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THE CLINICAL SIGNIFICANCE OF EARLY RADIOGRAPHIC PATHOLOGY IN AN ASBESTOS EXPOSED POPULATION

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Susan Abigail Korrick

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ABSTRACT

The Clinical Significance of Early Radiographic Pathology in an Asbestos Exposed Population

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The purpose of this study is to investigate the clinical significance of early radiographic pathology in an asbestos exposed population. Specifically, 477 men and women with moderate occupational or household asbestos exposures were seen in eight surveillance screenings conducted between 1982 and 1984. Based on chest radiograph evidence of parenchymal and/or pleural disease consistent with asbestos exposure, 75 of those screened were seen in follow-up by the Occupational Medicine staff of Yale-New Haven and Lawrence and Memorial Hospitals between 1982 and 1985.

By applying the 1980 ILO criteria for reading chest radiographs of the pneumoconioses, three categories of mild radiographic pathology were identified in this population: 1/0 parenchymal change, 1/1 - 1/2 parenchyma and benign pleural disease alone. Comparison of these three groups with each other and with the background population of normal chest radiographs revealed several significant findings. Radiographic abnormality was strongly associated with greater age, greater asbestos exposures, longer exposure latencies, and greater tobacco use. However, determination of the independence of these associations was beyond the

scope of this study. More importantly, the three groups were strikingly similar in terms of an excessive prevalence of pulmonary function abnormalities consistent with asbestosis and restrictive lung disease despite their mean tendencies toward normal pulmonary function. As a result, we conclude that radiographic identification of early asbestos-related lung disease be expanded to include not only those with category "1" parenchymal change but also those with so-called benign pleural disease. Furthermore, these results establish the clinical significance of 1/0 parenchymal disease and thereby legitimize continued health surveillance of individuals within that category.

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TABLE OF CONTENTS

TABLES (cont.)

INTRODUCTION

I. Overview and Purpose

The purpose of this study is to investigate the clinical significance of early radiographic pathology in an asbestos exposed population. Specifically, 477 individuals with moderate occupational or household exposure to asbestos were examined in health surveillance screenings. The information thereby obtained included occupational and environmental exposure histories, tobacco exposure histories, medical-surgical histories, symptomatology queries, physical exam findings, posteroanterior chest radiographs and results of portable spirometry. From this group, 34 individuals were found to have radiographic findings consistent with early asbestosis, in other words 1/0 parenchymal change according to the ILO (International Labor Office) 1980 guidelines for classification of radiographics of pneumoconiosis (29). Twelve of those screened had slightly more advanced radiographic findings of 1/1 or 1/2 grade by the ILO criteria. An addditional 52 of this group had benign bilateral pleural disease alone.

Understanding the clinical consequences of asbestos exposure is a significant challenge for physicians in the industrialized world. As with more readily recognized tobacco and/or alcohol exposed individuals, asbestos exposed individuals constitute a significant portion of industrialized populations. Their exposures vary in magnitude, duration and source. The clinical consequences are equally variable. The

understanding of those consequences is important not only in order to institute appropriate medical management for those who are ill, but also to understand the natural history of the disease in order to elucidate the prognosis for those who are not yet ill. In addition, the medical consequences of asbestos exposure bear legal consequences both in terms of legislating prevention or mitgation of future exposure and litigating against those liable for past exposure. Thus it is important to understand the disabilities and dangers associated with asbestos exposure as much for therapeutic and prevent measures as for adjucating legal retribution.

II. Definitions of Asbestos and Its Uses

It is necessary to know what asbestos is, where it is found and how it is used in order to appreciate the magnitude of its exposure hazards.

Asbestos is a naturally occurring hydrated silicate. It is mined in both surface and underground operations primarily in Canada, the Soviet Union and South Africa. Deposits have also been tapped in China, Taiwan, Japan, Korea, India, Turkey, Yugoslavia, Bulgaria, Cyprus, Finland, Rhodesia, Brazil, Bolivia, Australia and the United States. U.S. mining sites include Vermont, North Carolina, Maryland, Georgia, Texas, Arizona, California and Alaska.

Asbestos exists in one of two forms: amphibole or serpentine. The two forms differ in their associated cations, their crystalline structures and the geologic formations in which they are found. Thus amphibole asbestos, an iron silicate, forms irregular fibrous aggregates. It is found primarily in metamorphic rock. Serpentine asbestos, a

magnesium silicate, forms sheeted crystals, and is found in serpentine recrystallization veins in a variety of types of host rock. These two types also differ in ultrastructural morphology: amiphibole fibers are straight and needle-like whereas serpentine fibers are curly. The most frequently used amphiboles include crocidolite, amosite, anthophyllite, actinolite and tremolite. Chrysotile is the only widely used form of serpentine asbestos.

Asbestos types vary in color, texture and physical properties. Fibers may be white, green, blue, brown, gray or yellow. Their texture varies from coarse to silky. Asbestos fiber types are also distinguishable by their relative capacity to withstand stress from heat, acids or other chemicals, and mechanical wear. In general, asbestos is lauded for its incredible heat resistance as it is essentially noncombustible. It is relatively impervious to acids and other chemical insults, its tensile strength is approximately equal to that of steel, and it is well known for its abilities to insulate against heat, cold, electricity and noise. It protects against corrosion, enhances cellulose paper retention of filler and pigment, resists degradation from friction or vibration and withstands processing requirements such as mixing, pulping, fiberizing and slurry transport. It even protects from bacterial degradation. In addition to this unrivalled combination of properties, asbestos is both cheap and abundant. It is extremely easy to work with as it is readily woven or incorporated into a variety of other materials.

There is an impressive litany of uses found for asbestos which spans thousands of years and thousands of applications. Evidence of asbestos use has been found in stone age pottery, in the tales of Greek mythology, in the annals of Roman historians, in the battle armor of Medieval and

early Renaissance times, in 18th century wicks, textile and paper products and, of course, in the trappings of the industrial revolution of the 19th and 20th centuries. Contemporary uses of asbestos include incorporation in textile and paper products; construction materials, particularly insulation; electrical and mechanical parts; and insulated conduits. For example, asbestos is found in fireproof clothing, gloves and mitts, ironing board covers, theater curtains, firemen's clothing, welding blankets, felt, rope, wicks, paper, filters, stoves, boilers, engines, heat resistant cabinet surfaces and benches, insulation material, lagging, shingles, siding, flooring, roofing, clapboard, wallboard, fire doors, cement, fillers, mortar, grouting, water pipes, gaskets, cables, motors, transformers, pump and piston packing, clutch facings, brake linings, perpetual logs, tape, lamp sockets, paper mache, wine and beer filters, etc. An exhaustive catalogue of the uses of asbestos is impossible to construct. Still, a brief listing of its applications is enough to suggest the magnitude of potential exposures in both the manufacture and subsequent application of asbestos containing products. It is estimated that for every worker involved in direct manufacture of an asbestos containing product, another one hundred are involved in its use and application (52). In addition, one must include exposures incurred during direct processing -- mining and refining -- of asbestos itself, as well as incidental environmental exposures from consumers' wearing, living in, living with, drinking from and using asbestos containing products.

III. Historical Perspectives

The industrial revolution included among its accomplishments the beginnings of commercial use of asbestos in the mid 19th century. However, it was not until the beginning of this century that the deleterious health effects of asbestos were first recognized and subsequently incorporated into the medical, scientific and industrial literature. In pre-World War I England and continental Europe asbestos was noted to have a "weakening effect on the lungs" (55, p. 21). Increasing industrial activity during World War I facilitated official recognition of the association between asbestos exposure and certain disease states. By 1918, a vice president and statistician for Prudential Insurance Co., New York, acknowledged the hazards of asbestos dust by indicating that his company would no longer issue life insurance policies for asbestos workers (55, p. 22). At the same time, radiographic change associated witih asbestos exposure was first noted.

Literature recognizing morbidity and mortality associated with asbestos exposure begins with testimony received by the (British) Departmental Committee on Compensation for Industrial Diseases in 1906. Specifically, the Montague Murray Case was described as follows:

> The patient, a male aged 33, came under the care of Dr. Montague Murray at the Charing Cross Hospital in the beginning of 1899. He had worked with asbestos for 'some fourteen years', ten years as a cardroom hand, and the remainder in some other room of the factory, 'where there was much less dust'. He volunteered that of the ten people working in the cardroom when he went into it, he was the only survivor, and that all the others had died somewhere about 30 years of age. There is no note as to the nature of his work previous to that in the asbestos factory.

> He was treated in the Charing Cross Hospital for two months, and then returned to work. After a few months, however, he became ill again, and was re-admitted to the Hospital in April, 1900, where he died. The post-mortem examination confirmed the clinical diagnosis of extensive pulmonary fibrosis. There was no evidence of pulmonary tuberculosis, and examination of the sputum for M. tuberculosis was negative. (39, p. 198).

The first formally published case report of death secondary to pulmonary fibrosis in an asbestos worker was in the British Medical Journal in 1924 (55 p. 22). By 1927 the term "asbestosis" had been coined to describe the pulmonary fibrosis characteristic of the lung histology of asbestos exposed workers. Two years later "asbestos bodies" were first described in the lungs of exposed individuals. By 1930, labor and government interests throughout much of the industrialized world recognized the need for the careful health surveillance of the asbestos industry. Reports on asbestosis were given during an international medical conference in Johnannesberg in 1930 while, at the same time, the International Labor Organization (based in Geneva, Switzerland) called for review of working conditions in the asbestos industry (55, p. 23).

By 1935, the first case reports of deaths secondary to lung cancer with simultaneous note of asbestosis were made. However, the etiologic association between lung tumors (and malignant mesothelioma) and asbestos exposure was not recognized. In fact, it was not until the 1960's that enough epidemiological and experimental evidence had accrued to legitimize this claim in the U.S. although British investigators recognized an increased risk of lung carcinoma in asbestos workers by the late 1940's. The association of asbestos and mesothelioma was not recognized until 1960. Against this background of almost one hundred years of accumulated

epidemiological experience, contemporary elucidation of asbestos-related diseases continues. In more recent years the association between asbestos exposure and certain gastrointestinal malignancies (esophageal, gastric, colo-rectal) has been recognized. Laryngeal, buccal, renal and ovarian cancers are as yet only suspected to have an etiologic relationship with asbestos exposure.

IV. Scope of the Problem

The widespread industrial use of asbestos has created a public health hazard of significant magnitude. It has been estimated that between 1940 and 1979, 27,500,000 individuals had potential occupational exposures to asbestos (42). This estimate does not include exposures secondary to household contacts, environmental contamination, military service (engine room workers in naval vessels, for example) or daily use of asbestos containing products from hair dryers and ironing board covers to spackle compounds and automobile brakes. These categories account for countless additional mild to moderately exposed individuals. Recent estimates of asbestos-related cancer deaths range from 4,000 to 67,000 per year (49, 42). The most probable extimates by Nicholson et al. claim 8,200 annual cancer deaths secondary to asbestos exposure with a projected increase to 9,700 per annum by the year 2000 (42). One estimate from the Department of Health, Education and Welfare (1981) indicates 13 to 18 percent of all cancers in the near future will be related to asbestos exposures (42). For the subgroup of World War II shipyard employees, estimates of deaths secondary to lung cancer alone range from 25,000 to 120,000 (42).

Data on mortality secondary to to asbestosis is less extensive. Estimates of the prevalence of asbestosis range from 8,000 to 120,000 depending on the criteria used (59). Walker et al. estimate the 1980-1984 prevalence to be approximately 65,000 based on the assumption that the prevalence of asbestosis is linearly related to the incidence of mesothelioma (59). Mortality rates of those with asbestosis are approximately 2.8 times age matched rates among the general population (59). Mortality specifically attributable to asbestosis accounts for between 21 and 38 percent of those deaths (59).

Conservative estimates of the cost (in lost earnings) of asbestos related mortality indicate an average gross loss of $252,331 (present value, 1982) per worker's life lost (33). However this cost does not account for loss in quality of life prior to death nor associated mortality and/or morbidity of family members exposed via home contacts with workers and soiled work clothes.

Thus, at least 10 percent of the U.S. population is potentially at risk for asbestos-related disease. The cost incurred by mortality within this group is substantial. The additional cost of morbidity secondary to asbestos-related disability is as yet inestimable.

Current legislative and regulatory mandates have decreasaed but not eliminated continued exposure to asbestos in both occupational and non-occupational settings. The population exposed prior to regulatory stipulations for improved industrial hygiene practices in the 1970's is at risk for the development of asbestos-related disease well into the 21st century. It is the goal of the surveillance epidemiology upon which this paper is based to monitor asbestos exposed populations with the intention of identifying individuals at risk for development of disabling

and/or fatal consequences of their exposure. Once identified, these individuals should be followed medically in order to educate them about prevention of future exposures and, whenever possible, minimize the costly consequences of their past exposures.

V. Health Effects of Asbestos Exposure

The expansive capabilities of asbestos have been recognized since ancient times and exploited most intensively in contemporary times. The unfortunate health consequences of its inhalation and ingestion have been recognized for almost as long. However, clear documentation of these hazards is a relatively recent accomplishment. There are essentially three categories of disease ascribed, at least in part, to asbestos exposure: malignancies, interstitial fibrosis of the lung or asbestosis, and benign pleural disease. The malignancies proven to occur with greater frequency among asbestos workers include malignant mesothelioma of the pleura or peritoneum, bronchogenic cancer, and gastrointestinal malignancies of the esophagus, stomach, and colon or rectum. Laryngeal, buccal, pancreatic, renal and ovarian malignancies are suspected but not yet proven to be significantly associated with asbestos exposure. With the possible exception of mesothelioma, the relative risk of asbestos-related malignancies is linearly related to dose. Heavily exposed populations (without other risk factors such as smoking) have a five to ten-fold increase risk of bronchogenic cancer and two to three-fold increase risk of certain gastrointestinal malignancies. The latency for development of most asbestos-related tumors ranges from 15 to 40 years since first exposure. Although smoking does not affect the risk

of development of malignant mesothelioma, heavily exposed smokers have a relative risk of development of bronchogenic cancer of up to one hundred times that of nonexposed, nonsmokers or approximately ten times that of a nonexposed smoker.

Experience varies as to whether a history of exposure alone or concomittant radiographic evidence of asbestosis are associated with excess risk of bronchogenic cancers. The distinction is difficult because both asbestos-related tumors and the development of asbestosis demonstrate a dose-response relationship. However, British experience suggests the association is limited to those with asbestosis. This has not been confirmed by U.S. investigators.

The mechanism of carcinogenesis of asbestos is incompletely understood. There appears to be variation in carcinogenicity dependent on fiber type though all types have been incriminated in the development of malignancy. For example, malignant mesothelioma is most strongly associated with the amphibole asbestos, crocidolite. However, an excess risk of mesothelioma is found among U.S. insulators and the U.S. insulating trade generally does not use crocidolite asbestos.

The malignant transformation of epithelial surfaces (lung, gastrointestinal tract) after exposure to asbestos is most likely a product of several environmental influences (inhaled and ingested). For mesothelial surfaces (mesothelioma) asbestos alone is the most likely etiologic agent as other environmental agents have limited access to this site. In fact, malignant mesothelioma is an extremely rare tumor and was even less common before widespread use of asbestos began.

Several mechanisms of action for asbestos as a primary and co-carcinogen have been postulated. First, it has been suggested that

the physical action, particularly of fine fibers, is tumorogenic. Specifically, fiber contact induces cell membrane changes which interfere with cellular regulation and predispose tomalignant transformation. Alternatively, the irritation of fibers in tissue can induce increased cell multipulication which would increase the likelihood of abnormal clone formation. Substances adsorbed on fiber surfaces (hydrocarbons, for example) or processing contaminants (Ni, Cr, Be) may play a role in asbestos-related carcinogenesis. Lastly, it has been hypothesized that asbestos facilitates the action of latent or coincidental viral agents which then contribute to tumorogenesis.

The other major source of morbidity and mortality among asbestos exposed populations is asbestosis, or diffuse interstitial lung fibrosis. It is not clinically distinguishable from other forms of interstitial fibrosis (viral, cardiovascular, idiopathic) excepting the finding of a convincing history of asbestos exposure. Radiographically visible pleural scarring and the presence of asbestos bodies and/or asbestos fibers histologically are helpful in the diagnosis. In general, the diagnosis of asbestosis in its advanced stages is relatively straight forward. It requires the following: an appropriate history of asbestos exposure, radiographic parenchymal change equal to or greater than 1/0 (29), a restrictive pulmonary function deficit, bibasilar rates on physical exam, and symptoms of cough and/or shortness-of-breath. The presence of pleural plaques radiographically and/or finger clubbing on exam are frequent additional findings but they are not diagnostic.

The diagnosis of the early stages of asbestosis, however, is more difficult as the importance and order of appearance of the above criteria is not well established. For the purposes of surveillance of large numbers of exposed individuals, it would be useful to identify those at

risk for development of asbestosis based on early clinical signs. Preventive measures both in terms of industrial hygiene practices and medical care could then be instituted. In addition more quantitative estimates of disability and prognosis would thereby be possible for use in compensation and disability claims which are an invariable aspect of care of asbestos injured individuals.

The current epidemiologic literature concerned with interstitial lung disease among asbestos workers has dealt with criteria for its diagnosis: historical, radiographic, physiologic, clinical, and pathological (lung biopsy and/or post-mortem findings of diffuse interstitial fibrosis with asbestos bodies visible on light microscopy and/or asbestos fibers identified with ultrastructural techniques).

Radiographic findings may be divided into two categories: pleural and parenchymal. Information about the epidemiology of each is still evolving. Pleural calcifications, for example, were not officially recognized as part of asbestosis until the mid 1950's. Such belated acknowledgement was probably due to the natural history of the development of calcified plaques which often require at least a twenty year latency period.

The prevalence and natural history of pleural disease associated with asbestos exposure is difficult to construct because of lack of comparability among the literature. Convention on the subject depends on the population studied, the particular occupation or exposure source of concern, the definition of pleural disease applied, the types of radiographic studies obtained and the care with which other causes of pleural change are elicited through history.

In general, it is accepted that two categories of pleural changes may occur as a consequence of asbestos exposure: fibrosis or thickening and calcificaton. The fibrosis, in turn, may be localized or diffuse. These changes are primarily localized in the parietal pleura but are not confined to any particular region of the lung field. Thus plaques with or without calcifications may be found in the diaphragmatic, costal, mediastinal, apical or basal pleura. Changes can be seen along pericardial surfaces as well. Visceral plaques (with or without calcifications) extending into the interlobar fissures are also not uncommon.

Calcified pleural lesions are usually considered to be a later development of pleural fibrosis. However, it is possible to find evidence of pleural calcification without radiographically visible plaques and certainly radiographic plaques exist without apparent calcifications. Similarly, the parenchymal densities associated with asbestos exposure may or may not be evident in the presence of pleural changes.

Plaques may be unilateral or bilateral, the latter being considered pathognomonic of asbestos exposure in the absence of any other cause of apparent pleural scarring. Other causes comprise a lengthy list: thoracic trauma or surgery, rib fractures, empyema secondary to bacterial or tuberculous infection, bacterial or tuberculous pleurisy, hemothorax, obesity with deposition of subpleural fat, costal origins of chest wall muscles (serratus anterior and external oblique) and pleural metastases. In addition, so called "companion shadows" must be differentiated from plaques, the former most likely derived from a combination of intercostal muscle and fat, most commonly found on the medial surface of the first four ribs (20).

Assuming that alternative causes can be ruled out, plaques are clinically very useful as an indictor of asbestos exposure. Radiographically visible pleural changes are extremely rare with other forms of dust exposure. Plaques thereby have diagnostic (and legal) implications in defining asbestos-related disease.

Plaques alone, unless unusually diffuse and extensive, do not normally cause functional impairment and do not portend any increased risk of bronchogenic cancer or malignant mesothelioma above that already associated with the asbestos exposure from which the plaques derived.

The etiology of plaques is speculative. In general, their occurrence is related to the latency, duration and concentration of asbestos exposure. However, the specifics of this relationship are not well worked out. It is postulated that the physical dimensions of the asbestos fiber combined with the respiratory movements of the chest wall allow for fiber migration to the parietal pleural. The alleged conduit for their parietal destination is the lymphatic drainage of the visceral pleura. Fiber type may also play a role in migration of asbestos. It is further postulated that once localized, the chronic irritation of fibers residing in a mobile tissue structure initiates a fibrosing response. Histologically, plaques are composed primarily of avascular bundles of collegen in a hyaline matrix with occasional fibroblasts. Inflammatory cells are noteably absent. Grossly calcified zones are present in some, with microscopic calcifications found in many. Fine asbestos fibers can be identified in plaques ultrastructurally.

The diagnosis of plaques by radiographic criteria presents problems for several reasons. First, according to postmortem studies, plaques are oftentimes not radiographically visible (26). Thus the roentgenogram is

a specific but not particularly sensitive diagnostic tool in this case. Improved sensitivitiy can be achieved with increasing radiographic views (including oblique and lateral projections, for example) and thoracic computed tomography. Thoracic CT is especially useful for plaques in certain regions (along the mediastinum, paravertebral areas and diaphragmatic crura) as well as for distinction of normal anatomic structures (fat, muscle) from pleural disease. However, these techniques are often not financially or logistically feasible in the context of health survey activity for large populations of exposed groups. Second, any radiographic diagnosis is limited by inter- and intra-reader variability.

The epidemiology of plaques and their occurrence is also speculative. There is literature to both support and refute the view that not only asbestos exposure per se but also tobacco use, latency since first exposure, amount of exposure (in total years of exposure or cumulative fiber-year doses) and an individual's age are all independent contributors to the risk of development of plaques.

For example, in Quebec chrysotile miners where any pleural abnormality was recorded, the relationship between plaques and age was the only statistically significant ($p < 0.03$) determinant found (10). Age was also found to have a relationship to radiographic pleural disease in former railroad workers (57) and Swedish population surveys (25). However age was not identified as having a consistent or significant association with plaques in studies of ship repair workers (56), asbestos cement workers (16), and asbestos manufacturing plant workers (62).

From the same body of literature, smoking was found to increase the risk of bilateral plaques among asbestos cement workers (16) and cigarette smoking was found to be statistically significant in its association

with prevalence of plaques in asbestos manufacturing plant employees (62). However, the latter result was not corrected for age or cumulative exposure differences. Swedish population surveys also indicated an increased prevalence of smokers over expected among those with pleural plaques (25). However, in studies where adjustments for age and latency have been clearly made, tobacco exposure does not seem to be significantly associated with pleural disease.

There is an eclectic selection of literature on the prevalence of plaques. General population surveys for background prevalence findings range from 0 percent amongst Finnish and Bulgarian rural groups to 0.54 percent in urban Germany (26). Bilateral pleural plaques were found in less than 1 percent of 335 hospitalized women age thirty-five or older in a Philadelphia study (16). Hillerdale's review of a Swedish population survey of Upsala County (not heavily industrialized) found a .3 percent prevalence of bilateral pleural change with a 1 percent prevalence in males over 40 years of age (25). For those surveyed in the last year (1976), the prevalence of bilateral plaques was 1.6 percent for over 40 year old men and 3 percent in the 65 to 70 year old males. He found a bilateral plaque prevalence of 4 to 9 percent in those individuals in "asbestos occupations" with their employment having begun at least fifteen years prior to the survey, i.e., in 1960 or before (25). Frequencies of bilateral plaques of up to 22 percent were found among asbestos cement workers in Ontario (16). Other estimates of plaque prevalence among occupationally exposed groups range from 2.7 percent in Quebec chrysotile miners (10) to 38 to 53 percent among employees of an asbestos products plant (62). Selikoff et al. found a 54.6% prevalence of plaques in a population of ship repair workers (56). Hedenstierna

demonstrated radiographic evidence of pleural plaques in 62 percent of 423 construction workers studied (24). These figures, unless otherwise specified, all refer to any pleural thickening, including unilateral findings, not readily attributable to other causes.

When other causes can be eliminated, exposure to asbestos is clearly a risk factor for pleural change. Approximately twenty years' latency from exposure is usually required for development of pleural disease. Indices of total exposure (either through measurements of duration of exposure or estimates of cumulative dose of exposure) are less clear cut determinants of plaque formation. However, Finkelstein et al (16) demonstrated a log normal relationship between the 32 year risk of development of pleural abnormality and cumulative exposure. He also demonstrated a 23 percent risk of development of bilateral plaques five years after cessation of exposure.

Thus, pleural disease, in the absence of other causes, is a good indicator of asbestos exposure and likely represents a latency of as many as twenty years since that exposure. Cumulative exposure and/or intensity of exposure may affect the existence and extent, as well as latency of development of plaques. The role of smoking is equivocal. Age is unlikely to play a role when corrections for latency and cumulative exposure are made. Lastly, there are unknown background levels of asbestos exposure particularly in industrialized and urban areas of the world where asbestos and products containing asbestos have been manufactured and used. This incidental environmental source of dust exposure (both inhaled and ingested), could account for a theoretical, though highly specific for any particular environment and population, percentage of any prevalence figures for radiographic change.

The literature on radiologically defined parenchymal disease is equally diverse. Prevalence of small irregular opacities of grade 1/0 or greater (29) varies according to the population and exposure source studied. A 3 percent prevalence was found to be characteristic of an urban New Jersey population (16). Findings among occupationally exposed groups range from 2.1 percent for Quebec chrysotile miners (10) to 78.9 percent among ship repair workers (56). As with plaques, parenchymal findings have been significantly associated with age, tobacco history, latency of exposure and cumulative exposure by various authors. Similarly, age, tobacco history, latency, and cumulative exposure have each been discounted as having any significant independent effect on the development of parenchymal scarring secondary to asbestos exposure.

Histologically the parenchymal lesions associated with radiographic change include fibrosis of the lung beginning at the level of respiratory bronchioles, and eventually extending beyond peribronchiolar to diffuse interstitial fibrosis (6). Radiology usually only detects fairly advanced fibrosis.

The cellular mechanisms of these changes is hypothesized to include both the physical irritation of asbestos fibers and chemical insult secondary to leaching of associated ions and metals found in asbestos. These initiate an inflammatory response in peribronchiolar and interstitial regions which later progresses to the fibrosis characteristic of end stage disease. Disrupton of normal immune responses after macrophage ingestion of asbestos fibers has also been postulated to play a role in fibrogensis.

There is an increased risk of development of parenchymal fibrosis associated with smoking but whether this is an independent fibrogenic

effect of smoking itself or a synergistic effect or some combination of these is unclear. It has been postulated that smoking, by interfering with lung clearance mechanisms, potentiates the fibrogenic potential of asbestos. A related hypothesis has been formulated to explain the finding of some authors that ex-smokers are at greater risk for plaque formation than current smokers though both are clearly at greater risk than non-smokers. Weiss et al. postulated that immediate stimulation to clearance mechanisms by smoking itself served to protect against impairment of pulmonary clearance caused by tobacco (62). Ex-smokers would thereby suffer from tobacco related clearance problems without benefiting from its immediate stimulatory effects.

The pulmonary function or physiologic changes associated with asbestos exposure are the subject of yet another body of literature and controversy. In particular, the types of pulmonary defects, their frequencies, and the sequence of their appearance with the progression of disease have each been debated. In general, asbestosis is associated with a restrictive ventilatory defect. There is often an accompanying "alveolar-capillary block" or diffusion defect as well (63). Exertional hyperventilation often associated with arterial desaturation can be an additional finding. Increased respiratory rate is also characteristic of asbestosis in some settings. It is postulated to occur for a variety of reasons such as: increased ventilatory requirements in the setting of decreased diffusion capaciaty and resultant hypoxemia, excess stretch reflex stimulation secondary to decreased lung complicance, and increased oxygen demand because of increased work required for respiration in the setting of decreased lung compliance.

Good correlation exists between radiographic findings of advanced disease and pulmonary function abnormalities as outlined above. However, it is possible to have mild radiographic evidence of asbestosis without any evident ventilatory defect. The reverse is also true -- potentially asbestos-related pulmonary function abnormalities are found among exposed individuals with normal chest radiographs. In fact, many investigators believe that pulmonary function changes are the earliest sign of asbestos-related disease. Gaensler et al. found that, short of histological evidence through which the earliest lesions of asbestos exposure may be identified, funcional disorders often precede any radiographic evidence of asbestosis (19). Specifically, he demonstrated a decrease in lung volumes (total lung capacity and vital capacity) with parallel decrease in compliance. Others believe that reduction of diffusion capacity is an earlier finding in asbestosis. There is an extensive body of literature (3, 63) describing "alveolar capillary block" in asbestos exposed populations with characteristically decreased diffusion capacity and increased venous admixture. Lastly, there is evidence of an obstructive component to early asbestosis. This is localized in small airways purportedly obstructed because of peribronchiolar fibrosis (43) which in turn may contribute to decrease lung compliance (37) and decreased peak flows demonstrated by some authors (32) and attributed to increased upstream resistance. Small airways disease has been demonstrable as regional ventilation abnormalities in the fibrotic zones of asbestos exposed populations (50).

Although pulmonary function abnormalities may precede radiographic, symptomatic or physical exam signs of asbestos related lung disease, no consistent demonstrable correlation between change in pulmonary function

and indices of exposure (either in years or cumulative concentration) have been demonstrated. Lung perfusion has been shown to correlate significantly with years of asbestos exposure in workers with a wide range of exposures, chest radiograph findings and pulmonary function abnormalities (50). Vital capacity was the most sensitive reflection of exposure in chrysotile miners with wide ranges of exposure, but normal chest radiographs (32). A twenty-four man subgroup of this mining population with normal chest radiographs was evaluated with measurement of carboxyhemoglobin, lung volumes, lung flows, resting and exercise diffusion capacities as well as with pulmonary mechanics. After dividing the group into a more and less exposed subgroup, the authors were able to conclude:

> This study suggests that in men with normal chest films, exposure to asbestos dust produces measurable effects on the mechanical properties of the lungs in the absence of symptoms and signs of lung disease, in the absence of radiographic changes before other measurements of lung function are generally affected. . . The changes in pulmonary mechanics of the more exposed group (lower static pulmonary compliance and greater maximum elastic recoil pressure) are evident whether the results are compared with the less exposed group or with published data on subjects of comparable age who are considered normal. Furthermore, the other function changes in the more exposed group, although minor in degree, support the conclusion that the group differences are real, namely, the lower VC, the higher values of MMEF, and the evidence for greater regional inhomogeneity in gas distribution. . . it was found that the static recoil pressures of the lung were the most sensitive function measurements for detecting the early effects of exposure to asbestos dust. . . (32, pp. 529-532).

As with radiographically defined disease, the effects of age, sex, smoking habits and other exposures on physiologic abnormalities in asbestos exposed populations must be evaluated. In a study of 131

shipyard workers, Pearle found that smoking was a greater determinant of many functional and roentgenographic abnormalities than exposure (45). He found both smoking and exposure contributed to abnormal values for FEVI and FVC (< 80 percent predicted), but evidence of obstruction (FEV1/FVC < 70 percent) correlated only with smoking. Diffusion abnormalities were also strongly correlated to smoking history with only minimal association with exposure.

The correlation between radiographic abnormality and functional impairment has also been studied. Hedenstierna et al. found functional differences between asbestos exposed individuals with pleural disease (normal parenchyma) and nonexposed controls (normal chest radiograph) (24). Specifically, he noted reduced late expiratory flow rates, and increased closing volume in the exposed group. Both persisted when corrected with paired matching for differences in age, height and smoking habits. However, only the differences between exposed and nonexposed nonsmokers were statistically significant -- those between exposed and nonexposed smokers were not. Reductions in FVC, FEV1, and diffusion capacity in the exposed group did not attain significance after matched pairing. Good correlation between lung function abnormalities and radiographic change has been demonstrated in chrysotile miners (32).

By use of principle component analysis, Regan et al. attempted to determine the relative power of a variety of clinical, functional and radiographic variables for diagnosis of asbestosis and for differentiation from other lung disease, specifically obstructive defects attributable to tobacco exposure. In order of importance, diffusion capacity, vital capacity and age were the best predictors of severity of both asbestosis and COPD (47). Again, in descending order of importance, FEV1/VC,

productive cough, radiographic pleural disease, dry cough, and finger clubbing were the best variables for distinguishing between asbestosis and COPD. Low FEV1/VC and productive cough were consistent with COPD while plaques, dry cough and clubbing were associated with asbestosis.

MATERIALS AND METHODS

I. Overview

The information used in this study was derived from the retrospective review of eight field surveillance screenings of 477 asbestos exposed individuals. Additional information was obtained through follow up clinic evaluations for 75 of that group. The date was collected in several Connecticut communities during the three year period from February, 1982 to January, 1985.

With one exception, each surveillance was performed according to a fixed protocol by the staff of Yale University's Occupational Medicine Program. This protocol included a standardized exposure and medical history questionnaire, abbreviated physical exam, portable spirometry, chest radiograph (posteroanterior), and educational session. Earlier surveys also included the results of three home hemoccult cards. However, as this was eliminated from the protocol after 1982, information thereby obtained has been excluded from the present study.

Each participant was sent a letter summarizing the results of his/her screening evaluation and recommending additional medical follow up when clinically indicated. In all relevant cases advice regarding discontinuation of smoking, and its synergistic effects with asbestos, was given. The protocol further specified that all participants with certain radiographic and/or pulmonary function abnormalities be asked to come to the Yale-New Haven Hospital (New Haven, CT) or Lawrence and Memorial Hospital (New London, CT) Occupational Medicine Clinics for more detailed evaluation. Specifically, this latter group included anyone

with: 1) An abnormal chest x-ray because of interstitial fibrosis, bilateral pleural disease and/or mass lesion(s). Individuals with radiographic evidence of old granulomatous disease, chronic obstructive pulmonary disease, or congestive heart failure were not specifically referred for occupational medicine evaluation but were advised to seek medical follow up with their primary care physician when deemed appropriate in the context of the remainder of their screening results.

2) An abnormal pulmonary function test when indicative of a restrictive defect. Individuals with marked obstructive defects not attributable to prior tobacco exposure were also seen in follow up. However, those with obstructive defects and additional significant tobacco exposure (with or without radiographic evidence of COPD) were not seen unless they also demonstrated one of the above-mentioned radiographic abnormalities. Instead they were advised of the probable non-occupational etiology of their disease and the necessary measures for its palliation.

3) A history of cancer associated with asbestos exposure. Individuals with a history of upper or lower respiratory tract tumors, upper or lower gastrointestinal cancers or pleural or peritoneal malignant mesothelioma were invited for follow up to investigate the possible work-relatedness of their tumor. Because the data regarding increased relative risk of certain genitourinary malignancies among asbestos exposed populations is as yet inconclusive, individuals with a history of ovarian cancer, for example, were not seen unless otherwise indicated.

Each follow up visit was conducted according to specific guidelines. These included a detailed occupational and exposure history, a standard medical and surgical history, a review of systems query, a complete

physical exam (excepting genitourinary examination unless indicated because of historical information), chest radiograph (posteroanterior and lateral projections), and complete pulmonary functions including single breath diffusion capacity. Additional blood laboratories were obtained on an individual basis as necessary. Again, participants were sent a letter summarizing the results of their evaluation. Those without occupationally related disease or pleural disease only were so informed. However, those with radiographic evidence of parenchymal lung disease (greater than or equal to 1/0 ILO parenchymal classification) attributable to asbestos and/or the definitive diagnosis of asbestosis were advised to return for periodic follow-up. In addition, follow up individuals were advised about the prognostic and functional significance of any particular finding as well as given specific recommendations for cessation of culpable exposures (asbestos and/or tobacco). Advice regarding workman's compensation claims and/or disability entitlement was given where applicable.

II. Choice of Population for Study

The eight screenings reviewed in this study were chosen from among the cumulative experience of the Yale Occupational Medicine Program because the populations they encompass had histories or occupations consistent with moderate asbestos exposure. However, the original impetus for each survey was not specifically for research. Half of the surveillances were done because of trade union requests. Each of four different trades requested medical evaluations because of members' concern regarding use of or incidental exposure to asbestos during their work. These

included: bricklayers, plumbers and pipefitters, railroad machinists and sheetmetal workers. Three of the surveillance studies involved two particular industries, as opposed to trades. First, two surveys were performed on employees of the paper products manufacturing division of a conglomerate. These were done at the request of the employees. Second, at the request of management (rather than shop workers), employees of a gas utility corporation were evaluated. Members of management were included in this latter group because of documented environmental asbestos exposure secondary to exposed pipe insulation noted in managerial offices. The last of the eight groups consisted of wives of members of an insulators' union. This group's asbestos exposure was primarily from laundering their spouse's (and in some cases grandfather's and/or father's and/or brother's) work clothes. Again, union concern motivated this survey as members were aware of potential health hazards to household members involved in laundering asbestos covered clothing.

Thus, in all eight cases the health surveillance was sought by the participants whether workers or management or family. In all cases potential participants were recruited by their union or management, not by members of the Occupational Medicine Program. Participation was entirely voluntary and a single day was appointed during which time all available participants were evaluated for each screening.

This population does not include groups considered to have the heaviest asbestos exposures such as those who process raw asbestos, manufacture asbestos textile products, apply asbestos insulation, or work with asbestos in closed spaces (shipyard workers, for example). Instead one may loosely categorize this population as moderately exposed. It is difficult to be more quantitative as attempts at

quantifying asbestos exposures typical of a particular trade or industry are difficult. Inaccuracies occur on several levels. First, exposure levels vary by job site for skilled tradesmen and any given tradesman may change job sites every two to six months. Exposures vary by job assignment in a particular industry as incremental assemblage of finished products involves multiple jobs with variable risks. Exposures vary temporally as well. Exposures decreased in the years after the enactment of the 1970 Federal Occupational Safety and Health Act because of improved industrial hygiene via mandated changes in asbestos handling practices, ventilation and protective equipment requirements, and maximal allowable exposure levels.

Spraying of asbestos insulation was outlawed in 1973. Since 1975, the use of asbestos has declined in other capacities as well. Even in this post-regulatory era, exposures vary according to corporate as well as individual compliance and the politically dependent authority of government regulatory agencies. Some industries are more strictly compliant with regulatory requirements and some workers are more cooperative in the use of protective equipment. Although new products/processes containing asbestos have declined because of regulatory mandates, existing asbestos containing structures and materials still require maintenance, renovation or demolition activities all of which can involve significant fiber exposures.

Routine monitoring of dust levels in order to determine exposures (and maintain acceptable levels) is a fairly recent phenomenon. Equipment for doing so has a variety of limitations. Gravimetric (weight dependent) sampling was popular in the past but suffers from the inclusion of non-asbestos materials/dusts in its measurements. More recently,

impingers and membrane filters have been used but both are size selective methods and are usually only accurate for longer, larger diameter fibers. Timing, depending on how long people have been at work and what activities are in progress, and location for sampling will affect results. Personal monitors are best to assess an individual's exposure risk but such methods are infrequent and impracticable in many contexts. Frequency of monitoring will obviously impact on results. Ideally one would want continous levels, once or twice yearly is more common. For the years before regulation, when levels were the highest, very little, if any, monitoring data is available.

Quantifiable exposure levels are available for two of the eight groups included in this survey. The two screenings conducted on employees of a paper manufacturing industry included records of a 1977 inspection by the Connecticut Department of Labor's Division of Occupational Safety and Health. The plant involved was sited for exceeding acceptable ceiling concentrations of asbestos (> 10 fibers/cc for fibers > 5 u in length). The highest concentration found, 28 fibers/cc, was measured during fifteen minute ceiling value monitoring of one aspect of production. However, this information has limited value in terms of assessing cumulative exposure except to acknowledge that asbestos exposure occurred at levels noncompliant with acceptable ceiling concentrations. As asbestos standards are in large part legislative compromises, exposure within legally acceptable limits may not have physiologically acceptable insignificance. As in Peter's and Peter's caveat:

> The weight of presently available information suggests some small injury or insult from each asbestos fiber that enters the human body. There is no evidence that there are safe human exposure levels. . .that would pertain to all individuals . . .(46, p. 22).

Regardless of source or specific quantity, each of the eight populations had significant exposure to asbestos. For the above-mentioned paper products workers, exposures were possible during several phases of production as asbestos fibers are added to paper pulp and then sent through a series of refinements including, mixing, beating, calendar pressing, drying and cutting. Workers involved in preliminary handling and mixing of dry material and cutting of the dried final product were involved in the heaviest exposures.

The bricklayers and sheetmetal workers seen were exposed primarily because of activity of other trades on the same construction sites. In addition, mortar and fillers often contain asbestos such that those bricklayers involved in mixing asbestos containing compounds incurred exposures as a direct result of their trade as well. Because of variations in union structure and requirements, some sheetmetal workers applied their own insulation. This latter group, in particular, is at risk for higher exposures because duct construction by sheetmetal trades involves confined working spaces which therefore have greater concentrations of dust and fibers than open areas. Still, the simultaneous work of insulators and laggers most likely contributed to the bulk of bricklayers' and sheetmetal tradesmen's exposures.

Plumbers and pipefitters are also exposed because of proximity to other trades' application of pipe insulation. However, they also must cut and repair pipes with asbestos containing jackets in place and their work can involve significant dust exposures. In addtion, they frequently operate in closed and/or poorly ventilated spaces which enhance dust concentrations.

The railroad machinists' repairs of locomotive boilers, fireboxes, pipes and passenger cars involve manipulation, removal or replacement of lagging which usually contains approximately 15% asbestos (57). Absbestos containing jackets were especially common in U.S. steam engine construction during the 1950's.

The natural gas company employees were exposed in two settings. Shop workers had exposures secondary to repair and maintenance of hot and cold pipes and boilers constructed with asbestos-containing insulation. Managerial employees were exposed in their offices because of exposed piping covered with friable asbestos insulation.

The families (wives, children, siblings) of asbestos insulators were exposed via household contact with dusty workclothes before legislation in the 1970's required industry responsibility for cleaning and/or disposal of protective garments. Wives and children often laundered garments after vigorously shaking them and thereby creating significant household fiber levels. Epidemiologic surveys of such populations have confirmed their exposures via radiographic and clinical findings as well as patterns of mortality. (52).

III. Demographics

The population reviewed can be characterized as follows: of the 477 screened, 392 or 82.2 percent were male and 85 or 17.8 percent were female. The age range was from 21 to 79 years with a mean age of 49 years for 457 individuals on whom age was available. The asbestos exposure

of 419 or 87.8 percent was primarily occupational whereas 58 or 12.2 percent were exposed via household contacts. All of the individuals in the latter category were female. Current or previous smokers represented 342 or 74.8 percent of those on whom smoking histories were available. An additional 13 or 2.8 percent claimed a history of cigar and/or pipe smiking without use of cigarettes. At the time of this review one, or 0.2 percent of the original 477 had died. The cause of death in this case was bronchogenic carcinoma.

IV. The Questionnaire

Questionnaires were distributed prior to the day of surveillance in seven of the eight screenings. In one group, the railroad machinists, no questionnaire was used. During the screening, the questionnaire was reviewed by each participant with an interviewer from the clinic staff to ensure its completion and accuracy. Information thereby obtained included: (1) basic demographic attributes of each participant such as age, sex, race, height, weight, place of birth and residence, (2) exposure histories including a review of the extent and time course of occupational and environmental exposures as well as extensive smoking histories, (3) a review of systems designed to elicit symptoms of respiratory disease (quality, frequency and timing of cough, shortness-of-breath, dyspnea on exertion, pleurtic chest pain), of cardiac disease (exertional or ischemic chest pain, orthopnea, paroxysmal nocturnal dyspnea, pedal edema), of tumor (significant weight loss, anorexia, skin lesions, dysphagia,

anorexia, dysphagia, voice changes, hemoptysis, hematochezia), (4) a medical history including queries regarding pneumonia, bronchitis, asthma, emphysema, tuberculosis, cancer, abnormal chest radiographs, rib fractures, thoracic surgery, hypertension, diabetes, heart disease, peptic ulcer disease, regular medications, and pulmonary function tests, and (5) a summary of the participant's marital status and family composition.

V. The Physical Exam

For surveillance purposes each participant received an abbreviated physical examination designed to elicit signs relevant for asbestos-related lung disease. This exam was performed by physicians, nurse practitioners or senior medical students affiliated with the Yale Occupational Medicine Clinic. It included ausculation of the heart and lungs and examination of the extremities for evidence of cyanosis, clubbing or edema. The railroad machinists, however, did not receive physical exams. Those individuals seen in follow up clinic visits received complete physical exams performed by clinic physicians.

VI. The Chest Radiograph

Chest radiographs obtained for surveillance purposes were done by contracted private radiologists and scheduled according to the convenience of participants over several weeks' time. Whenever possible,

the same radiology group performed all radiographic analyses for a given screening to ensure consistent quality. Posteroanterior projections were the only views obtained. After all chest radiographs had been obtained from a given survey, they were read blind during a one day reading session by two Grade B readers (i.e. readers certified for application of the 1980 International Labor Office standards for reading chest radiographs of the pneumoconioses). After discussion, the two readers' concensus was given as a final evaluation. Chest radiographs obtained during follow up included both posteroanterior and lateral projections. In most cases they were read by at least one Grade B reader in the context of available clinical information.

The International Labor Office (ILO) 1980 crieria for reading radiographs of pneumocomoses were applied to all of the radiographic data of this paper (29). It is the most current system for evaluating such data and represents over fifty years of cumulative international experience and collaborative trials. Its classifications are purely descriptive of two sites of radiographic lesions: pleural and parenchymal. An additional commentary section for non-pneumocoiosis related findings such as emphysema, lung cancer, tuberculosis, pneumonia, pneumothorax, etc., is included.

For each of parenchymal and pleural findings, a system for describing both the morphology and profusion of lesions has been devised. Thus pleural plaques, when present, may be qualified as circumscribed or diffuse, bilateral or unilateral, with their anatomic location specified and their widths and extents each assigned to one of three size categories. Similarly, parenchymal change is described according to its quality, round regular or irregular, and size, small or large. Its

profusion is classified into one of twelve categories each representing a point along a continuum of radiographic disease. "0/-" "0/0" and "0/1" represent progressive gradiations of essentially normal parenchymal densities and "3/+" represents the most profuse parenchymal densities. There are eight intervening categories.

As will be described in more detail below, the categories of profusion are based on comparison with four standard radiographs representing the middle of four categories: 0 (normal), 1, 2, and 3. Different standards are available for different pneumoconioses, such as silicosis and asbestosis, because of the differences in morphology of their characteristic lesions on chest radiograph. The numerator of fractional readings represents the final category into which a film is placed and the denominator any adjacent category seriously consider if applicable.

The development of this system required multiple revisions to design a more accurate and clinically meaningful diagnostic tool. Its beginnings are in the early decades of this century when it was first recognized that radiographic abnormalities accompanied heavy occupational dust exposure. By World War I, pneumoconioses constituted an international health epidemic the most common diseases being silicosis and coal workers' pneumoconiosis. Through the International Labor Office (ILO), worldwide interest in occupationally related lung disease was channeled into the development of an international system of radiographic classification of disease. In fact, the premortem diagnosis and management of pneumoconioses were primarily dependent on radiographic findings as analysis of tissue samples or quantifiable measures of pulmonary function were not readily available.

Early 20th century South African miners employed in a variety of mining operations were exposed to several types of fibrogenic dusts. Appropriately, it was in this setting that the first set of radiographic classifications of pneumonoconioses was established in 1916. This system was accepted on an international scale in 1930 by the ILO sponsored first international conference on pneumoconioses in Johannesburg. The participants were primarily concerned with classification of silicosis. In so doing, they defined three stages of disease. The definitions were not only descriptive of progressive radiographic findings, but included an associated rquirement of specific decrements in work capacity. This system was difficult to apply because of inclusion of non-radiographic criteria of disease. By 1950, yet another international conference attempted to define radiographic stages of pneumoconioses, primarily silicosis and coal workers'. However, the verbal definitions of this system were also difficult to apply in practice. Findings were not reliably reproduceable nor clinically meaningful. As with subsequent modifications, the distinction between the upper limits of normal and the beginning of radiographic disease was paraticularly difficult (8).

By 1958, the so-called Geneva classifications were established. This was the first purely descriptive system for defining pneumoconoses. No pathologic process nor assessment of pulmonary function was included in its stages. Rather, it was intended to be purely descriptive of radiographic findings, again primarily for silicosis and coal workers' pneumoconioses. This was the first classification system to include recommendations for technical quality of film as well as standard radiographs for comparison with films to be judged. The system was organized first in categories descriptive of the shape and size of

parenchymal opacities (linear, rounded, small or large) and then further subdivided by a three point (1, 2, 3) gradation of the profusion of opacities. Optional commentary on the presence or absence of pleural disease was included. This system was particularly difficult to implement for pneumoconioses in which nonuniform parenchymal change occurred. In such cases, a variety of shapes of densities, each of different profusions might occur simultaneously. Also standard films were intended to represent midcategory change such that classification of films falling between two standards was difficult.

In 1967 with these criticisms in mind, the International Union Against Cancer (UICC) established a system in which profusion of densities rather than their qualitative features (linear versus round versus large or small) was emphasized. In fact, the profusion rather than the morphology of radiographic densities is believed to be the better reflection of exposure and any dose-related pathology. The UICC expanded the classifications system from a three to a four point scale (0, 1, 2, 3) and then further subdivided these grades into twelve fractions to allow for between standard equivocation. Thus the numerator became the category to which a film was assigned (i.e, 0, 1, 2, or 3). If an adjacent category had also been seriously considered, this became the denominator, otherwise the numerator and denominator were the same. The range of possible profusion was thereby defined as 0/- (absolutely no densities) to 3/4. The ten categories between included 0/0, 0/1, 1/0, 1/1, 1/2, 2/1, 2/2, 2/3, 3/2, and 3/3. The system thus aquired more universal applicability. In particular, asbestosis could now be categorized.

The following year (1968), the ILO incorporated portions of the UICC system into its own to form what was then called the extended classification system. This adopted the emphasis on profusion of density with the twelve point scale and added a system for elaborating on pleural change via both qualitative and quantitative description. This included localization of pleural change with differentiation of diffuse versus circumscribed thickening and calcified versus non-calcified changes. Pleural plaques were further described by both width and extent.

By 1971 the ILO/UICC systems were fully integrated with elimination of ILO category "Z" which had been used to describe chest radiograph changes suspicious for pneumoconiosis but not definitely classifiable as such. The current standards were established in 1980 by the joint efforts of the Commission of the European Communities, the National Institute of Occupational Safety and Health (a subdivision of what was then the U.S. Department of Health, Education and Welfare), and the American College of Radiology. New mid-category standards were included and, for the first time, were a mandatory part of the classification process.

This long litany of revisions has been based on continuing review of the international experience of experts and organizations concerned with the study of occupational lung disease. The standard films used in the 1980 system were selected by controlled trials in an attempt to maximize the reproduceability of classifications. Reproduceability is an issue not only betwen readers but also for the same reader on repeat readings and for different readers from different national backgrounds as the latter have been found to have consistent differences in their patterns of radiographic interpretations. Validation has required ongoing efforts

to determine the clinical significance (regarding disability, prognosis and treatment) of any given radiographic classification and to clarify the relationship between historical exposure information and radiographic findings.

VII. Pulmonary Function Testing

With two exceptions, pulmonary function assessment during surveillance was obtained with a portable Breon versus model 2400 spirometer. The plumbers and pipefitters were screened with a Collins Eagle II Spirometer and computer generated values of FVC, FEV1, FEV1/FVC and flow rates (PEFR, MMEF, FEF25, FEF50, FEF75). Information about pulmonary function equipment used in screening the railroad machinists is not available.

For all those screened with spirometry, results were based on the best of two efforts. Values abstracted from graphic results included FEV1, FVC and FEV1/FVC. Predicted FEV1 and FVC values were corrected for age, sex, height and race according to Morris (Oregon) tables for predicted values. On the basis of this information, participants were categorized as having normal, restrictive, obstructive or mixed pulmonary function deficits. A restrictive defect described individuals with FVC less than 80 percent of predicted and FEV1/FVC greater than 75 percent.

Obstruction was applied to individuals with FEV1 less than 80 percent of predicted and FEV1/FVC less than 75 percent. A mixed defect thereby included those with FVC and FEV1 less than 80 percent of predicted and FEV1/FVC less than 75 percent. All others were considered normal.

Pulmonary function tests obtained for those seen in follow up at Yale-New Haven Hospital were obtained with a Warren E. Collins maximodular lung analyzer and included lung volumes, flows and a single breath diffusion capacity. Assessment of those seen at Lawrence and Memorial Hospital was done on a P.K. Morgan (U.S.A. transfer) spirometer and included lung volumes, flows and a single breath diffusion capacity.

VIII. Statistical Methods

Both nonparametric and parametric statistical methods were applied to the data obtained in this study. For comparison of proportions in independent samples, chi-square calculations with one degree of freedom were applied. The validity of the chi-square calculation was discounted for comparisons in which the expected count for any category of information was less than five. For comparing mean values the *t* test for independent means was applied in which a pooled estimate of common variance was used. This evaluation rested on the assumption that the standard deviations in the underlying populations were equal. For *t* tests of significance a two-tailed *t* distribution was used. In all comparisons, statistical significance was determined at the five percent level.

RESULTS

I. Overview

A total of 477 workers were seen during the eight surveillance screenings of this study. Of these, 446 (93.5 percent) obtained readable chest radiographs. Of the remainder, 28 (5.9 percent) had not obtained readable roentgenograms at the time of this review despite requests to do so issued according to the screening protocol. An additional three (0.6 percent) chest radiographs were of sufficiently poor quality as to be deemed inappropriate for ILO grading.

Most of those screened with radiographs were found to have normal parenchyma by the 1980 ILO grading system (29). A total of 400 (89.7 percent) normal parenchymal designations were assigned. The remaining forty-six radiographs were classified into one of three categories of parenchymal abnormality: thirty-four were designated as 1/0, ten as 1/1, and two as 1/2. The prevalence of parenchymal abnormality was therefore 10.3 percent most of which (34 out of 46 or 73.9 percent) was of the lowest possible grade (1/0). Only twelve abnormal films demonstrated more severe parenchymal change but all of these were still category "1" films. The highest grade found, 1/2, was assigned to only two individuals.

Pleural disease was more prevalent among those with abnormal parenchyma. Fifty-two (13 percent) of the 400 individuals with normal parenchyma demonstrated bilateral pleural disease that could not readily be attributed to causes other than asbestos exposure. Of those with 1/0 category parenchyma, eleven (32.3 percent) had bilateral pleural changes

attributable to asbestos exposure and seven (58.3 percent) of those with either 1/1 or 1/2 grade parenchyma were noted to have bilateral pleural disease.

II. Clinical Findings

This study was designed to determine if there are reliable clinical criteria, in addition to radiographic findings, which distinguish individuals with 1/0 parenchymal disease from those with normal lung parenchyma as assessed radiographically. The criteria examined included: pulmonary function parameters consistent with restriction; physical exam findings, specifically the presence or absence of bilateral rales not attributable to reversible atelectasis; and the presence or absence of symptoms of shortness-of-breath and/or cough. Because of the design of the screening protocol, data for detailed clinical assessment was obtained only on individuals seen for clinic follow up appointments. This group included all those with lung parenchymal abnormalities assessed by ILO radiographic criteria, i.e. those with 1/0, 1/1 or 1/2 findings in the population. In addition, those with bilateral pleural disease but normal parenchyma were recommended for follow up. Thus this latter group served as controls for comparison of results.

Ninety-eight individuals were classified in one of the three categories of radiographic abnormality seen in follow up. At the time of this study, 75 (76.5 percent) of those recommended for follow up had been seen. Of the 75 on whom data was available approximately half had normal parenchyma and half abnormal. Specifically, thirty (40 percent) were

individuals with 1/0 radiographs, ten (13.3 percent) were individuals with 1/1 or 1/2 findings and thirty-five (46.7 percent) had normal parenchyma but bilateral pleural disease.

Follow up rates for those with parenchymal abnormalities were much better than the normals. Thus 30 out of 34 (88.2 percent) of those in the 1/0 category were seen and 10 out of 12 (83.3 percent) of those with 1/1 or 1/2 ratings were seen. Only 35 out of 52 (67.3 percent) of those with normal parenchyma but bilateral pleural plaques were seen. Follow up requests were worded such that those with parenchymal disease were given more emphatic invitations for additional evaluation as pleural disease alone is generally considered a relatively benign and nonprogressive consequence of asbestos exposure. This bias in requests most likely contributed to the difference in response rate.

The results of this analysis demonstrated very limited clinical differences among the three radiographically defined populations: 1/0, 1/1 - 1/2 and bilateral pleural disease only. First, there were no statistically significant differences in prevalence of criteria for restrictive disease among the three groups (see Table I). Thus for each of total lung capacity, residual volume and diffusion capacity, the frequency of values less than eighty percent of predicted did not vary significantly among the three groups. Mean values for these variables (TLC, RV and DLCO expressed as precent predicted) were comparable among all three radiographic groups and without any evident abnormality (see Table II). The means of abnormal percent predicted values of TLC or RV did not demonstrate any significant difference among the three groups (see Table III). Diffusion capacity, however, was much less for those with 1/1

or 1/2 findings compared with 1/0 or normal groups. The statistical significance of these differences was not tested.

Evaluation of evidence of obstructive pulmonary deficits was more revealing. The prevalence of findings consistent with obstructive disease (FEV1/FVC less than 75 percent) did not vary significantly among groups (see Table I). The mean of FEV1/FVC was within normal limits for each group. However, the mean of abnormal FEV1/FVC values were consistently less in those with 1/1 or 1/2 radiographs versus either 1/0 or normal groups (see Table III). Again the statistical significance of these differences is beyond the scope of this study.

Symptoms of asbestos related lung disease did not distinguish among radiographic groups. Thus there was no statistically significant difference in frequency of complaint of cough and/or shortness-of-breath among the three groups (see Table IV).

The sign of bilateral rales on ausculation was found among half of those with 1/1 or 1/2 radiographs. There was a statistically significant increase in prevalence of this finding on exam in the 1/1 - 1/2 group when compared with those with 1/0 radiographs ($.001 < p < .01$) and with those with normal parenchyma ($.01 < p < .05$). (See Table V). The differences between 1/0 and bilateral plaque groups on physical exam were not significant, only about 10 percent were positive in each group.

The concomitant existence of physical exam, symptomatic and pulmonary function changes consistent with asbestosis were infrequent enough findings to make meaningful comparison impossible.

Other disease processes can cause radiographically visible changes in lung parenchyma similar to that of asbestos exposure. In a population with documented histories of asbestos exposure other environmental or

even viral sources of fibrogenic lung disease are less likely. Cardiac dysfunction, however, cannot be similarly ruled out. Formal cardiac function testing, either through imaging and/or stress techniques, was not within the scope of this study. However, historical information relevant to cardiovascular disease was obtained, including histories consistent with myocardial infarction, coronary artery bypass surgery, or hypertension. Abnormal radiographic findings of an enlarged cardiac silhouette and/or vascular redistribution suggestive of congestive heart failure were included in chest radiograph readings. With the exception of those with histories of hypertension, the frequency of other cardiac findings were small enough to make meaningful statistical analysis difficult (see Table VI). For hypertensives, those in the bilateral plaque, normal parenchyma category were a significantly larger proportion than found among the total screened population ($.001 < p < .01$) or the total population of normal chest radiographs ($.01 < p < .05$) (see Table VII). The proportion of hypertensives among those with 1/0 or greater than 1/0 findings did not differ significantly from those with bilateral pleural disease nor from the background screening population.

The question of radiographic congestive heart failure was raised more frequently among 1/0 individuals than any other group (see Table VI). This finding was statistically significant when the 1/0 group was compared to all those with normal radiographs ($.01 < p < .05$) as well as when compared to all those screened with radiographs ($.01 < p < .05$). (See Table VII). However, this finding was in the context of extremely small frequencies (less than 5 expected cases) which make its significance of questionable value.

In summary, then, each radiographic group demonstrated associated significant clinical findings. However only in the group of 1/1 - 1/2

radiographs were these findings consistent with the criteria for diagnosis of asbestosis. In this case, the finding of bibasilar rales on physical exam was significantly more prevalent than in either the 1/0 group or bilateral plaque group. There was also more obstructive disease among the 1/1 - 1/2 group compared to those with bilateral plaques when obstruction was evaluated by the means of all values FEV1/FVC < 75 percent. With one exception, the 1/0 group did not distinguish itself clinically. The exception was the increased prevalence of radiographic signs of congestive heart failure compared with the total population of radiographs as well as with all normal radiographs. This difference was of limited significance because of the small numbers involved. Lastly, those with normal parenchyma but pleural disease distinguished themselves by a significant increased frequency of hypertension (historical information) compared with all those radiographed as well as with all those with normal radiographs.

III. Epidemiological Patterns

The demographic characteristics and exposure experiences of the three radiographic groups were more distinguishing than clinical differences. Comparison of the total population with the three subgroups of chest radiograph findings (1/0 parenchyma, 1/1 - 1/2 parenchyma and normal parenchyma with bilateral pleural changes) revealed several general trends (see Table VIII). First, a larger percentage of those with parenchymal or pleural abnormalities were over fifty years of age than in the background population (see Table IX). Conversely, a smaller portion

of these same groups were relatively young, i.e. under forty, than in the overall population. Specifically, the greater mean age of each abnormal radiographic group was found to be statistically significant when compared to normals from the same population (see Tables X and XI). Among the three categories of abnormality, the 1/1 - 1/2 and bilateral plaque disease categories were found to have statistically significant mean age differences when compared to 1/0 individuals (see Table XI). Those with bilateral pleural disease alone were significantly older on average than those with 1/0 findings ($.02 < p < .05$). Similarly those with 1/1 - 1/2 findings were significantly older than the 1/0 category members ($.02 < p < .05$). There was no statistically significant mean age difference between the 1/1 - 1/2 and bilateral pleural disease categories.

Although females represented a consistently small proportion of normal as well as abnormal groups, several sex related trends were noteable. First, 17 percent of all those with chest radiographs were women. Similarly, 70 or 20 percent of all normal chest radiographs belonged to female participants. However women represented an even smaller proportion of all categories of abnormality. Specifically, 3 or 8.8 percent of those with 1/0 profusion, none of those with 1/1 - 1/2 profusion, and 2 or 3.8 percent of those with bilateral pleural disease were female participants. The differences in prevalence of women for any of the three categories of radiographic abnormality were not statistically significant. However, for those with bilateral pleural disease, there was a significantly lower proportion of women when compared to all those radiographed as well as to all those with normal roentgenograms.

Exposure histories and smoking habits also varied in association with radiographic findings. Thus the prevalence of those with histories of

twenty or more years of total asbestos exposure, twenty or more years' latency since first exposure, and histories of cigarette use was greater among those with radiographic abnormalities (see Tables XII and XIII). A consistently larger percentage of those with normal radiographs were less than twenty years away from their first asbestos exposure, with only 10-19 years of total estimated exposure and histories devoid of any cigarette, cigar or pipe use.

The means for total years of asbestos exposure, years of latency since first asbestos exposure, and years exmployment in the trade in which exposure occurred, were consistently greater for each category of radiographic abnormality when compared to normals from the entire screening population (see Table X). These differences were statistically significant for all comparisons excepting that between normals and 1/1 - 1/2 categories regarding total years of exposure (see Table XI).

When comparing those with bilateral plaques and normal parenchyma to those with parenchymal abnormalities, the former had longer mean total years of asbestos exposure, latencies since first exposure, and years in the trade in which exposure occurred than either 1/0 or 1/1 - 1/2 categories (see Table X). The one exception to this generalization occurred for latency since first exposure which was approximately the same for the bilateral plaque and 1/1 - 1/2 groups. These differences were statistically significant in only two cases: bilateral plaques versus 1/0 groups in mean years in a given trade ($.02 < p < .05$) and in bilateral plaques versus 1/0 groups in mean years of latency since first asbestos exposure ($.01 < p < .02$). (See Table XI).

Comparison of the mean exposures, latencies and trade experiences of those with 1/0 and those with 1/1 - 1/2 parenchymal change revealed an

inconsistent pattern of differences none of which were statistically significant. These differences included a greater number of mean latency years and mean trade experience for individuals with higher grade radiographic abnormalities but essentially the same mean years of exposure for the two groups (see Table X).

Comparison of smoking habits among the three groups with radiographic abnormality demonstrated several trends. As assessed by mean pack-year experience, all three groups smoked significantly more than normals. The heaviest smokers were those with 1/1 - 1/2 radiographs, followed by those with bilateral plaques (see Table X). The lightest smokers were those in the 1/0 category. The 1/1 - 1/2 individuals had statistically significant greater mean pack-year experience than either those with 1/0 parenchyma or with normal parenchyma and bilateral plaques (see Table XI). However, the differences between the 1/0 group and those with bilateral pleural disease were not statistically significant.

In general, any of the three categories of radiographic abnormality (1/0, 1/1 - 1/2 or bilateral pleural disease) of this survey was associated with an older and more heavily exposed (to both asbestos and tobacco) population when compared with those screened with normal chest roentgenograms. For the population with abnormal radiographic findings, the 1/0 group distinguished itself by being the youngest and the least exposed to tobacco. The 1/1 - 1/2 group had the heaviest pack-year experience while those with bilateral plaques had the greatest number of mean years of asbestos exposure, latency and trade experience. The 1/0 and 1/1 - 1/2 groups had comparable asbestos exposures.

DISCUSSION

I. Limitations in Methodology

In order to appreciate the significance of the results of this study, it is important to recognize its limitations. Despite the standardization and quantification of the radiographic criteria upon groups were defined, these criteria lack ideal rigor.

Certain limitations are inherent in the ILO system. First, the use of a diagnostic test the reproduceability and validity of which are still being defined is problematic. Second, despite its fifty plus year history of application and refinement, the system was originally designed for assessment of silicosis and coal workers' pneumoconioses. It is relatively recently that expansion to include all pneumonconioses, and asbestosis in particular, has been acccomplished. Furthermore, the radiographic lesions of asbestosis are more difficult to identify than other pneumoconioses such as silicosis.

The twelve point profusion rating system is intended to represent discrete points on what is presumed to be a continuum of radiographic change. Use of mid-category standards is therefore difficult in cases where the boundaries between standards are poorly understood and/or poorly standardized between different observers and observations. Use of twelve ratings to describe four categories was one attempt to alleviate this problem. The denominator allows for some between category equivocation. The use of boundary standards, rather than mid-category, has been considered as a way to eliminate inter- and intra-observer variations

based on variable boundary definitions. Fletcher et al. employed a system of standards representative of the lower limit of each category to readings of coal workers' pneumoconiosis (18). By comparing both experienced and inexperienced groups of readers and describing readings with and without standard films, he concluded that standards enabled most readers to improve their diagnostic accuracy (appropriate diagnosis was defined as the mean of several independent readings). Experienced readers were particularly aided in identification of normal films whereas the inexperienced primarily improved their accuracy in the diagnosis of degree of abnormality.

The idenfification of the upper limits of normal required to identify normal films is perhaps one of the most difficult and crucial boundaries for film readers. It is of note that with a system of boundary standard films (rather than mid-category), experienced readers were more accurate in their identification of normal. Unfortunately direct comparison with use of mid-category film standards is not available. Regardless of the type of standard employed, consultative readings (with at least two, and preferrably three, participants) are believed to improve diagnostic accuracy. Some authors also believe films should be read on at least two occasions (by the same readers) with an average final reading to optimize accuracy (18). This study was limited to the consensus of two readers. Furthermore, the radiographs for each survey were read only once with the eight reading sessions spread over the three years during which the screenings were conducted. Intersession variability represents another source of inaccuracy.

II. The Population Studied

A volunteer population was chosen for study. Rather than a random sample of the seven industries investigated, the data was limited only to those who volunteered to paraticipate and furthermore were available for participation on a single day. In addition, the impetus for each screening was through participants' requests such that the choice of industries and trades is also a biased selection. Self-selection has the potential to skew results in one of two ways. The group representatives who seek initial evaluation and the individuals who then participate may tend to be sicker than their background population base and thus more actively involved in pursuit of medical evaluation. Conversely, more conscientious employers and/or employees who are thereby more likely to be fastidious about industrial hygiene and health care, may be those most likely to pursue assessment. In this case one would be selecting for a better informed, more compliant, less exposed and healthier population.

The response rate for followup, although reasonable in the 1/0 and 1/1 - 1/2 profusion categories (88.2 percent and 83.3 percent respectively), was poor for those with normal parenchyma but bilateral pleural disease (67.3 percent). The selective response of this latter group may have biased results in one of two ways. A sicker, more symptomatic, older and/or more exposed population might be more likely to seek medical care. Conversely, those with established rapport with a physician because of poor health might be less likely to comply with follow up request from yet another health care provider.

The population studied is further constrained by virtue of its eclectic composition. The seven exposure sources -- paper products

production, bricklaying, plumbing and pipefitting, sheetmetal work, natural gas utility operation, railroad machinist work and household laundry exposure -- from which these individuals were taken are only roughly comparable. In fact, there is significant potential for variability of exposure (and resultant disease risk) within any given trade, industry or household setting.

III. The Bias of Good Health

Summary statistics reflect the net outcome of this diverse mixture. By radiographic criteria, the population surveyed was relatively healthy. Normal chest radiographs (at least in terms of evidence of parenchymal or pleural disease associated with asbestos exposure) were found for the vast majority or 348 (78 percent). An even greater proportion, 89.7 percent, was free of any parenchymal findings. Of the 10.3 percent with abnormal parenchyma, all were within the lowest abnormal perfusion category, i.e. "1". The majority of the latter, 34 or 73.9 percent, were classified as having the lowest grate, 1/0, of category "1" film. The 10.3 percent prevalence of parenchymal abnormality, therefore, is relatively low for a predominantly occupationally exposed population. It is certainly greater than Cordier et al.'s finding of a 2.1 percent prevalence among Quebec chrysotile miners (10) but significantly less than the 78.9 percent found by Selikoff et al. among ship repair workers (56). The former group was exposed to low level fiber concentrations, the latter to heavy. Given a

hypothetically linear dose response relationship between exposure and parenchymal change, one may assume this population's exposure falls in the middling ground of so-called moderate levels.

Although the prevalence of bilateral pleural disease is primarily dependent on latency since first asbestos exposure, there is evidence that extremely heavy doses of asbestos can shorten the latency for development of plaques. For the population studied here, approximately two-thirds (of those whom year of first exposure was available) were twenty or more years away from first exposure. The prevalence of bilateral pleural disease in this population is consistent with light to moderate exposure in a group the bulk of whom have experienced at least 20 years' latency since first exposure.

A general finding of 15.7 percent of all radiographs with bilateral plaques is approximately comparable to that of 22 percent among asbestos cement workers in Ontario with at least 20 years' latency (16), 20 percent among railroad workers with at least 30 years' latency (57), or 14.7 percent found in asbestos textile workers with 10-20 years' latency (10). It is certainly greater than that of 2.7 percent prevalence of any pleural change among Quebec chrystile miners with 10-27 years' latency (10) or of 4-9 percent bilateral pleural change among Swedes in "asbestos occupations" (25). A 15.7 percent frequency also contrasts with Selikoff's finding of 54.6 percent prevalence of plaques in ship repair workers with at least 20 years' latency (56) and Hedenstierna's finding of pleural disease in 62 percent of construction workers studied with 15 years average latency (24). However, both Selikoff's and Hendenstierna's figures include any pleural abnormality (unilateral, for example) not attributable to other than asbestos exposure.

At the time of the screenings there was one case of bronchogenic carcinoma diagnosed subsequent to screening findings (n = 446), three individuals with histories of colon cancer out of 380 on whom such information was available, and one case with a history of ovarian cancer of the 85 women screened. The one death among this group was the above-mentioned case of bronchogenic carcinoma. These figures are too small to allow meaningful estimates of the relative risk of asbestos-related malignancies in the screening population. Furthermore, with the exception of the case of bronchogenic cancer, this information reflects prevalence not incidence of disease, the latter being more useful for assessment of prognosis for the population as a whole. It has already been established that asbestos exposed populations are at increased risk of certain malignancies. Although ovarian cancer is still only suspected of association with asbestos exposure, both bronchogenic and colonic malignancies are clearly exposure related. However, it is beyond the scope of this study and the limitations of this data to infer anything about malignancy in this population. Thus we will confine assessment of the overall state of health of the individuals screened to parameters for evaluation of interstitial lung disease only.

IV. Data Limitations

With the exception of follow up pulmonary function testing and physical examination, the nonradiographic data used in this analysis was confined to historical information the only source of which was individual participants. Such information is deficient because of

subjective and interpretive influences as well as memory limitations. For the most part, no previous medical records or diagnostic test results were available except for former chest radiographs obtained when necessary in follow up. In addition, the subgroup with abnormal pulmonary function findings may have been larger had more extensive functional parameters, such as measures of pulmonary mechanics, been available.

V. Clinical Findings

The 446 chest radiographs evaluated in the eight surveys represented a relatively healthy population. Furthermore the abnormal radiographic findings were only mildly so. Analysis of the subgroup with abnormal roentgenograms demonstrated a striking prevalence of pulmonary function abnormalities despite the fact that, as a group, they too were relatively healthy. On average they had normal pulmonary functions. Although each of the three groups had frequent symptomatic complaints, there was no distinguishing difference in prevalence of cough and/or shortness-of-breath among them. The only discriminating clinical feature of this population was the finding of significantly greater prevalence of bibasilar rales on physical examination in the 1/1 - 1/2 profusion category when compared with the other two. This was also the most severe category of radiographic abnormality studied. When examined only in terms of mean pulmonary function values, the 1/1 - 1/2 and the 1/0 profusion categories as well as those with normal parenchyma but bilateral pleural disease were all apparently healthy. In the case of

those with bilateral plaques alone, this finding is consistent with the epidemiologic experience of most authors. In contrast, those with 1/1 -1/2 parenchyma, as a group, might be expected to be sicker than our data indicate while those with 1/0 findings represent a poorly understood group, the clinical profile of which has not been clearly identified in the literature.

Still, the mean value of any given pulmonary function parameter for each of the three groups has no predictive value for any given individual in that group. When the data for all three forms of radiographic abnormality are evaluated in terms of prevalence of pulmonary function abnormalities, the appearance of health is lost. From this perspective, these populations are clearly not normal. Thirteen out of the 30 in category 1/0 had evidence of abnormal lung volumes (TLC < 80 percent predicted or RV < 80 percent predicted) and 6 out of 30 had abnormal diffusion capacities (see Table I). These figures represent a substantial proportion of illness. Furthermore, these ratios did not differ significantly among the three groups with radiographic abnormality. Although more rigidly defined restrictive defects (TLC < 80 percent predicted and RV < 80 percent predicted) were not as prevalent as any one criterion, lung volumes suggestive of early restriction with maintenance of total lung capacity at the expense of residual volume were common among all three radiographic groups (see Table I). Thus 8 out of 30 in category 1/0 had TLC < 90 percent predicted and RV < 70 percent predicted (see Table I). Again these proportions did not differ significantly among the three groups.

There are several important implications of these results. First, it is commonly accepted that an asbestos exposed individual with 1/1 - 1/2 radiographic profusion is likely to have other clinical abnormalities consistent with asbestos-related pulmonary fibrosis. Similarly it is commonly accepted that an asbestos exposed individual with radiographic change limited to benign pleural disease is likely to be otherwise healthy. The 1/0 population is less well characterized. This study challenges the above views. Not only do all three groups demonstrate a large prevalence of early restrictive pulmonary deficits, but all three groups are approximately comparable in degree of pathology. It is even more significant to find consistent abnormality within a population which is healthy overall and which by both historical and radiographic criteria is only moderately exposed to asbestos.

To validate this finding, it is important to determine its specificity for the presumed etiologic agent, asbestos. One possible confounder is other respirable expsoures. Tobacco is the most common and culpable agent in this category. However, the three groups' smoking habits were distinguishbale in only one case. Those with 1/1 - 1/2 profusion had significantly greater overall pack-year experience than either those in the 1/0 or those in the bilateral plaque categories (see Table XI). All three groups had comparable prevalences of smokers and nonsmokers (see Table XIII). The problem is to determine if the distinctions of 1/1 - 1/2 radiographic profusion and physical exam abnormalities are thus a function of asbestos exposure or tobacco exposure or some combination of the two. The 1/1 - 1/2 group did not vary from the other two in prevalence of abnormal FEV1/FVC values (see Table I). The only distinguishing feature for 1/1 - 1/2 individuals regarding obstructive

deficits was the finding that those with abnormal values of FEV1/FVC tended to be more abnormal than either those with 1/0 or bilateral pleural findings (see Table III). The 1/1 - 1/2 group did not have significantly greater asbestos exposure when compared with either of the other two groups. This generality held when comparisons were based on mean years of exposure, mean years in a trade, or mean years of latency since first exposure as well as on prevalence of exposure categories ($<$ 10 years, 10-19 years, $\geq$ 20 years) or latency categories ($<$ 20 years, or $\geq$ 20 years) (see Tables XI and XII). Whether or not cigarette smoking is responsible for the distinctive finding of 1/1 - 1/2 radiographic profusion with one associated physical examination abnormality is difficult to determine within the scope of this study. Clearly the 1/1 - 1/2 group has greater cigarette exposure and slightly more severe obstructive deficits among the subpopulation with this functional abnormality. Although the three groups have significantly greater asbestos exposure than the background population, the differences in exposure criteria among the three were not statistically significant. It is possible, therefore, that the 1/1 - 1/2 category results demonstrate that smoking acts in synergy with asbestos exposure to enhance radiographic pathology, physical exam abnormalities and obstructive functional deficits. In any case, the contribution of smoking cannot be ignored based on the above data and it appears to play a role particularly in the clinical profile of the 1/1 - 1/2 group.

Cardiovascsular disease which may present with clinical findings, particularly radiographic, similar to asbestosis represents another confounder. However, the five criteria used to assess cardiovascular status (cardiac catheterization proven coronary artery disease, history

of hypertension, history of coronary artery bypass surgery, history of myocardial infarction and chest radiographic findings consistent with congestive heart failure) occurred so rarely in this population that statistically meaningful evaluation was not possible. The only exception was the significantly increased prevalence of hypertensive disease among those with bilateral plaques when compared to the background population as well as the subgroup with normal radiographs. The role of this finding in terms of radiographic pathology is unclear. They did not have more experience with thoracic surgery, at least as assessed by histories of coronary artery bypass grafts, which might account for pleural scarring. In general, cardiovascular disease affects parenchymal but not pleural appearance. It is possible, however, that the unexpected degree of functional abnormality among those with benign pleural disease may in part be related to their relatively compromised cardiovascular status. Alternatively, exclusion of those with unilateral pleural disease from the category of benign pleural disease may have selected for a sicker population. The increased prevalence of questionable radiographic congestive heart failure among those in the 1/0 category (versus normals) cannot be evaluated because the numbers of individuals are too small. This finding is more likely a result of the technical difficulties of identifying 1/0 profusion. Thus within the limitations of the available data, one may conclude that cardiovascular disease did not play any significant role in the radiographic pathology of this population. Cardiovascular disease, therefore, could not have played any significant role in this population's functional pathology with the possible exception of those with bilateral pleural disease.

For both 1/1 - 1/2 profusion and benign pleural disease, asbestos exposure cannot be identified as the only factor significantly associated with their functional and physical exam abnormalities. The 1/1 - 1/2 group is also strongly associated with smoking, the bilateral plaque group with hypertensive disease. These two groups are distinguishable on demographic grounds as well. Both are significantly older than the 1/0 population. The 1/1 - 1/2 group is, on average, six years older and the bilateral plaque group is, on average, four years older than those with 1/0 profusion. Greater age could also contribute to increased functional and physical exam abnormality. In the case of those with 1/1 - 1/2 profusion age as well as smoking could contribute to radiographic pathology as well. For benign pleural disease, age has been identified elsewhere as an independent risk factor. In this population, those with benign pleural disease had greater mean total years of asbestos exposure, latency since first exposure and trade experience when compared with both 1/1 - 1/2 and 1/0 groups though only in comparison with the latter did these differences reach statistical significance (see Table XI). Based on the experience of other investigators, it is likely that when adjusted for latency and total years of exposure, age would not play an independent role in the development of benign pleural disease in this population.

The clinical significance of mild radiographic pathology in this population is a complicated issue not only for the traditionally poorly characterized subgroup with 1/0 profusion but also for those with 1/1 - 1/2 profusion and benign pleural disease. The populations represented in all three categories are, on average, older than those with normal radiogrphs and have a greater proportion of older ($\geq$ 50 years) and smaller

proportions of younger (< 40 years) members than their normal counterparts. Similarly all three have significantly greater mean pack-year experience and greater proportions of smokers than normals studied. Whether or not age or tobacco use are each independent risk factors for any of the three forms of early radiographic pathology investigated is beyond the scope of this study. In general, the epidemiologic literature supports an increased risk of development of parenchymal fibrosis associated with smoking. Still, appropriate corrections would have to be made for the greater exposure years, latency years and trade years among all three abnormal radiographic categories when compared to normals. With one exception, the latter finding is supportive of asbestos-related pathology. The one exception, that 1/1 - 1/2 individuals and normals have approximately the same mean total years of exposure, is especially surprising. This finding does not support an approximately linear dose-response relationship between asbestos exposure and radiographic change. It may simply be that total years of asbestos exposure is too crude an exposure index. However, the 1/1 - 1/2 group was also most strongly associated with smoking and the increased risk of development of parenchymal fibrosis in smokers may be related to the degree of radiographic pathology they demonstrate. This would explain the comparable restrictive pathology between the 1/1 - 1/2 and 1/0 group with the former including somewhat more severely obstructed individuals. The 1/1 - 1/2 category of this study is probably a group with 1/0 asbestos-related pathology who are older and thereby have greater cumulative tobacco experience as a result of which they have developed slightly more progressive radiographic change and more advanced obstructive deficits. Although the 1/1 - 1/2 group did not have

significantly more years of exposure when compared to the other two groups, their greater age not only implies more accumulated tobacco use but also suggests more concentrated exposures as they would have relatively greater work experience during the decades before regulation. This possibility may be an equally, if not more, important determinant of their more advanced radiographic pathology.

It is of note that the population least strongly associated with criteria other than asbestos exposure (age, smoking, cardiovascular disease) is the 1/0 group. Granted, they smoke more and are older than normals but they are the youngest and least heavily exposed to tobacco among those with radiographic abnormalities. It is possible that in the early stages of disease or in disease related to moderate rather than heavy asbestos exposure, radiographic change is particularly sensitive to tobacco exposure and/or age. A few extra years of urban living and smoking experience or slightly more concentrated asbestos exposures may be the necessary catalysts for crossing the boundary between normal and abnormal or 1/0 and 1/1 - 1/2. This hypothesis may be evidence for the subtlety of these distinctions but does not discount a significant role for asbestos exposure nor a significant predictive value for these categories in indentification of asbestos-related disease.

The above analysis is more difficult to apply to those with benign pleural disease as clinically they appeared very similar to those with 1/0 profusion. They are older, heavier smokers and more heavily exposed (by trade years and latency years) than the 1/0 group and yet have no evidence of parenchymal disease radiographically. If comparison of 1/0 and 1/1 - 1/2 categories suggests that not only exposure but also age and smoking experience are associated with progressive parenchymal change,

then it is inconsistent that this relationship does not hold for those with benign pleural disease. There are several possible explanations. Within the limitations of this study, each of age, tobacco use and asbestos exposure seems to play a role in the etiology of nonradiographic disease as well as radiographically apparent parenchymal and now pleural disease. The problem is when does an older, more heavily asbestos exposed, heavier smoker become more likely to develop parenchymal rather than pleural change and vice versa. The data suggests that the older, more heavily asbestos exposed, heavier smoker is likely to develop both parenchymal and pleural disease. Thus only 13 percent of normal chest radiographs demonstrated bilateral plaques while approximately 1/3 of the 1/0 category and 2/3 of the 1/1 - 1/2 castegory had pleural disease. The finding of benign pleural disease in the absence of parenchymal changes suggests that some other factor(s) may play a role. Idiosyncratic host susceptibility may be important. Variations in predominant fiber type to which an individual is exposed may also be a factor. Those with benign pleural disease may have had lower cumulative exposures since latency rather than dose is more important for plaque formation. Similarly development of parenchymal disease may reflect a greater fiber burden. Unfortunately, however, the specific fiber content as well as cumulative fiber burden of the population studied are not available.

The purpose of this study was to determine the clinical significance of early radiographic pathology, specifically 1/0 parenchymal profusion, in an asbestos exposed population. Our null hypothesis was therefore that 1/0 parenchymal change is not significantly associated with any other clinical criteria for asbetsos related lung disease. This was not the case. In fact the 1/0 group demonstrated a substantial prevalence of

reduced lung volumes, in particular residual volume. 43 percent of its members were found to have RV less than 80 percent of predicted. Volumes consistent with an early restrictive deficit were also relatively common with a prevalence of from 17 to 29 percent depending on the criteria used (see Table I).

An incidental finding was the apparently homogeneous clinical profiles of all three radiographically defined groups. Except for the significantly more common finding of bibasilar rales in the 1/1 - 1/2 group, the three categories were functionally and symptomatically very similar. In general 1/1 - 1/2 profusion should reflect the greatest amount of disease and benign pleural disease the least, with 1/0 somewhere in between. This was not the case. Contrary to expectations based on prior epidemiologic experiences, the differences among groups were not apparent in pulmonary function parameters or symptom queries. However, the finding of bibasilar rales in the 1/1 - 1/2 group is consistent with the experience of other authors. In fact, rales on exam are considered to be an early and sensitive manifestation of asbestosis in some populations. Here the radiographically defined categories differed most clearly in epidemiologic grounds. Thus the 1/1 - 1/2 finding was closely associated with greater age and heavier tobacco exposure and those with bilateral plaques had more hypertensive disease and fewer women than expected when compared with the total population. These findings suggest that our initial assumption that the 1/0 category represents the earliest form of radiographic disease may be an oversimplification. It appears more useful to think of all categories studied, 1/0, 1/1-1/2 and benign plaques as consistent with early radiographic pathology. Within the limits of the data, there is a clear association between indices of

asbestos exposure and these three forms of radiographic change. Although these radiographic manifestations of moderate asbestos exposure appear to be affected by other factors such as exposure to tobacco and age, the pathognomonic finding of frequent bilateral pleural disease (39 percent of those with parenchymal disease) and prevalent early restrictive lung function changes all support a significant role for asbestos itself. The ILO classification system has not been overinclusive in its designation of 1/0 radiographs as abnormal. These individuals are abnormal by functional criteria as well.

We have identified a population at risk for disease through radiographic screening. The disease process of concern, i.e. early asbestosis, was confirmed to be present through early restrictive pulmonary function changes in all three categories of radiographic abnormality studies. As a result, we conclude that radiographic identification of early asbestos-related lung disease be expanded to include not only those with category "1" parenchymal change but also those with so-called benign pleural disease. Furthermore, these results establish the clinical significance of 1/0 parenchymal disease and thereby legitimize continued health surveillance of individuals within that category. Unfortunately, however, this study was limited to historical and cross-sectional information which tell us nothing about future prognosis. The next challenge is to follow the course of this group in order to elucidate the natural history and progression of early asbestosis and thereby better manage its consequences.

TABLE I: PREVALENCE OF CXR FINDINGS ACCORDING TO PULMONARY FUNCTION ABNORMALITIES

	1/0 PROFUSION	1/1 - 1/2 PROFUSION	BILATERAL PLAQUES ONLY
LUNG VOLUMES			
TLC < 80% Predicted	1/30	2/10	5/34
RV < 80% Predicted	13/30	6/10	12/34
DIFFUSION CAPACITY			
DLCO < 80% Predicted	6/30	2/10	3/34
FLOW RATES			
FEV1/FVC < 75%	10/30	3/10	12/35
RESTRICTIVE DEFICIT			
TLC AND RV < 80% Predicted	1/30	2/10	4/34
TLC and RV and DLCO < 80% Predicted	1/30	1/10	0/34
"EARLY" RESTRICTION			
TLC < 90% Predicted and RV < 80% Predicted	8/30	2/10	7/34
TLC < 90% Predicted and RV < 70% Predicted	5/30	2/10	6/34

TABLE II: MEANS FOR LUNG VOLUMES AND DIFFUSION CAPACITY

	1/0 PROFUSION (n = 30)	1/1 - 1/2 PROFUSION (n = 10)	BILATERAL PLAQUES ONLY (n = 34-35)
MEAN PERCENT PREDICTED TLC (RANGE)	95.13 (68-121)	94.60 (53-121)	94.70 (70-118)
MEAN PERCENT PREDICTED RV (RANGE)	83.53 (58-131)	85.80 (62-155)	90.50 (46-148)
MEAN PERCENT PREDICTED DLCO (RANGE)	96.97 (51-120)	92.90 (24-131)	100.97 (54-168)

TABLE III: MEANS FOR ABNORMAL PULMONARY FUNCTION VALUES

	1/0 PROFUSION	1/1 - 1/2 PROFUSION	BILATERAL PLAQUES ONLY
MEAN PERCENT PREDICTED FOR TLC < 80% (RANGE)	68.00 (68-68) n = 1	64.50 (53-76) n = 2	75.80 (70-79) n = 5
MEAN PERCENT PREDICTED FOR RV <80% (RANGE)	67.08 (58-77) n = 13	66.67 (62-75) n = 6	63.50 (46-78) n = 12
MEAN PERCENT PREDICTED FOR DLCO < 80% (RANGE)	69.00 (51-77) n = 6	38.00 (24-52) n = 2	61.33 (54-68) n = 3
MEAN FOR FEV1/FVC < 75% (RANGE)	67.90 (53-73) n = 10	54.67 (38-70) n = 3	67.33 (57-74) n = 12

TABLE IV: PREVALENCE OF CXR FINDINGS ACCORDING TO SYMPTOMS AND SIGNS OF RESPIRATORY DISEASE

	1/0 PROFUSION	1/1 - 1/2 PROFUSION	BILATERAL PLAQUES ONLY
COUGH AND/OR SHORTNESS-OF-BREATH	15/29	4/10	20/35
BIBASILAR RALES ON PHYSICAL EXAM	2/30	5/10	4/35

TABLE V: P VALUES FOR VARIABLE FREQUENCIES OF SIGNS AND SYMPTOMS OF RESPIRATORY DISEASE BY RADIOGRAPHIC CATEGORY

	1/1 - 1/2 PROFUSION	1/0 PROFUSION	P VALUE
BIBASILAR RALES ON PHYSICAL EXAM	5/10	2/30	$.001 < P < .01$

	1/1 - 1/2 PROFUSION	BILATERAL PLAQUES ONLY	P VALUE
BIBASILAR RALES ON PHYSICAL EXAM	5/10	4/35	$.01 < P < .05$

	1/0 PROFUSION	BILATERAL PLAQUES ONLY	
BIBASILAR RALES ON PHYSICAL EXAM	2/30	4/35	$P > .10$

TABLE VI: PREVALENCE OF HISTORICAL AND RADIOGRAPHIC EVIDENCE OF CARDIOVASCULAR DISEASE

	ALL CXR's n = 352	ALL NORMAL CXR's n = 269	1/0 PROFUSION n = 29	1/1 - 1/2 PROFUSION n = 9	BILATERAL PLAQUES ONLY n = 41
CARDIAC CATHETERIZATION PROVEN CORONARY ARTERY DISEASE	1	1	0	0	0
HISTORY OF HYPERTENSION	65	45	4	2	14
S/P CORONARY ARTERY BYPASS SURGERY	4	1	1	1	1
S/P MYOCARDIAL INFARCTION (BY HISTORY)	9	6	3	0	0
? CONGESTIVE HEART FAILURE BY CXR	8	4	3	1	0

TABLE VII: P VALUES FOR VARIABLE PREVALENCES OF CARDIOVASCULAR ABNORMALITIES BETWEEN RADIOGRAPHIC GROUPS

	HISTORY OF HYPERTENSION	S/P CORONARY ARTERY BYPASS SURGERY	S/P MYOCARDIAL INFARCTION (BY HISTORY)	CONGESTIVE HEART FAILURE BY CXR
ALL CXR'S	65	4	9	8
1/0 PROFUSION	4	1	3	3
P VALUE	$P > .10$	$P > .10$	$P > .10$	$P < .05$
ALL CXR's	65	4	9	8
1/1 - 1/2 PROFUSION	2	1	0	1
P VALUE	$P > .10$	$P > .10$	$P > .10$	$P > .10$
ALL CXR's	65	4	9	8
BILATERAL PLAQUES ONLY	14	1	0	0
P VALUE	$.001 < P < .01$	$P > .10$	$P > .10$	$P > .10$
NORMAL CXR's	45	1	6	4
1/0 PROFUSION	4	1	3	3
P VALUE	$P > .10$	$P > .10$	$P < .10$	$P < .05$
NORMAL CXR's	45	1	6	4
1/1 - 1/2 PROFUSION	2	1	0	1
P VALUE	$P > .10$	$P > .10$	$P > .10$	$P > .10$

(Table continues on next page)

TABLE VII (cont.)

	HISTORY OF HYPERTENSION	S/P CORONARY ARTERY BYPASS SURGERY	S/P MYOCARDIAL INFARCTION (BY HISTORY)	CONGESTIVE HEART FAILURE BY CXR
NORMAL CXR	45	1	6	4
BILATERAL PLAQUES ONLY	14	1	0	0
P VALUES	$.01 < P < .05$	$P > .10$	$P > .10$	$P > .10$
1/0 PROFUSION	4	1	3	3
1/1 - 1/2 PROFUSION	2	1	0	1
P VALUE	$P > .10$	$P > .10$	$P > .10$	$P > .10$
1/0 PROFUSION	4	1	3	3
BILATERAL PLAQUES ONLY	14	1	0	0
P VALUE	$.05 < P < .10$	$P > .10$	$P > .10$	$P > .10$
1/1 - 1/2 PROFUSION	2	1	0	1
BILATERAL PLAQUES ONLY	14	1	0	0
P VALUE	$P > .10$	$P > .10$	$P > .10$	$P > .10$

TABLE VIII: PREVALENCE OF CXR FINDINGS ACCORDING TO SEVERAL VARIABLES

	ALL CXR's	ALL NORMAL CXR's	CXR = 1/0	CXR = 1/1 - 1/2	CXR = BILATERAL PLAQUES ONLY
MALES	371	278	31	12	50
FEMALES	75	70	3	0	2
TOTAL	446	348	34	12	52
AGE (YEARS)					
$\leq$ 40	94	92	1	0	1
40-49	120	102	9	1	8
$\geq$ 50	213	137	23	11	42
None Given	19	17	1	0	1
TOTAL	446	348	34	12	52
SMOKING					
Never Smoked	94	82	4	1	7
Cigar/Pipe Only	10	8	0	1	1
Cigarettes	322	239	29	10	44
No History Given	20	19	1	0	0
TOTAL	446	348	34	12	52
YEARS EXPOSED					
$\leq$ 10	32	29	2	1	0
10-19	105	96	5	1	3
$\geq$ 20	232	153	26	9	44
Not Available	77	70	1	1	5
TOTAL	446	348	34	12	52
LATENCY SINCE FIRST EXPOSURE					
$\leq$ 20 years	96	86	6	1	3
$\geq$ 20 years	191	122	23	9	37
Not Available	159	140	5	2	12
TOTAL	446	348	34	12	52

TABLE IX: AGE DISTRIBUTION

	< 40 YEARS %	40-49 YEARS %	≥ 50 YEARS %	AGE NOT AVAILABLE %	TOTALS %
ALL CXR's (n = 446)	21.0	26.9	47.8	4.3	100
ALL NORMAL CXR's (n = 348)	26.4	29.3	39.4	4.9	100
CXR = 1/0 (n = 34)	2.9	26.5	67.6	2.9	100
CXR = 1/1 - 1/2 (n = 12)	0	8.3	91.7	0	100
CXR = BILATERAL PLAQUE ONLY (n = 52)	1.9	15.4	80.8	1.9	100

TABLE X: MEANS FOR AGE, TOBACCO USE, AND EXPOSURE HISTORIES ACCORDING TO RADIOGRAPHIC PROFUSION

	NORMAL CXR's	PROFUSION 1/0	PROFUSION = 1/1 - 1/2	BILATERAL PLAQUES ONLY
AGE				
Mean Years (Range)	47 (n = 331) (21-79)	53 (n = 33) (35-66)	59 (n = 12) (49-72)	57 (n = 51) (37-78)
SMOKING				
Mean Pack-Year Experience (Range)	20.24 (n = 284) (0-135)	31.21 (n = 32) (0-70)	52.54 (n = 11) (0-100)	31.53 (n = 45) (0-144)
Mean Pack-Year Experience For Smokers (Range)	29.61 (n = 194) (3-135)	35.64 (n = 28) (5-70)	64.22 (n = 9) (30-100)	38.32 (n = 37) (2-144)
EXPOSURE				
Mean Total Years (Range)	18.26 (n = 269) (0-49)	24.31 (n = 29) (4-40)	23.30 (n = 10) (8-42)	25.05 (n = 41) (3-44)
Mean Years in Trade Exposure Occurred (Range)	20.30 (n = 273) (1-49)	26.18 (n = 33) (4-42)	28.18 (n = 11) (9-42)	30.35 (n = 46) (13-45)
Mean Year of 1st Exposure (Range)	1960 (n = 208) (1933-1982)	1956 (n = 29) (1939-1980)	1950 (n = 10) (1928-1971)	1950 (n = 40) (1929-1968)

TABLE XI: SIGNIFICANCE OF MEAN AGE, PACK-YEAR AND EXPOSURE DIFFERENCES BETWEEN RADIOGRAPHIC GROUPS

	NORMAL CXR	PROFUSION = 1/0	P VALUE
MEAN AGE (YEARS)	47	53	$.001 < P < .01$
MEAN PACK-YEAR EXPERIENCE	20.24	31.21	$.01 < P < .02$
MEAN PACK-YEAR EXPERIENCE FOR SMOKERS	29.61	35.64	$P > .10$
MEAN TOTAL YEARS EXPOSURE	18.26	24.31	$.001 < P < .01$
MEAN YEARS IN TRADE	20.30	26.18	$.001 < P < .01$
MEAN YEAR OF 1st EXPOSURE	1960	1956	$.02 < P < .05$

(Table continues on next page)

TABLE XI: (cont.)

	NORMAL CXR	PROFUSION = 1/1 - 1/2	P VALUE
MEAN AGE (YEARS)	47	59	$P < .001$
MEAN PACK YEAR EXPERIENCE	20.24	52.54	$P < .001$
MEAN PACK YEAR EXPERIENCE FOR SMOKERS	29.61	64.22	$P < .001$
MEAN TOTAL YEARS EXPOSURE	18.26	23.30	$P > .10$
MEAN YEARS IN TRADE	20.30	28.18	$.001 < P < .01$
MEAN YEAR OF 1st EXPOSURE	1960	1950	$.001 < P < .01$

(Table continues on next page)

TABLE XI: (cont.)

	NORMAL CXR	BILATERAL PLAQUES ONLY	P VALUE
MEAN AGE (YEARS)	47	57	$P < .001$
MEAN PACK YEAR EXPERIENCE	20.24	31.53	$.001 < P < .01$
MEAN PACK YEAR EXPERIENCE FOR SMOKERS	29.61	38.32	$.02 < P < .05$
MEAN TOTAL YEARS EXPOSURE	18.26	25.05	$P < .001$
MEAN YEARS IN TRADE	20.30	30.35	$P < .001$
MEAN YEAR OF 1st EXPOSURE	1960	1950	$P < .001$

(Table continues on next page)

TABLE XI: (cont.)

	PROFUSION = 1/0	BILATERAL PLAQUES ONLY	P VALUE
MEAN AGE (YEARS)	53	57	$.02 < P < .05$
MEAN PACK-YEAR EXPERIENCE	31.21	31.53	$P > .10$
MEAN PACK-YEAR EXPERIENCE FOR SMOKERS	35.64	38.32	$P > .10$
MEAN TOTAL YEARS EXPOSURE	24.31	25.05	$P > .10$
MEAN YEARS IN TRADE	26.18	30.35	$.02 < P < .05$
MEAN YEAR OF 1st EXPOSURE	1956	1950	$.01 < P < .02$

(Table continues on next page)

TABLE XI: (cont.)

	PROFUSION 1/0	PROFUSION = 1/1 - 1/2	P VALUE
MEAN AGE (YEARS)	53	59	$.02 < P < .05$
MEAN PACK-YEAR EXPERIENCE	31.21	52.54	$.01 < P < .02$
MEAN PACK-YEAR EXPERIENCE FOR SMOKERS	35.64	64.22	$P < .001$
MEAN TOTAL YEARS EXPOSURE	24.31	23.30	$P > .10$
MEAN YEAR OF FIRST EXPOSURE	1956	1950	$P > .10$
MEAN YEARS IN TRADE	26.18	28.18	$P > .10$

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TABLE XI: (cont.)

	PROFUSION = 1/1 - 1/2	BILATERAL PLAQUE ONLY	P VALUE
MEAN AGE (YEARS)	59	57	$P > .10$
MEAN PACK-YEAR EXPERIENCE	52.54	31.53	$.05 < P < .10$
MEAN PACK-YEAR EXPERIENCE FOR SMOKERS	64.22	38.32	$.02 < P < .05$
MEAN TOTAL YEARS EXPOSURE	23.30	25.05	$P > .10$
MEAN YEARS IN TRADE	28.18	30.35	$P > .10$
MEAN YEAR OF 1st EXPOSURE	1950	1950	$P > .10$

TABLE XII: ASBESTOS EXPOSURE EXPERIENCE

	TOTAL YEARS OF EXPOSURE					YEAR OF 1st EXPOSURE			
	< 10 YEARS	10-19 YEARS	≥ 20 YEARS	NOT AVAILABLE	TOTAL	< 20 YEARS PRIOR TO CXR	≥ 20 YEARS PRIOR TO CXR	EXPOSURE NOT AVAILABLE	TOTAL
	%	%	%	%	%	%	%	%	%
ALL CXR's (n = 446)	7.2	23.5	52.0	17.3	100	21.5	42.8	35.7	100
ALL NORMAL CXR's (n = 348)	8.3	27.6	44.0	20.1	100	24.7	35.1	40.2	100
CXR = 1/0 (n = 34)	5.9	14.7	76.5	2.9	100	17.6	67.6	14.7	99
CXR = 1/1 - 1/2 (n = 12)	8.3	8.3	75.0	8.3	100	8.3	75.0	16.7	100
CXR = BILATERAL PLAQUE ONLY (n = 52)	0	5.8	84.6	9.6	100	5.8	71.2	23.0	100

TABLE XIII: SMOKING HABITS

	NEVER SMOKED	CIGAR/PIPE USE ONLY	CIGARETTE SMOKERS	TOBACCO HISTORY NOT AVAILABLE	TOTALS
	%	%	%	%	%
ALL CXR's (n = 446)	21.1	2.2	72.2	4.5	100
ALL NORMAL CXR's (n = 348)	23.6	2.3	68.7	5.4	100
CXR = 1/0 (n = 34)	11.8	0	85.3	2.9	100
CXR = 1/1 - 1/2 (n = 12)	8.3	8.3	83.3	0	100
CXR = BILATERAL PLAQUES ONLY (n = 52)	13.5	1.9	84.6	0	100

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