III. EFFECTS ON HUMANS

Nonmalignant Respiratory Diseases

(a) Historical Studies

The use of asbestos dates back thousands of years; however, the modern industry dates from about 1880, when it was used to make heat and acid resistant fabrics, (Hendry, 1965; Hueper, 1966). With the increasing use of asbestos materials, reports of asbestos-related disease emerged.

The first record of a case of asbestosis was reported in England by Montague Murray in 1906. Hoffman (1918) reported that it was the practice of American and Canadian insurance companies not to insure asbestos workers due to unhealthful conditions in that industry. Pancoast et al (1917) commented on x-ray changes resembling pneumoconiosis in 15 individuals exposed to asbestos. The first complete description of asbestosis and of the "curious bodies" seen in lung tissue appeared when Cooke (1927) reported on a case of asbestosis, and McDonald (1927) reported on the same and another case. Each author gave reasons for believing that these "curious bodies" originated from asbestos fibers that had reached the lungs. Mills (1930) reported the first case of asbestosis in the United States, and in the same year, Lynch and Smith (1930) reported on "asbestosis bodies"* found in the sputum of asbestos workers. Early studies led many investigators to conclude that people exposed to asbestos

*"Ferruginous bodies" is a more descriptive term, as other inhaled fibers, eg, fibrous glass, may also become iron coated.

dust developed the disease "asbestosis" if the dust concentration was high or their exposure was long (Merewether and Price, 1930; Merewether, 1934; Fulton et al 1935; Dreessen et al, 1938).

(b) Epidemiologic Studies

Harries (1968) reported that although first impressions would lead one to believe that only workers continuously exposed to asbestos are at risk of developing asbestosis, further consideration of the industry and processes should have suggested that many other workers were also at risk. For example, some trades worked in confined spaces where asbestos was used. Work in shipboard trades was accepted by the Pneumoconiosis Panel of the United Kingdom as associated with asbestosis.

Murphy et al (1971a) found that asbestosis was 11 times more common among pipe insulators involved in new ship construction than among a control group. Asbestosis first appeared 13 years after exposure or at about 60 mppcf-years. The prevalence was 38% after 20 years. They also reported a case of extensive pleural calcification in a worker whose only known asbestos exposure was during sanding asphalt and vinyl tile floors (Murphy et al, 1971b).

Lorimer et al (1976), in a study of brake repair and maintenance workers exposed to asbestos, found that 25% of the workers showed evidence of x-ray abnormalities consistent with asbestosis. One quarter also had restrictive pulmonary function test findings.

Meurman et al (1973) found a three-fold risk of dyspnea and a two-fold risk of cough for asbestos workers as compared with controls, after adjusting for smoking.

Weill et al (1975) reported a decreased lung function in relation to increasing cumulative dust exposure in a group of asbestos cement manufacturing workers. Ayer and Burg (1976) reported a decrease in pulmonary function in asbestos textile workers with less than ten years of exposure.

In a study of 232 former insulation plant employees, Selikoff (1976a) reported positive x-ray findings among individuals having exposures to asbestos known to be as short as 1 day. More recently, Anderson et al (1976) reported x-ray findings consistent with asbestosis in household and family members having no known exposure to asbestos other than residing with a known asbestos worker. These two studies demonstrate the presence of asbestos disease in the absence of continuing new known exposures.

Wagoner et al (1973) demonstrated a significantly increased risk of death from nonmalignant respiratory disease and for diseases of the heart, which in part were secondary to pulmonary disease, among a cohort of workers in a major manufacturing complex using predominately chrysotile. Among those workers observed 20 or more years after onset of employment, a four-fold increased risk of death due to nonmalignant respiratory disease was observed. Further evaluation of these deaths revealed that the majority occurred within 1 year after termination of employment and at an average age of 53.8 years.

Newhouse (1969) reported an increased risk of death from nonmalignant respiratory disease in male asbestos textile and insulation workers with low to moderate exposure.

Enterline and Henderson (1973) reported that for all ages, only 18 deaths from asbestosis occurred in several asbestos plants studied from 1941 to 1969. It is significant to note, however, that the state of New

Jersey alone, in the years 1969-1970, had awarded workman's compensation for asbestosis to 455 workers from one of the plants in the study. (Heymann, 1971; Serraino, 1970)

Selikoff (1976a) reported a significant excess of deaths due to asbestosis among a group of workers in the US and Canada. Out of 17,800 asbestos insulation workers, there were 119 observed deaths attributed to asbestosis. Although it was not reported, the expected death rates from asbestosis in the general population would be virtually zero.

(c) Description of Asbestosis

Asbestosis is a chronic lung disease due to the inhalation of asbestos fibers and is characterized by diffuse interstitial fibrosis, frequently associated with pleural fibrosis (thickening) or pleural calcification.

The characteristic x-ray changes of asbestosis are small irregular opacities in the lower and middle lung fields, often accompanied by pleural thickening and pleural calcifications.

The pulmonary fibrotic changes develop slowly over the years--often progressively even without further exposure--and their radiographic detection is a direct correlate of their extent and profusion. In some cases, minor fibrosis with considerable respiratory impairment and disability can be present without equivalent x-ray changes. Conversely, extensive radiographic findings may be present with little functional impairment.

Commonly found in asbestosis are pulmonary rales, dyspnea, finger clubbing and cyanosis, but any or all can be absent in any one case.

Pulmonary hypertension is frequently associated with advanced asbestosis and the resultant cor pulmonale (right-sided heart failure) may be the cause of death.

Carcinogenicity

(a) Occupational Exposure

(1) Historical Studies

In 1935, 55 years after the start of large-scale usage of asbestos in industry, suspicion of an association between asbestosis and lung cancer was reported by Lynch and Smith (1935) in the USA and by Gloyne (1935) in the UK. About 10 years later, case reports of pleural and peritoneal tumors associated with asbestos appeared (Wedler, 1943, a,b; Wyers, 1946). Epidemiologic evidence from Doll (1955) showed a ten-fold excess risk of lung cancers in those UK asbestos textile workers who had been employed before 1930, before regulations produced improved dust conditions in factories. Similar findings were reported in the USA in 1961. Mesotheliomas were also detected but this fact was not published until later (Mancuso and Coulter, 1963; Selikoff et al, 1964). Possible variations in risk with different types of fiber were rarely considered in the early reports. Since 1964, following the recommendations of the UICC Working Group on Asbestos Cancers (UICC 1965) for new studies, there has been an expansion of epidemiologic studies in many parts of the world.

(2) Epidemiologic Studies

(A) Lung Cancer, Pleural and Peritoneal Mesotheliomas

(i) Mixed Types of Fiber

In most industrial processes different types of fiber are mixed, so that pure exposures to a single asbestos type are rare. Mortality studies of defined populations of asbestos-manufacturing, insulating, and shipyard workers have provided the most concrete evidence concerning the association between bronchial cancer, pleural, and peritoneal mesotheliomas and exposure to asbestos. Reports have come from several countries: (UK) Newhouse, 1969; (FRG) Bohlig et al, 1970; (USA) Selikoff et al, 1970; (UK) Elmes and Simpson 1971; (The Netherlands) Stumphius, 1971; (Italy) Rubino et al, 1972.

A seven-fold excess of lung cancer was found in a group of insulation workers whose exposures had been to chrysotile and amosite but not crocidolite (Selikoff et al, 1971). Enterline and Henderson (1973) reported a 4.4 times increased risk of respiratory cancer mortality among retired men who had worked as production or maintenance employees in the asbestos industry and who had been exposed to mixed fibers. Among men with mixed exposure to crocidolite and chrysotile in the asbestos cement industry, the rate was 6.1 times the expected rate. In a British naval dockyard population, Harries (1976) showed that there had been a steep rise in mesotheliomas since 1964. However, the full biologic effects of asbestos in shipyard workers would not have been expected to be detected until the 1970's and thereafter (Selikoff, 1976a).

Edge (1976) reported that shipyard workers with mixed asbestos exposure and pleural plaques (without evidence of pulmonary fibrosis) had a 2.5 times increased risk of developing carcinoma of the bronchus, when compared with matched controls without plaques. In a study of sheet metal workers (Cooper et al, 1975) with measurable and mixed asbestos exposure, an excess of deaths from malignant neoplasms (24.7% of deaths for two cohorts selected for 5 or more years worked in the trade, 19.1% of deaths for a group with death claims where 14.5% was expected) was largely attributed to an excess of malignant tumors of the respiratory tract. Of the 307 deaths in the first cohort, 32 lung cancer deaths were significantly in excess (1.7 times the expected). One pleural mesothelioma was observed.

Additional confirmatory evidence of the association between mesotheliomas and past exposure to asbestos comes from many institutes and departments of pathology and cancer registers, eg, (France) DeLarjarte et al, 1973; (Italy) Gobbato and Ferri, 1973; (South Africa) Webster, 1973; (UK) Greenberg and Lloyd Davies 1974; (FRG) Hain et al, 1974; (Finland) Nurminen and Markku), (German Democratic Republic) Sturm, 1975; (The Netherlands) Zielhuis et al, 1975). These studies have shown an association between asbestos and mesothelioma even with exposures as brief as 1 day; however, approximately 15% of the mesotheliomas are not known to be related to exposure to asbestos. Three studies (McDonald et al, 1973; Greenberg and Lloyd Davies, 1974; Newhouse et al, 1972) showed a poor correlation between certified cause of death and histologic diagnosis of mesothelioma. There is still a need to reduce the inter-observer variation in the diagnosis of these rare and pleomorphic tumors (McCaughey and Oldham, 1973).

The ratio of pleural to peritoneal tumors appear to be associated with heavier exposures (Newhouse et al, 1973). Among a number of occupationally exposed groups studied, approximately 5 - 7% of deaths have been from mesotheliomas (Gilson, 1973; Hammond and Selikoff, 1973; Selikoff, 1976b). More recently however, an estimate has projected that 11% of asbestos workers' deaths in England will be from mesotheliomas

(Newhouse and Berry, 1975).

(ii) Individual Types of Fibers

Crocidolite - In 1956, Wagner started investigating the occurrence of pleural and peritoneal mesotheliomas in the crocidolite mining areas of the Northwest Cape Province in South Africa. It was shown that these tumors occurred in the nonmining population living in the vicinity as well as among men working in the mines and mills and in the transportation and handling of the fiber (Wagner, 1960). Asbestosis was not invariably present. The latent period between first exposure and clinical recognition of the tumor was long - a mean of 40 years. Subsequent surveillance of the mining population in all the asbestos-producing areas in South Africa has added support for a major difference in the incidence of mesotheliomas within the crocidolite mining areas of that country. (Harrington et al, 1971; Webster, 1973). The mining of crocidolite in northwest Australia has been associated with mesotheliomas (McNulty 1962). Jones et al (1976) have reported a high incidence of mesotheliomas among women who worked with crocidolite in a factory producing gas mask canisters during World War II.

Chrysotile - McDonald et al (1973, 1974) reported that the overall death rate among 11,500 workers born between 1891 and 1920 and employed in the chrysotile mines and mills of Quebec was lower than for Quebec Province as a whole. An increased lung cancer risk was found and considered to be dose-related, and those who had been most heavily exposed to the dust showed about a five-fold risk compared with the least exposed. Of the 3,270 deaths, 134 were from respiratory cancer, with 129 being lung cancer and 5 mesotheliomas. Recently, the authors (McDonald and McDonald, 1976) have observed 3,938 total deaths among males through 1973, of which 224 were from lung cancer and 7 from mesothelioma. The authors suggested that the respiratory cancer mortality in the Quebec chrysotile industry as a whole was greater than that expected on the basis of regional mortality data.

Kogan et al (1972) investigated the cancer mortality among workers in asbestos mining and milling industries between 1948 and 1967. The total cancer mortality rate among workers was 1.6 times higher than that found in the general male population; for female workers the rates were 0.8 for those in mines and 1.3 for those in mills. The lung cancer risk for male miners and millers was twice that of the general male population. For females in mines and mills, the risks were 2.1 and 1.4 times that of the general female population, respectively. For those workers over 50 years of age, the risk of lung cancer was greater: for men in mining, 4.9; those in milling, 5.9; for women in mining, 9.5; and for those women in milling, 39.8 times that found in the general population. No mesotheliomas were found, but Kogan et al (1972) indicate that this might be explained by the insufficient experience of pathologists with this rare type of cancer in that geographical area. Also, the number of people in the study populations were not reported.

Wagoner et al (1973) reported on the cancer risk among a cohort of workers in a major manufacturing complex utilizing predominately chrysotile asbestos in textile, friction, and packaging products. An excess of respiratory cancer occurred among asbestos workers in each duration-of-employment category down to and including 1-9 years. They observed statistically significant standard mortality ratios of 122 for all malignant neoplasms and 244 for malignant neoplasms of the respiratory system. The asbestos workers in this study were located in an area of predominately Amish Dutch population with known low frequencies of smoking. The authors, nevertheless, used the general white male US population as a control group, which would tend to underestimate the degree of risk.

Enterline and Henderson (1973) found that for retired men who had worked as production or maintenance employees in the asbestos industry and who had reached 65 years of age, those who had been exposed only to chrysotile had a respiratory cancer risk two - four times than that expected. Among men within the asbestos cement industry exposed only to chrysotile, a one- to four-fold excess of respiratory cancer was found. Of 802 deaths, only one mesothelioma had been recorded in the several plants investigated. In contrast, a subsequent investigation by Borow et al (1973) found 70 cases of mesothelioma from only one of these plants. The discrepancy was due to methodologic variations, for example, Enterline and Henderson (1973) had limited their investigation to men age 65 or over, while many of the mesothelioma cases reported by Borow et al (1973) had died before that age.

Amosite - In a study of a group of miners exposed to amphibole fibers in the cummingtonite-grunerite ore series, Gillman et al (1976) demonstrated mortality from malignant respiratory disease to be three times than that found in the general population.

Exposures to amosite alone in a factory making insulation material were reported by Selikoff (1976 a & b). Ten mesotheliomas were found in addition to an increased risk of lung cancer in workers who were observed 20 years or longer. The excess lung cancer risk in the amosite workers was shown to increase with duration of employment. There was a three-fold increase in lung cancer among those with less than 3 months employment and among those with less than 1 month employment there was a 2.25-fold increase.

In a retrospective study of 914 men who had worked periodically during World War II in a plant manufacturing insulating materials from amosite for the US Navy, Seidman et al (1976) concluded that the group of 65 men who had worked for less than 1 month had experienced excess mortality, on the age-specific basis, from lung cancer during the 30 years since the beginning of their exposure, but not from all cancers or all causes of death. Men who had worked for a full month or longer had excess mortalities from all three causations examined, the risk of death from lung cancer increasing with duration of exposure.

Anthophyllite - In Finland, anthophyllite mining has been associated with an excess bronchial cancer risk of 1 - 4 times the expectation overall, and about double this figure for those with more than 10 years' exposure (Meurman et al, 1974).

There was also a higher prevalence of dyspnea and cough in the miners. However, no mesotheliomas were found despite the presence in Finland of an unusually high incidence of pleural thickening and calcification as detected by radiographic and pathologic surveys (Kiviluoto, 1960; Meurman, 1966).

(B) Other Types of Cancer

Epidemiologic studies of the already defined populations have consistently shown an excess risk of other cancers, especially of the gastrointestinal tract (Mancuso and El Attar, 1967; Elmes and Simpson, 1971; Kogan et al, 1972; Newhouse, 1973; Wagoner et al, 1973; McDonald et al, 1974; Selikoff et al, 1974); however, it has been less than that of lung cancers.

Schneiderman (1974), in a literature review with an emphasis on dose-response, concluded that "good dose-response data, with quantitative estimates of dose are uncommon; however, in all the literature reviewed, only one paper did not support the conclusion that increased exposure to inhaled asbestos particles leads to increased digestive system cancer."

Stell and McGill (1973) found that out of 100 men with squamous carcinoma of the larynx, 31 had known exposure to asbestos compared with only three in matched controls. Similar associations have been reported by Morgan and Shettigara (1976). Newhouse and Berry (1973) found two cases of cancer of the larynx (ICD 161) in their cohort of over 4,000 workers compared with an expected 0.4.

(b) Nonoccupational Exposure

Household contact with asbestos is associated with an increased mesothelioma risk. Anderson et al (1976) have recently reviewed 34 such cases of mesothelioma from nine countries and reported four new cases among the traced family members of 1,664 asbestos workers. Cases of mesotheliomas have also occurred in nonoccupationally exposed individuals living in the neighborhood of industrial sources of asbestos (Wagner et al, 1960; Newhouse and Thompson, 1966; Bohlig and Hain, 1973). Studies of the geographical distribution of cases of mesothelioma in the UK over a 10-year period indicate that the new cases are nearly all from areas in which there has been a recognized industrial source of asbestos (Gilson, 1970; Greenberg and Lloyd Davies, 1974).

Lesions among nonoccupationally exposed persons in Finland have been reported where anthophyllite asbestos is mined. In this study, 118 cases of the total 126 cases of roentgenologically-diagnosed pleural calcification studied, excluding those individuals with hemothorax, emphysema, and tuberculosis, lived or have lived in areas immediately adjacent to asbestos mines (Kiviluoto 1960). The results of this study suggest a health hazard from community exposure to ambient asbestos.

SYNERGISM

There is marked enhancement of the risk of lung carcinoma in those workers exposed to asbestos who also smoke cigarettes (Selikoff et al, 1968; Doll, 1971; Berry et al, 1972; Hammond and Selikoff, 1973); Hammond and Selikoff (1973) interpret the excess lung carcinoma risk from asbestos in nonsmokers to be small. No link between cigarette smoking and mesotheliomas has been observed in a prospective study by Hammond and Selikoff (1973). A preliminary study (Lemen, 1976) on female workers employed between January 1940 and December 1967, in a predominately chrysotile asbestos textile plant, revealed 7 lung cancer deaths among 580 women when only 0.63 deaths were expected ($p<0.01$). One lung cancer death was observed in a smoker, two in women of undetermined smoking history, and four in "never" smokers as determined from hospital admission charts.

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

FIBER ANALYSIS IN TISSUE

The physical characteristics of asbestos fibers which penetrate to the lung parenchyma have been studied by Timbrell (1965 and 1972) who demonstrated fiber respirability to be largely a function of fiber diameter.

Two kinds of data are relevant. Timbrell et al (1971) and Timbrell (1972) have shown that the crocidolite mined in Northern Cape Province, South Africa, and in Western Australia is associated with a high incidence of pleural mesothelioma among the local populations and has finer and shorter fibers than the crocidolite or amosite mined in the Transvaal Province, which is associated with a relatively lower incidence of pleural mesothelioma among the exposed population. As crocidolite and amosite are similar in chemical composition, there is reason to assume that the risk difference may be attributable to the differing physical characteristics of fibers.

Preliminary studies (Fondimare et al, 1974) concerning diameter and length of 5,000 asbestos fibers from the lungs of 10 deceased persons who had been occupationally exposed, showed that these fibers were all less than 0.5 μm micrometer in diameter. When separated according to type of asbestos, 90% of chrysotile fibers and 70% of amphibole fibers were less than 5 μm in length.

Asbestos bodies have been found in large numbers by light microscopy in occupationally exposed individuals (Ashcroft and Heppleston, 1973). Numerous asbestos fibers, either of chrysotile or amphibole or both types, have been found by electron microscopy in lungs of industrially exposed men (Pooley, 1972, 1973; Fondimare et al, 1974). A quantitative topographic study of asbestos fibers in the lung has been carried out in 12 industrially exposed men which showed that heavily exposed cases with lung fibrosis and carcinomas had fewer fibers in the fibrotic lower lobes than in the less fibrotic type. In less exposed cases with lung cancer but without lung fibrosis, a higher concentration of asbestos fibers, mostly of the chrysotile type, was clearly demonstrated in peripheral areas of the lung.

Optical and electron microscopic study of pleural plaques revealed the presence of some coated fibers and large numbers of uncoated fibers, mostly short, ultimate fibrils of chrysotile (Fondimare et al, 1974).

Pooley (1973) found that 93% of 120 mesothelioma cases studied had asbestos fibers in their lungs visible by electron microscopy versus less than 50% of 135 nonmesothelioma cases. Higher concentrations of fibers were observed in mesothelioma than in nonmesothelioma cases. In mesothelioma cases, the fiber types were either amphibole or chrysotile, or both, but amphibole was predominant; in nonmesothelioma cases, chrysotile fibers were predominant. In the three cases included in the study by Fondimare et al (1974), the percentage of chrysotile fibers was from 44 to 97% in the peripheral areas of the lung. The ratio of amphibole to chrysotile has been found to decrease from the central toward the peripheral areas of the lung (Fondimare et al, 1974; LeBouffant et al, 1976).

Coated fibers ("asbestos" or "ferruginous bodies") have been found in the lungs of most adults who have lived in urban areas (Gross et al, 1969; Bignon and Goni, 1969; Selikoff et al, 1972; Thompson et al, 1966; Davis and Gross, 1973; Oldham, 1973). The number of coated fibers in the lung has been compared in cases with and without lung carcinoma. Meurman (1966), who took cigarette consumption into account, could find no significant difference.

Doniach et al (1975) found an increased incidence of asbestos bodies in men with stomach cancer and in women with breast cancer, but not in lung cancer cases. Warnock and Churg (1975) found that lung cancer cases had more coated fibers in their lungs, even though only one case had known occupational exposure. The variations in percentage are probably from methodologic differences. In general, methods involving the counting of fibers/unit of weight or volume of lung tissue have greater associations with health outcomes in epidemiologic studies. However, coated fibers are not specific to asbestos (Gross et al, 1968) and cannot be related to asbestos unless the core has been identified as such by electron diffraction and/or x-ray analytical techniques (Pooley, 1970, 1975; Langer and Pooley, 1973, 1974; Fondimare et al, 1975).

Transmission electron microscopy has demonstrated the presence of chrysotile fibers or fibrils in the lungs of most consecutive autopsy cases in London (Pooley et al, 1970), New York (Langer et al, 1971) and Pittsburgh (Gross et al, 1973).

Although some differences in both the fibrotic and the carcinogenic responses to asbestos fibers may depend on the type of fiber administered, all types have definitely shown both these kinds of action (eg, Karacharova et al (1979), Shin and Firminger (1973), Wagner et al (1976). Godwin and Jagatic (1970), Gross et al (1973), and Taskinen et al (1973) reported finding fibers in lymph nodes and in the spleen, abdomen, and intestinal mucosa of occupationally exposed patients with mesotheliomas and pleural nodules. These findings emphasize the practical importance of penetration and transport of the small fibers of asbestos from their initial sites of impaction. They also stress the importance of guarding against the entrance of asbestos fibers into the body by any route.

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TABLE III-1

STUDIES OF HUMAN POPULATIONS-NONMALIGNANT RESPIRATORY DISEASE

Author	Date	Finding	Group and Exposure
<u>Historical Studies</u>			
Murray	1906	First reported case of asbestosis	Asbestos workers
Cooke	1927	Case of asbestosis reported	"
McDonald	1927	Two cases of asbestosis reported	"
Mills	1930	First case of asbestosis reported in U.S.	"
Lynch and Smith	1930	Ferruginous or "asbestosis bodies" found in sputum	"
<u>Epidemiological Studies</u>			
Murphy	1971	Asbestosis	Pipe insulators
Lorimer et al	1976	X-ray abnormalities consistent with with asbestosis and restrictive pulmonary function testing	Brake repair maintenance workers
Meurman et al	1973	Dyspnea and cough	Asbestos workers
Weill et al	1975	Decreased lung function	Asbestos cement manufacturing workers
Ayer and Burg	1976	Decrease in pulmonary function	Asbestos textile workers with less than 10 yr exposure
Selikoff	1976a	Asbestosis	Former insulation plant employees with as little as one day exposure
Anderson et al	1976	X-rays consistent with asbestosis	Household and family members of asbestos worker
Wagner et al	1973	Death due to nonmalignant respiratory disease and diseases of heart, in part secondary to pulmonary disease	Chrysotile workers
Newhouse	1969	Death due to nonmalignant respiratory disease	Male asbestos textile and insulation workers
Enterline and Henderson	1973	Death due to asbestosis	Asbestos plant workers
Selikoff	1976a	"	Insulation workers and factory workers exposed to asbestos
Bohs	1968	X-ray evidence of asbestos	Workers in asbestos industry in Britain after 1933 with perponderance of less than 20 yr exposure
Lewinsohn	1972	X-ray abnormalities	Asbestos workers in Britian
Gillam et al	1976	Nonmalignant respiratory disease	Amosite miners

TABLE III-2

STUDIES OF HUMAN POPULATION CARCINOGENICITY

Author	Date	Finding	Group and Exposure
Occupational Exposure			
Historical Studies			
Lynch and Smith	1935	Suspicion of association	Asbestos workers
Gloyne	1935	Between asbestos and lung cancer	"
Wedler	1943a,b	Case reports of pleural and peritoneal tumors associated to asbestos	"
Doll	1955	Lung cancer	Asbestos textile workers employed before 1930
Mancusco and Coulter	1963	Lung cancer and mesotheliomas	Asbestos workers
Selikoff	1964	"	"
Epidemiological Studies			
Lung, Pleural and Peritoneum			
Mixed Types of Fibers			
Newhouse (UK)	1969	Bronchial cancer, pleural and peritoneal mesotheliomas	Asbestos manufacturing, insulation and shipyard workers
Bohlig et al (FRG)	1970	"	"
Selikoff et al (USA)	1970	"	"
Elmes and Simpson (UK)	1971	"	"
Stumphius (Netherlands)	1971	"	"
Rubino et al (Italy)	1972	"	"
Selikoff et al	1973	Lung cancer	Insulation workers, chrysotile and amosite asbestos exposure
Enterline and Henderson	1973	Respiratory cancer	Retired production and maintenance workers in asbestos industry
Harries	1976	Mesotheliomas	Naval dockyard workers
Edge	1976	Carcinoma of bronchus	Shipyard workers

TABLE III-2 (CONTINUED)

STUDIES OF HUMAN POPULATION CARCINOGENICITY

Author	Date	Finding	Group and Exposure
Mixed Types of Fibers			
DeLajarte et al (France)	1973	Evidence of association between mesotheliomas and past exposure to asbestos	Occupational exposures in some cases as brief as one day
Gobbato and Ferri (Italy)	1973	"	"
Webster (South Africa)	1973	"	"
Greenberg and Lloyd Davies (UK)	1974	" "	" "
Hain et al (Fed. Rep. Germany)	1974	"	"
Nurminen (Finland)	1975	"	"
Stunn (Ger. Dem. Rep.)	1975	"	"
Zielhuis (The Netherlands)	1975	"	"
Newhouse et al	1973	Peritoneal tumors associated to heavy exposures	"
Gilson	1973	5% to 7% asbestos workers' deaths due to mesotheliomas	"
Hammond and Selikoff	1973		"
Selikoff	1976	"	"
Newhouse and Berry	1975	11% asbestos workers deaths due to mesotheliomas	"
Single Types of Fibers			
Crocidolite			
Wagner	1960	Pleural and peritoneal cancer	Workers in mines, mills and in transportation and handling of crocidolite and population in vicinity of mines
Harrington et al	1971	Mesotheliomas	Mining population of crocidolite mines
Webster	1973		
McNulty	1962	"	Miners of crocidolite
Jones et al	1976	"	Women working with crocidolite in WWII gas mask canister factories

TABLE III-2 (CONTINUED)

STUDIES OF HUMAN POPULATION CARCINOGENICITY

Author	Date	Finding	Group and Exposure
Chrysotile			
McDonald et al	1973,1974	Lung cancer	Chrysotile mine and mill workers
Kogan et al	1972	Total cancer Lung cancer	Workers in asbestos mining and milling, men and women
Wagoner et al	1973	Respiratory cancer	Workers in manufacturing of textile, friction and packaging products using chrysotile
Enterline and Henderson	1973	"	Men 65 yr and older, retired production or maintenance employees in asbestos industry exposed only to chrysotile
Borow et al	1973	Mesotheliomas	Workers at plant using chrysotile, all ages
Amosite			
Gilliam et al	1976	Malignant respiratory disease	Miners exposed to amphibole fibers in cummingtonite-grunerite ore series
Selikoff et al	1976a,b	Mesotheliomas, lung cancer	Insulation workers in factory using amosite
Anthophyllite			
Neurman et al	1974	Bronchial cancer, dyspnea and cough	Anthophyllite mining employees
Other Cancer			
Mancuso and El Attar	1967	Cancer of gastrointestinal tract	Asbestos workers
Elmes and Simpson	1971	"	"
Kogan et al	1972	"	"
Newhouse	1973	"	"
Wagoner et al	1973	"	"
McDonald et al	1974	"	"
Selikoff et al	1974	"	"
Stell and McGill Morgan et al	1973 1976	Squamous carcinoma of larynx	Workers with exposure to asbestos
Newhouse and Perry	1973	Cancer of larynx	Asbestos workers

TABLE III-2 (CONTINUED)

STUDIES OF HUMAN POPULATION CARCINOGENICITY

Author	Date	Finding	Group and Exposure
Nonoccupational Exposure			
Anderson et al	1975	Mesotheliomas	Family members of asbestos workers
Wagner et al	1960	"	Individuals in neighborhood of industrial sources of asbestos
Newhouse and Thompson	1965		
Bohlig and Hain	1973		
Gilson	1970	"	New cases from areas with recognized industrial source of asbestos
Greenburg and Lloyd	1974		
Davies			
Kiviluoto	1960	Pleural plaques	Persons in farming region of Bulgaria where minute quantities of anthophyllite, tremolite and sepiolite in soil and non-occupationally exposed persons in anthophyllite mining area of Finland
Other Studies			
Newhouse	1969-	Cancer, mesothelioma	Women factory workers exposed to chrysotile, amosite and crocidolite
Newhouse et al	1972	"	
Howard et al	1976	Lung cancer	Workers in asbestos industry from 1933 to 1950 and after 1950
Cooper et al	1975	"	Sheet metal workers with 5 or more years exposure