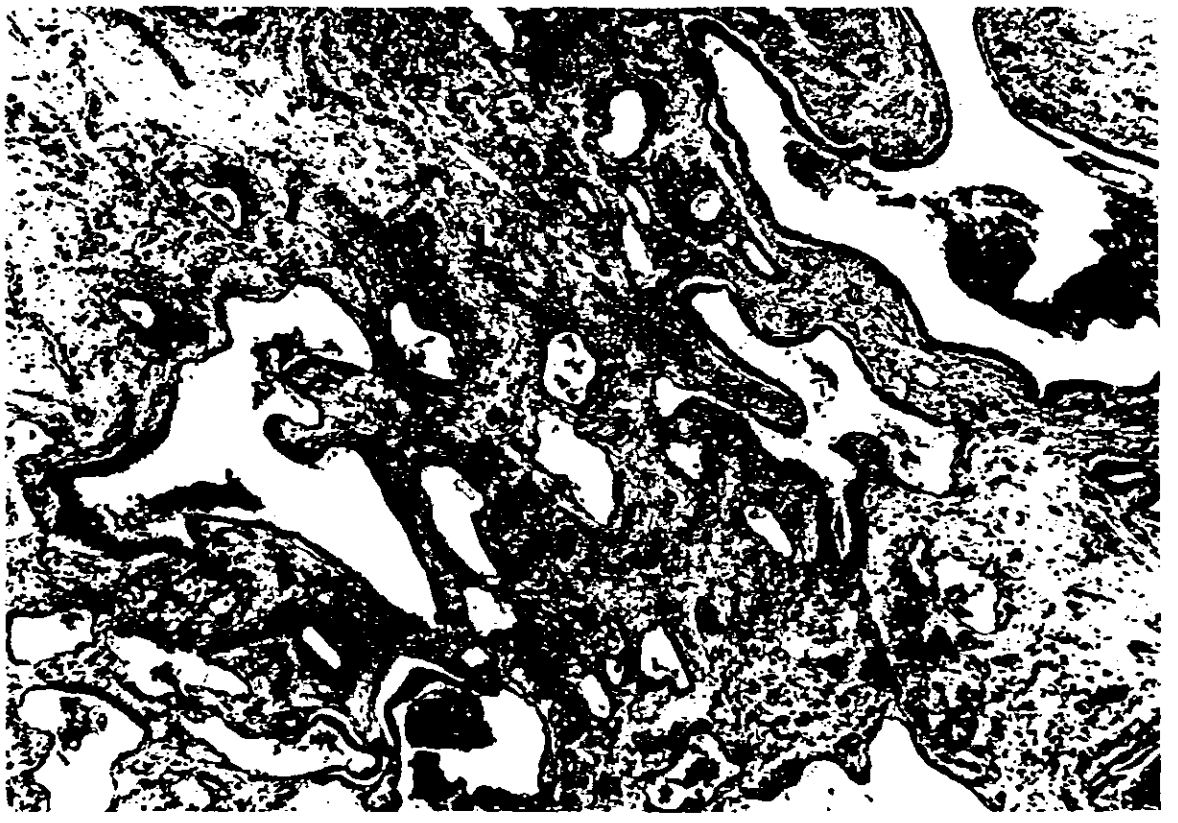

Figure II-17. Section of lung showing honeycombing. The pulmonary architecture has been replaced by thick bands of fibrous tissue outlining cystic spaces. There is a moderate chronic inflammatory cell infiltrate of the parenchyma. Hematoxylin and eosin × 40.

showing a preponderance of adenocarcinomas.

Metaplastic and pre-malignant changes have been observed in the bronchi and within areas of fibrosis in asbestosis (42)(101). It has yet to be determined whether sputum cytology is of value in early detection of carcinoma in asbestos workers (35).

Mesothelioma

Mesothelioma is a rare tumor arising from the mesothelial cells that line the pleural, pericardial, and peritoneal cavities. The first case associated with asbestos exposure was reported by Wyers in 1946 (165). In 1960 this association was firmly established by Wagner and co-workers in a study of individuals exposed to crocidolite asbestos in the Northwest Province of South Africa (152). Since then, cases have been reported from all major industrial countries. Exposure to crocidolite and amosite (45) (125) appear to carry the greatest risk for developing mesothelioma, whereas workers exposed predominantly to chrysotile asbestos appear to have the least risk (18) (45). The tumor is almost invariably associated with asbestos exposure—a positive history being obtained in 80-90% of cases (13)(151); however, there is no evidence for a dose-response relationship. Although exceedingly rare in the general population, mortality from mesothelioma may approach 10% among some groups of asbestos workers (127).

The tumor occurs in both sexes and has a latency period in excess of 20 years—usually 30 to 40 years. There is no association with cigarette smoking. The tumors are ivory colored and, in typical cases of pleural mesothelioma, encase the lungs in a rubbery mass of tissue. Pleural plaques and asbestosis may also be present, though in the majority of cases mesotheliomas occur in the absence of these lesions. The tumor tends to spread along the interlobar fissures and to invade the subpleural portions of the lungs. Direct invasion of adjacent organs, such as heart, diaphragm, and liver and extension into surgical incisions and aspiration needle tracts are characteristic. Metastases to local lymph nodes and the

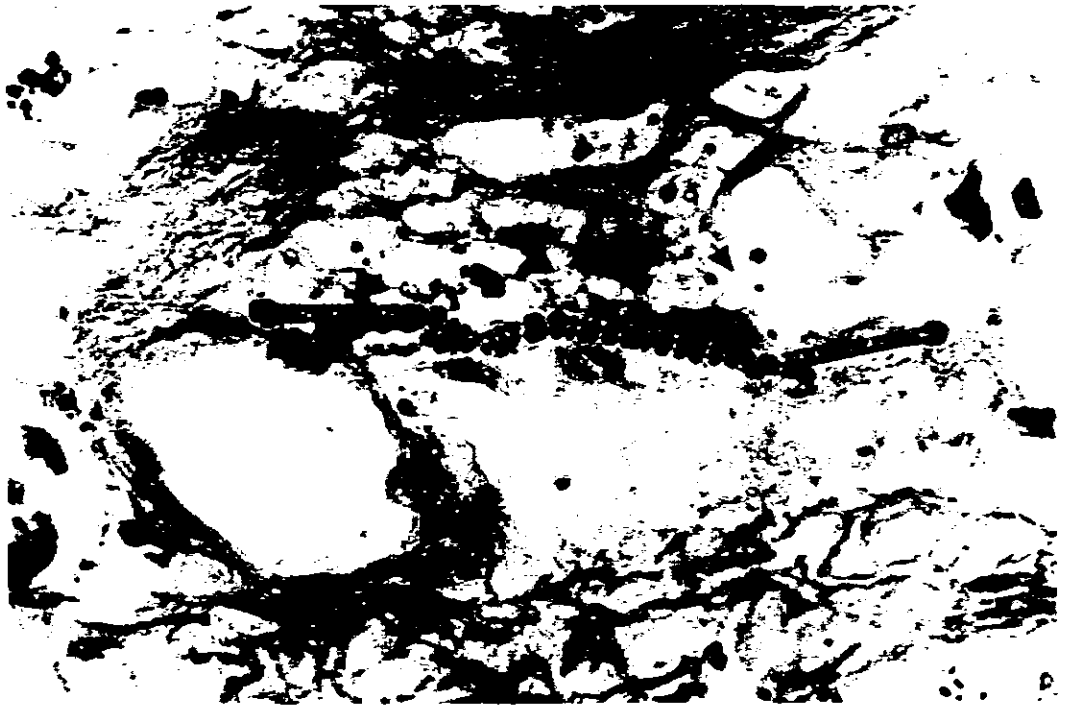

Figure II-18. Asbestos body within an area of fibrosis. The body is composed of a translucent core fiber with a beaded iron-protein coat. An uncoated fiber is also seen (arrow). Hematoxylin and eosin X 600.

lung are also fairly common. Extrathoracic metastases are relatively rare, and their presence should raise a suspicion as to the authenticity of the tumor.

Microscopically, the tumor can be classified into tubo-papillary, sarcomatous, and mixed types. The tubo-papillary is the most common type and is easily confused with metastic carcinoma from the lung or elsewhere. Special stains may aid in differentiation in some cases. Mesotheliomas usually contain the mucopolysaccharide, hyaluronic acid, which stains with Hale's colloidal iron and with alcian blue. The specificity of the reaction can be determined by pretreatment of the tissue section with hyaluronidase (16). Hyaluronic acid may also be demonstrated by electrophoresis of tumor tissue (154). Adenocarcinomas usually contain intracytoplasmic mucin droplets rather than hyaluronic acid (16). More recently it has been suggested that the absence of carcinoembryonic antigen (CEA) may be a useful adjunct for diagnosis (153). In the United States and Canada, special panels of pathologists (mesothelioma panels) exist to provide a diagnostic referral service (50).

CLINICAL EVALUATION

Clinical evaluation of the asbestos-exposed worker should include a full occupational and environmental history, full medical history, chest radiographs, and spirometry. Evaluation of the occupational and environmental history is especially important. The patient may have had only a few weeks of employment in construction or a shipyard as a summer job years before; yet, it is well documented that such brief exposures may manifest in asbestos related diseases 20 to 30 years later. It is important to assess other occupational exposures, such as coal or hard rock mining, which may produce rounded opacities on radiographic evaluation. Family history is also important. Asbestos insulation workers, as in many trades, tend to work in that trade from generation to generation. Therefore, the possibility of asbestos exposure in the home as a child should not be overlooked. Although a single PA radiograph is recommended for screening for

asbestos related disease in the clinical evaluation, a lateral chest radiograph should also be obtained to evaluate the lung zones behind the heart and provide a baseline for future evaluation. Although impairment is better correlated with radiographic abnormality in asbestosis than in other forms of pneumoconiosis, it is still highly variable. Therefore pulmonary function evaluation is required to assess the nature and extent of lung function abnormality.

Symptoms and Signs: Unlike silicosis and coal workers' pneumoconiosis, the asbestos worker may present with dyspnea in the absence of radiographic abnormality. Exertional dyspnea is the most prominent symptom with progression and is the major complaint in asbestosis. A chronic cough which is usually dry, but which may be productive especially among smokers and those working a dusty job, is another common finding. This is consistent with epidemiological studies showing increased bronchitis and airways obstruction especially among smoking asbestos workers. With progression of asbestosis, dyspnea becomes marked and is accompanied by tachypnea.

Pleural plaques or thickening are typically not accompanied by symptoms and may therefore be present years before detection. Some of these patients will report chest tightness or difficulty taking a deep breath. With marked pleural thickening, dyspnea is usually the principal complaint. Asbestos induced pleural effusions are not unusual and may cause pleuritic pain, but pleural pain is often not present even when a friction rub is heard.

Physical examination is usually not remarkable, especially in early cases of asbestosis. In most cases, the first sign, and often the only sign, is crisp basal crepitations usually best detected anteriorly and laterally at the end of a full inspiration. Clear mid-inspiratory crepitations may be heard over the mid and lower lung zones in more advanced cases of asbestosis. Digital clubbing is found in advanced asbestosis. Cyanosis, like clubbing, is a late sign in those with far advanced disease.

Physical findings in patients with pleural plaques or thickening are few unless the thickening is marked or an effusion is present. In such instances decreased thoracic expansion, dullness to percussion, and diminished breath sounds are found. Pleural friction rubs may also sometimes be detected in patients with pleural involvement.

Radiographic Findings: The radiographic findings of asbestosis and asbestos related pleural plaques and thickening are best described through systematic application of the 1980 ILO Classification for interpretation of the pneumoconioses (44). Guidelines for obtaining a technically satisfactory radiograph and for its interpretation are included in the 1980 ILO Classification. Because of the well known variation in interpretation of radiographs from reader to reader, it is recommended that the ILO standard films be used as a guide and that more than one independent reading be obtained (89). This is especially important in evaluation of clinical series and in population studies.

The small irregular opacities of asbestosis are most commonly distributed in the mid and lower lung zones. Their profusion (number of opacities per unit area) is dependent on the degree and length of asbestos exposure and may be quantified into categories (0,1,2,3, by the 1980 ILO Classification). The size and shape of the opacities may be described by using the symbols "s" (irregular opacities less than 1.5 mm in diameter), "t" (irregular opacities 1.5 to 3.0 mm in diameter), or "u" (irregular opacities greater than 3 mm, but less than 10 mm in diameter). Rounded opacities (p,q,r) may also be seen, but if profuse should alert the reader to the possibility of other siliceous dust exposure—this pattern is not uncommon among asbestos miners and asbestos cement manufacturers. With progression, all lung zones may be affected and radiological evidence of honeycombing in the lower zones is not unusual (Figure II-19). Rarely coalescence of opacities may produce large opacities which are ill defined and may be several centimeters in diameter (Figure II-20). Other late manifestations include irregular diaphragmatic, pleural and cardiac borders ("shaggy heart"), often associated with pleural thickening or plaques (Figure II-21).

It is, however, the early cases of asbestosis rather than the advanced cases which are difficult to interpret. It is known that smoking and repeated infections (bronchitis and pneumonia) may produce irregular opacities, especially in older individuals. Morgan et al. have shown that as a consequence, the frequency distributions of small opacities in persons with and without pneumoconiosis may be expected to overlap each other at a low profusion level (90). This obser-

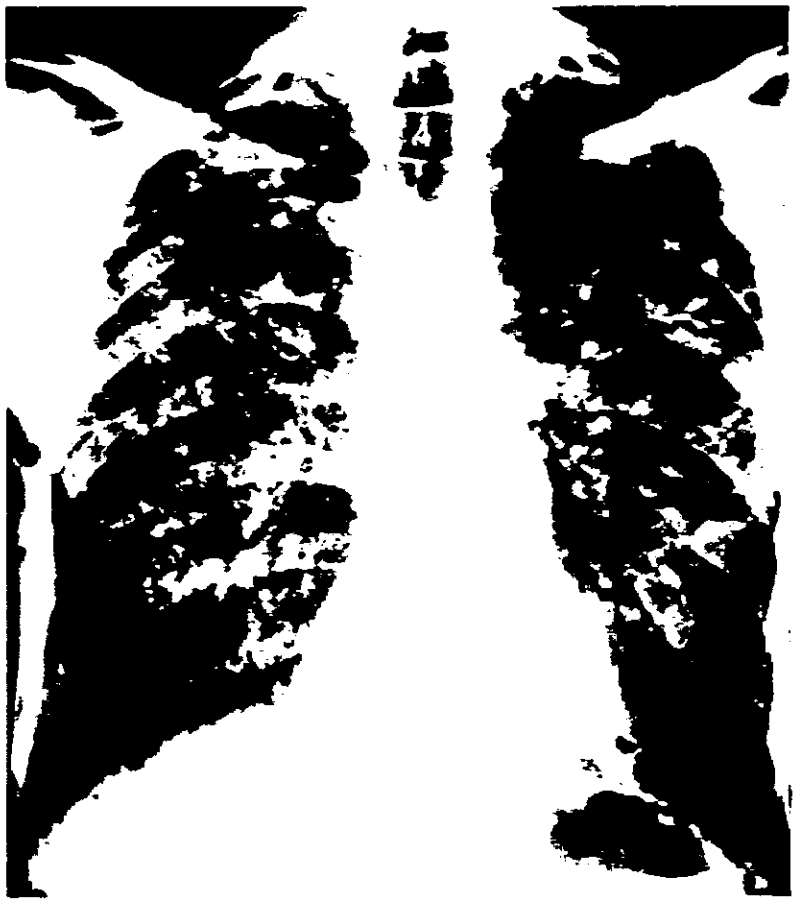

***Figure II-19. Advanced asbestosis—profusion 3/3 with all lung zones involved with s/t opacities.**

*Source: American College of Radiology Teaching Module on Asbestos Related Disease. American College of Radiology, Chevy Chase, Maryland, 1981 NIOSH contract.

vation, together with reader variability, means that caution must be used in ascribing low levels of profusion (0/1,1/0) to asbestos exposure, without consideration of other factors or etiologies—scleroderma, lipoid pneumonia, desquamative interstitial pneumonitis, and sarcoid may all present with basal irregular opacities similar to asbestosis.

Pleural plaques are fibrotic processes which begin below the surfaces of the parietal pleura, are usually smooth or nodular, are often bilateral, and are rarely over 1 cm in thickness. They are most commonly found on the posterolateral or anterior chest walls between the sixth and tenth ribs and in the aponeurotic portion of the diaphragm. Pleural plaques tend to spare the apices and costophrenic angles and, with time, tend to calcify. Plaques vary from small circular or linear opacities to large irregular opacities—some may encircle the lung. Even without calcification, they are sufficiently characteristic that an asbestos etiology should be presumed whenever they are seen. They greatly assist in the assessment of early parenchymal disease.

The 1980 ILO Classification provides an expanded and complete scheme for codifying pleural changes arising from asbestos exposure (44). The reader is asked to note whether the diaphragm and costophrenic angles are affected. Classification is provided for both diffuse and circumscribed plaques by width (O, A, B, C) and extent (0, 1, 2, 3) evaluated en face on projections. Finally, pleural calcification on the diaphragm, chest wall, or other sites may be specified.

Pleural plaques are often mimicked by the images of small divisions of the external abdominal oblique and the serratus anterior muscles which originate from the external surfaces of the

***Figure II-20. Advanced asbestosis—profusion 2/3 with all lung zones involved with s/t opacities. Large opacities in left mid-zone. Poorly differentiated squamous cell carcinoma of the right hilum.**

*Source: American College of Radiology Teaching Module on Asbestos Related Disease. American College of Radiology, Chevy Chase, Maryland, 1981 NIOSH contract.

ribs posteriorly and laterally. Unlike most plaques, however, these images are bilaterally symmetrical, occur in rhythmic sequence along the lateral chest walls, are generally smooth, regular, and less opaque than plaques. Oblique radiographs are often useful in differentiating these shadows from plaques or to better define plaques.

Lung Function: Lung function testing has been applied to the study of asbestosis since its introduction to clinical medicine in the 1940's. The specific type of lung function test is dictated by the type of investigation. Spirometry has served well as a tool for industrial medical surveillance and for prospective epidemiological studies. Assessment of lung volumes and gas exchange (D_{LCO} and arterial blood gases) have been useful additional laboratory tests used to evaluate those exposed to asbestos.

Classically, advanced asbestosis has been considered as a disease which restricts lung volumes (especially VC, and to a lesser extent, RV) and produces gas exchange measurements consistent with an "alveolar capillary" block (i.e., decreased D_{LCO} and in more advanced cases, depressed resting Pa_{O2})(3). CO_2 exchange is usually not affected. In far advanced cases arterial oxygen desaturation is observed; this usually corresponds to central cyanosis and marked dyspnea.

Recent papers on lung function among those with asbestosis have suggested that a mixed restrictive and obstructive pattern and obstructive defect are also commonly found among those with asbestosis. In 1972, Muldoon and Turner-Warwick reported 13 of 60 asbestos workers evaluated at the Brompton Hospital had a pure

***Figure II-21. Chronic calcified fibrous pleuritis involving the right chest wall and costophrenic angle.**

*Source: American College of Radiology Teaching Module on Asbestos-Related Disease. American College of Radiology, Chevy Chase, Maryland, 1981 NIOSH contract.

obstructive ventilatory defect; 3, a mixed pattern; 32, restriction; and 12 were normal (72). In 1975, Fournier-Massey and Becklake reported that among 1,000 Canadian asbestos miners and millers, 12.8% had a restrictive pattern and 12.2% an obstructive pattern (30). Murphy et al. in a study of shipyard workers, found no more obstruction among asbestos workers than matched controls (94). However, Rodriquez-Roisen et al. recently reported an obstructive pattern, defined by reductions in forced expiratory flow at 75% of the vital capacity, in 34 of 40 asbestos workers referred to the Pneumoconiosis Medical Panel and the Brompton Hospital, London (114). Although only 7 of 34 were considered nonsmokers, the authors suggest that airways obstruction, particularly affecting small airways, is a common functional abnormality attributable to asbestos exposure. This view is consistent with pathological observations which show peribronchiolar fibrosis to be an early lesion in asbestosis (see Pathology). The extent and severity of obstructive defects among asbestos workers, however, still needs full epidemiological evaluation with attention to other risk factors, especially smoking.

Other Medical Tests: Serological tests of those with asbestosis have shown increased levels of antinuclear factor (ANF) and rheumatoid factor (RF)(142)(147). Others have reported normal levels in mild cases, suggesting that these findings may be the result of nonspecific lung damage (24)(144). However, Gregor et al. have recently reported a series of 119 subjects followed prospectively at the Brompton Hospital and assessed for progression in asbestosis relative to auto-

antibody status (36). Although the numbers were small, there was some suggestion that those who showed a progression over three to seven years had higher antinuclear antibody titers and with greater frequency. These authors suggest that this finding, if confirmed, might indicate a greater degree of inflammation associated with greater alveolar macrophage turnover; this may be an important event in rapid progression among some with asbestosis.

HLA phenotype is another serological test which has been studied in relationship to asbestosis, extent of radiographic profusion, and progression of asbestosis. In a preliminary study, Merchant et al. reported a slight increase in HLA-27 phenotype among men with asbestosis and this was associated with a greater degree of fibrosis (radiographic profusion) (82). However, upon prospective evaluation of the HLA system in asbestosis, Turner-Warwick concluded that HLA phenotype was not of significant importance in the etiology of asbestosis (146).

PREVENTION

Available epidemiologic data support a linear, no threshold dose-response relationship between asbestos exposure and the risk of lung cancer. Additionally, no threshold has been convincingly demonstrated for nonmalignant respiratory diseases associated with asbestos exposure. Thus, any asbestos exposure carries with it some increased risk of asbestos related diseases. Accordingly, asbestos exposure should be eliminated or reduced to the lowest level possible.

The most effective method for eliminating asbestos related diseases is substitution of less toxic materials or modification of a process or product to eliminate asbestosis. Materials commonly used for substitution include fibrous glass, rock wool, slag wool, and various ceramic and man-made fibers. Asbestos pipe insulation has been satisfactorily replaced with calcium-silicate insulation block. These substitute materials are not totally without risk; thus appropriate work practices and engineering controls are still required.

Appropriately designed and maintained engineering techniques are the control method of choice where asbestos substitutes cannot be used. Processing of asbestos in a wet state has been shown to be an effective control method in many asbestos processing industries, including the asbestos textile industry. The most commonly used control measure in asbestos processing plants is local exhaust ventilation whereby liberated dust is collected at the dust source and removed from the breathing zone of workers. Methods of local exhaust ventilation also have been developed for handtools such as saws and drills used in the construction industry.

Appropriate work practices are an important component of any dust control program. These include use of wet methods or high efficiency vacuum cleaners for cleaning of asbestos contaminated areas and proper disposal of asbestos contaminated waste. Showering and changing of work clothes at the end of the work shift are important in eliminating "take-home" exposures. Respiratory protection is appropriate for short-term jobs or operations where controls may be unfeasible; however, use of respirators is not an acceptable substitute for engineering controls.

The combined effects of asbestos exposure and cigarette smoking in increasing the risks of lung cancer and asbestosis are well established. In addition to reducing or eliminating asbestos exposures, asbestos workers should be educated on the multiplicative risks of smoking and asbestos exposures and encouraged not to smoke. Anti-smoking programs are important for asbestos workers.

Various regulations have been promulgated in the United States specifying exposure limits, exposure monitoring requirements and medical surveillance requirements. In 1972, the Occupational Safety and Health Administration promulgated its first exposure standard for asbestos fibers, specifying a limit of five fibers/cc of fibers longer than 5μm (fibers/cc) on an eight hour time-weighted-average basis. This was reduced to two fibers/cc on July 1, 1976. Subsequent reviews of new literature on health hazards of asbestos prompted the National Institute for Occupational Safety and Health to recommend an eight hour exposure limit of 0.1 fiber/cc and elimination of all but essential uses of asbestos.

Research Priorities: Although asbestosis is well characterized clinically and has been the subject of a good deal of epidemiological research, a number of research priorities remain:

1. Epidemiological studies are needed to further characterize: potential asbestos risk from exposure in the railroad in-

dustry; tremolite exposure from contaminated vermiculite and talc in the users of these products; the risk (if any) among those working in the crushed stone industry; and to assess the risk of pleural abnormalities in the absence of parenchymal changes.

2. Research is needed to further assess differences in lung cancer and pneumoconiosis risks for various manufacturing and mining populations.
3. Pathological standards developed to characterize asbestosis need to be tested for reliability and validity in a controlled trial.
4. More sensitive and specific tests are needed to assess asbestos lung deposition and injury.
5. Immunological, serological, and bronchial lavage studies of the progression of asbestosis are needed to better characterize the natural history of asbestosis.
6. Experimental animal and clinical trials with promising chemotherapeutic modalities, for both asbestosis and asbestos associated cancer, should be a high priority.
7. Research must continue on other fibrous materials, such as wollastonite and fine fibrous glass and mineral wool, to document other health effects which may be associated with these fibrous materials.

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OCCUPATIONALLY INDUCED LUNG CANCER EPIDEMIOLOGY

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INTRODUCTION

It has been estimated that lung cancer will kill approximately 77,000 men and 28,000 women in the United States during 1981 (16). This accounts for 34% of all types of cancer deaths in males and for 15% in females. It is expected that 122,000 new cases of lung cancer will occur in the United States in 1981. This will account for a total of 22% of deaths in males and 8% of deaths in females. The age-adjusted lung cancer death rates have increased steadily in men from 5 per 100,000 deaths in 1930 to about 70 per 100,000 deaths in 1980. In females, the rate did not climb as steadily: from 2 to 3 per 100,000 deaths in 1930 to about 7 to 8 per 100,000 deaths in the mid-sixties. However, from the mid-sixties to 1980, the rate has increased rapidly to approximately 18 per 100,000 deaths. It has been suggested that the rapid rise in lung cancer among females is because of the increasing number of women in the work force and because many more women have taken up smoking (128).

ASBESTOS

Occupational Exposure—Historical Studies

In 1935, 55 years after the usage of asbestos was introduced on a large-scale basis in industry, suspicion of an association between asbestosis and lung cancer was reported by Lynch and Smith (75) in the United States and by Gloyne (38) in the United Kingdom. About 10 years later, case reports of pleural and peritoneal tumors associated with asbestos began to appear (144)(145)(149). Epidemiologic evidence from Doll showed a tenfold risk of lung cancers in the U.K. asbestos textile workers who had been employed from 1930, that was prior to regulations that were written to help workers improve dust conditions in factories (27). Similar findings were reported in the United States in 1961. Mesotheliomas were also detected, but this fact was not published until later (81)(119). Possible variations in risk with other types of asbestos fibers were rarely considered in the earlier reports. Since 1964, following the recommendations of the UICC Working Group on Asbestos Cancers (UICC 1965)(136) for new studies, there has been an expansion of epidemiological studies in many parts of the world.

Epidemiologic Studies—Lung Cancer

Mixed Fiber Types

In most industrial processes different fiber types are mixed, so that pure exposures to a single asbestos type are rare. Mortality studies of defined populations of asbestos manufacturing, insulating, and shipyard workers have provided the most concrete evidence concerning the association between bronchial cancer and exposure to asbestos. Reports received from several countries: England (30)(92), Germany (12), the United States (118), the Netherlands (129), and Italy (112) have confirmed this evidence.

Elmes and Simpson (31) have extended their earlier report (30) to include deaths occurring since 1965 through 1975. The mortality trend has shifted from a preponderance of asbestosis and gastrointestinal deaths to malignancies from lung cancer and mesothelioma, (diseases associated with longer latent periods). These authors report that their findings would suggest any standard based "on the prevention of asbestosis, may not provide adequate protection against neoplasia."

A sevenfold excess of lung cancer was found in a group of insulation workers who had been exposed to chrysotile and amosite asbestos, but not crocidolite (121). Enterline and Henderson reported a 4.4 times increased risk of (respiratory cancer) mortality among retired men who had

worked as production or maintenance employees in the asbestos industry and who had been exposed to mixed fibers (32). Among men with mixed fiber exposure (crocidolite and chrysotile) in the asbestos cement industry, the rate was 6.1 times the expected rate. In a British naval dockyard population, Harries showed that there had been an increased rise in mesotheliomas since 1964 (43). However, the full biologic effects of asbestos in shipyard workers would not have been expected to be detected until the 1970's and thereafter (117).

Edge reported that shipyard workers with mixed asbestos exposure and pleural plaques (without evidence of pulmonary fibrosis) had a 2.5 times increased risk of developing carcinoma of the bronchus, when compared with matched controls without plaques (29). In a study of sheetmetal workers with measurable and mixed asbestos exposure, an excess of deaths from malignant neoplasms (24.7% of the deaths for two cohorts, selected for 5 or more years, who worked in the trade; with 19.1% of deaths for a group where 14.5% was expected) was largely attributed to an excess of malignant tumors of the respiratory tract (21). Of the 307 deaths in the first cohort, 32 lung cancer deaths were significantly in excess (1.7 times the expected level).

Weill et al. reported on the mortality experience of a cohort of 5,645 men employed in the production of asbestos cement products and who had at least 20 years since first exposure (146). These workers were exposed largely to chrysotile with some crocidolite and amosite. Among this group, 601 persons were identified as deceased by the Social Security Administration. The vital status of 25% was unknown, and were assumed to be alive, which probably resulted in underestimation of the true risk. Death certificates were obtained for 91% of the known dead. Dust exposures were estimated, using each worker's employment history in conjunction with historical industrial hygiene data.

Weill et al. observed increased respiratory cancer mortality only among those with exposure in excess of 100 mppcf-year, where 23 cases were observed vs. 9.3 expected (146). The unusually low SMR for all causes in the low-exposure groups suggests the possibility of a selection bias and any interpretation of risks at low exposures should be done with caution. Separating the cohort by fiber type exposure, the authors concluded that the addition of crocidolite to chrysotile enhanced the risk for respiratory malignancy; however, an excess risk was observed among those not exposed to crocidolite with cumulative exposures in excess of 200 mppcf-months. Both average concentration of exposure and duration of exposure were found to be related to cancer risk.

McDonald and McDonald studied the mortality of 199 workers exposed to crocidolite during gas mask manufacture in Canada from 1939 to 1942 (84). This cohort was followed through 1975, when by this time 56 deaths occurred. Out of these 56 deaths, 4 (7%) were from mesothelioma and 8 (14%) from lung cancer.

Chrysotile

McDonald et al. reported an increased risk of lung cancer among men employed in Quebec chrysotile mines and mills (85)(86). The risk of lung cancer among those workers most heavily exposed was five times greater than those least exposed.

Kogan et al. investigated the cancer mortality among workers in asbestos mining and milling industries between 1948 and 1967 (54). The total cancer mortality rate among workers was 1.6 times higher than that found in the general male population; for female workers the rates were 0.8 times higher for those in mines and 1. for those in mills. The lung cancer risk for male miners and millers was twice that of the general male population. For females in mines and mills, the risks were 2.1 and 1.4 times that of the general female population, respectively. For workers over 50 years of age, the risk of lung cancer was greater: for men in mining, 4.0; those in milling, 5.9; for women in mining, 9.5; and those in milling, 39.8 times that found in the general population.

Wagoner et al. reported on the cancer risk among a cohort of workers in a major manufacturing complex utilizing predominantly chrysotile asbestos in textile, friction, and packaging products (143). An excess of respiratory cancer occurred among asbestos workers in each duration-of-employment category down to and including one through nine years. They observed statistically significant standard mortality ratios of 122 for all malignant neoplasms of the respiratory system. The asbestos workers in this study were located in the area of predominantly Amish dutch population with known low frequencies of smoking. The authors, nevertheless,

used the general white male U.S. population as a control group, which most likely resulted in an underestimation of the degree of risk.

Robinson et al. (106) reported an additional 8 years of observation and 385 deaths to the Wagoner et al. (143) study of mortality patterns of workers among one facility manufacturing asbestos textile, friction, and packing exposed predominately to chrysotile. Except for 3 years (during World War II), chrysotile constituted over 99% (per year) of the total quantity of asbestos processed. During those 3 years, amosite was selectively used to a limited extent because of Naval specifications and accounted for approximately 5% of the total asbestos used per year. Crocidolite and amosite (for the other years) accounted for less than 1% of the total usage in very selected areas. Exposures to these two types may have played a role in the etiology of disease; however, due to the overwhelming exposure of the cohort to chrysotile, it is likely that the other exposures played a minor role in the overall mortality patterns. Robinson et al. confirmed the observations of Wagoner et al. that statistically significant excess deaths were due to bronchogenic cancer.

Weiss reported no unusual mortality experience over a 30-year period for a cohort of workers employed in a paper and millboard plant, reported to be using only chrysotile (147). The author concluded the study results were suggestive of a minimal hazard from chrysotile. This conclusion must be viewed in light of the limitations inherent in the study. First, the population studied was small (n = 264) and only 66 workers had died at the time of the analyses. Moreover, the unusually low SMR for many of the contrasts in the Weiss et al. paper suggests the possibility of a selective bias greater than usually seen when contrasting industrial populations are contrasted with the general population.

Enterline and Henderson found that retired men who had worked as production or maintenance employees in the asbestos industry, and had been exposed only to chrysotile, and who had reached 65 years of age, had a respiratory cancer risk 2 to 4 times greater than that expected (32). Among men within the asbestos cement industry exposed only to chrysotile, a one- to four-fold excess of respiratory cancer was found.

Anthophyllite

In Finland, anthophyllite mining has been associated with an excess bronchial cancer risk of 1 to 4 times the overall expected and about double this figure for those with more than 10 years' exposure time (53)(87)(88).

Synergism

There is marked enhancement of the risk of lung carcinoma in those workers exposed to asbestos who smoke cigarettes (11)(25). Hammond and Selikoff interpret the excess lung carcinoma risk from asbestos in nonsmokers to be small (41). No link between cigarette smoking and mesotheliomas has been observed in a prospective study by Hammond and Selikoff (41). A preliminary study on female workers employed between January 1940 and December 1967, in a predominantly chrysotile asbestos textile plant, revealed 7 lung cancer deaths among 580 women when only 0.63 deaths were expected ($p<0.01$) (64). One lung cancer death was observed in a smoker, two in women of undetermined smoking history, and four in women who "never" smoked cigarettes (as determined from hospital admission charts).

It is important to note that the historic documentation of cigarette consumption patterns is lacking for most retrospective cohort studies done on asbestos workers. It is also important to note that a sizable portion of the general population, the group usually selected for comparison in these studies, are cigarette smokers. Therefore, the risk of lung cancer demonstrated for these industrial groups exposed to asbestos is of such magnitude that it precludes the identification of an independent etiologic role for cigarette smoking.

Hammond et al. have attempted to correct this methodological problem by comparing 12,051 asbestos insulation workers having complete smoking histories to a control population, with no smoking histories (42). Their control population consisted of 73,763 men from the American Cancer Society's prospective cancer prevention study who were similar to the asbestos workers in that they were white males; nonfarmers; had no more than a high school education; a history of occupational exposure to dust fumes, vapors, gases, chemicals, or radiation; and were alive as of January 1, 1967. Non-smoking asbestos workers showed a five times greater risk of dying from lung cancer than their smoking controls. Both smokers and nonsmokers exhibited a fivefold relative risk; however, the attributable risk was greater among the smokers. This higher attributable risk can be accounted for by the large

number of smokers in the asbestos-exposed population and the comparison population.

Liddell et al. has also studied the smoking patterns among asbestos workers through administering questionnaires to living workers or relatives of deceased workers, who died after 1951 (68). The authors report SMR's of 48 and 46 for nonsmokers and ex-smokers, increasing to 206 for heavy smokers. This study is unreliable however, because specific smoking death rates were not used for the calculation of expected lung cancer deaths, and this underestimated the risks among nonsmokers.

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