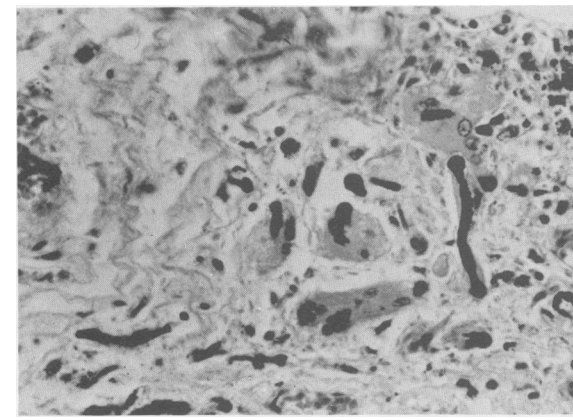

Figure 4.—High power view of asbestos bodies with alveolar wall thickening and numerous macrophages laden with a coarse granular material in the alveolar spaces. (Hematoxylin and eosin, oil immersion reduced 50 percent from ×1500)

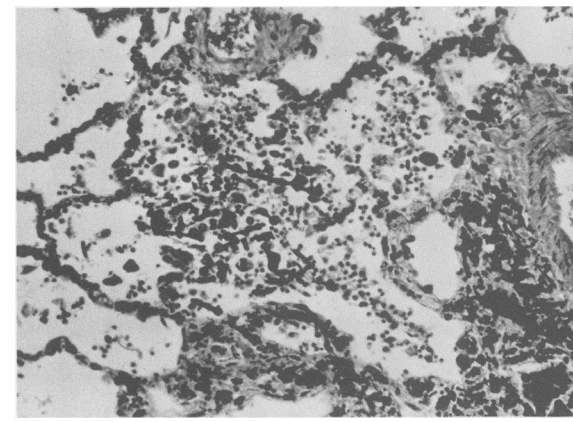

Figure 5.—Asbestos bodies shown in advanced fibrosis with collagenisation apparent. (Reduced 50 percent from ×700)

provided standard samples of various types of asbestos for research.

Closely associated with the chemical combination and the particle size, is the ability of the asbestos fibers in the virgin state to adsorb hydrocarbons subsequent to mining, as well as the varying contents of oil, waxes and other organic matter contained within the fibers themselves. Chrysotile can absorb the carcinogen 2-4 benzpyrene, and such compounds are found adsorbed to native crocidolite and amosite.[27,28]

One theory to account for the difference in carcinogenic risk between asbestos found in South Africa and that in Canada was based on the idea that jute bags used for shipping South African asbestos contain carcinogenic oils which later become adsorbed, whereas the fibers from Canada

are shipped in plastic bags.[27] This theory is untenable, because the fibers are equally carcinogenic in South Africa before they have been put into the jute bags and shipped.

Tissue Reaction

The initial tissue reaction to asbestos fibers is a fluid exudation with an inflammatory response that coats the particle with a protein film. In guinea pigs, under experimental conditions, this process takes about seven days but it may take longer in human beings. The protein film is impregnated with iron and becomes a golden brown "asbestos" or "ferruginous" body.[29] If the fibers are of a suitable size, they are then phagocytized by alveolar macrophages. Fourteen days after the guinea pig inhalation of the fibers there is a progressive bronchiolitis which proceeds to collagenisation and fibrosis. Later the paratracheal nodes become involved, and electron microscopy has shown that the microscopic fibers travel through the lymphatics to these regional nodes. They may cause more tissue injury than the larger and more obvious fibers which are found in the lung and sputum. Fibrosis occurs initially in the lung bases and then progresses upwards as the disease spreads. One of the difficulties in the diagnosis of asbestosis is that the "ferruginous body" can be caused by fibers other than asbestos.[30] Such bodies are found in the lungs of coal miners and those who work with graphite, fiberglass, ceramics, carborundum and even diatomaceous earth.[30] Thus, it is not safe to diagnose asbestosis merely by the presence of "ferruginous bodies" in the sputum or lungs, particularly as asbestosis is almost a normal finding in city dwellers (Figures 1-5).

Pulmonary Asbestosis

The first case of pulmonary asbestosis reported was from the Charing Cross Hospital in London in 1900.[1] The name was first given to it by Dr. W. E. Cooke in 1924, referring to a woman who had died after twenty years of working as an asbestos textile operator.[31] Fifty years later it is still a very difficult disease to define. Many authors adopt their own criteria, adding to the confusion in the literature. Murphy[32,33] devised a definition which has much to recommend it. He required at least three of five criteria:

1. Dyspnea after climbing one flight of stairs.
2. Fingernail clubbing with a hyponychial angle greater than 198°.
3. Rales present in two or more of eight sites.
4. A forced vital capacity less than 80 percent of the predicted level.
5. A radiographic film of the chest showing moderate or advanced asbestosis.

To overcome the radiological problem of defining asbestosis, he required that three radiologists assess the film separately and assign a score of five or six on a six point arbitrary scale.

Pulmonary function studies are helpful in making the diagnosis. The most consistent finding is a decrease in the diffusing capacity for carbon monoxide. This correlates highly with the level of dyspnea.[34] The total lung volume is reduced, probably by the fibrotic reaction both in the lungs and in the pleura causing reduced thoracic expansion. There is also a considerable ventilation-perfusion inequality, and the alveolar-arteriolar difference is characteristically increased.[34] A very consistent finding is reduction in the forced vital capacity (fvc) and the forced expiratory volume in one second (fev-1).[36] It is known that asbestosis causes a pronounced reduction in pulmonary compliance, presumably from the reduction in the total number of lung units and their mechanical restriction by interstitial and pleural fibrosis.

Field surveys to identify workers who have been affected by asbestosis have been successful using a simple spirometer to determine the fvc and the fev-1, providing a ratio of fev-1 to fvc as a percentage. For example, in a study of 57 wall board manufacturers, Wegman et al found that the duration of exposure to asbestos was more reliably related to the loss of fvc and fev-1 than age, height or smoking. They found that the mean of fev-1 to fvc was 76.3 percent and that only three of the 57 workers had figures below 60 percent (60 percent or below is taken as being characteristic of obstructive disease[36]).

The symptom complex is manifested mainly by dyspnea, although this is usually a late occurrence. In a series of 1,170 asbestos workers, some of whom smoked and some of whom did not, dyspnea developed in 1 percent after ten years of exposure, in 7 percent after 20 years and in over 50 percent of those who survived after 40 years.[37] Finger clubbing, cyanosis and fine basal rales all occur somewhat late.[38] An obvious bronchitis is relatively infrequent in contrast to other types of pneumoconiosis. An asymptomatic and non-inflammatory bronchiectasis can occur as a result of distention of the bronchi and bronchioles caused by the contraction of the interstitial fibrous tissue. It is a little surprising that obstructive pulmonary

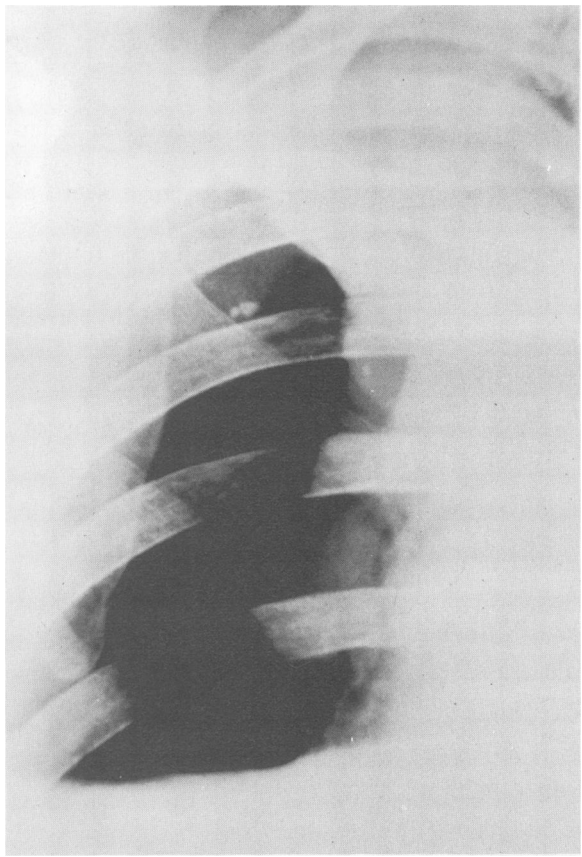

Figure 6.—A pneumothorax leaving visible pleural calcification on the parietal pleura.

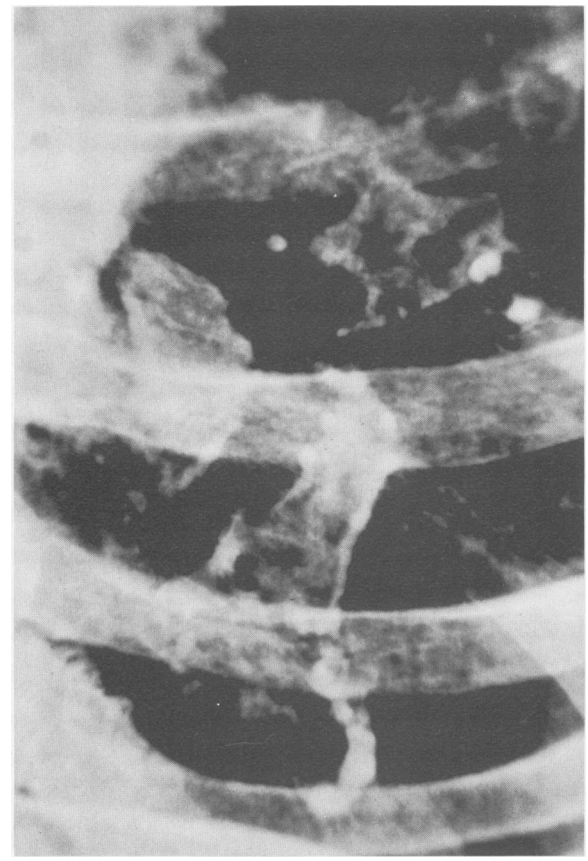

Figure 7.—The typical "leaf" pattern of asbestos pleural calcification with a rolled edge.

emphysema is not a feature of asbestosis, although the alveolae do become distended and distorted by the fibrosis in the same way as the bronchial tree. This fibrosis is truly interstitial, and the differential diagnosis histologically must include any of the many other causes of similar fibrosis.

Asbestos pleural effusion has been noted in 21 percent of all patients with asbestosis in one laboratory. It is frequently recurrent, usually bilateral, accompanied with chest pain and composed of a sterile exudate.[39]

Radiographic Signs in Pulmonary Asbestosis

There is yet no international definition of the radiographic changes of asbestosis. Many radiological features have been described, but since there is no basis on which to define "asbestosis" these findings cannot be satisfactorily correlated. If 50 percent of the urban population have asbestos in their lungs, then the presence of number of "ferruginous bodies" in the lungs or sputum is no guide to the extent of the disease. Furthermore, pulmonary function studies do not always show good correlation with radiological abnormalities.[40,44] Perhaps more important, neither can be perfectly correlated with the pathologic changes which are eventually discovered by lung biopsy or autopsy. In its early stages, histological diagnosis is unreliable and radiographic evidence to confirm the diagnosis may be entirely missing. The radiological abnormalities have been described in many articles and can be summarized under two headings: changes in pleura and changes in the lungs themselves.

The one common finding in people exposed to asbestos is subsequent calcification of the pleura and the diaphragm. Pleural calcification is often inexplicably unilateral, but autopsies have shown that pleural fibrosis forming characteristic plaques is nearly always bilateral. Because of a different rate of progression on each side, the radiological finding may appear unilateral. These "asbestos" plaques are nearly always in the parietal pleura; yet in spite of quite severe fibrosis, the two layers of the pleura do not always become adherent. A pneumothorax may easily be induced even when

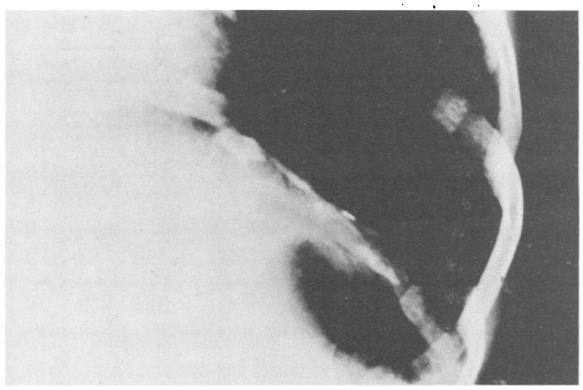

Figure 8.—Calcification in the diaphragm from asbestos. A South African patient.

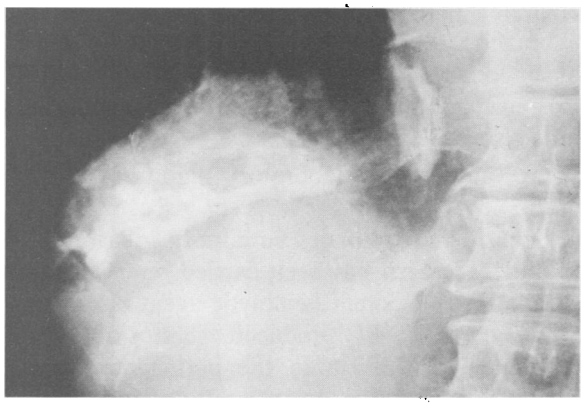

Figure 9.—Calcification in the diaphragm. A chance finding during a gastrointestinal series on an American with no industrial history.

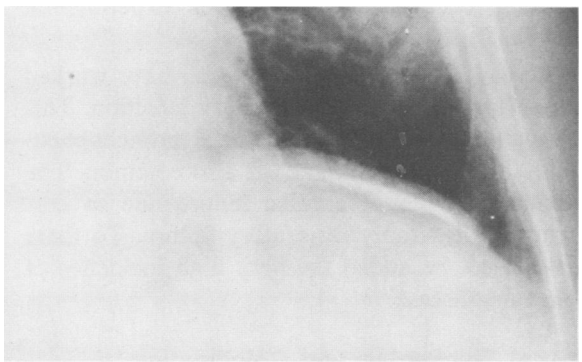

Figure 10.—Calcification in the diaphragm in a shipyard worker from America.

there are obvious radiological changes which have proceeded as far as calcification (Figure 6). Only in the latest stages do the two layers of the pleura become adherent.

The pattern of calcification is unique for asbestos, resembling a leaf with a rolled and nodular

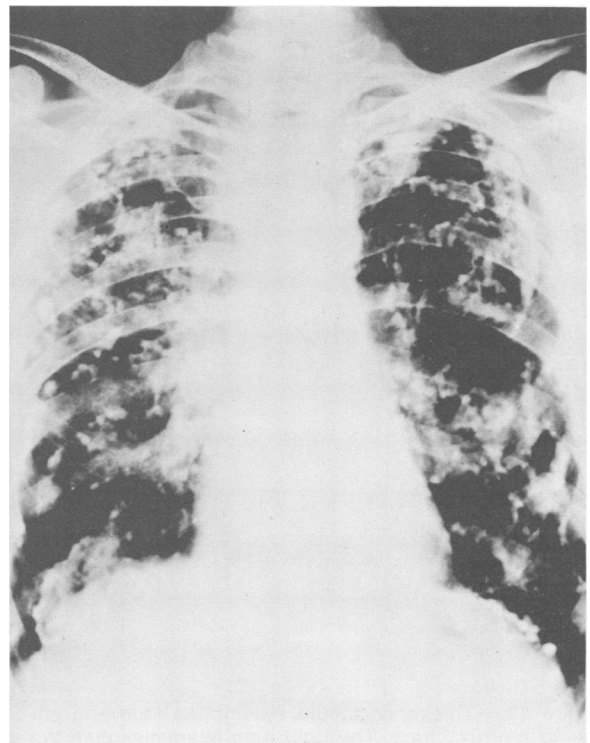

Figure 11.—Bilateral advanced asbestos calcification.

edge (Figure 7). It can be distinguished from calcification following trauma, either surgical or otherwise. The calcification is most frequent in mid zones and the bases in some geographic areas, where as in others it is infraclavicular as well, spreading throughout the rest of the chest.

Equally diagnostic is calcification on and in the diaphragm. Sections of specimens show calcification actually within the diaphragm at any depth. We do not know of any other circumstance in which similar diaphragmatic calcification occurs except, rarely, following trauma. The diaphragmatic calcification can be unilateral or bilateral and may occur in part of either diaphragm. It may be thick or thin and it seldom affects the movement of the diaphragm until it becomes extensive (Figures 8-10). It is associated with fibrosis in its latest stages but may be seen with an entirely normal lung above it. It is often an unexpected finding, for example, on a routine chest x-ray film (Figure 11). Even before calcification, the diaphragm may thicken, either in short segments or throughout its dome, bilaterally or unilaterally.

The pleura may also thicken to two or three centimeters without calcification. It may resemble fluid on the chest x-ray film, but none may be found (Figure 12). The lungs become encased

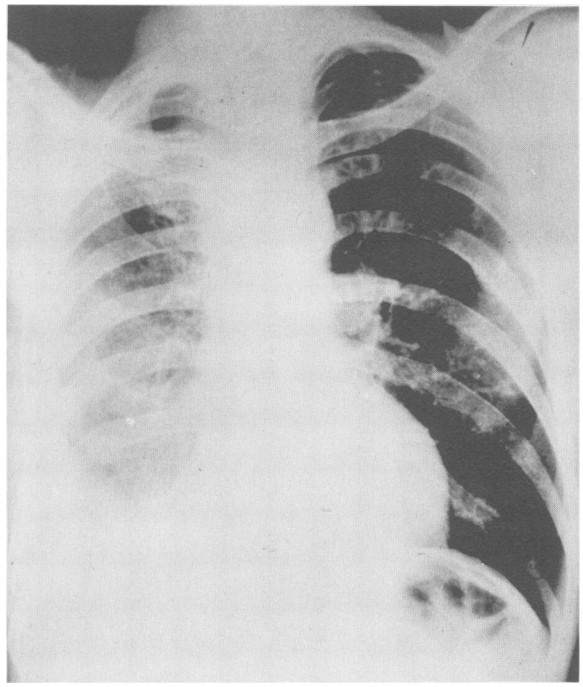

Figure 12.—Thickened pleura resembling fluid and encasing the right lung. The right lung is smaller than the left.

and movement is then restricted. As with other changes in asbestosis, the abnormalities may be more extreme on one side than on the other and the thoracic cage may be notably asymmetrical. Almost any combination of these changes occur. The pleura or the diaphragm may be separately affected, there may be calcification or plaque formation, and all or none may be present with or without obvious underlying lung disease.

The reverse is also true: there may be pronounced underlying lung disease without any obvious changes in the pleura or diaphragm. The lung abnormalities may be summarized as a diffuse ground-glass parenchymal fibrosis with a fine stippling. These changes may vary with the type of asbestos and particularly with its mineral content.

An additional feature described for many years is blurring of the cardiac outline, called a "shaggy heart." It also is by no means constant. The pulmonary and cardiac changes are much less reliable and helpful in diagnosis than the pleural and diaphragmatic calcification. There is evidence that the radiological abnormalities increase in number and severity with the length of asbestos exposure, but do not follow any firm rule of progression[42] (Table 1). After this description of the

TABLE 1.[2]—*Radiologic Changes in Asbestos Insulation Workers*

Onset of Exposure (years)	*Number*	*Percent Normal*	*Percent Abnormal*	*Asbestosis Grade:* 1	2	3
40+	121	5.8	94.2	35	51	28
30-39 ...	194	12.9	87.1	102	49	18
20-29 ...	77	27.2	72.8	35	17	4
10-19 ...	379	55.9	44.1	158	9	0
0-9 ...	346	89.6	10.4	36	0	0
TOTALS ..	1,117	51.5	48.5	366	126	50

radiological findings, it should be emphasized that the chest x-ray film may appear to be quite normal even when all other diagnostic findings are significantly abnormal. In searching for a means of early recognition of lung damage it is probable that a combination of pulmonary function testing, supplemented with questionnaires, physical and radiologic examination provides an epidemiologic method suitable for field surveys.

Unfortunately, the laboratory findings are not helpful. The chemical effects of asbestos have been considered by many authors in great detail and much research has been carried out. Chrysotile asbestos is a potent hemolytic agent but other forms of commercially produced asbestos are relatively inactive.[43] Silica, in the particulate form, also has a lytic action on intracellular structures. Asbestos produces no systemic poisoning, and there are no distinctive findings in the blood or in the urine. No minimum lethal dose has been established and there is no evidence of allergy in either occupational groups or experimental animals.

The cause of death in those who have worked with asbestos is usually pulmonary infection. This is usually severe bronchitis and bronchopneumonia, but lobar pneumonia is also common. The patients may die of cardiac failure due to cor-pulmonale or simply respiratory failure. To these causes must be added the very high incidence of malignant disease.

Pleural Thickening and Calcification

The presence of pleural calcification is significant. It carries with it so many unsolved questions that it is worthy of further comment. It has been thoroughly studied in Finland by Kiviluoto: he compared the chest x-ray films of 6,312 adults living near an asbestos mine with 7,101 chest x-ray films of adults who lived in a similar area but one without an asbestos mine near by.[44] There

TABLE 2.[2]—*Pleural Calcification Among Asbestos Insulation Workers*

Onset of Exposure (years)	Number	Percent Normal	Percent Calcification	Extent of Calcification 1	2	3
40+	121	42	58	37	20	13
30-39	194	65	35	46	15	6
20-29	77	89	10	8	0	0
10-19	379	99	1	5	0	0
0-9	346	100	0	0	0	0
TOTAL ...	1,117					

were 499 cases of pleural calcification among those who lived near an asbestos mine, but there were none in the control series. He called it "endemic pleural asbestos."[44] Selikoff has found pleural calcification in approximately 50 percent of insulation workers with greater than 20 years experience (Table 2).

But even this association is not as simple as it seems. Asbestos has been mined in the town of Shabani in Rhodesia for 60 years. There are large mine dumps of waste material in and around the town. Yet a personal search by one of the authors over a ten year period found no diaphragmatic calcification, pleural plaques or pleural calcification. Three independent radiological surveys of the miners and their families who lived in this area were reviewed by two experienced chest physicians, specially looking for diaphragmatic calcification, pleural plaques and pleural calcification. They found none, even when these surveys were repeated after a period of four years.[45] There was one exception, and it served to underscore the accuracy of the method of the examination. The exception was a miner who had worked for many years in the northwestern Cape of South Africa where pleural calcification is almost a normal finding in the population.[46] It seems likely that other factors relating to the asbestos industry apart from the asbestos itself are significant. MacDonald stated that the factor which causes asbestosis is not the same as that which causes pleural calcification.[47] So far, only an association has been shown and not a proven casual relationship. Nor does the occurrence of unilateral or bilateral calcified plaques imply the presence of an underlying asbestos pneumoniconiosis. It may occur in isolation, but it has been shown that the more severe the degree of the lung changes among asbestos workers, the greater the frequency of pleural calcification.[2]

Exposure to Low Concentrations of Asbestos

To make the diagnosis the possibility of the disease must be constantly borne in mind, even when there are patients who have been exposed to low concentrations of asbestos. The effects of such low concentrations in industry were reported by Murphy and associates in 1971.[32] In surveying 101 pipe coverers engaged in the construction of new ships, they found that asbestosis (using the aforementioned criteria) was 11 times more common in those exposed to low concentration than it was in workers employed in the same shipyard who had no exposure. Even when the concentration of asbestos was low, it was possible to detect asbestosis after 13 years of exposure, and after 20 years the prevalence had reached 38 percent. A very careful history may be required to provide the one vital clue which puts the whole picture together.

Asbestos Carcinogenesis

Finally, the vexing problem of carcinogenesis associated with asbestosis should be considered. There is no doubt that inhaling asbestos fibers carries a considerable carcinogenic risk, not only to the lungs, pleura, peritoneum and larynx[48] but possibly to the oropharynx, pancreas and gastrointestinal tract. Thompson predicted that asbestos will rival cigarettes as a cause of lung cancer in the future, because the production of asbestos has increased 1,000-fold during the last century.[49,50] The long delay period in producing its changes, from 20 to 40 years of exposure, may mean that we are yet to face the onslaught of malignant disease which could result.

But why should asbestos be carcinogenic? One possibility is that asbestos enhances and prolongs the carcinogenic effects of benzpyrene by adsorbing the carcinogen.[51] Some researchers take a different view because animal studies show that the trace metals nickel, chromium, manganese and iron are also carcinogenic agents and are found in asbestos.[52] Stanton took yet another position and reported that the structure of the fibers is responsible for carcinogenicity. He found that fibers between 0.5 and 5 microns in diameter and less than 80 microns in length were the most carcinogenic and suggested that this was the result of a physical irritation rather than a biochemical one.[53] The fact remains that all commercially-used types of asbestos have been shown to be carcinogenic.

Richard Doll reported that the average risk of

TABLE 3[55]—*Mortality Data=623 Asbestos Insulation Workers NY-NJ, January 1, 1943-December 31, 1971. All with 20 or More Years of Exposure to Asbestos*

	1943-1951		1952-1961		1962-1971		TOTAL 1943-1971	
	E	O	E	O	E	O	Expected	Observed
Total cancer	11.3	28	18.3	57	17.6	104	47.2	189
Lung cancer	1.5	13	3.5	23	5.1	48	10.1	84
Pleural mesothelioma	..	1	..	2	..	5	..	8
Peritoneal mesothelioma	..	1	..	3	..	20	..	24
GI	4.1	7	5.0	18	3.9	16	13.0	41
All other sites	5.7	6	9.8	11	8.6	15	24.1	32
Asbestosis	..	1	..	10	..	22	..	33
All other causes	65.1	44	89.4	94	78.3	61	232.8	199
TOTAL ALL CAUSES	76.4	73	107.7	161	95.9	187	280.0	421

Expected rates are based upon age-specific health rate data of U.S. National Office of Vital Statistics from 1949-1967.

carcinoma of the lung among employees who have worked for over 20 years or more in asbestos factories is ten times as high as that of the general population.[54] Selikoff concluded that malignant disease was the most important complication of asbestos exposure and found that 45 percent of New York insulation workers died of cancer.[55,56] In his study of the causes of death for 623 asbestos insulation workers, 84 were shown to have died of lung cancer, whereas the expected number was 10.1.[55,57] There were 42 deaths from mesothelioma, and gastrointestinal malignancies occurred three times the expected rate (Table 3).[55] Selikoff then attempted to assess the effect of smoking and followed 370 of the original group from 1963 to 1967. He found the risk of lung cancer for an asbestos worker who smoked was 92 times greater than for a non-smoker in the general population.[58]

In another study, Selikoff reviewed the histories of 17,800 American and Canadian insulation workers, following them from 1967 until December 1971. In a group this size, 44 deaths from lung cancer would be expected but the actual number proved to be 213. Of those who smoked, approximately 25 percent (134 out of 596) of the deaths were due to lung cancer.[55] Later, the same author tried to exclude the possible effects of other insulation materials by studying death rates for employees in a factory that specifically used asbestos.[59] In this series of 484 deaths, 73 were due to lung cancer, instead of the expected 11.4. There were an additional seven deaths due to mesothelioma and a larger than expected number of gastrointestinal neoplasms. He suggested that the typical latent period for carcinoma of the lung was more than 20 years after the onset of the exposure to asbestos, with a variation in exposure from one day through many years.

This apparently firm conclusion is not straightforward. The people living near or working in the mines around Shabani in Rhodesia (already referred to because of their strange lack of pleural and diaphragmatic calcification) have a similar low incidence of malignancy.[45,46] The control series was provided from a small population in a nearby gold mining town. Osburn reported a high incidence of malignancy in the gold miners in Gwanda but none has occurred in Shabani.[60] The findings are true of both White and African miners and their way of life and the background of all concerned in these two studies are very similar. Thus, for some inexplicable reason, exposure to asbestos in the town of Shabani over a period of many years does not carry an increased risk of malignancy. This same discrepancy has been demonstrated in Canada. A survey by MacDonald[17] of 1,200 asbestos miners in Quebec showed no unusually high rates of mortality from lung cancer. If this series is then examined more closely, it is found that those who were heavily exposed did have an increased rate of lung cancer, as much as five times as high as those who were lightly exposed, but the overall rate for the population was not increased.

A similar problem arises with mesotheliomas. These are tumors of the pleura and the peritoneum and are extremely rare, with an expectancy of about one in 10,000 deaths among the general population.[61] But Selikoff found that 7 percent of deaths among asbestos workers were due to mesotheliomas. Wagner from South Africa reported a series of 33 patients with mesotheliomas, of which 32 had exposure to asbestos.[62] This series needs

care in interpretation, because the area from which these patients were drawn has an extremely high asbestos exposure and it would be difficult to find many members of the population who have not been exposed to this dust. Nevertheless, there is not the slightest doubt that the incidence of mesotheliomas in the Cape Province of South Africa is incredibly high, yet in the Transvaal a few hundred miles to the east a similar high incidence is not found.[63] After sixty years' exposure in Shabani, Rhodesia, there have been no mesotheliomas.[45] An excess of mesotheliomas has not been found in the asbestos mining regions of Canada.[64]

Minimal exposure does not seem to provide protection from mesotheliomas. Newhouse reported 76 patients with mesothelial tumors of which approximately half (53 percent) had a history of either occupational or other asbestos exposure.[65] If they did not work with asbestos themselves they lived with an asbestos worker. Of the patients, 31 percent lived within half a mile of the asbestos factory. Either asbestos fibers or asbestos bodies were found in the lungs of 30 of 38 patients. However, this is near the percentage found in urban populations and its significance must therefore be doubtful. The length of exposure in the series varied from 16 to 55 years, but mesotheliomas have been reported in children aged six years or less. In England, Owen studied 17 patients from Liverpool with mesotheliomas and found that only 11 had a history of handling asbestos and only two worked directly with the material.[66]

Equally uncertain is the role of exposure to asbestos in increasing the risk of malignant disease in other parts of the body, particularly in the stomach, colon and rectum. Selikoff found a two-to-three times increased risk for gastrointestinal cancer in his studies, but a personal investigation by one of the authors in the Cape Province of South Africa did not find any significant increased incidence of malignant disease of the stomach or elsewhere in the alimentary tract. Asbestos exposure has recently been linked with laryngeal carcinoma.[48] It has been suggested that because an asbestos body has been found in the pancreas, this too may be the cause of increased pancreatic carcinoma. However, such isolated cases are of doubtful significance. It is not unreasonable to suspect that asbestos bodies will be found almost anywhere in the tissues of urban populations, if they are sought with sufficient care.

Occupational Standard

The present federal standard for occupational exposure to asbestos dust is five fibers per cubic centimeter greater than 5 microns in length as an eight-hour time-weighted average.[17] By 1976, the Department of Labor will reduce the standard to two fibers per cubic centimeter. Thus, the asbestos worker who typically inhales 6 to 8 million cubic centimeters of air per day will inhale 30 to 40 million asbestos fibers under the present standard, to be reduced to a mere 12 to 16 million under the future standard.[67,68] No one knows whether the two fibers per cubic centimeter standard will protect the occupationally-exposed worker from asbestos related disease.[68] There is still considerable debate concerning the development and implementation of this new standard.[69,70] Moreover, there are numerous fibers less than 5 microns in length (especially less than 1 micron as identified by the electron microscope). These minute fibers, not even mentioned in the occupational standards, are easily inhaled and may be particularly injurious.[71]

Conclusions

The literature on asbestos is so extensive that this survey has only skimmed the surface. However, certain conclusions seem clear.

Asbestos is, indeed, a "lethal dust" and exposure to it carries many and considerable risks. The major risk is of pulmonary fibrosis. That risk is increased many times if the patient is also a smoker. But exposure to asbestos also increases the risk of carcinoma of the lung, and again if the patient smokes this is increased further. It seems probable that exposure to asbestos, particularly in small amounts, increases the likelihood of a mesothelioma developing. A close relationship to the degree of exposure is not firmly established, and why a mesothelioma should develop in some patients while in others a carcinoma of the lung develops is not understood. In some geographical areas, exposure to asbestos carries an increased risk of malignant disease of the alimentary tract, though it is not certain that this is a risk in every locality.

For each of these conclusions, with which most researchers would agree, there remain many unanswered questions. Why do apparently similar mines carry a totally different risk of pleural or malignant disease? Why are calcified pleural plaques unilateral in many cases? How can fibers pass through an apparently normal lung, subse-

quently damage the pleura or the diaphragm, or even pass through both these tissues to irritate the peritoneum? Is there a firm relationship between the amount of pleural fibrosis and the development of mesotheliomas? Is there a positive or a negative correlation?

A statement made about other malignant disease seems particularly applicable to exposure to asbestos: "An individual who develops a malignant process must possess firstly a susceptibility to the specific carcinogenic activity and secondly survive long enough to develop a malignant neoplasm."[72] We also agree that asbestos by itself is probably not the sole cause; possibly some other factor or factors in association with it will be shown to cause the presently inexplicable variation in the malignant diseases of asbestos workers.

The authors have been unable to find any consistent common denominator associated with asbestos. Indeed, we find that we have not really progressed much further than Ramazzini, a physician of Padua, who in 1746 stated "Diseases arise from the offensive quality of the matter which tradesmen handle in the way of their business. Under this head, I reckon the diseases which affect mine diggers and all workmen who work upon minerals."[73]

Medicine may not have progressed in this respect, but civilization undoubtedly has, and unfortunately the problems of asbestos are no longer confined to "mine diggers and those who work upon minerals." We are all at risk and only time will tell what havoc will be wreaked on all, human and animal, who live in this asbestos age.

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