WORKPLACE EXPOSURE TO ASBESTOS
Review and Recommendations

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Asbestos Work Group
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MEMORANDUM FOR: *Dr. Eula Bingham*
Assistant Secretary for
Occupational Safety and Health

Dr. Anthony Robbins
Director, National Institute for
Occupational Safety and Health

FROM: *Asbestos Work Group*

SUBJECT: *The Updated Scientific Information on Asbestos and Recommended Occupational Standard for Asbestos Exposure*

In the fall of 1979, a NIOSH/OSHA committee was formed at the direction of Dr. Eula Bingham, Assistant Secretary of Labor for Occupational Safety and Health, and Dr. Anthony Robbins, Director of the National Institute for Occupational Safety and Health (NIOSH), to review the scientific information concerning asbestos-related disease and assess the adequacy of the current OSHA occupational health standard of * 2,000,000 fibers per cubic meter greater than 5 μm in length (2Mf/m^3). Since the 1972 promulgation of this 2,000,000 f/m^3 standard, OSHA, in 1975, proposed lowering the standard to 500,000 f/m^3; NIOSH, in 1976, recommended lowering the standard to 100,000 f/m^3; and the British Advisory Committee on Asbestos, in 1979, recommended lowering its occupational exposure standards. The NIOSH/OSHA committee has reviewed the most recent scientific information, including documents concerning the above developments and the 1977 International Agency for Research on Cancer (IARC) review of the carcinogenicity hazards of asbestos, and presents the following major conclusions and recommendations. A detailed updating of significant scientific literature since the 1976 NIOSH Criteria Document and the 1977 IARC Monograph is attached.

*Effective January 19, 1989, the OSHA Permissible Exposure Limit (PEL) was changed to 0.2 f/cc. Federal Register, Vol. 54, No. 12, pp. 2332-2983.

1. Definition of Asbestos. Having considered the many factors involved in specifying which substances should be regulated as asbestos, the committee recommends the following definition:

> Asbestos is defined to be chrysotile, crocidolite, and fibrous cummingtonite-grunerite including amosite, fibrous tremolite, fibrous actinolite, and fibrous anthophyllite. The fibrosity of the above minerals is ascertained on a microscopic level with fibers defined to be particles with an aspect ratio of 3 to 1 or larger.

2. Sampling and Analysis of Airborne Asbestos. The committee concludes that the membrane filter-phase contrast microscopy method represents the only technique available that can reasonably be used for routine monitoring of occupational exposures and sampling for compliance purposes. However, the committee recognizes the lack of specificity of this method for fiber identification, and recommends the use of supplementary methods such as electron microscopy for fiber identification in cases of mixed fiber exposures. In recommending the primary use of light microscopy, the committee also wants to stress the inability of this method to detect short asbestos fibers to which workers are exposed. The toxicity of asbestos fibers shorter than the 5-micrometer detection limit of light microscopy cannot be dismissed on the basis of current scientific information.

3. Biologic Effects of Exposure to Asbestos. Animal studies demonstrate that all commercial forms and several noncommercial forms of asbestos produce pulmonary fibrosis, mesothelioma, and lung neoplasms. Chrysotile is as likely as crocidolite and other amphiboles to induce mesotheliomas after intrapleural injection, and also as likely to induce lung neoplasms after inhalation exposures.

Human occupational exposures to all commercial asbestos fiber types, both individually and in various combinations, have been associated with high rates of asbestosis, lung cancer, and mesothelioma. While significant excesses of cancer of several other sites have been observed in exposed workers, presently available information is insufficient to determine the role of specific fiber types.

On the basis of available information, the committee concludes that there is no scientific basis for differentiating between asbestos fiber types for regulatory purposes. Accordingly, the committee recommends that a single occupational health standard be established and applied to all asbestos fiber types.

Available data show that the lower the exposure, the lower the risk of developing asbestosis and cancer. Excessive cancer risks, however, have been demonstrated at all fiber concentrations studied to date. Evaluation of all available human data provides no evidence for a threshold or for a "safe" level of asbestos exposure. Accordingly, the committee recommends that, to the extent uses of asbestos cannot be eliminated or less toxic materials substituted for asbestos, worker exposures to asbestos must be controlled to the maximum extent possible.

4. Inadequacy of Current 2,000,000-Fiber Occupational Standard. The committee concluded that a variety of factors demonstrates that the current 2,000,000-fiber standard is grossly inadequate to protect American workers from asbestos-related disease. First, the 2,000,000-fiber standard was designed in 1969 by the British Occupational Hygiene Society (BOHS) for the limited purpose of minimizing asbestosis. Disease prevalence data from the BOHS study population collected subsequent to 1969 strongly suggest that this standard is insufficient to prevent a large incidence of asbestosis. Second, all levels of asbestos exposure studied to date have demonstrated asbestos-related disease, and a linear relationship appears to best describe the shape of the dose-response curve. These considerations led the committee to conclude that there is no level of exposure below which clinical effects do not occur. Third, the absence of a threshold is further indicated by the dramatic evidence of asbestos-related disease in members of asbestos-worker households and in persons living near asbestos-contaminated areas. These household and community contacts involved low level and/or intermittent casual exposure to asbestos. Studies of duration of exposure suggest that even at very short exposure periods (1 day to 3 months) significant disease can occur.

Although various models can be and have been fashioned to postulate possible dose-response relationships involving asbestos, the committee believes that the limited current data preclude the creation of any one empirical curve to describe *the exact* dose-response relationship. Over the last three decades, measurement techniques for asbestos have changed in several crucial respects, and there have been no suitable methods available to date to compare the results of prior techniques to current methods.

In addition, no adequate epidemiological information is available on the disease experience of workers exposed below the current standard and followed for a sufficient period to identify long latent effects. Consequently, the committee cannot present a precise dose-response relationship for the variety of asbestos-related diseases. However, the committee firmly believes that compelling evidence demonstrates that prevention of asbestos-related diseases requires that an occupational standard minimize all asbestos exposures, and definitely be set far below the current 2,000,000-fiber standard.

5. Recommended Occupational Standard for Asbestos Exposure. Given the inadequacy of the current 2,000,000-fiber standard, the committee urges that a new occupational standard be promulgated which is designed to eliminate non-essential asbestos exposures, and which requires the substitution of less hazardous and suitable alternatives where they exist. Where asbestos exposures cannot be eliminated, they must be controlled to the lowest level possible. A significant consideration in establishing a permissible exposure limit should be the lowest level of exposure detectable using currently available analytical techniques. At present this level would be 100,000 fibers greater than 5 μm in length per cubic meter averaged over an 8-hour workday. Regardless of the choice of a permissible exposure limit, the best engineering controls and work practices should be instituted, and protective clothing and hygiene facilities should be provided and their use required of all workers exposed to asbestos. Respirators are not a suitable substitute for these control measures. The committee also reiterates its judgment that even where exposure is controlled to levels below 100,000 fibers, there is no scientific basis for concluding that all asbestos-related cancers would be prevented.

6. Medical Surveillance Program. Appropriate medical surveillance is crucial to detect and minimize the progression of some asbestos-related diseases. Considerable emphasis should be placed on baseline medical examinations for all workers potentially exposed or who have been exposed to asbestos at any level. These examinations should include the following: (1) a 14" x 17" postero-anterior chest X-ray; (2) spirometry including forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1); (3) a physical examination of the chest including auscultation for the presence or absence of rales, rhonchi,

and wheezing; (4) an assessment of the presence or absence of finger clubbing; and (5) a history of respiratory symptoms and conditions including tobacco smoking.

An occupational history should include a history of exposure to asbestos and exposure to other substances of real or potential medical significance. Performance criteria for these procedures, including the periodicity of subsequent medical surveillance, should be developed by NIOSH in consultation with OSHA and professional societies and organizations concerned with the diagnosis and prevention of respiratory diseases. The committee does not recommend comprehensive annual medical examinations as presently required. Sputum cytology should be evaluated in the development of an improved medical surveillance program. The committee believes that sputum cytology may prove to be a valuable supplement to X-ray evaluation.

It is also crucial that all required medical surveillance be promptly evaluated and the results reported to the employee. Furthermore, the standard should provide for periodic reporting of aggregate medical information concerning an employer's entire workforce. Results at a minimum should be displayed in a non-identifiable, aggregate format so that the employer, employees, and OSHA can see the prevalence of abnormalities possibly associated with asbestos-related disease, and also see how this prevalence has changed over time.

The committee recognizes that OSHA's recent lead standard contains a multiple physician review mechanism whereby workers can get independent medical evaluations by physicians of their choice. The lead standard also contains a medical removal protection program whereby workers can obtain special health protection where necessary, accompanied by appropriate economic protection. The committee feels that these programs are relevant to asbestos workers and should be considered as part of a new occupational asbestos standard.

Medical records generated due to the standard's medical surveillance program should be maintained for at least 40 years or for 20 years after termination of employment, whichever is longer.

7. Other Recommendations. The committee further recommends the following: (1) Due to the widespread current and past uses of asbestos products in the maritime and construction in-

dustries, it is vital that any new asbestos standard address these industry sectors as well as other workplaces with employees exposed to asbestos. Regulation of these industries should be structured around the principle that where work must be done using asbestos, only those employees needed to do this work should be present, and only for the minimum period of time needed to complete this work.

(2) Due to the sampling and analytical difficulties concerning asbestos, manufacturers of asbestos-containing products such as construction materials should perform detailed monitoring of exposures which could result from all foreseeable uses of their products, including misuse. This monitoring should include electron microscopy to identify fiber type mix and exposures to fibers less than 5 μm in length. This monitoring data should accompany these products downstream so the users not only know that asbestos exposures may occur, but also know the nature of potential exposures. This monitoring data could, if appropriate, avoid the need for small employers who use asbestos-containing products to have to conduct monitoring on their own.

(3) Due to the fact that other agencies regulate occupational exposures to asbestos (such as the Mine Safety and Health Administration), these agencies should be urged to participate in the development of a new standard and adopt this new standard.

(4) Because cigarette smoking enhances the carcinogenic effect of asbestos exposure on the lung, particular emphasis should be placed on this in any educational program developed under a new standard.

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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ASBESTOSIS

John M. Dement
James A. Merchant
Francis H. Y. Green

INTRODUCTION

Occupational exposure to asbestos minerals constitutes a major health hazard in the United States and in most industrialized nations of the world. Because of their unique properties such as resistance to heat and chemical attack, asbestos minerals have long been used by man. Finnish potters are known to have used soils containing anthophyllite asbestos dating from 2500 B.C. (103). Use of asbestos in lamp wick was described by Theophrastus, Strabo, and Plutarch. Herodotus (456 B.C.) described cremation clothes made of woven asbestos. Marco Polo described tablecloths of asbestos seen during his journeys (66).

Despite early uses, large scale use of asbestos came with industrialization and particularly the steam engine which required heat resistant materials for packings and seals. The first asbestos textile mill in the United States began production in about 1896. Today, commercial uses of asbestos are countless and nearly every manufacturing sector may be involved with production or use of asbestos-containing products.

The term "asbestos" is applied to a group of naturally occurring fibrous silicate minerals. Although many minerals are fibrous in nature, only six are regulated by Occupational Safety and Health Administration (OSHA) standards. These minerals fall into two major mineralogical subdivisions: chrysotile, which belongs to the serpentines; and the amphiboles, including crocidolite, asbestiform actinolite, asbestiform tremolite, amosite, and anthophyllite. Only amosite, chrysotile, and crocidolite are of economic importance. Chrysotile is basically a sheet silicate mineral rolled into itself to form a hollow tube. This tube constitutes the basic fibril of chrysotile. All amphibole asbestos types are similar in crystal structure: they consist of double chains of linked silicon oxygen tetrahedra between which metallic ions are sandwiched (128). Chemical composition and trace metal contamination (Cr, Co, Mn, Ni associated with chrysotile) of asbestos fibers may vary considerably between deposits from different mining regions (43).

More than 90% of all asbestos used in the United States is of the chrysotile variety. Total U.S. consumption of asbestos in 1977 was 610,000 metric tons, down from peak comsumption of 795,000 metric tons in 1973 (12). By contrast, only 93,000 metric tons were produced in U.S. mines and mills; Canada furnished 95% of all imported raw asbestos fiber. U.S. asbestos consumption by end use for 1978 is shown in Table II-9. Asbestos cement products constitute the major use of asbestos followed closely by floor products or materials used in the construction industry. Materials containing asbestos have been extensively used in construction and shipbuilding for purposes of fireproofing and for decoration. These have often been applied by spray application.

DEFINITION

Asbestosis is the name of the pneumoconiosis produced by the inhalation of asbestos fibers. It is characterized by diffuse interstitial fibrosis of the lung parenchyma, often accompanied by thickening of the visceral pleura and sometimes calcification of the pleura. Clinical findings include dyspnea on exertion, non-productive cough, rales at the lung bases, bronchi, and in advanced cases, finger clubbing. Lung function measurements usually demonstrate a restrictive impairment with reduced diffusing capacity.

Table II-9

U.S. ESTIMATED ASBESTOS CONSUMPTION IN 1978 BY END USE CATEGORY

Product	Consumption (Metric Tons)			
	Chrysotile	Crocidolite	Amosite	Anthophyllite
Asbestos cement pipe	119,800	23,300	2,700	
Asbestos cement sheet	28,400		800	
Flooring products	122,400			
Roofing products	58,200	100		
Packing and Gaskets	23,200	100		
Thermal insulation	14,300			
Electrical insulation	3,200			
Friction products	81,000			600
Coating and compounds	29,100			
Plastics	5,300	500		
Textiles	5,700			
Paper	28,400	700		
Other	33,100			2,100
Total	552,100	24,700	3,500	2,700

Source: (12)

CAUSATIVE AGENTS

Asbestosis is perhaps the most widely studied of the known occupational hazards; however, its mechanisms are still not fully understood. Both clinical and epidemiological data have conclusively shown that asbestos is associated with asbestosis and respiratory cancer in man. Animal bioassay data fully support these findings and suggest that pathological responses to asbestos may be more related to physical characteristics of the fibers than to chemical composition. Animal data have shown a wide variety of fibrous minerals and small diameter glass fibers to be capable of producing tumors upon pleural injection or implantation (110)(111)(139). Interstitial fibrosis has also been produced in animals intratracheally injected with small diameter glass fibers (63).

POPULATION AT RISK

Asbestos has over 3,000 commercial uses and is ubiquitous in the general environment. Because of the mineral's resistance to thermal and chemical degradation, exposures may take place starting from initial mining of the fibers through manufacture, use, and eventual burial of asbestos containing waste.

Mining and milling of asbestos in the United States is not extensive: fewer than a thousand workers are employed (148). However, amphibole minerals and, to a lesser extent, serpentines, are sometimes found as contaminants of other types of ore bodies, such as talc, vermiculite, crushed stone aggregates, and in ores from various metal mining operations (19)(64)(115) (140). There have been no systematic studies of mining operations in the United States to identify specific ores containing asbestos as contaminants and the degree to which workers are exposed.

Estimates of the number of workers exposed to asbestos in primary manufacturing of asbestos products are given in Table II-10. In the primary manufacturing sector approximately 18,000 workers are estimated to be potentially exposed; however, this number could be as high as 37,000 (17). A large variety of asbestos products and materials produced in primary manufacturing are fabricated and processed with other materials in secondary industries to produce the more than 3,000 end products containing asbestos. The secondary fabrication and processing industry is very large and has been estimated to employ more than 300,000 workers (17).

By far the largest number of workers with potential asbestos exposures may be found in industries which utilize asbestos products such as the construction industry, the automobile servicing industry (including remanufacturing of

Table II-10
ESTIMATES OF WORKERS EXPOSED TO ASBESTOS IN PRIMARY MANUFACTURING

Manufacturing Sector	Estimated Number of Potential Exposed Workers
Asbestos cement pipe	1,755
Asbestos cement sheet	980
Friction materials	5,605
Floor coverings	3,500
Asbestos paper products	2,120
Packing and gaskets	1,125
Paint, coating and sealant	815
Asbestos textiles	1,800
Total	17,700

Source: (17)

asbestos containing parts), and the shipbuilding and repair industry. In the construction industry, including those doing demolition and repair, an estimated 180,000 to 408,000 workers are potentially exposed to asbestos. The automobile servicing industry includes brake and clutch servicing garages, rebuilding and refacing friction components, and repackaging of friction products. Within this sector, 2 million workers are potentially exposed to asbestos (17). Approximately 3,800 workers are potentially exposed to asbestos in shipbuilding and repair.

A total of 2.3 to 2.5 million workers are estimated to be currently (potentially) exposed to asbestos. However, because of the long latency (20 to 30 years) required before asbestos related diseases become clinically manifest, past asbestos workers must also be considered at risk. These estimates are especially difficult to develop and are subject to controversy (29). Nonetheless, large numbers of previous asbestos workers are now completing their latency period and are at risk of asbestos related diseases.

EPIDEMIOLOGY

Early Observations

Asbestosis

The first well documented case of asbestosis was reported by H. Montague Murray in 1906, although there were several anecdotal reports prior to this time (66)(95). Murray documented a case of pulmonary fibrosis at autopsy in a worker engaged in the production of asbestos textiles. This worker reported that he was the sole survivor of 10 men who started with him in the carding room; the others had died.

Following the report by Murray, Pancoast et al. (1917) reported 17 cases of pulmonary fibrosis in a Pennsylvania plant (105). In 1924, Cooke published another detailed autopsy report of a 33-year-old woman suffering from asbestosis (14). Necropsy findings included pulmonary fibrosis, pleural thickening, pleural calcification, and heart enlargement. Further cases were reported by Mills in 1930, Donnelly (1933), Lynch and Smith (1931), Seiler and Gilmour (1931), Wood and Gloyne (1930), Oliver (1927), Simson (1928), Stewart (1928), and Pancoast and Pendergrass (1926) (21)(70)(88)(104)(106)(120)(134)(141)(164). By 1930, more than 75 asbestosis cases had been reported in the literature.

Early case reports stimulated concern and in 1928 the first detailed epidemiologic study of asbestos workers was undertaken by the Ministry of Labour in Great Britain. Results were published by Merewether and Price in 1930 (84). This was a cross-sectional chest x-ray study of 363 workers engaged in production of asbestos textiles. Of this group, 95 (26.2%) were found to have pulmonary fibrosis and the prevalence of fibrosis with 20 or more years employment was over 80%.

In the United States, Donnelly (1936) reported a cross-sectional chest x-ray study of 151 asbestos workers which found a pulmonary fibrosis prevalence of 59% among workers employed 4 years of more (22). Schull (1936) reported chest x-ray studies of 100 workers dismissed from North Carolina asbestos plants due to disability and found a 55% prevalence of moderate or advanced asbestosis (131).

In 1937 the U.S. Public Health Service undertook the first detailed epidemiologic study of asbestos workers in the United States with results published by Dreessen et al. in 1938 (23). A total of 511 employees were studied in this cross-sectional study and worker exposures were estimated by the impinger method. A relationship was found between extent of asbestos exposure and clinical symptoms of asbestosis although many workers had only short periods of exposure at the time of the study. This study resulted in a recommended occupational exposure

limit of 5 million particles per cubic foot of air (mppcf) in the United States.

Lung Cancer and Mesothelioma

The first indication that asbestos might be a human carcinogen came in 1935. Lynch and Smith (in the United States) and Gloyne (in England) independently reported three cases of lung cancer detected during autopsy studies of asbestos workers (34)(71). All three workers had died of asbestosis. Other case reports followed by Egbert and Geiger in 1936, Gloyne in 1936, and Nordmann in 1938 (26)(33)(102). In the 1947 annual report of the Chief Inspector of Factories in England, Merewether stated that of 365 asbestosis deaths, 65 (17.8%) also had cancer of the lung at autopsy (83). This compared to a prevalence of lung cancer of only 1.3% for cases certified at death as having silicosis.

Despite early suggestions, the first detailed epidemiologic study to conclusively demonstrate an association between asbestos exposure and lung cancer was not published until 1955 by Doll (20). Doll studied the mortality experience of a cohort of 113 asbestos textile workers employed more than 20 years. Among this group, 11 lung cancer deaths were observed compared to only 0.8 expected—based on the mortality experience of England and Wales.

Asbestos exposure is associated with mesothelial tumors of pleural and peritoneal tissues. Lee and Selikoff have reviewed early reports associating asbestos exposures and mesothelioma (66). The first cases were reported in 1946 by Wyers (165). However, conclusive evidence of an association between asbestos exposure and mesothelioma was not available until 1960 when Wagner et al. reported 33 pleural mesotheliomas in the crocidolite mining area of South Africa (152).

Mortality

Epidemiologic studies have repeatedly demonstrated an association between asbestos exposure and increased mortality due to asbestosis, lung cancer, pleural and peritoneal mesothelioma, and gastrointestinal cancer. In some studies, asbestos exposure has also been associated with increased risks for laryngeal cancer and cancer of the buccal cavity and pharynx. Table II-11 contains a brief summary of important mortality studies and significant findings. In this section, mortality studies are reviewed with emphasis on asbestosis and lung cancer risk differences by fiber type, industry, and smoking patterns.

Mixed Fiber Exposures

In most plants processing asbestos, several different types of asbestos may be used or have been used in the past. Typically, chrysotile and one or more amphiboles are used.

Asbestos insulation workers have been extensively studied in the United States and other countries. Selikoff et al. studied the mortality experience of 632 insulation workers followed between 1943 and 1962 and observed 45 lung cancer deaths whereas only 6.6 were expected (123). Of the 255 deaths in this cohort, 28 (11%) were due to asbestosis and 3 (1.2%) to mesothelioma. An SMR of 309 was observed for cancer of the stomach, colon, and rectum (although it was based on a small number of observed cases).

A much larger cohort of 17,800 insulation workers was followed by Selikoff et al. between 1967 and 1976 (126)(127). Among this cohort, 2,271 deaths were observed including 429 lung cancers (SMR-406), 78 asbestosis deaths, and 49 deaths due to mesotheliomas. Significant increased mortality was also observed for cancers of the esophagus, stomach, colon-rectum, larynx, buccal cavity and pharynx, and kidney. Only 2 of the 78 asbestosis deaths occurred prior to 20 years from onset of employment, based on death certificate information. Review of all available autopsy, surgical, and clinical material indicated an additional 90 deaths were due to asbestosis, 57 to lung cancer, and 126 to mesothelioma.

Elmes and Simpson studied the mortality of 162 insulation workers in Belfast between 1940 and 1975 (27)(28). Among this cohort, 122 deaths were observed including 16 (13.1%) due to asbestosis and 13 (10.7%) to mesothelioma. A large excess due to respiratory cancer was observed.

There are several important studies of mortality among textile workers exposed to mixed asbestos types. In an early study in the United States published in 1963, Mancuso and Coulter observed more than a threefold excess risk of lung cancer among workers producing textile and friction products (73). Fourteen percent of 195 deaths were due to asbestosis and 2 (1%) were due to mesotheliomas.

Mortality among employees in the plant initially studied by Doll in 1955 has been in-

Table II-11

SUMMARY OF MORTALITY STUDIES OF ASBESTOS EXPOSED POPULATIONS

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Doll	1955	113 textile workers employed 20 or more years	Mixed	Retrospective cohort 1922-1953	11 lung cancers observed versus 0.8 expected, 14 death certificates mentioned asbestosis.
Mancuso and Coulter	1963	1,495 workers producing textile, friction products	Mostly chrysotile	Retrospective cohort, 1940-1960	28 asbestosis deaths, 19 lung cancers observed versus 5.6 expected, 5 peritoneal neoplasms (2 were mesotheliomas).
Selikoff, Churg and Hammond	1964	632 insulation workers with 20 or more years employment	Mixed	Retrospective cohort, 1943-1962	12 asbestosis deaths, 45 lung cancers observed versus 6.6 expected. Increased gastro-intestinal cancer, 3 pleural mesotheliomas.
Knox et al.	1965, 1968	1,014 textile workers	Mixed	Retrospective cohort, 1922-1966	27 lung cancers observed versus 10.75 expected, 42 with asbestosis on death certificate. Authors suggested reduced risks after controls added in 1933.
Newhouse	1969, 1973	4,500 textile workers	Mixed	Retrospective cohort, 1933-1968	Significant excesses for lung cancer among workers in highest exposure category; 24 mesotheliomas among males.
Newhouse et al.	1972	922 female textile and friction product workers	Mixed	Retrospective cohort, 1942-1968	14 lung cancers observed versus 0.5 expected in those working 2 years in highest exposure jobs. Approximately threefold excess of respiratory disease mortality in this group. Overall 1 mesothelioma.

Table II-11

SUMMARY OF MORTALITY STUDIES OF ASBESTOS EXPOSED POPULATIONS (Continued)

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Selikoff, Hammond and Churg	1968	370 insulation workers with >20 years employment	Mixed	Retrospective cohort, 1963-1967	Observed strong interactive effect between asbestos exposure and smoking for lung cancer; 10 mesothelioma deaths observed and 15 asbestosis deaths.
Elmes and Simpson	1971, 1977	162 insulation workers	Mixed	Retrospective cohort, 1940-1975	16 asbestosis deaths, 13 mesotheliomas. Large excess risk for respiratory cancer throughout follow-up period.
McDonald, et al.	1971, 1974, 1979, 1980,	11,379 asbestos miners and millers	Chrysotile	Retrospective cohort, 1926-1975	Among those achieving >20 years latency, overall lung cancer SMR = 125, with 42 pneumoconiosis deaths and 11 mesothelioma deaths. Linear dose-response observed for lung cancer and pneumoconiosis.
Enterline and Henderson	1972, 1978	1,075 retired asbestos product worker's	Chrysotile and amphiboles	Retrospective cohort, 1941-1973	Lung cancer SMR = 270; 19 asbestos deaths. Linear dose-response observed for lung cancer with SMR = 198 at 62 mppcf-yrs. and SMR = 778 at 976 mppcf-yrs.; 2 mesothelioma deaths.
Selikoff et al.	1973, 1979	17,800 insulation workers	Mixed	Retrospective cohort, 1967-1976	429 lung cancers observed versus 105.6 expected; 78 asbestosis deaths and 49 mesotheliomas.
Meurman et al.	1974	1,092 asbestos mine and mill workers	Anthophyllite	Retrospective cohort, 1936-1974	21 lung cancers observed versus 13 expected; 13 asbestosis deaths but no mesotheliomas. A strong interactive effect on lung cancer with smoking and asbestos exposure was observed.

Table II-11

SUMMARY OF MORTALITY STUDIES OF ASBESTOS EXPOSED POPULATIONS (Continued)

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Peto et al. and Peto	1977, 1979	1,106 textile workers employed >10 years	Mixed	Retrospective cohort	36 respiratory cancers observed versus 19.3 expected among those only employed in controlled areas. Significant excess of non-malignant respiratory diseases.
Weiss	1977	264 paper and millboard workers	Chrysotile	Retrospective cohort, 1945-1974	2 asbestosis deaths among a total of 66 deaths. No excess of lung cancer but numbers were small; no mesotheliomas reported.
Jones et al.	1976, 1979	1,088 gas mask workers during WW II	Crocidolite	Retrospective cohort, 1939-1976	12 lung cancers observed versus 6.3 expected in women; 17 mesothelioma deaths. Linear dose-response for mesothelioma with employment duration; 3 mesotheliomas observed among those exposed 5-10 months.
Edge	1976, 1979	429 shipyard workers with pleural plaques	Mixed	Prospective follow-up 1968-1974	19 broncogenic cancers observed versus 4.0 expected; 23 mesotheliomas observed. Shipyard workers with plaques had 2.5 times lung cancer risk when compared to matched controls without plaques.
Hughes and Weill	1979	5,645 asbestos cement workers >20 years latency	Chrysotile and crocidolite	Retrospective cohort, 1940-1973	23 lung cancers observed versus 9.3 expected among those with cumulative fiber exposures>100 mppcf/yr.; 2 pleural mesotheliomas observed versus 4.4 expected among those not exposed to crocidolite.

Table II-11

SUMMARY OF MORTALITY STUDIES OF ASBESTOS EXPOSED POPULATIONS (Continued)

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Sheers	1979	410 dockyard workers with pleural plaques or pleural fibrosis	Mixed	Prospective follow-up 1967-1976	6 mesothelioma deaths among those with plaques and 2 with only pleural fibrosis. Author suggested pleural plaques are of greater biological significance than simply a marker of exposure.
Seidman, Selikoff and Hammond	1979	820 men producing insulation between 1941-1945	Amosite	Retrospective cohort, 1961-1975	83 lung cancers observed versus 23.9 expected. Among 61 men employed<1 month, 3 lung cancers observed versus 1.3 expected. 4 mesotheliomas by death certificate diagnosis but an additional 10 identified using necropsy data. 15 deaths observed due to asbestosis.
Hammond, Selikoff	1979	12,051 insulation workers with >20 years latency	Mixed	Retrospective cohort, 1967-1976	Asbestos workers who did not smoke had a fivefold risk of lung cancer compared to nonsmoking controls. Smoking asbestos workers had 53 times the lung cancer risk of nonasbestos exposed persons who also did not smoke.
Robinson, Lemen and Wagner	1979	3,276 workers producing textile, friction products	Mostly chrysotile	Retrospective cohort, 1940-1975	Overall lung cancer SMR = 136 for males and 824 among females. Some increasing trends in lung cancer with employment duration. Large excesses due to asbestosis. 17 mesothelioma deaths observed.

Table II-11

SUMMARY OF MORTALITY STUDIES OF ASBESTOS EXPOSED POPULATIONS (Continued)

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Nicholson et al.	1979	544 chrysotile miners and millers, >20 years employment	Chrysotile	Retrospective cohort, 1961-1977	28 lung cancers observed versus 11.1 expected; 26 cases of asbestosis observed; 1 pleural mesothelioma observed.
Dement et al.	1980	768 textile workers	Chrysotile	Retrospective cohort, 1940-1975	26 lung cancers observed versus 7.47 expected; 15 asbestosis deaths and 1 mesothelioma death. Linear dose-response for lung cancer with SMR = 223 at cumulative exposures <30 fiber/cc x yrs.
Brown, Dement, and Wagoner	1979	398 talc miners and millers	Anthophyllite and tremolite	Retrospective cohort, 1947-1975	9 lung cancers observed versus 3.3 expected. Significant excess due to nonmalignant respiratory diseases; 1 mesothelioma death.

vestigated by Knox et al. (59)(60), and more recently by Peto et al. (108)(109). Peto studied 1,106 men and women who had worked 20 or more years in asbestos exposed areas. Among those who were first employed after 1933 (when control regulations were enacted), 31 lung cancer deaths were observed whereas 19.3 were expected. Additionally, 35 deaths were observed due to nonmalignant respiratory disease versus 25 expected, and there were 5 deaths due to pleural mesothelioma. Dust exposures in this plant were reported to be generally above 5 fiber/cc until about 1970.

Newhouse (96)(97) and Newhouse et al. (98) have studied patterns of mortality among 4,600 male and 922 female workers in a plant which chiefly produced asbestos textiles but later asbestos insulation products. Exposures were classified as low to moderate (5-10 fibers/cc) and severe (>10 fibers/cc). Among males, there were 46 mesothelial tumors and an SMR for lung cancer of 538 was observed for those employed more than ten years in the severe exposure group. In those with lowest exposure, a lung cancer SMR of 154 was observed. Deaths from chronic respiratory diseases were 1.8 times expected in the highest exposure group. A remarkable cancer SMR was observed among females in the highest exposure group (21 observed versus 0.8 expected). Both males and females were found to have smoked more than the comparison population; however, this could only account for 10% to 20% of the observed excess lung cancer mortality.

The asbestos cement product industry is one of the largest consumers of asbestos in the United States. In addition to their asbestos exposure, workers in this industry may also be exposed to low levels of crystalline silica and other materials associated with cement dust. Weill et al. reported mortality patterns among 5,645 asbestos cement product workers with a minimum of 20 years since initial employment (156). Exposures for the cohort were estimated and expressed as mppcf × yrs. Among those exposed to greater than 100 mppcf × yrs., 23 lung cancers were observed versus 9.3 expected. No excess lung cancer risk was reported among those with cumulative exposures less than 100 mppcf × yrs. Two pleural mesothelioma deaths were observed. Weill et al. reported that exposure to crocidolite in addition to the (predominant) chrysotile used in cement products increased the lung cancer risk in comparison to chrysotile exposure alone. The unusually low SMRs for all causes regardless of exposure category suggest that cohort follow-up and death certificate ascertainment was less complete than desired.

Crocidolite

Wagner et al., in 1960, reported 33 pleural mesotheliomas among men working in crocidolite mines and mills and the population living in the vicinity of these mills in the Northwest Cape Province of South Africa (152). The high incidence of mesotheliomas in this area has been confirmed by other investigations (13)(39)(155).

Crocidolite was commonly used in the production of gas mask canisters during World War II and mortality among these workers has been investigated. Jones et al. studied the mortality of 1,088 workers exposed between 1940 and 1945 and followed through 1976 (46)(47). Twenty-two pleural and 7 peritoneal mesotheliomas were observed and a linear relationship was observed between employment duration and the risk of mesothelioma. There was also a modest excess of bronchial carcinoma. Similar results have been reported by McDonald and McDonald who studied a smaller cohort of gas mask workers in Canada and found that 7% of all deaths were due to mesotheliomas (75).

Amosite

Mortality patterns among a cohort of workers producing amosite asbestos insulation between 1941 and 1945 have been reported by Selikoff et al. (125) and more recently by Seidman et al. (118)(119). This group of 820 men were observed over a 35 year period during which 528 deaths occurred: by death certificate information 15 (2.8%) were due to asbestosis and 1 was due to mesothelioma. Review of available surgical, pathological, and clinical data for this group identified 13 additional mesotheliomas and 15 additional cases of asbestosis not listed on death certificates. Overall there were 83 lung cancers observed whereas 23.1 were expected and among those employed less than one month, 3 lung cancers were observed versus 1.3 expected. Anderson et al. have observed four confirmed cases of mesothelioma among household contacts of workers at this plant (1).

Anthophyllite and Tremolite

The only location in the world where anthophyllite has been commercially mined and processed is Finland. These ores are also known to contain smaller quantities of tremolite. Mortality among workers in two Finnish mines and mills has been studied by Meurman et al. (86) (87). In their first report, 1,092 workers were followed from 1936 until 1974. A relative risk for lung cancer of 1.6 was observed and there were 13 (5.2%) asbestosis deaths but no deaths due to mesothelioma. Their subsequent study concerned 793 workers with known smoking histories with 10 additional years of follow-up. A relative risk for lung cancer of 19 was observed for smoking asbestos workers and 1.6 for asbestos workers who did not smoke. Asbestosis mortality was found to be equally frequent among smokers and nonsmokers. All lung cancer cases with more than 10 years of exposure were also found to have asbestosis.

Chrysotile

Chrysotile is the major asbestos fiber type used in the United States, but most of this fiber is imported from Canada. The mortality of Quebec chrysotile miners and millers has been extensively studied by McDonald et al. (76) (79-81). The most recent report for this cohort included 10,939 men who had been employed one or more months and followed between 1926 and 1975. An overall SMR for lung cancer of 125 was observed; 42 deaths were due to asbestosis and 11 to mesothelioma. A nearly linear dose-response relationship was reported for lung cancer. Increased mortality was also observed for cancer of the stomach and esophagus but no other gastrointestinal sites. Similar patterns of lung cancer and asbestosis mortality have been reported by Rubino et al. in Italian chrysotile miners and millers where an SMR for lung cancer of 206 was observed among those with sufficient latency (117).

The McDonald et al. studies demonstrated a low lung cancer risk even in the highest exposure group. Nicholson et al. have reported larger excesses from lung cancer and asbestosis in their study of chrysotile miners and millers in Quebec (99). This latter study cohort consisted of 544 miners and millers with at least 20 years seniority and followed between 1961 and 1977. A total of 28 lung cancers were observed versus 11.1 expected (SMR = 252). There were 30 deaths due to noninfectious respiratory diseases whereas only 6.7 were expected. Of these 30 deaths, 26 were due to asbestosis. Only one mesothelioma (pleural) was observed.

Mortality among chrysotile asbestos miners and millers in the Urals has been investigated by Kogan et al (61). The overall cancer mortality risk was found to be 1.6 times that for the general male population and was higher in mining than in milling. Among males, the relative risk for lung cancer was 2.0 and ranged from 1.4 to 2.1 for females. The lung cancer risk was considerably greater in older age groups having the longest latency. No mesotheliomas were reported; however, Kogan et al. attributed this to insufficient experience of pathologists in that geographic area (61). Nonetheless, the low mesothelioma risk is consistent with other studies of chrysotile-exposed populations.

There have been several studies of factory populations exposed only to chrysotile. Weiss studied a small cohort of 264 workers in a plant producing asbestos millboard and reported no excess cancer mortality (160). However, there were only 66 deaths (2 of which were due to asbestosis) and cancer latency was not taken into account in the analysis.

A facility manufacturing asbestos textile, friction, and packing products has been studied by Robinson et al. (113). Chrysotile constituted over 99% of the total quantity of asbestos processed per year in this plant except during World War II; the remaining 1% was crocidolite and amosite. The cohort consisted of 2,722 males and 544 females followed between 1940 and 1975. Among males, an overall lung cancer SMR of 135 was observed but among females the excess lung cancer risk was much higher with an overall SMR of 824. There were 76 deaths in males due to noninfectious respiratory disease but only 16.4 expected. Again, the chronic respiratory disease risk was higher among females with an SMR of 1,555. There were 4 mesotheliomas among females and 13 in males.

Dement et al. have reported mortality among a cohort of asbestos textile workers exposed only to chrysotile (18). This cohort consisted of 768 white males employed at least 6 months and followed between 1940 and 1975. There were 26 lung cancers observed versus 7.47 expected. Of the 191 deaths in this cohort, 15 (7.9%) were due to asbestosis or pulmonary fibrosis and 1 (0.5%) was due to a peritoneal

mesothelioma. Linear relationships were demonstrated between cumulative fiber dose and the risk of mortality for lung cancer and noninfectious respiratory diseases. An SMR for lung cancer of 223 was observed for the lowest cumulative exposure category of less than 30 fibers/cc × years.

Fibers and Asbestos-like Contamination of Other Minerals

Both serpentines and amphiboles may be found as contaminants in other mined and processed ores and may result in significant fiber exposures to workers in these operations.

Fibers and cleavage fragments of fibrous grunerite occur where ore from some iron formations are crushed and comminuted and have been found in high concentrations in Lake Superior as a result of mining and milling operations (64). Gillam et al. studied mortality among gold miners exposed to cummingtonite-grunerite and found a threefold excess risk of lung cancer and a twofold excess of nonmalignant respiratory disease, excluding influenza and pneumonia (32). However, workers in this mine were also exposed to silica. McDonald et al., in a subsequent study of the same mine, examined the mortality experience of persons with at least 21 years of employment with the company (78). This study demonstrated excess mortality due to pneumoconiosis (mainly silicosis), tuberculosis, and heart disease but no overall excess of malignant diseases was found. However, when the population was stratified by exposure, respiratory cancer was elevated (but was not statistically significant) in the highest exposure group.

Commercial talc deposits are sometimes found to contain serpentines (chrysotile, antigorite, and lizardite) and fibrous and nonfibrous amphiboles. Kleinfeld et al. demonstrated significantly increased proportionate mortality due to lung cancer and nonmalignant respiratory disease among talc miners and millers in New York State exposed to fibrous anthophyllite and fibrous tremolite (53)(58). Brown et al. have reported a further mortality of talc miners and millers in one company mining this same ore body (9). This cohort consisted of 398 workers followed between 1947 and 1975. Among this cohort, 10 respiratory cancers were observed whereas only 3.5 were expected. Approximately a threefold excess risk of nonmalignant respiratory disease was reported; however, only one death due to mesothelioma was observed.

Effects of Smoking

Smoking and asbestos exposure are more than additive in their combined ability to increase the risk of lung cancer. Hammond et al. reported results of their 10-year follow-up of 8,220 asbestos insulation workers with known smoking status (38). The mortality experience of these workers was compared with that expected among smokers and nonsmokers of the American Cancer Society's prospective cancer prevention study. Asbestos workers who did not smoke showed approximately a fivefold risk of lung cancer compared to the nonsmoking control population. On the other hand, a more than sixtyfold risk of lung cancer was observed for smoking asbestos workers compared to nonsmoking controls. A similar multiplicative effect was observed by Selikoff et al. among a factory cohort producing amosite insulation (129).

Although less striking, cigarette smoking may also contribute to the risk of death due to asbestosis. Hammond et al. reported that asbestosis death rates of smoking asbestos workers were 2.8 times as high as that of nonsmoking asbestos workers. Meurman found less association between asbestosis mortality and smoking; he reported 7 of 42 asbestosis deaths among nonsmokers (86).

Mortality and Pleural Radiographic Changes

The relationship between pleural thickening and calcification and subsequent mortality is important insofar as surveillance of asbestos workers is concerned. Edge studied the mortality of 429 shipyard workers with plaques and compared this to matched controls without plaques (25). Among those with plaques, 23 mesotheliomas were observed and workers with plaques had 2.5 times the lung cancer risk of those without plaques. Sheers observed 6 mesothelioma deaths among 410 dockyard workers with plaques, but he found just 2 mesotheliomas in those with only pleural fibrosis (130). Neither of these studies established causality between pleural changes and subsequent development of mesothelioma or lung cancer because neither asbestos exposure or latency were controlled for in the analysis. Meurman has shown that anthophyllite asbestos workers have a high prevalence

of pleural changes but a minimal mesothelioma risk (86)(87). However, plaques and pleural thickening do indicate an asbestos exposure and this fact alone places the workers at an increased risk for lung cancer and asbestosis.

Respiratory Morbidity

All types of asbestos have been shown in epidemiologic studies to be associated with asbestosis, pleural thickening, and pleural calcification. Available evidence from cross-sectional and prospective respiratory disease studies provide little evidence that any one type of asbestos is more biologically active than another insofar as x-ray or clinical changes are concerned (149) (164). These findings are fully supported by animal bioassay data.

Important epidemiologic studies of respiratory morbidity among asbestos workers are summarized in Table II-12. In these studies, various objective measures of effect or disease outcome have been used including chest roentgenographs, spirometry, measures of diffusion capacity, and chest auscultation. Subjective data such as respiratory symptoms obtained by questionnaire have also been used. In the diagnosis of "definite asbestosis," most studies have relied upon combinations of objective and subjective data.

Mixed Fiber Exposures

Early cross-sectional studies of chest roentgenographs of asbestos workers by Merewether and Price, Donnelly, Schull, and Dreessen et al. demonstrated a striking prevalence of pulmonary fibrosis of as much as 80% for workers employed more than 20 years (22)(23)(84)(131).

Several studies have been conducted among insulation workers. Selikoff et al. studied chest films of 1,117 insulation workers exposed to chrysotile and amosite (122)(124). A 50% overall prevalence of pulmonary fibrosis was observed increasing to 90% among those employed more than 30 years. Pleural calcification showed an increasing prevalence with latency reaching 57.9% at 40 years since initial employment. Pleural fibrosis (thickening) occurred earlier than calcification. Murphy et al. also studied shipyard insulation workers and found a prevalence of asbestosis 11 times that of age matched, nonexposed controls (92)(93). Exposures among this group were thought to be low.

Cross-sectional data from an asbestos textile plant processing a mixture of asbestos types were used by the British Occupational Hygiene Society (BOHS) in establishing occupational exposure standards (8). Among 290 workers employed after dust controls were installed in 1933, only 8 workers (2.7%) demonstrated x-ray changes considered consistent with asbestosis. Basal rales was taken as an early disease marker with a 1% risk estimated for a working lifetime of 50 years at an average exposure of 2 fibers cc. Workers at this same plant were subsequently studied cross-sectionally by Lewinsohn (67). This latter and much larger study demonstrated a significantly greater prevalence of pulmonary fibrosis; reaching 40.5% among workers employed from 30-39 years. Pleural fibrosis (thickening) was observed in 1.6% of those employed 1-9 years and in 50% of workers employed more than 40 years.

Berry et al. reported the results of a prospective study of workers employed in the same plant studied by Lewinsohn (67). This study consisted of 379 persons completing 10 or more years employment by 1971. Possible asbestosis was diagnosed based on one or more combinations of basal rales or crepitations, radiological changes, a falling transfer factor and restrictive lung function changes. Among these 379 men, 60 cases of possible asbestosis were diagnosed by the factory medical officer, whereas 85 cases were diagnosed by an independent clinician. Using plant exposure data, it was estimated that the cumulative dose necessary for a 1% incidence for crepitations, possible asbestosis, and certified asbestosis was 43 fiber/cc-yr, 55 fiber/cc-yr, and 72 fiber/cc-yr, respectively. Two cases of certified asbestosis were observed among nonsmokers and nine among ex-smokers, suggesting a contributory smoking role. Weiss reported similar findings in his study of 100 asbestos textile workers where a 24% prevalence of pulmonary fibrosis was observed in nonsmokers versus 40% for smokers (159)(161). Gregor et al. demonstrated a progression of radiological changes in asbestos workers referred to the British Pneumoconiosis Medical Panel without further asbestos exposures (36).

Lung function and chest film effects of exposure to asbestos cement dust have been studied by Weill et al. (157)(158). This study included 859 workers in two asbestos cement plants who were administered respiratory symptom questionnaires, spirometry, and chest films. Cumulative dust exposures were estimated and expressed as mppcf-yr. Both small rounded and linear opac-

Table II-12

SUMMARY OF RESPIRATORY MORBIDITY STUDIES OF ASBESTOS EXPOSED POPULATONS

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Selikoff, Churg, and Hammond	1965	1,117 insulation workers	Chrysotile and amosite	Cross-sectional, no external controls	50% prevalence of pulmonary fibrosis. Increasing prevalence of all chest film changes with employment duration increasing to 90% prevalence at >30 years
Kilviluoto et al.	1960, 1965, 1979	Persons in Central Finland	Anthophyllite tremolite	Case series	Pleural calcification observed in persons only secondarily exposed to asbestos. Pleural changes unrelated to lung cancer mortality.
Selikoff	1965	1,117 insulation workers	Chrysotile and amosite	Cross-sectional, no external controls	Pleural calcification showed increasing prevalence reaching 57.9% among those with 40 years since first exposure. Pleural fibrosis occurred earlier than calcification, 50% of cases were bilateral.
McDonald et al.	1972	1,015 chrysotile miners and millers	Chrysotile	Cross-sectional, no externals	Shortness of breath increased with estimated cumulative dust exposure but bronchitis showed little correlation.
Becklake et al.	1972	1,105 chrysotile miners and millers	Chrysotile	Cross-sectional, no externals	FVC found to decrease with estimated cumulative dust exposure in smokers and nonsmokers. Same trends seen in FEV_1. Obstructive impairment seen in high exposure group. Few trends in diffusing capacity.

Table II-12

SUMMARY OF RESPIRATORY MORBIDITY STUDIES OF ASBESTOS EXPOSED POPULATONS (Continued)

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
McDonald et al.	1974	5,082 miners and millers with chest films	Chrysotile	Mortality follow-up	Increased mortality observed for those with parenchymal changes but not in those with only pleural changes, 32 deaths observed due to all respiratory diseases versus 8 expected.
Liddell et al.	1977	267 miners and millers with chest films	Chrysotile	Prospective follow-up	During 20-year period, the following cumulative incidence was reported: small opacities 16%, pleural thickening 5.3%, pleural calcification 5.3%, obliteration of c/p angle 7.3%
Weiss	1971	100 asbestos textile workers	Unknown	Cross-sectional, no external controls	Overall prevalence of fibrosis 36% with 24% prevalence in nonsmokers and 40% in smokers. None of 11 nonsmokers with exposures less than 20 years showed fibrosis.
BOHS	1968	290 asbestos textile workers	Mixed	Cross-sectional, no external controls	Basal rales used as early disease marker, 1% risk estimated for a working lifetime of 50 years at 2 fibers/cc.
Lewinsohn	1972	1,287 asbestos textile workers	Mixed	Cross-sectional, no external controls	Prevalence of pulmonary fibrosis 0% with 0-9 years exposure up to 40.5% with 30-39 years exposure. Pleural fibrosis prevalence 1.6% in 0-9 years and 50% in 40-49 years exposure group.

Table II-12

SUMMARY OF RESPIRATORY MORBIDITY STUDIES OF ASBESTOS EXPOSED POPULATONS (Continued)

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Berry et al.	1979	379 asbestos textile workers	Mixed	Prospective follow-up	6.6% of workers had "possible" asbestosis after 16 years follow-up and an average exposure of 5 fibers/cc. Cumulative exposure for 1% incidence of "possible asbestosis" for 40 years employment estimated to be 55 fibers/cc X years.
Weill et al.	1973	908 asbestos cement workers	Mixed	Cross-sectional, no external controls	Overall prevalence of small rounded opacities 1/0 or greater was 3.1%, for small irregular opacities prevalence was 2.5%. Reduced FEV_1, FEF_{25-75} and FEV_1/FVC ratio found in those with x-ray abnormalities.
Weill et al.	1975	859 asbestos cement workers	Mixed	Cross-sectional, no external controls	Prevalence of small rounded and irregular opacities, 4% in lowest exposure group and 30% in highest. Pleural changes 11% in lowest exposure group and 30% in highest. FVC and FEV_1 reduced in those with x-ray changes.
Weiss and Theodas	1978	98 workers age 40 or over in two plants	Chrosotile and amosite	Cross-sectional, no external controls	Prevalence of profusion (1/1) 17.5% in chrysotile workers and 16.5% in mixed fiber workers. Pleural thickening prevalence, 17.5% in chrysotile workers and 35.4% in mixed fiber workers. Smoking found to be significant factor in those exposed to amosite.

Table II-12

SUMMARY OF RESPIRATORY MORBIDITY STUDIES OF ASBESTOS EXPOSED POPULATONS (Continued)

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Selikoff et al.	1977	485 miners and millers	Chrysotile	Cross-sectional, no external controls	10% prevalence of all radiographic abnormalities. Pleural changes seen in 3% of all workers. Prevalence of abnormalities among those employed less than 5 years was 5% with 3% being parenchyma changes (profusion $\geq$ 1/0).
Jones et al.	1979	204 asbestos cement workers	Mixed	Prospective follow-up 1970-1976	Progression of small opacities dependent upon both average and cumulative exposure. Lung function declines were associated with smoking and cumulative exposure. Pleural abnormalities progressed more as a function of time with little association with additional exposure.
Anderson	1979	Household contacts of factory workers	Amosite	Cross-sectional, age, sex matched controls	35.9% prevalence of x-ray abnormalities compared to a 4.6% prevalence in the control group. Pleural abnormalities more prevalent than parenchymal changes.
Gamble, Fellner, and DiMeo	1979	121 talc miners and millers	Anthophyllite and tremolite	Cross-sectional, external comparison populations	Talc workers with greater than 15 years employment had increased prevalence of pleural abnormalities compared to comparison populations, FEV_1 and FVC reduced in association with dust and fiber exposures.

Table II-12

SUMMARY OF RESPIRATORY MORBIDITY STUDIES OF ASBESTOS EXPOSED POPULATONS (Continued)

Author(s)	Date	Study Population	Fiber Type	Study Design	Summary of Important Findings
Irwig et al.	1979	1,801 miners and millers with chest films	Crocidolite and Amosite	Cross-sectional, no external controls	Prevalence of pleural changes increased from 2.5% for workers with less than 1 year employment to 33.6% for workers with 15 or more years. Parenchymal changes (>1/0 ILO) found in 2.3% of workers employed less than 1 year and 26.7% in workers employed more than 15 years.
Gregor et al.	1979	119 asbestos workers referred to Pneumoconiosis Medical Panel	Mixed	Prospective follow-up	One-third of workers showed progression after 6 years follow-up and no further asbestos exposure. Progression frequency higher among those with profusion>1/1 or 1/2 (ILO).
Rubino et al.	1979	56 retired chrysotile miners and millers surviving>3 years	Chrysotile	Prospective follow-up	39% of persons with abnormal films (profusion>1/0 ILO) showed progression after an average follow-up of 8 years. 7.9% of workers with normal initial films developed radiographic changes.
Murphy et al.	1971, 1978	101 shipyard pipe coverers and 95 controls	Mixed	Cross-sectional with further follow-up matched controls	Prevalence ratio of asbestosis 11 times greater than controls. Asbestosis evident after cumulative exposures of 60 mppcf-years.

ities were observed, indicating the possible role of small quantities of silica present in cement dust. Among those with a cumulative exposure less than 50 mppcf-yr, and approximately 4% prevalence of small opacities (rounded or irregular, profusion ≥1/0 was observed; the prevalence of these changes increased to 30% with an exposure of more than 400 mppcf-yr. Pleural changes were seen in 11% of those in the lowest exposure category. Both FVC and FEV_1 were reduced in those with x-ray changes. There was no apparent interaction effect of cigarette smoking on the development of diffuse fibrosis.

Jones et al. studied the progression of radiographic abnormalities and lung function changes among 204 asbestos cement workers between 1970 and 1976 (48). Films were read side by side in known order and ranked according to progression. These authors concluded that: (1) progression of small opacities depended upon both average and cumulative exposure; (2) declines in lung function were related to both smoking and cumulative exposure; and (3) pleural abnormalities progressed as a function of time. Disease incidence was not estimated in relation to exposure.

Anthophyllite and Tremolite

Respiratory morbidity among Finnish anthophyllite miners and millers has been studied by Meurman et al. (87). Among 787 active employees, a threefold excess of dyspnea and a twofold excess of cough was observed among asbestos workers compared to controls. The prevalence of dyspnea was not found to be associated with smoking habits.

A high prevalence of pleural plaques has been reported among persons residing near anthophyllite mines and mills in Finland (51)(85). In two mining communities where mass roentgenological surveys were conducted, prevalences of pleural plaques of 9% and 6.5% were observed compared to less than 0.1% for the Finnish population.

Talc deposits found in upper New York State contain both anthophyllite and tremolite. Workers in talc mines and mills in this area have been shown to experience pulmonary fibrosis, pleural changes, and restrictive lung function changes (52)(54-57)(107)(132)(133). A recent cross-sectional study of lung function and chest x-rays among talc workers in this area was reported by Gamble et al. (31). Compared with coal and potash miners, talc miners and millers were found to have an increased prevalence of cough and dyspnea along with reduced FEV_1, FVC, and flow rates. Talc workers with more than 15 years employment were found to have a 33% prevalence of pleural calcification and pleural thickening. Recent exposures in these operations were reported by Dement and Zumwalde (19). Time-weighted-average fiber exposures were found to range from 0.8 to 16.0 fibers/cc with 12-19% identified as tremolite and 38-45% anthophyllite.

Chrysotile—Radiological changes, lung function, and respiratory symptoms among Canadian chrysotile miners and millers have been extensively studied by McDonald et al. (76) (77) and Becklake et al. (4). A total of 1,015 current employees were given chest x-rays, underwent pulmonary function studies, and were administered a standard British Medical Research Council Questionnaire on respiratory symptoms. Both persistent cough and phlegm (bronchitis) and breathlessness on exercise were found to increase with exposure. The prevalence of bronchitis rose to 50% among smokers in the highest dust exposure categories. The prevalence of breathlessness was not affected by smoking but rose to greater than 40% in those with cumulative dust exposures over 800 mppcf-years. The prevalence of irregular small opacities (>1/0 ILO/UC) in the lowest exposure category was found to be 1.8% for the Thetford mine and 6.4% for the Asbestos mine. Prevalences increased to 26.4% for Thetford and 10.9% for Asbestos in the group with exposures more than 800 mppcf-yr. The prevalence of pleural thickening was found to be less strongly related to exposure. Among various lung function parameters measured, both FVC and FEV_1 declined more with exposure. Those with small opacities of category 2/1 or greater were found to have significantly reduced functional residual capacity, residual volume, and single breath diffusing capacity at rest. Only FVC and FEV_1 were reduced in those with earliest roentgenographic changes.

Cross-sectional respiratory disease studies have been conducted among chrysotile miners and millers in Newfoundland and Corsica (7) (121). Selikoff studied 485 current employees

of a chrysotile mine in Newfoundland and found a 5% prevalence of parenchymal abnormalities (ILO U/C ≥1/0) (121). This prevalence increased to 11.5% among those employed more than 10 years. The prevalence of pleural changes was less than that observed for parenchymal changes.

Boutin et al. studied chest films of 16 ex-workers of chrysotile mines and mills in Corsica which had been closed in 1965 (7). Compared with controls, chrysotile miners and millers had 2.4 times the risk of parenchymal abnormalities and 2 times the risk of pleural abnormalities. Exposure levels among those workers were extremely high, ranging from 85 to 267 mppcf.

The above studies of chrysotile asbestos workers have been cross-sectional by design and have likely underestimated risks since: (1) those who develop severe disease are likely to have already left employment, and (2) chest film changes may develop after termination of employment, or changes may be progressive without additional exposure. Liddell et al. studied chest film changes in a 20-year longitudinal study of chrysotile miners and millers (62). These authors observed a 20-year cumulative incidence for small irregular opacities of 16%, a pleural calcification incidence of 5.3%, and a pleural thickening incidence of 5.3%. Only the incidence of small opacities was strongly associated with smoking. Rubino et al. studied the progression of chest film changes among retired chrysotile asbestos miners and millers and found that 39% of those who had initial films with a profusion of 1/0 or greater, demonstrated progression without further exposure (116). Becklake et al. also studied radiological changes after withdrawal from asbestos exposure (5). Parenchymal progression was observed in 7% of the films, pleural progression in 19.8%, and both parenchymal and pleural progression in 2.3%. These changes were found to be independent of age and smoking, but parenchymal "attacks" occurred more among those with higher asbestos exposure prior to employment termination.

Relationships between radiological findings and subsequent mortality among chrysotile miners and millers have been studied by Liddell and McDonald (69). This study consisted of 4,559 whose latest film had been read according to the UICC/Cincinnati classification system with mortality follow-up from time of film assessment through 1975. Overall, this cohort experience significantly increased mortality for all causes (SMR = 144), lung cancer (SMR = 177), pneumoconiosis (31 cases), other respiratory diseases (SMR = 127), diseases of the heart (SMR = 136), cancer of the esophagus or stomach (SMR = 170), and cerebrovascular diseases. There were 5 pneumoconiosis deaths among those classified as having normal radiographs; however, the risk of death due to pneumoconiosis was 11.75 times greater among those with "less-than-normal" films. The lung cancer relative risk for those with chest film changes was 3.24 and most who died of lung cancer were found to be smokers. Small parenchymal opacities were present in most but not all persons whose deaths were attributed to lung cancer. The authors concluded that the chest radiograph was useful for surveillance of asbestos workers but was limited due to radiological progression after withdrawal from exposure and by the carcinogenic risk associated with dust retained in the lung.

PATHOLOGY

Pleural Plaques

Hyaline plaques of the parietal pleura occur in association with exposure to all commercial types of asbestos. They are more common than the pulmonary parenchymal lesions of asbestosis, thus their presence does not necessarily imply coexistent asbestosis. The majority occur in men, 20 years or more after first exposure. The plaques almost invariably involve the parietal pleura; less commonly they are found on the visceral pleura or parietal pericardium. They are usually bilaterally symmetrical and appear as well circumscribed, pearly white or creamy, fibrotic elevations of the pleura (Figure II-11). Their surface is smooth and glistening with either a flat, plateau-like or nodular contour. They range in size from a few millimeters to several centimeters in diameter. Most commonly they are found following the lines of the lower ribs posteriorly or on the diaphragm. On cut section, they have the consistency of cartilage. Histologically, the plaques are composed of avascular and acellular bundles of hyalinized collagen arranged in a reticulated mesh or "basket weave" pattern (Figure II-12). Some of the more nodular plaques show a whorled pattern of collagen fibers. Focal

calcification is fairly common and elastic fibers are sometimes demonstrable within the plaque (112). Although the plaques are almost acellular, lymphocytes and plasma cells may be present around blood vessels beneath the plaque. The origin of the plaque is not known; histological studies suggest an extrapleural rather than a pleural origin (145). Asbestos bodies are rarely seen in pleural plaques, though they can usually be detected in the underlying pulmonary parenchyma (40)(112). Short, uncoated fibers may be present in a proportion of plaques (40) (65). Pleural plaques rarely, if ever, undergo malignant change.

Asbestosis

In early or mild cases of asbestosis, the lungs may be of normal size and shape; in advanced cases, they show a marked reduction in volume. The visceral pleura is usually pale, opaque, and thickened, particularly over the lower lobes. Adhesions between the visceral and parietal pleura may be present. In the absence of other exposures, pleural pigmentation is usually slight.

The lungs may appear grossly normal in cases showing histological evidence of mild disease. However, on careful palpation, it is usually possible to detect an increased firmness of the parenchyma. With advancing disease, the lungs are dark tan in color and show a pale reticular fibrosis. Characteristically, the fibrosis is most prominent in the lower lobes and dependent parts of the upper and middle lobes. In the late stages of the disease, the lungs have firm, spongy texture and show dense fibrosis with areas of cyst formation (honeycombing). The honeycomb

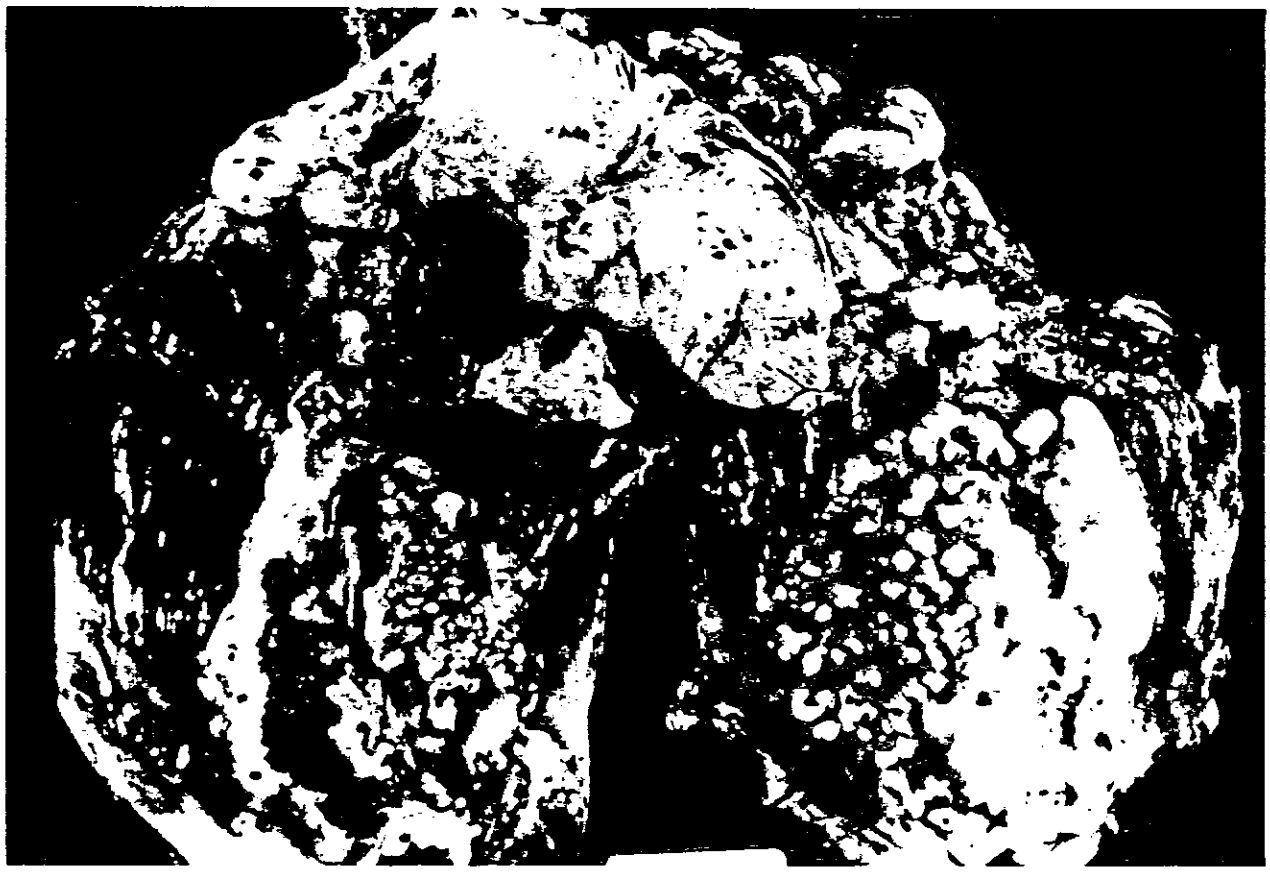

Figure II-11. Diaphragmatic pleura of 68-year-old ex-construction worker. Numerous dome shaped and flattened, ivory colored plaques are seen over both hemidiaphragms.

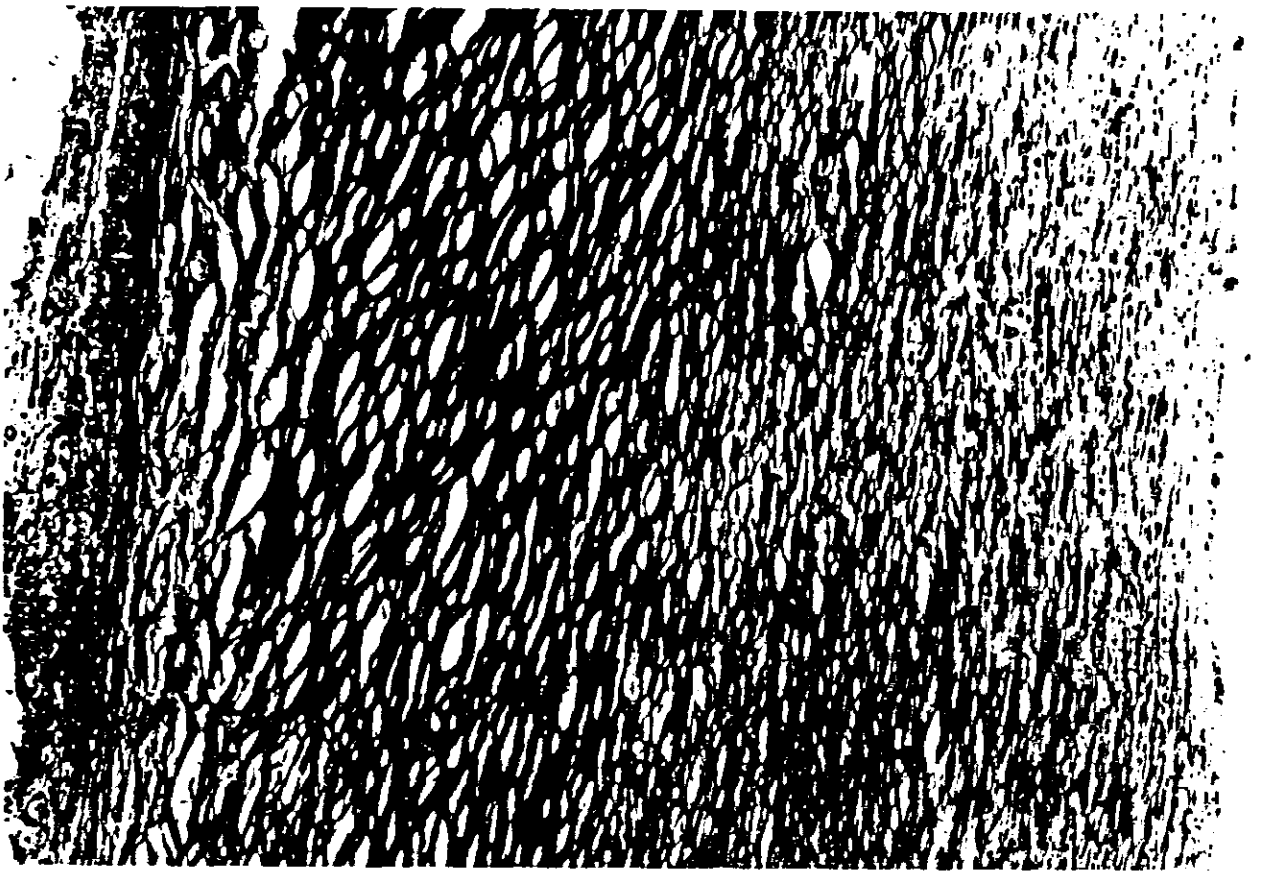

Figure II-12. Histological section of pleural plaque. The plaque is composed of acellular bundles of collagen fibers arranged in a "basket weave" pattern. Hematoxylin and eosin × 64.

cysts vary in size from a few millimeters to a centimeter or more in diameter and are most prominent in the lower lobes and subpleural areas of the lungs (Figure II-13, A & B). Emphysema is unusual and, when present, is not related to asbestos exposure. Massive fibrosis is a less common feature of asbestosis and probably results from mixed dust exposure. Necrotic nodules similar to Caplan's lesions in coal workers have been described in patients with asbestosis and circulating rheumatoid factor (91).

Microscopically, the earliest lesion attributable to asbestos inhalation involves the respiratory bronchiole. Fibers deposited on the walls of respiratory bronchioles and adjacent alveoli stimulate a macrophage response. Depending on fiber size, giant cells may form. The macrophagic response is followed by the deposition of reticulin and collagen in the walls of the respiratory bronchioles (Figure II-14). Asbestos bodies and fibers are found in association with the lesions of the respiratory bronchioles and within alveoli. A similar lesion has been described in cigarette smokers (100). The early lesion of asbestosis differs from the respiratory bronchiolitis of cigarette smokers only with respect to the presence of asbestos bodies. The diagnosis, therefore, of asbestosis depends upon the recognition of asbestos bodies within the lesion.

As the disease evolves, the fibrosis extends out to involve the walls of adjacent alveoli. Eventually, adjacent acini are affected resulting in a diffuse interstitial fibrosis (Figure II-15). With further progression of the disease, the pulmonary architecture becomes distorted. Intra-alveolar fibrosis leads to obliteration of alveolar spaces

Figure II-13 (A). Freeze dried whole lung section from 51-year-old male plumber exposed to asbestos lagging for 16 years. There is marked honeycombing of the mid and lower zones.

and eventually to areas of conglomerate fibrosis (Figure II-16). Despite the obliteration of alveolar spaces, the outline of the walls of the alveoli usually remain intact and can be demonstrated with elastic stains (138). Eventually, fibrous-walled (honeycomb) cysts form (Figure II-17). The cysts are lined by flattened or metaplastic epithelial cells of ciliated cuboidal, goblet, or squamous type. These changes are nonspecific and may occur in the late stages of pulmonary fibrosis, whatever the etiology. This pathogenetic sequence of events forms the basis for a grading system developed by a committee of U.S. pulmonary pathologists assembled under the auspices of the National Institute for Occupational Safety and Health and the College of American Pathologists (16).

The above features appear to be common to all the commercially available types of asbestos. Several other types of tissue response have been described in association with asbestosis. These include chronic inflammatory cell infiltrates, desquamative interstitial pneumonia (15), and the formation of intra-epithelial eosinophilic hyaline bodies (62). These features are not specific for asbestos.

Asbestos Bodies and Fibers

Two types of fibers are encountered in the lungs; uncoated fibers that resemble the inhaled particle and coated fibers or asbestos bodies. The ratio of uncoated fibers to coated bodies is high, ranging from 5:1 to 10,000:1 (10).

Asbestos bodies are an index of asbestos exposure and are considered an essential feature for the histological diagnosis of asbestosis (16). They may be formed in the lungs as early as two months after first exposure (135). Asbestos bodies tend to form on the larger fibers, i.e., those greater than 5μm in length and result from the deposition of iron-protein complexes on the core fiber by alveolar macrophages (143). In hematoxylin and eosin stained sections they appear as golden brown segmented structures with a clear central core fiber. In Perl's iron stained sections they appear blue. The morphology of the coating is variable, with club-shaped or beaded bodies predominating (Figure II-18). Similar structures may form around other minerals such as carbon, ceramic aluminum silicate fibers, and fiberglass, and they have been termed ferruginous bodies (37)(42). They usually lack the clear central core of a typical asbestos body. These types of bodies are relatively uncommon, however, and for practical purposes, it can be assumed that a typical asbestos body contains an asbestos fiber. Although all major commercial types of asbestos can produce asbestos bodies, the majority of the core fibers, when analyzed by selected area electron diffraction, are found to be amphibole asbestos (11). Several procedures exist for the quantification and identification of fibers in tissues (11)(16)(137)(150). The majority of these fibers are too small (<5 μm in length) to be

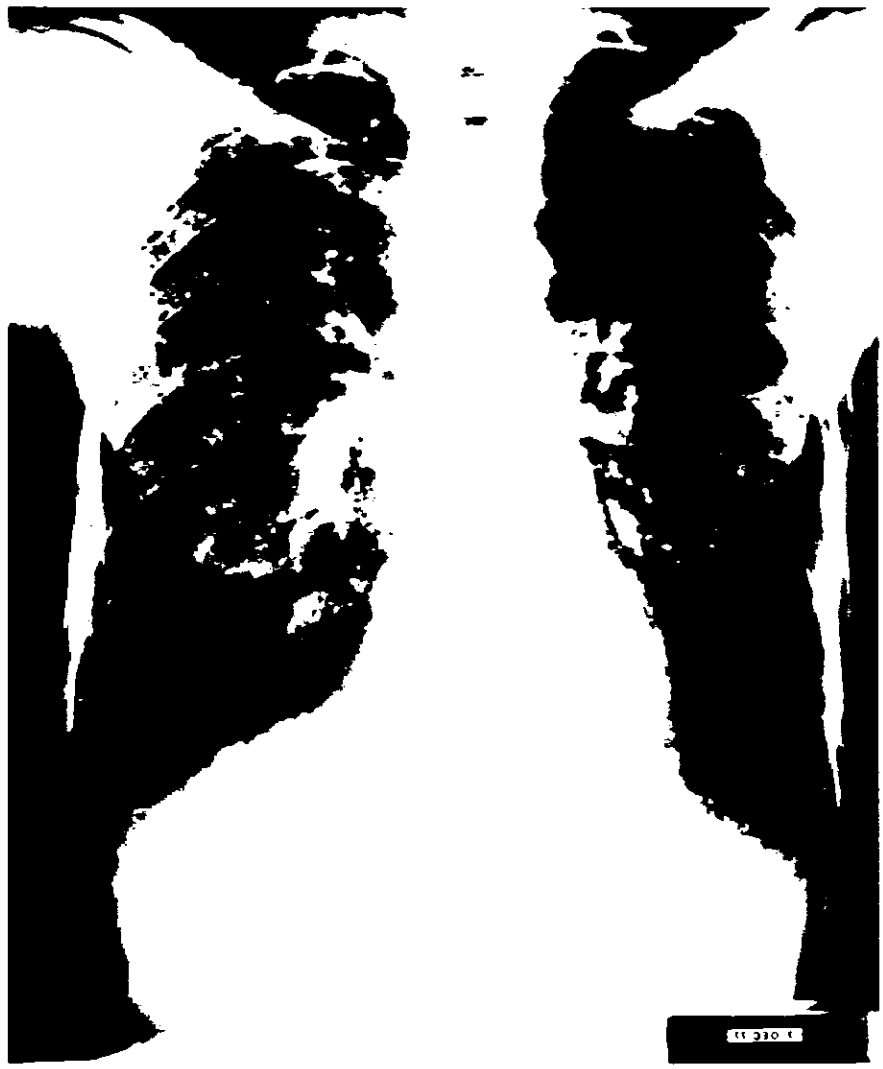

Figure II-13 (B). Roentgenogram showing marked interstitial disease with honeycombing which is most severe in the mid zones.

resolved by the light microscope. Electron microscopical studies on selected cases have shown that occupationally exposed workers have pulmonary asbestos fiber counts orders of magnitude greater than the general population (16)(163). The value of these techniques is to establish exposure and to identify the mineral type and should not be considered a substitute for more conventional diagnostic methods. Currently, the role of the short fibers in the pathogenesis of asbestosis and asbestos-associated lung cancer has not been resolved.

Lung Cancer

The association between asbestos exposure, smoking, and lung cancer is now firmly established. The majority of asbestos-associated bronchial carcinomas arise in lungs that also show asbestosis. Autopsy and mortality studies indicate that the prevalence of lung cancer in persons with asbestosis ranges from 12-55% (42) (136).

The lung cancers associated with asbestos exposure occur at a slightly earlier age than in nonexposed individuals (74). They arise in relation to the fibrotic lesions and are thus more common in the periphery of the lower lobes (49)(162). All histological types of cancer occur with most (41)(42)(162), but not all (49), studies

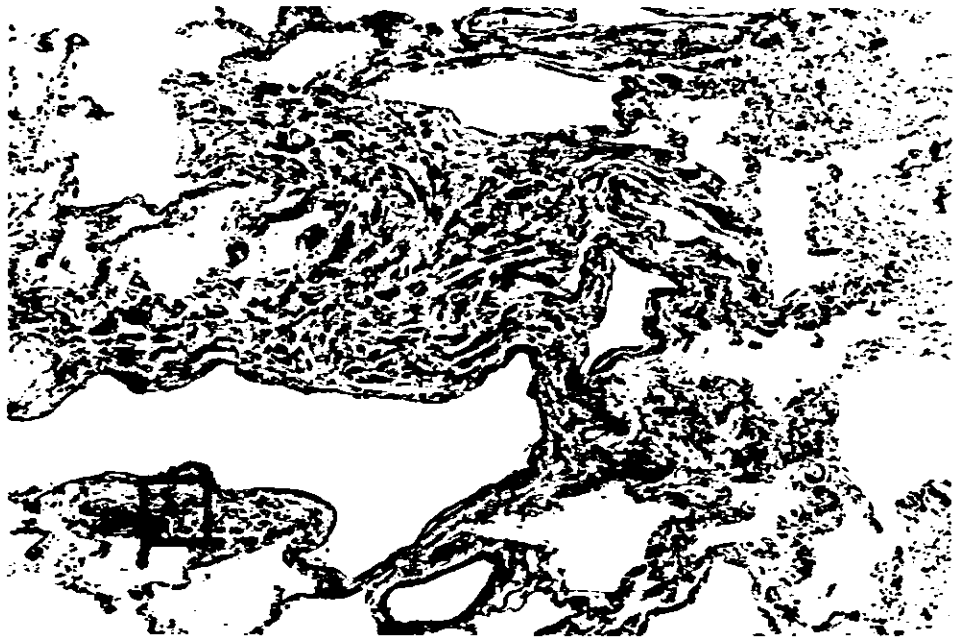

Figure II-14. Section of lung from 68-year-old asbestos insulation worker showing the histological features of mild asbestosis. The lesion is characterized by peribronchiolar fibrosis in which there are numerous asbestos bodies. Inset shows an asbestos body. Hematoxylin and eosin × 100.

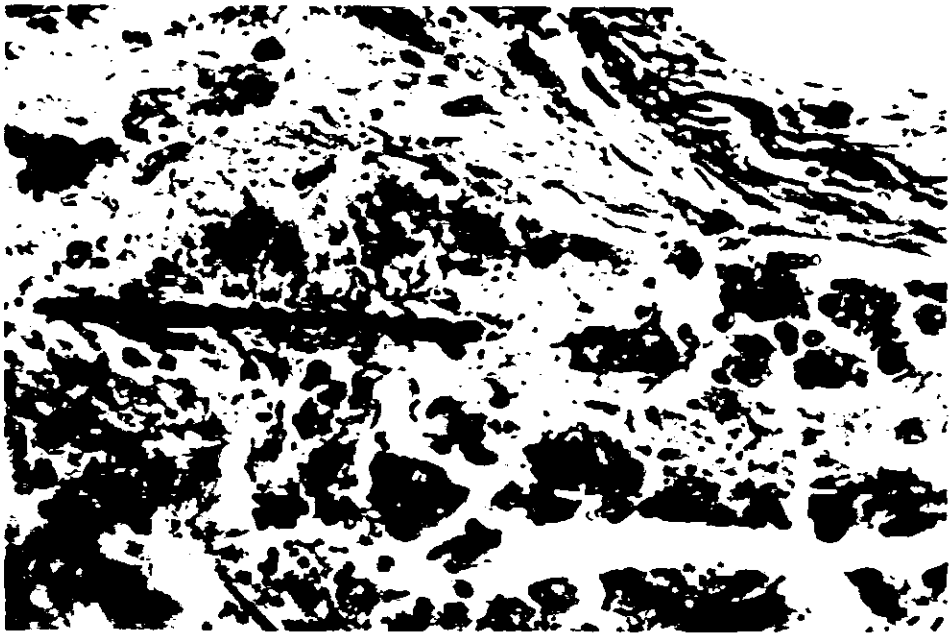

Figure II-14 (Inset).