metric equivalents in ital
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PLAINTIFF'S EXHIBIT

UC-4636

ORNL-EPA-17
November 30, 1974

REVIEW OF THE ENVIRONMENTAL EFFECTS OF ASBESTOS

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ABSTRACT

Available data indicate that asbestos is a widespread environmental pollutant present in air, water, soil, food, drugs and beverages. All types of asbestos have been found to be pathogenic in animals and humans, causing asbestosis, lung cancer, mesotheliomas and pleural lesions. Because of the large number of variables influencing the effects of asbestos, the mechanisms of pathogenicity are poorly understood and the physicochemical properties of various asbestos types as related to biological effects are incompletely defined. The general population is widely exposed to asbestos via inhalation and ingestion, however, the hazards of chronic environmental exposure have not been determined.

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1.0 GENERAL SUMMARY

1.1 FINDINGS

Asbestos exposure is pathogenic to humans, causing asbestosis, lung abnormalities such as pleural plaques, lung cancer, pleural and peritoneal mesotheliomas, and gastrointestinal tract cancers. Its pathogenicity is well supported both by experimental animal data and human epidemiological studies of occupationally exposed populations.

An ideal summation of animal data would be a dose-response curve showing doses of various types of asbestos plotted against the incidence of asbestosis and cancer in different experimental animals; it is hoped that the results could then be extrapolated to humans. Unfortunately, these investigative data do not yet exist. We can conclude from available data, however, that all commercially important types of asbestos have the potential to produce asbestosis and cancer in all commonly used laboratory animals, including mice, rats, hamsters, guinea pigs, and monkeys (Section 4.0).

Species differ in the intensity and speed with which they respond to asbestos exposure (Section 4.4.1.3.1). The fibrotic response in the rat usually is multifocal and nonprogressive unless a chronic infection is present (Section 4.4.1.3.1). In guinea pigs, fibrosis is diffuse and progressive (Section 4.4.1.3.1). Considerable controversy exists concerning the fibrogenic potential of various asbestos types and fiber sizes (Section 4.4.1.3.2 and Section 4.4.1.3.3). Firm conclusions about pathogenic mechanisms are impossible because of the large number of physical and chemical variables that may influence the pathogenicity of asbestos (Section 4.2).

Drawing conclusions about the carcinogenic potential of asbestos is also problematic; neither mechanisms of action nor quantitative dose-response relationships have been defined (Section 5.3.3). Lung cancer and mesothelioma induction are positively associated with asbestos exposure, as shown in many epidemiological investigations of humans. Mesotheliomas in humans are associated with inhalation of crocidolite, amosite, and chrysotile asbestos fibers. The risk is greatest with crocidolite and less with amosite and chrysotile (Section 5.3.4.3). In animal experiments, chrysotile, amosite, as well as crocidolite, produce mesotheliomas when injected intrapleurally into rats

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(Section 4.4.2.1). Mesotheliomas have been induced following inhalation exposure of animals to crocidolite, chrysotile and amosite (Section 4.4.2.1). The data clearly show that asbestos exposure can lead to asbestosis, lung cancer, and mesothelioma in animals, but quantitative dose-response relationships have not been obtained. However, the data also suggest that mesothelioma may indeed occur with little exposure and that the incidence is not necessarily proportionate to the dose (Section 6.0).

Asbestos inhalation causes several interrelated respiratory diseases in humans (Table 1.1) (Section 5.3). The symptoms include cough, dyspnea, rales, emphysema, pleuritis, altered serum protein concentrations, reduced lung function, pulmonary fibrosis, pleural effusion, pleural thickening, finger clubbing, and pleural plaques. Diagnoses can be made from a history of exposure, biopsy, x-ray, and examination of sputum, tumor, or lung tissue for the presence of asbestos bodies. Removal from exposure and symptomatic treatment are direct measures that can be taken against asbestos-related health problems. The most prevalent condition is asbestosis--a chronic, progressive disease characterized by pleural lesions and interstitial pulmonary fibrosis with functional impairment of the lungs. Symptoms include cough, weight loss, and shortness of breath (Section 5.3.1). There is no effective treatment for asbestosis or its complications (Section 5.3.1). Once asbestos fibers reach the lung, they induce diffuse fibrous degeneration, primarily in the lower lobes (Section 5.3.1); this condition may develop as early as 3 to 6 years after initial exposure and continues to progress even after exposure has ceased (Section 5.3.1). The gradual progression of fibrosis results in the distortion of terminal bronchioles and air spaces (Section 5.3.1), leading eventually to severe pulmonary insufficiency and death.

Abnormalities of the pleural lining surrounding the lungs commonly accompany asbestotic lung fibrosis (Section 5.3). The main pleural lesions involved are hyaline plaques, which are layers of hyalinized fibrous protein formed by the proliferation of connective tissue fibers (Section 5.3.1.2). This fibrous response is attributed to the abrasive action of asbestos fibers that reach the pleura via penetration of lung tissue (Section 5.3.1.2).

Dose-response relationships between asbestos inhalation and asbestosis are poorly defined for humans. Nearly all of the positive evidence linking asbestos with human health effects comes from epidemiological and clinical studies, most of which lack quantitative exposure histories (Section

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Table 1.1 RESPIRATORY CONDITIONS CAUSED BY ASBESTOS

Condition	Definition
Asbestosis	Lung fibrosis caused by inhalation of asbestos dust.
Pleural calcification	Hardening of pleural tissue.
Pleural plaques	A patch or small differentiated area on the surface of the pleura.
Pleural and peritoneal mesothelioma	A rare neoplasm derived from the lining cells of the pleura and peritoneum.
Lung cancer	Various types of malignant neoplasms, most of which invade surrounding tissues, and may metastasize to several sites.

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5.3.3). Consequently, only a minimal association has been established between human epidemiological data and environmental exposure, and even this reflects a noticeable lack of definitive information concerning causal relationships (Section 5.3.1). Generally, the development of asbestosis appears to be closely related to the dose and duration of asbestos exposure and to the length of asbestos residence in the lungs; the incidence increases with increasing dose and/or duration (Section 5.3.3). However, a 38% incidence of asbestosis has been reported in 101 shipyard workers exposed to a small dose of approximately 5 million particles per cubic foot (mppcf) for more than 20 years (Section 5.5.3.3). These results suggest that prolonged exposure to low concentrations is hazardous and that the current threshold limit value (TLV) of 5 fibers per ml should be lowered (Section 5.3.3).

Other studies show that the inhalation of large doses for short durations can be as harmful as the cumulative effect of low concentrations over many years of exposure (Section 5.3.3).

Several types of human cancers have been attributed to asbestos inhalation (Section 5.3.4). A recent report estimates that 50% of the persons with asbestosis also develop lung cancer (Section 5.3.4.1.1). Mesotheliomas of the pleural and peritoneal tissues are rare primary tumors of the serosa; approximately 80% of these cancers occur in persons exposed to asbestos (Section 5.3.4.1.2). The prognosis for mesothelioma in either site is poor, and the condition usually results in tumor progression, mesothelioma or obliteration of the abdominal cavity by peritoneal mesothelioma (Section 5.3.4.1.2.2).

Asbestos inhalation enhances the risk of cancer of the stomach and colon. Persons with asbestosis demonstrate an increased incidence of gastrointestinal cancer (Section 5.3.4.1.3). Ingestion of asbestos fibers after inhalation may be the route of exposure that leads to this increased risk (Section 5.3.4.1.3). For example, the extremely high rate of stomach cancer among the Japanese may result from the ingestion of rice that is treated with asbestos-contaminated talc (Section 5.3.4.1.3). Asbestos contamination of drinking water in Duluth, Minnesota, has not yet produced any apparent increases in cancer mortality within the surrounding population. The findings are inconclusive, however, because cancer induction requires more than twenty years ~~any years and~~ there is a ~~significant~~ lack of ~~experimental and~~ epidemiological information concerning the effects of asbestos ingestion in humans (Section 5.3.4.1.3).

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Numerical
~~Well-defined~~ dose-response relationships between asbestos exposure and cancer induction cannot be derived readily from available data. The greatest risk occurs with long, heavy exposure, which is most likely to occur in industrial situations (Section 5.3.4.2). ~~An exception may be the development of carcinoma in one patient exposed to asbestos for only 12 months~~ (Section 5.3.4.2). Mesotheliomas have also been reported in persons who were indirectly exposed to asbestos through contact with clothing of occupationally exposed relatives, and in persons who live in the vicinity of asbestos industries (Section 5.3.4.2).

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Some epidemiological studies indicate that crocidolite is more carcinogenic than other types of asbestos; it is associated with a higher incidence of mesothelioma and lung cancer than are chrysotile, amosite, and anthophyllite (Section 5.3.4.3).

Cigarette smoking ~~may be~~ is a cofactor in lung cancer induction by asbestos ~~(Section 5.3.4.4)~~, Asbestos inhalation combined with cigarette smoking significantly increases lung cancer incidence over that occurring with exposure to either factor alone (Section 5.3.4.4).

Until 1969, diseases associated with asbestos exposure were considered only as occupational hazards (Section 5.3.6.2). More recently, investigators have realized that exposure of the general population to environmental asbestos pollution may also be hazardous, particularly in urbanized areas (Section 5.3.6.2). Asbestos bodies are commonly found in the lungs of urban residents, both in Europe and the United States (Section 5.3.6.2.1). Data are ~~insufficient to indicate the significance of the concentrations detected; nevertheless,~~ reports of mesotheliomas and pleural lesions in persons who reside in the vicinity of asbestos industries indicate that ~~pollution of the environment~~ (increased exposure) by asbestos may be a ~~serious~~ human health hazard (~~Section 5.3.6.2.2~~).

Asbestos is disseminated widely in the human environment (Section 6.2.1). Asbestos particulates are released into water, air, and soil, mainly from industrial sources, and are readily transported by wind or water (Section 6.2.2). Because of technical difficulties in monitoring the concentrations and distribution of asbestos in the environment, there is a significant lack of data concerning types, amounts, and size of asbestos fibers that contaminate the environment (Section 6.2.1). Ambient air concentrations in urban areas are considerably higher than for nonurban sites. Contamination of North American water

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resources may be widespread. Asbestos particles have been detected in drinking water samples from various cities in Canada and the United States--Ottawa, Atlanta, Boston, Chicago, Dallas, Denver, Duluth, Kansas City, New York City, Philadelphia, San Francisco, and Seattle, for example (Section 6.2.1.2). In addition, significant concentrations of asbestos contaminate beverages, foods, and drugs that are processed through asbestos filters during manufacture (Section 6.2.1.4).

adults future are detectable in

Although the general population is widely exposed to asbestos--both by inhalation and ingestion--the hazards of chronic, environmental exposure have not been determined. The reason, in part, is a paucity of information concerning human dose-responses, effects of asbestos ingestion, ambient concentrations and distribution of asbestos in the environment, the environmental cycling of asbestos, and related biological interactions including transmission through food chains (Section 7.0).

(insert) but no health effect has been demonstrated,

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1.2 CONCLUSIONS

a. All types of asbestos are pathogenic in animals and humans, causing asbestosis, lung cancer, mesotheliomas, pleural lesions, and gastrointestinal cancer.

b. Because of the large number of variables that influence the effects of asbestos, the mechanisms of pathogenicity are poorly understood. The etiological significance of fiber size or type is controversial, and the physicochemical properties of various asbestos types as related to biological effects are incompletely defined. (To correct this situation, the Third International Conference on the Physics and Chemistry of Asbestos Minerals will be held in Laval University, Quebec City, August 17 to 25, 1975.)

c. Little is known about the clearance rates of asbestos from tissues, the transport of asbestos within the organism, or the metabolic alteration of asbestos in the body.

d. Animal models necessary to accurately predict the potential effects of asbestos in humans have not been developed.

e. Quantitative dose-response relationships between asbestos inhalation and related diseases have not been determined for animals or humans, and minimal exposure levels required to cause disease are not known. Generally, however, the incidence of asbestosis and cancer among occupationally exposed persons increases with increasing dose and/or duration of exposure. The inhalation of high concentrations for short durations can be as harmful as prolonged exposure to low concentrations.

f. Malignancies that arise after long-term occupational exposure have been most often studied. However, malignancies result from short-term, occupational exposure and nonoccupational exposure in the vicinity of asbestos industries.

g. A causal relationship between gastrointestinal cancer and asbestos ingestion has not been

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established unequivocally. The potential effects of ingested asbestos--either directly into the gastrointestinal tract or indirectly via lung clearance mechanisms--are only scantily (often peripherally and speculatively) mentioned in a limited number of reports. ~~The recent gathering of asbestos experts at the 1973 Joint National Institute of Environmental Health Sciences – Environmental Protection Agency Conference on the Biological Effects of Ingested Asbestos signals the scarcity of quantified and quantifiable data.~~

h. Tobacco smoking increases the incidence ~~of~~ asbestosis and lung cancer among asbestos workers.

i. Available data indicate that the presence of asbestos is a widespread ~~environmental pollutant~~ in air, water, soil, food, ~~drugs, and beverages. However, efficient~~ methods for quantitatively identifying the concentrations, size distributions, and types of asbestos fibers in the environment ~~have not been~~ are lacking developed ~~adequately with uniform scientific~~ acceptance.

j. ~~The~~ No human health hazards of chronic environmental exposure to asbestos ~~are not known because of the~~ have been demonstrated. This is a paucity of information concerning human dose-responses, ambient concentrations and distribution of asbestos in the environment, the transmission of asbestos through food chains, and the effects of asbestos ingestion.

k. Since ~~any~~ a non-occupational asbestos exposure standard must be based on knowledge of environmental levels and related hazards, ~~it is obvious that~~ the available environmental and biological data are insufficient to enable ~~the~~ scientifically based establishment of such standards. ~~Evidence clearly indicates, however, that personal health protection both for asbestos workers and for the general population demands more attention for the safe mining, processing, utilization, and waste disposal of asbestos.~~

Persons working in potentially hazardous dust areas should have thorough physical examinations routinely; new employees should be examined at the start of employment and periodically thereafter.

No reference to Dept. Education & Welfare's recommendations

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Asbestos literature to date is confusing. To present dependable, clinical lung function data of asbestos-related disease is difficult; reports rarely supply complete data.

Suggest this instead:

Due to many new publications and reports (Insume?) that are being generated, the data base on asbestos is continually being updated.

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2.0 PHYSICAL AND CHEMICAL PROPERTIES

2.1 SUMMARY

The name "asbestos" refers to a group of hydrated, silicate minerals that possess a fiber-like structure. Widespread commercial use of asbestos stems from physical properties such as flexibility and high tensile strength (Table 2.1), which are imparted by the chemical composition and crystal structure of the fibers. Asbestos minerals consist of two main groups, serpentine and amphibole, as determined by their crystal structures. The serpentine group contains chrysotile, a commercially important, nearly pure magnesium silicate that comprises 90 to 95% of the world's asbestos production (Speil and Leineweber, 1969). The amphibole group contains five asbestiform minerals with varying amounts of magnesium, iron, sodium and calcium cations. Of these five--actinolite, tremolite, amosite, anthophyllite, and crocidolite--only the last three are commercially important. Differences in the chemical composition and in the crystal structure account for slight variations in physical properties among different types of asbestos (Table 2.1).

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2.2 PHYSICAL PROPERTIES AND USES

Industrial uses of asbestos include the following (U.S. Department of Interior, 1970; U.S. Geological Survey, 1973)

a) Building materials and cement pipe (70 percent of total uses)

b) Floor tile (10 percent of total uses)

c) Brake linings, gaskets, paints, insulations, pipe coverings and others (20 percent of total uses)

Since the industrial uses of asbestos depend on the physical characteristics of the fibers, and since there is some evidence to indicate that its harmful effects in the body are related to the dimensions of the fibrils, much recent work has been done with the electron microscope on the structure of the smallest units. Investigations of the structure of the most common form of asbestos, chrysotile (Bates, et al., 1950; Turkevick and Hillier, 1949; Whittaker, 1953; Whittaker, 1955), indicate that the fibrils are approximately hollow cylinders with varying amounts of

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Table 2.1 PROPERTIES OF COMMERCIALLY IMPORTANT TYPES OF ASBESTOS

Property	Chrysotile	Amosite	Anthophyllite	Crocidolite
Composition	Hydrous silicates of magnesia	Silicate of Fe and Mg	Mg silicate with iron	Silicate of Na and Fe with water
Chemical formula	$Mg_3Si_2O_5(OH)_4$	$(Fe^{++}Mg)_7Si_8O_{22}(OH)_2$	$(MgFe^{++})_7Si_8O_{22}(OH)_2$	$Na_2Fe_3^{++}Fe_2^{+++}Si_8O_{22}(OH)_2$
Color	White, grey, green, yellowish	Ash grey, greenish, or brown	Greyish-white, brown-grey, or green	Lavender, blue, greenish
Length	Short to long	Long	Short	Short to long
Texture	Soft to harsh; also silky	Coarse, but somewhat pliable	Harsh	Soft to harsh

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an amorphous material on the inside and outside of the tubes. Pundsack (1961), by water-vapor adsorption, estimated an average outer diameter of 20 to 25 nm and an inner diameter of 2 to 5 nm for these particles. Moderate applications of heat to chrysotile can be used to improve its bulk, absorption, filtration, and electrical properties (Badollet, 1951); but above 600 degrees centigrade, decomposition (with loss of water) begins to take place (Pundsack, 1955). The tensile strength of chrysotile fibers has been variously reported to be between 70,310 and 281,240 kg per sq cm (100,000 and 400,000 psi) (Badollet, 1951; Pundsack, 1955). The density is reported at 2.4 to 2.6 gm per ml (Pundsack, 1961). The surface area varies with the degree of fiberization. The fibers, as mined, have surface areas of 4 to 12 sq m per g. These values can be increased to as high as 50 sq m per g by mechanical breakup of the fibers. This value is greater than that of any other natural or synthetic textile fiber (Zukowski and Gaze, 1959).

The asbestiform amphibole minerals (crocidolite, amosite, anthophyllite, tremolite and actinolite) all have a similar crystal structure with double silica chains (Si_4O_{11}) sandwiching metal cations. Easy cleavage parallel to the silica chains results in the asbestiform character of the minerals. The various amphibole minerals are characterized by the amount of iron, magnesium, calcium, or sodium filling the cation positions in the structure. Amphibole fibers are solid rather than hollow and are usually wider than chrysotile (Hodgson, 1966). As a result the fiber is coarser and generally less flexible than chrysotile.

The tremolite-actinolite series of amphibole minerals contains calcium with variable amounts of magnesium and iron: $Ca_2(MgFe)_5Si_8O_{22}(OH)_2$. Tremolite is a magnesium-rich member of the actinolite-tremolite series. Tremolite fibers have variable morphologies and are often found associated with talc. Actinolite contains more iron than does tremolite. Actinolite fibers are smaller and more brittle than tremolite.

Anthophyllite is a magnesium silicate in which a small amount of the magnesium is replaced by iron. The fibers vary from soft, to semiharsh, to brittle. They have good heat resistance, but tensile strength is less than 281 kgm per sq cm.

Amosite is an asbestiform mineral in the cummingtonite-grunerite series of amphiboles. It is used commercially as

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asbestos and is mined in South Africa. Amosite fibers are generally straight, harsh, and brittle.

Crocidolite fibers from different parts of the world show marked differences in fiber structure, but they contain the lowest magnesium and highest iron concentrations of all the amphiboles (Timbrell et al., 1971).

2.3 CHEMICAL PROPERTIES

The serpentine type of asbestos (chrysotile), which comprises 90 to 95 percent of the world's asbestos production, is essentially a pure magnesium silicate with the empirical formula, $3MgO \cdot 2SiO_2 \cdot 2H_2O$. Small amounts of other oxides are generally present, either in the crystal structure or as impurities. The most abundant are iron oxides, (which may be as high as 6 percent by weight), calcium oxide (up to 5 percent), and aluminum oxide (as much as 1.5 percent). Other minerals occur in trace quantities, and considerable interest is shown in these by investigators who believe that the deleterious effects of asbestos in the body may be due, at least partially, to these impurities. A recent review of this question is given by Cralley and Lainhart (1973). The metals of most interest seem to be chromium, cobalt, manganese, nickel, and scandium. Analyses of different types of asbestos from different locations show wide variations in the levels of these impurities (Morgan and Cralley, 1973). In addition to the interest shown in the inorganic material, considerable attention has been directed toward the analysis of various oils and other organic compounds that may be present.

Different types of asbestos vary considerably in resistance to attack by acids and alkalis. Chrysotile is readily attached by acids; 25 percent hydrochloric acid will dissolve up to 56 percent by weight of this asbestos type. Amosite is less readily dissolved (12 percent). Anthophyllite and crocidolite are more resistant, with less than 5 percent of their weight lost in hydrochloric acid (Badollet, 1951). Amosite is least resistant to a 25-percent sodium hyroxide solution which can leach 7 percent of its weight. The other types are more resistant, each losing less than 2.2 percent by weight.

The crystal structure of all asbestos varieties can be destroyed at elevated temperatures. This temperature varies with the different types from about 400 to 800 C. Anthophyllite is the most heat resistant, followed by chrysotile.

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2.4 ANALYTICAL METHODS

Analytical work with asbestos is concerned either with the determination of the type by various chemical and physical measurements or with analyses of various trace contaminants and impurities.

2.4.1 Determination of Asbestos Types and Levels

Bulk samples of asbestos fibers can be analyzed by classical chemical procedures to determine the empirical chemical composition of magnesium, silicon, iron, calcium, aluminum, sodium, and water. This information, together with gross physical properties such as fiber length and texture, is generally sufficient to identify the type. X-ray diffraction methods can distinguish the serpentine asbestos type (chrysotile) from the amphiboles due to differences in their crystal structures (Crable, 1966; Goodhead and Martindale, 1969). However, when dealing with many environmental and biological samples, only one or a few fibers may be present, and these may be contaminated with a large amount of foreign material of a similar chemical composition. Collection of asbestos fibers in atmospheric samples usually is made by membrane filtration, which also collects other dust particles at the same time (Asbestosis Research Council, 1971). In such cases, the asbestos type may be determined from its morphology and electron diffraction pattern in a transmission electron microscope. Alternatively, through the use of a scanning electron microscope and an energy dispersive x-ray spectrometer, the asbestos type can be determined through an elemental analysis. Electron microprobe methods can also be used (Langer 1973).

The Environmental Sciences Laboratory at the Mount Sinai School of Medicine has done considerable work on the identification of the fibers found in the cores of "asbestos bodies" removed from lungs of patients. This laboratory has developed a technique that combines electron microscopy, electron diffraction, and x-ray spectrometry (Langer et al., 1970). Another method that has been used to determine inorganic trace metals in small samples of asbestos is neutron activation analysis. Not only can this technique determine the usual cations of aluminum, iron, magnesium, and sodium, but also those of antimony, cesium, chromium, nickel, cobalt, manganese, and scandium (Morgan and Holmes, 1970). Since the various types of asbestos contain these trace metals in different proportions, the total gamma-ray spectrum after neutron irradiation can serve to identify the

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type and/or source of the material. A brief review of all the techniques that can be used to identify asbestos in biological tissues has been given by Langer (1973).

The problem of determining total amounts of asbestos in ambient air is a difficult one, and no totally satisfactory method has been achieved. Although satisfactory sampling can be done with a membrane filter and a pump, the chief difficulty is the identification of only a few asbestos fibers in the presence of a relatively large number and variety of other inorganic particles found in the same sample. The most direct method, counting of particles with an optical microscope, is both tedious and inaccurate. Some of the fibers are too small in diameter to be resolved by the optical microscope, and an electron microscope must be used. Rickards (1973) used electron microscopic methods in an effort to obtain lower detection limits than he had previously obtained by x-ray diffraction (Rickards, 1972). X-ray diffraction methods have been used by other workers (Crable, 1966; Goodhead and Martindale, 1969), and they have the advantages of speed and the possibility of a total mass determination. Their disadvantage is that they do not furnish a fiber count or fiber-size distribution. In a literature review by Sullivan and Athanassiadis (1969), references are cited describing the following methods and instruments for determining types and levels of asbestos:

a. Microscopic particle counting of samples on membrane filters

b. Thermal precipitators

c. Impingers

d. Royce particle counter

e. Mass concentration methods

f. Microsieving

g. Digestion

h. Column chromatography of organics adsorbed on the surface

i. X-ray diffraction

j. Low-temperature ashing

k. Atomic absorption spectrophotometry

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l. Electron microprobe

m. Neutron activation

n. Owens jet counter

o. Konimeter

2.4.2 Determination of Contaminants

Several theories relate the carcinogenic activity of asbestos fibers to trace impurities, either organic or inorganic, present on the particles (See Section 5.3.4.3). Some of these apparently are present in the original material as mined, and others become adsorbed during the milling, storage, or shipping of the asbestos product. An exhaustive study has been carried out at the Royal Cancer Hospital in London to determine the exact chemical composition of both organic and inorganic impurities of various types of asbestos. Results showed that some types contain as much as 0.3 percent material extracted by organic solvents, and that in some samples, the known carcinogen, benzo(a)pyrene can be measured. Indirect evidence indicates that some of this material is of secondary origin, either through contamination or intentional application during milling. Measurements of naturally occurring radioactivity in asbestos indicate that the total flux is so low as to be of no practical significance. Analyses for trace metal concentrations by spectrochemical procedures have detected 14 in varying amounts. Of particular significance seem to be nickel and chromium in chrysotile, manganese and zirconium in amosite, and zirconium in crocidolite (Harington, 1965). Harington clearly demonstrated that asbestos adsorbed oils from jute bags used for storage, and a related work showed that the same phenomenon occurred with certain polyethylene bags (Gibbs, 1969). Further work has shown that the substance adsorbed is 3,3',5,5'-tet tetratertiary butyl diphenoquinone (Timbrell, 1970).

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2.5 REFERENCES

1. Asbestosis Research Council. The Measurement of Airborne Asbestos Dust by the Membrane Filter Method. Technical Note 1, Oscar Blackford, London, England, 1971.

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NOT FOR QUOTATION

DOW 02029

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 25 of 114 asbestosclaims.law/library/19184/25

2. Badollet, M. S. Asbestos, a Mineral of Unparalleled Properties. Trans. Can. Inst. Mining Met. 54:152, 1951.

3. Bates, T. F., L. Sands, and J. F. Mink. Tubular Crystals of Chrysotile Asbestos. Science 111:512-513, 1950.

4. Crable, J. V. Quantitative Determination of Chrysotile, Amosite and Crocidolite by X-ray Diffraction. Am. Ind. Hygiene Journal 27:293-298, May-June 1966.

5. Cralley, L. J., and W. S. Lainhart. Are Trace Metals Associated with Asbestos Fibers Responsible for the Biologic Effects Attributed to Asbestos? J. Occup Med. 15(3):262-266, 1973.

6. Gibbs, G. W. Some Problems Associated with the Storage of Asbestos in Polyethylene Bags. Amer. Ind. Hyg. Assoc. J. 30(1):458-464, January-February 1969.

7. Goodhead, F., and R. W. Martindale. The Determination of Amosite and Chrysotile in Airborne Ducts by an X-ray Diffraction Method. Analyst. 94:985-988, November 1969.

8. Harington, J. S. Chemical Studies of Asbestos. Ann. N.Y. Acad. Sci. 132(1):31-47, December 1965.

9. Hodgson, A. A. Fibrous Silicates. Lecture Series 1965. The Royal Institute of Chemistry, London, England, 1966. 46p.

10. Langer, A. M. Identification of Asbestos in Human Tissues. J. Occup. Med. 15:287-295, March 1973.

11. Langer, A. M., I. Rubin, and I. J. Selikoff. Electron Microprobe Analysis of Asbestos Bodies. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, 1970. p. 57-69.

12. Morgan, A., and L. J. Cralley. Chemical Characteristics of Asbestos and Associated Trace Elements. In: Proceedings of the Conference on Biological Effects of Asbestos. Lyon, 1973.

13. Morgan, A., and A. Holmes. Neutron Activation Techniques in Investigations of the Composition and

DRAFT
NOT FOR QUOTATION

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Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 26 of 114 asbestosclaims.law/library/19184/26

Biological Effects of Asbestos. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, 1970. p. 52-55.

14. Pundsack, F. L. The Pore Structure of Chrysotile Asbestos. J. Phys. Chem. 65:30-33, 1961.

15. Pundsack, F. L. The Properties of Asbestos. I. The Colloidal and Surface Chemistry of Chrysotile. J. Phys. Chem. 59:892-895, September 1955.

16. Rickards, A. L. Estimation of Submicrogram Quantities of Chrysotile Asbestos by Electron Microscopy. Anal. Chem. 45:809-811, April 1973.

17. Rickards, A. L. Estimation of Trace Amounts of Chrysotile Asbestos by X-ray Diffraction. Anal. Chem. 44:1872-1873, September 1972.

18. Sullivan, R. J., and Y. C. Athanassiadis. Preliminary Air Pollution Survey of Asbestos, A Literature Review. U.S. Dept. of Health, Education and Welfare, Public Health Service, Raleigh, North Carolina, 1969. p. 39.

19. Timbrell, V. Characteristics of the International Union Against Cancer Standard Reference Samples of Asbestos. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, 1970. p. 28-36.

20. Timbrell, V., D. M. Griffiths, and F. D. Pooley. Possible Biological Importance of Fibre Diameters of South African Amphiboles. Nature 232:55-56, July 1971.

21. Turkevick, J., and J. Hillier. Electron Microscopy of Colloidal Systems. J. Anal. Chem. 21(4):475-485, April 1949.

22. U.S. Department of Interior. Bureau of Mines Bulletin 650, 1970.

23. U.S. Geological Survey. U.S. Mineral Resources. Professional Paper 830, 1973.

24. Whittaker, E. J. The Diffraction of X-rays by a Cylindrical Lattice 1 and 2. Acta Cryst. 8:261-265, 1955.

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NOT FOR QUOTATION

ST0066240

DOW 02031

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 27 of 114 asbestosclaims.law/library/19184/27

25. Whittaker, E. J. The Structure of Chrysotile. Acta. Cryst. 6:747-748, 1953.

26. Zukowski, R., and R. Gaze. Tensile Strength of Asbestos. Nature 183:35-37, 1959.

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NOT FOR QUOTATION

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Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP…
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3.0 BIOLOGICAL ASPECTS OF ASBESTOS IN PLANTS AND MICROORGANISMS

No information was found on the effects of asbestos on plants or microorganisms, however, data concerning the effects of taconite tailings on phytoplankton (suspended algae), periphyton (algae attached to submerged objects) and bacteria in Lake Superior are available and have been summarized (U.S. Environmental Protection Agency, 1973).

In the presence of sunlight, phytoplankton and periphyton transform inorganics to sugars and other foods on which other biota depend. Because of the importance of algae to other biota, many experiments have been performed to determine whether taconite tailings inhibit or stimulate algal growth.

In general, comparisons of algal growth studies are difficult, as there are numerous ways to measure growth (Mount, 1973). Cell counts, pigment analysis and carbon fourteen fixation have all been employed to quantify algal growth (Swain et al., 1970; Shapiro, 1973).

After reviewing tests performed by other researchers using Lake Superior water, Mount (1973) concluded that taconite tailings may mildly stimulate algal growth by providing supplemental manganese and other elements essential to plants. Researchers generally concur that approximately 1 percent of the taconite tailings are soluble in water and that manganese, a mild plant growth stimulant, is released by these tailings (U.S. Environmental Protection Agency, 1973).

Though the increase in algal populations appears to be the result of chemical stimulation, the increase in bacteria in lakes containing taconite tailings may be due to the physical presence of the tailings. (Mount, 1973) Bacteria are generally associated with tailings as well as with natural suspended solids, which may act as platforms for bacterial growth. Many heterotrophic bacteria are stimulated by the presence of tailings; however, recent laboratory studies do not confirm the stimulation of coliforms or certain pathogens (Fischer et al., undated).

Although the data are incomplete, it appears that tailings have a stimulatory effect on bacteria, phytoplankton, and periphyton under some conditions (Mount, 1973).

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asbestosclaims.law/library/19184/29

3.1 References

1. Fischer, J., C. Thomas, M. Ievin, V. Cabelli (undated). Multiplication of Bacteria in Lake Superior Water Containing Taconite Tailings. Studies Regarding the Effect of the Reserve Mining Co. Discharge on Lake Superior, U.S. EPA, Washington, D.C.

2. Mount, D. I., 1973. A Summary of the Studies Regarding the Effect of the Reserve Mining Company Discharge on Lake Superior. Studies Regarding the Effect of the Reserve Mining Co. Discharge on Lake Superior, U.S. EPA, Washington, D.C.

3. Shapiro, Joseph, 1973. The Effects of Taconite. Tailings on the Phytoplankton of Lake Superior. Studies Regarding the Effect of the Reserve Mining Co. Discharge on Lake Superior, U.S. EPA, Washington, D.C.

4. Swain, W. R., T. A. Olson, T. O. Odlaug, 1970. The Ecology of the Second Trophic Level in Lakes Superior, Michigan, and Huron. Water Resources Research Center, niversity of Minnesota Graduate School.

5. U.S. Environmental Protection Agency, 1973. Studies Regarding the Effect of the Reserve Mining Company Discharge on Lake Superior, Washington, D.C.

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4.0 BIOLOGICAL ASPECTS OF ASBESTOS IN ANIMALS

4.1 ANIMAL EXPOSURE TO ASBESTOS IN THE NATURAL ENVIRONMENT

Almost no data are available on exposure of animals to asbestos in the natural environment, as opposed to the large amount of data from experimental studies. Schuster (1963) reported a case of asbestosis in a dog that lived in an asbestos factory for 10 years. No asbestos bodies were found in the lungs, although the histology was typical of asbestosis. The dog was exposed to unknown doses of white, blue, and brown asbestos and survived for 8 years before symptoms appeared. Kiviluoto (1965) found anthophyllite asbestos fibers in the lungs of a cow living near an asbestos mine.

Interstitial fibrosis, asbestos fibers, and asbestos bodies were found in the lungs of a donkey that had worked 10 years at an amosite mine and in the lungs of a baboon that lived near a crocidolite mill (Webster, 1963). Asbestosis was also found in field rats trapped around the same crocidolite mill.

4.2 RELEVANCE OF ANIMAL EXPERIMENTS

There is no doubt that asbestos in its various forms is pathogenic to humans; the intent of this section on animal studies (and in fact the aim of most animal experiments with asbestos) is not so much to show that asbestos exposure is harmful, but rather to show why and how it exerts its pathogenic effects. Unfortunately, there are no conclusive answers to these questions-only possible answers and hypotheses that are supported by some data and disputed by others.

Although inhalation is the major route of asbestos uptake in humans, intrapleural, intraperitoneal, intratracheal, and subcutaneous injection have been more commonly used in animal studies. The primary reason is that injection permits greater control over dose than does inhalation, and it also permits the sample to be deposited at the area of interest in amounts not otherwise achievable.

In addition to this possible objection, data extrapolation from animals to humans is difficult because the amount of asbestos dust usually required to produce a pathologic effect in animals is much larger than the amount encountered in human exposure. Also most exposures in man

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are to undetermined mixtures of dusts, metals, oils, and other substances. The effectiveness of lung clearance mechanisms differs among animals, and the actual amount of asbestos deposited in the lungs in inhalation studies cannot be accurately determined. Other variables that must be controlled are the physical and chemical natures of the asbestos fibers. Any combination of the following may be involved in the pathogenicity of asbestos: fiber length, shape, diameter, weight, surface area, chemical composition of surface, trace metal content, and polycyclic hydrocarbon content. Because of the problems mentioned above, establishment of human dose-response curves from animal experiments is not feasible. However, since mammals do possess some similarities, perhaps the determination of mechanisms of action in animals will aid the identification of ways to modify asbestos to make it less hazardous to mankind.

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4.3 ANIMAL METABOLISM

4.3.1 Uptake, Distribution, and Fate

The fate of asbestos in humans apparently depends on the size, shape, and route of entry of the asbestos fibers. Inhalation and ingestion are the primary routes of entry into man, but injection of various pharmaceutical preparations containing asbestos as a contaminant may also be of consequence. The animal studies presented here were conducted in an attempt to clarity and understand events that have occurred and been observed in man. Exposure of laboratory animals to asbestos has taken three general approaches: (1) inhalation experiments, (2) injection of asbestos into any one of several body cavities and, (3) ingestion. The effects and responses of the animals to asbestos will be discussed in Section 4.3.

4.3.1.1 Inhalation--Inhalation studies have great significance in that many of the apparent deleterious effects of asbestos in humans have followed the uptake of asbestos into the respiratory tract. Experimental studies using inhalation procedures have been performed primarily in rats and guinea pigs as well as other rodent species. The asbestos is usually presented to the test animal as a dust or aerosol. Exposure times have been as minimal as a single 1-hour exposure or as great as 400 hours over a 4-week period. In general, data interpretation is difficult because of a lack of uniformity of the experiments with respect to fiber types and sizes and with respect to the

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concentration of asbestos and the duration of animal exposure. The studies presented here have attempted to define the distribution and fate of various types and sizes of asbestos following inhalation in animals.

Holt et al. (1964) studied the distribution of Rhodesian chrysotile fibers in rat lung following exposure of the animals to the dust at a rate of 5,000 particles per ml of air for 100 hours over a period of 30 days. Approximately 84 percent of the particles were 5 micrometers or less in length. The lungs of the rats killed on the 14th day of exposure were found to contain small quantities of asbestos dust. A few fibers were present in the focal inflammatory lesions produced. Almost all the fibers found in the lungs were less than 2 micrometers long, so it appeared that the clearance mechanism in the rat lung was effective in removing particles larger than 2 micrometers.

The results of a study reported 1 year later (Wagner and Skidmore, 1965) demonstrated that the chemical and physical properties of asbestos may, at least in the rat, affect the distribution and fate of inhaled asbestos particles. In this study, a method of aerosol exposure was developed to deposit equal amounts of chrysotile, crocidolite, and amosite in the lungs of rats by inhalation. Ninety-five percent of the fibers were less than 10 micrometers long. Rats were exposed to 30 daily dusting sessions over a period of 6 weeks at average respirable dust concentrations (in mg per cubic meter) of 26.1 $\pm$ 6.3 for chrysotile, 28.8 $\pm$ 6.7 for crocidolite, 31.0 $\pm$ 12.5 for amosite, and 31.0 $\pm$ 6.0 for powdered glass. All dust tended to accumulate in the alveoli arising directly from the respiratory bronchioles. Equal amounts of each dust were probably deposited in the lungs initially; however, the elimination rate of Rhodesian chrysotile was three times greater than that of crocidolite or amosite.

Although the chemical and physical properties of asbestos may influence its distribution following inhalation, the animal species being studied must also be considered. Indeed, the results of studies comparing the distribution of and response to anthophyllite asbestos (Botham and Holt, 1968; 1972a) and Northwest Cape (NWC) crocidolite dust (Botham and Holt, 1972b) in guinea pigs and rats suggest that species differences must be considered when evaluating data. In the latter study (Botham and Holt, 1972b), guinea pigs and rats were exposed to NWC crocidolite dust for a total of 400 hours over a 4-week period.

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The fiber length varied from 0.11 micrometers to 1.6 mm, with diameters from 0.01 micrometers to 3.48 micrometers; most fiber diameters, however, were less than 1.0 micrometers. All guinea pigs that had inhaled NWC crocidolite died within 273 days from the start of dusting. Some long fibers were found in giant cells and macrophages in interalveolar septa throughout the lungs. A few fibers reached the subpleural region and were seen in rats after about 500 days. Many long fibers were present in the peribronchiolar septa and in the muscular coats of bronchioles in older rats. Fibers were found projecting into the pleura in the older animals toward the end of the experiment (848 days). In these older animals, fibers had also penetrated the muscular coats of the bronchioles and arteries.

In contrast to guinea pig lung, rat lung showed fewer asbestos fibers in alveolar septa following inhalation of NWC crocidolite (Botham and Holt, 1972b).

Results of another study conducted by Botham and Holt (1972a) again suggest that rats are capable of clearing asbestos fibers from their lungs more efficiently than guinea pigs. In this study, the response of guinea pigs and rats to Finnish anthophyllite was compared. The animals were exposed to the dust for a maximum of 24 hours. Both species cleared most of the extracellular fibers from the terminal bronchioles within 2 weeks after the end of exposure; however, intracellular fibers were seen earlier in the rat--after 3 hours of exposure in the rat and 24 hours in the guinea pigs. Clearance from the respiratory bronchioles was similar in both species. Extracellular fibers were cleared rapidly during the first week after dusting. Intracellular fibers took longer to clear. Fibers spread into the alveoli near respiratory bronchioles within 3 hours after the start of dusting. Giant cells formed in guinea pig lungs but seldom in rat lungs. Since giant cells are more difficult to remove than individual macrophages, asbestos fibers are cleared more rapidly from rat lungs.

Radioactive tracer techniques have also been used to determine the distribution of asbestos in the respiratory tract of animals (Evans et al., 1973). Rats were exposed to an aerosol of radioactive UICC (International Union Against Cancer) standard crocidolite (made radioactive by neutron irradiation) at a concentration of 13.0 or 8.1 micrograms per liter. Median fiber length was 3 to 5 micrometers as measured by optical microscopy. The rats were exposed for 1 hour and received 36 to 74 micrograms of crocidolite. The mean value of asbestos located in the lower respiratory

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tract was 50 ± 5 percent of the total respiratory deposition. Clearance from the upper respiratory tract to the gastrointestinal tract was almost complete in 1 hour and was seen as a short-term component in fecal elimination of the crocidolite. The half-time of the short-term component was 0.43 days. Crocidolite deposited in the lower respiratory tract was eliminated with a mean half-time of 29 days. Autoradiographs of thin lung sections showed that, in general, fibers deposited in the bronchioles were longer and thicker than those deposited in the alveolar region. Timbrell (1970, 1972) concluded on theoretical grounds that deposition by sedimentation is controlled mainly by fiber diameter, since the falling speed of a fiber is more dependent on its diameter than its length. In small airways, interception is more important than sedimentation and is controlled by fiber length. In actual measurements, Timbrell (1970) found that the average fiber lengths of amosite in rat lung alveolar tissues were shorter than those in air ducts, which were shorter than those in the inhaled dust.

The fate of inhaled asbestos is not limited to the pulmonary system. Mesotheliomas and gastrointestinal cancers have been reported to be produced in rats exposed to asbestos through inhalation, indicating translocation of fibers from the lungs.

4.3.1.2 Ingestion--Little information is available on the effects of asbestos ingestion on animals or man. The key question in the evaluation of ingestion as a route for the introduction of asbestos fibers into the animal is whether or not fibers can pass through the gastrointestinal tract wall and become lodged in the mucosa or the peritoneum, or be transported to other sites in the body.

A wide variety of particles, 2 to 120 micrometers in diameter, have been shown to penetrate the gastrointestinal tract and be transported throughout the body in experiments with animals and humans (Volkheimer, 1973). Dyed plant fibers were given orally and later found in blood and urine samples, with no such fibers in control samples (Schreiber, 1974). Rats fed a 6-percent chrysotile asbestos diet had fibers in their colon tissue as revealed by electron microscopy (Westlake et al., 1965). Chrysotile asbestos fibers administered to the stomach of rats appeared in the blood shortly thereafter and accumulated in various tissues in the rats (Cunningham and Pontefract, 1973).

A recent report by Gross, et al. (1974) of several ingestion experiments with rats concluded that no evidence was found for transmigration of fibers from the

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gastrointestinal tract. Although some amphibole fibers were found in tissues from exposed rats and none in tissues from controls, it was felt that these fibers could have been present as a result of contamination. Some cancers were found in the long-term feeding study, but cancers also appeared in the controls.

4.3.1.3 Injection--Although injection is not a source of industrial asbestos exposure to humans, it is possible that a small amount of asbestos might be injected as a contaminant in various drugs that are filtered through asbestos pads during production (Duma, 1973). The value of injection as a route of exposure in animal studies, however, is not that it simulates human exposure but that it permits studies not possible in inhalation experiments. Injection experiments permit the examination of response once the asbestos is present in the pleural or peritoneal cavity in a large enough number of animals to give significant results. In animals, the main routes of injection used are intratracheal, intrapleural, intraperitoneal, and subcutaneous. Intrapleural, intraperitoneal, subcutaneous, intragastric and intravenous injection are discussed below.

4.3.1.3.1 Intrapleural injection--The translocation and fate of radioactive Rhodesian chrysotile injected into the pleura of two 3-month-old rats was studied by Holmes and Morgan (1967). Neutron irradiation of the asbestos forms gamma-emitting isotopes of the trace metals in the asbestos. In chrysotile, these are principally scandium-46, chromium-51, iron-59, and cobalt-60. The distribution and elimination of the trace metals and of fibers can thus be determined.

Urine samples contained chromium-51 and cobalt-60. After 50 days, 19 percent of the chromium-51 and 57 percent of the cobalt-60 had been excreted in the urine, indicating that they are leached from chrysotile in vivo. The small amounts of all four nuclides found in feces could be a result of some asbestos fibers entering the lungs from the pleura, with subsequent clearance to the gastrointestinal tract (Holmes and Morgan, 1967). Small amounts of all four nuclides were also found in tissue samples. For example, iron-59 was found in blood and liver.

About 90 percent of the remaining nuclides at time of death were located in the lungs and pleural cavity. In general, Holmes and Morgan (1967) concluded that though some translocation of fibers does occur, the process is comparatively slow.

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The same technique was used in a later study (Morgan et al., 1971) to determine the in vivo solubilities of trace metals in chrysotile from Rhodesia, Quebec, and British Columbia. All trace metals were soluble to some extent when the asbestos samples were injected intrapleurally into specific pathogen free (SPF) Wistar rats. As found in the previous experiment, only chromium-51 and cobalt-60 were present in significant amounts in urine. Scandium-46 was found in the feces, as were small amounts of iron-59. Tissue distribution was similar to the previous report, that is, chromium was found in the liver and carcass, and scandium was found in all tissues except blood. Chrysotile was distributed mostly in the heart, lungs, diaphragm, and chest wall.

4.3.1.3.2 Intraperitoneal injection--Chrysotile dust injected intraperitoneally into rats was found to migrate into the peribronchial and perivascular tissues of the lung and was found in alveolar epithelial cells (Karacharova et al., 1969).

In another study, 20 mg per week, for 5 weeks, of UICC standard amosite, anthophyllite, or crocidolite was injected intraperitoneally into female Wistar rats (Friedrichs et al., 1971). The animals were killed 4 months after the first injection and histologically examined. Transport of fibers from the site of injection was found to be dependent on fiber length, beginning with fibers 20 micrometers long and increasing with decreasing fiber length.

4.3.1.3.3 Subcutaneous injection--Roe et al. (1967) observed that following subcutaneous injection of crocidolite, amosite, or chrysotile asbestos into the flanks of female CBA mice, fibers of all three types were transported, apparently specifically, to the mesothelium of the pleural, pericardial, and peritoneal spaces. Transport was probably through lymphatic channels, although no direct proof was obtained.

A more detailed follow-up study by Kanazawa et al. (1970) examined the migration of asbestos fibers following subcutaneous injection into mice. Improved staining, microincineration, and electron microscopy techniques led to a confirmation of lymphatic transport and showed that the transport was less than formerly believed. Fibers accumulated in lymphoid tissues, mainly in axillary lymph nodes, but also concentrated in inguinal, mediastinal, and lumbar nodes. Some fibers were found in the spleen and in nonlymphoid organs such as the liver, kidneys, and brain, thereby suggesting that some fibers had entered the

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bloodstream. Most asbestos fibers probably travel inside macrophages, although some larger fibers may be free in the lymph or blood (Kanazawa et al., 1970). Selective transport of fibers to the subserosal tissue, as suggested in the earlier study, was not supported by the present evidence.

4.3.1.3.4 Intragastric injection--Two to four days after chrysotile fibers were injected into the stomachs of rats (9.4 billion fibers in the two-day group and 94 billion fibers in the 4-day group), fibers were isolated from the blood, spleen, liver, kidney, omentum, muscle, lung, and brain (Cunningham and Pontefract, 1973). The omentum surrounding the small intestine had the most asbestos at 4 days after injection (18.25 million fibers per g). Tissues of control rats contained surprising amounts of asbestos: the levels were similar to those found in tissues of humans who died of natural causes (0.114 to 0.378 million fibers per g in brain, 0 to 0.253 in spleen, and 0.773 to 0.915 in peritoneum). How fibers were absorbed is undetermined.

A recent report by Gross et al. (1974) questions the validity of this experiment because of artifacts inherent in Cunningham and Pontefract's technique.

4.3.1.3.5 Intravenous injection--Asbestos administered intravenously was shown to accumulate mostly in the liver and lungs (Cunningham and Pontefract, 1973). Later, transplacental transport of asbestos in rats was demonstrated by these same workers (Cunningham and Pontefract, 1974). Chrysotile asbestos at a dose of 1 to 3 mg (1 mg per ml in water) was injected intravenously at 2-day intervals into pregnant Wistar rats from the 10th through 14th day of gestation. Total dose varied from 4 to 12 mg of asbestos. Fetuses were removed by Caesarean section the day before parturition in a manner preventing cross contamination from the mother. The livers and lungs were analyzed by electron micrcscopy. Values of asbestos found were quite variable, with livers from some fetuses containing large numbers of asbestos fibers. Whether transport is by individual fiber penetration, a mass breakthrough, or by both methods is unknown.

4.4 Animal Effects

Effects occurring in vivo in various experimental animals exposed to asbestos can be generally classified as fibrogenic or carcinogenic and are treated separately in subsections. Subjects to be discussed under the fibrogenesis heading include phagocytosis of asbestos fibers, giant cell formation, collagen production, fibrosis,

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asbestos body formation, and factors possibly controlling the fibrogenic potential of various asbestos types. The carcinogenic potential of asbestos and factors possibly affecting this potential will be discussed under the carcinogenic heading.

Although both fibrogenic responses and carcinogenesis can result from the same exposure, a separate discussion for each is justified because fibrosis is a fast response to asbestos exposure, and tumor production takes a relatively long time.

4.4.1 Fibrogenesis

4.4.1.1 Phagocytosis--One of the first responses to asbestos exposure is phagocytosis of asbestos fibers by macrophages. The number of macrophages in rat and hamster lungs was shown to be increased by intratracheal injection of chrysotile dust (Brian, 1971). During phagocytosis, individual macrophages may fuse, producing multinucleated giant cells (Holt et al., 1964; Botham and Holt, 1972b; Shin and Firminger, 1973; Davis, 1964, 1970a, 1970b; Smith et al., 1965a; Holt et al., 1966). This occurs commonly in quinea pigs and hamsters and rarely in rats.

Although asbestos fibers are phagocytosed mainly by macrophages, both types A and B alveolar epithelial cells, and occasionally terminal bronchiolar cells of hamsters, have been shown to phagocytose chrysotile fibers (Holt et al., 1966; Suzuki et al., 1968; Suzuki et al., 1972). Following phagocytosis, type B cells lose their microvilli and osmiophilic lamellar inclusions (Holt et al., 1966; Suzuki et al., 1968).

It was suggested that asbestos is only fibrogenic when ingested by phagocytes (Holt et al., 1964).

4.4.1.2 Asbestos Body Formation--Asbestos bodies are structures commonly found in the lungs of humans who have worked with asbestos or asbestos products and to a lesser degree in the lungs of many persons with no known exposure to asbestos. Asbestos bodies also occur in the lungs of experimental animals following inhalation or intratracheal injection of asbestos.

Formation of an asbestos body may occur in the following manner (Davis, 1970b): macrophages and giant cells secrete mucopolysaccharides, which are adsorbed by asbestos fibers; the mucopolysaccharide layer then becomes impregnated with ferruginous granules. At this stage, the

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asbestos fiber is termed an asbestos body. Only fibers partly surrounded by a macrophage or giant cell can be coated; free fibers are not coated.

A similar process was reported following brief exposure (3 or 50 hours) of guinea pigs to anthophyllite dust (Botham and Holt, 1968). The asbestos caused a release of red blood cells from alveolar capillaries. Granules of iron-containing degradation products of hemoglobin (hemosiderin) from these red blood cells were found in macrophages along with a solubilized iron-containing substance (possibly ferritin). This substance was then adsorbed onto an asbestos fiber in the macrophage, with only one fiber per cell (usually the longest) being coated. Additional information on asbestos body formation can be found in papers by Suzuki and Churg (1969a, 1969b).

Guinea pigs, Vervet monkeys, and rabbits were exposed to chrysotile, amosite, or crocidolite dusts (Wagner, 1963). Asbestos bodies were produced in all three species by each dust but were more plentiful after amosite exposure.

Asbestos bodies are not produced in rats (Botham and Holt, 1972a, 1972b; Davis, 1970b; Gross and De Treville 1967).

Gross et al., (1967) proposed the term ferruginous body instead of asbestos body, since identical-appearing structures were formed after exposure to materials other than asbestos (e.g., following intratracheal injection of aluminum silicate into hamsters). Similar results were reported by Davis et al. (1970). The term asbestos body should be used only when the central fiber is identified as asbestos.

4.4.1.3 Fibrotic Response--Dissimilarities in the fibrogenic potential of different asbestos types (Wagner, 1963), as well as species differences in extent and severity of the fibrotic responses (Davis 1964) have been shown in experimental animals. Several methods of asbestos administration have been used to induce and study asbestosis. Fibrosis of the lung following the inhalation or intratracheal injection of various asbestos types has been observed in rats (Holt, et al., 1964; Davis, 1964, 1970a, 1970b; Gross et al., 1967b; Burger and Engelbrecht, 1970, and Wagner et al., 1974), guinea pigs (Davis, 1964; Wagner, 1963; Szymczykiewicz, 1970; and Holt et al., 1966), hamsters (Gross and De Treville, 1967), dogs (Motlagh and Falor, 1968), rabbits (Ford, 1972), monkeys (Zaidi et al., 1973), baboons (Webster, 1963), and donkeys (Webster, 1963). Local

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fibrotic responses have also resulted following the injection of asbestos into either the peritoneal or pleural cavity (Karacharova et al., 1969; Davis, 1970a, 1970b, 1971, 1972; Shin and Firminger, 1973; Jagatic et al., 1967; Smith et al., 1965a). Stanton et al. (1969) used an asbestos-saturated fibrous-glass pad applied to the pleura and pericardium of rats to induce fibrosis as well as cancer. Results of these studies indicate that asbestos of any type is capable of causing fibrosis. Still unclear however, is the impact of fiber length on the fibrotic response: however, electron microscopic procedures have suggested that small uncoated fibers are the most fibrogenic (Miller et al., 1965).

4.4.1.3.1 Species differences--As noted above, the fibrotic response may depend, in part, on the species being studied. Davis (1964), in a species comparison experiment, exposed rats and guinea pigs by inhalation to chrysotile dust (particle size range: 1 to 10 micrometers in length and 0.02 to 1.0 micrometers in diameter). Pathological effects occurred in three stages: formation of small nodular lesions (usually in the walls of terminal bronchioles), fibrosing interstitial pneumonia widely scattered throughout the lungs, and complete lung consolidation in some areas. In the rat lung, consolidation tended to resolve itself after exposure stopped. Subsequent investigations have similarly demonstrated that the fibrotic response in the rat is usually multifocal, rather than diffuse, and nonprogressive when exposure stops (Holt et al., 1964; Davis, 1970a, 1970b; Gross et al. 1967b; Burger and Engelbrecht, 1970). The fibrotic response in the guinea pig, however, tended to be progressive and diffuse.

The guinea pig and rat differ also in their responses to asbestos fibers of different lengths. Burger and Engelbrecht (1970) concluded from their studies in rats that short fibers (less than 10 micrometers) tend to be less fibrogenic than longer fibers. Beck et al., (1971a) reach a similar conclusion. On the other hand, Holt et al. (1964, 1965) stressed the importance of very fine, short particles of asbestos in fibrosis in guinea pig lungs. Inhalation of very fine particles of chrysotile by guinea pigs resulted in a bronchiolitis within a few days (Holt et al., 1966). This result occurred at a time when very small amounts of dust and no long fibers were visible with the light microscope. After 30 weeks, cell degeneration started, and fibrosis appeared. A further discussion on the importance of fiber length is found in Section 4.4.1.3.3.

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Another example of a species difference in the fibrotic response following inhalation of asbestos was demonstrated by Gross and De Treville (1967). Chrysotile dust was administered to rats and hamsters either intratracheally or by inhalation. Lung clearance was less effective in hamsters than in rats. Hamster lung tissue was more reactive, and a progressive fibrosis was noted.

Species differences were also noted by Wagner (1963). In that study, guinea pigs, Vervet monkeys, and rabbits were exposed to chrysotile, amosite, or impure crocidolite (only 10% asbestos) dust. Impure crocidolite produced severe lesions in guinea pigs and monkeys, and these animals succumbed more readily to respiratory infections. Chrysotile produced no effect in rabbits.

The injection of asbestos into the pleural or peritoneal cavity has demonstrated that species differences in the fibrotic response is not restricted to lung tissue.

The injection of chrysotile or crocidolite into the pleural cavity of mice, rats, and guinea pigs lead to granular formations by 7 days (Davis, 1970a). Generally, the fibrotic response to asbestos following pleural or peritoneal injection appears to be qualitatively similar but quantitatively greater than the fibrotic response in the lungs. In the guinea pig, the granulomas were composed mainly of giant cells and were surrounded by capsules of fibrous tissue. In rats and mice, the granulomas contained mostly mononuclear cells and no distinct capsule was present. In guinea pigs, the granulomas remained cellular for 6 to 12 months, in mice, 11 to 15 months, and in rats, only 3 to 4 months.

4.4.1.3.2 Asbestos type—The potential of UICC reference amosite, anthophyllite, crocidolite, Canadian chrysotile, or Rhodesian chrysotile for causing fibrosis was investigated by Wagner et al. (1974). Rats were exposed via inhalations of 6 hours per day, 5 days per week, with total exposure times ranging from 1 day to 24 months. Almost all rats exposed for less than 12 months survived during the total length of their planned exposure. Only 53 percent of the rats survived for the full length of their planned exposure in the 24-month group.

All samples produced asbestosis; and after 6 months of exposure, asbestosis was progressive, even when exposure stopped. The progressive response was in contradiction to other work in the rat (Holt et al., 1964; Davis, 1964; 1970a; Gross et al., 1967b; Burger and Engelbrecht, 1970).

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However, the large cumulative dose after 6 months probably overwhelmed the ability of the animal to make repairs. The mean dose varied from 1,880 mg per cubic meter-hour for a 5-week exposure to 33,400 mg per cubic meter-hour for a 24-month exposure. Asbestosis increased with the dose for all asbestos types, but amosite gave the lowest incidence throughout the experiment; anthophyllite and Canadian chrysotile produced the greatest incidence of asbestosis after 6 months or longer exposure.

The results of the above study in rats are in conflict with an earlier observation by Wagner (1963) with respect to the fibrogenic potential of amosite. In the earlier study, amosite inhalation resulted in more severe and earlier lesions than chrysotile in guinea pigs, Vervet monkeys, and rabbits. Although species differences is an obvious conclusion, the question of the fibrogenic potential of amosite compared to other asbestos types has not been clarified.

The fibrogenic potential of the different asbestos types has also been studied following intraperitoneal administration. In a comparison of the fibrogenic potential of 50 mg of chrysotile, actinolite, tremolite, or brucite ($Mg(OH)_2$) dust administered intraperitoneally, Karacharova et al. (1969) observed that all produced a fibrogenic response in the mesentery. Cell nodules consisting of dust macrophages formed and were surrounded by collagen fibers. Chrysotile and brucite were found to be the most fibrogenic.

Differences in tissue response dependent on the type of asbestos administered were also repeated by Shin and Ferringer (1973). Their study of intraperitoneal injection of chrysotile or crocidolite into rats killed 40 percent of the animals within 8 days as a result of acute peritonitis. It was noted that tissue response of the survivors depended on the type of asbestos injected. Chrysotile fibers were covered by hyaline-like material during the acute inflammatory stage. The material was later replaced by dense hyalinized tissue. Crocidolite produced primarily a foreign-body, giant cell reaction as early as 5 days after injection. Both types of asbestos produced equal localized or diffuse fibrosis, but a typical mesothelial proliferation was more prevalant with chrysotile. The physical and chemical properties of the fibers were concluded to be responsible for the toxicity.

From the above discussions it is apparent that some differences, resulting from fiber types, may exist in the potential to produce fibrosis. However, it is important to

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remember that most fiber types studied have produced a fibrotic response.

4.4.1.3.3 Fiber size--In addition to the controversy that surrounds the fibrogenic potential of asbestos types, the input of fiber length is also controversial. In this regard, the results of Burger and Engelbrecht (1970) have already been discussed (Section 4.4.1.3.1). The effect of fiber length on tissue response was also studied by Szymczykiewicz (1970). Sixty mg of chrysotile dust containing fibers either 5 or 10 micrometers long were administered intratracheally to guinea pigs. The dynamics and extent of the fibrotic reaction were most marked in the bronchi and peribronchial tissue, probably because of selective filtration by air passages. Location and site of fibrotic reaction were concluded to be dependent on structure of the fiber. The injurious effect on lung tissue was also attributed to the crystalline structure of the fibers.

Davis (1972) studied the relative fibrogenicity of a series of mineral dusts that were injected intrapleurally into mice. The chrysotile sample had fiber bundles ranging in size from 200 micrometers long by 10 micrometers in diameter to 1 micrometer long by 25 to 30 micrometers in diameter; most fibers, however, were less that 5 micrometers long by 0.1 to 1.0 micrometers in diameter. All dust samples produced granulomata in the pleural cavity with collagen production. The final degree of fibrosis was paralleled by the initial accumulation of cells around the injected material. Long fiber samples produced much larger and more cellular lesions and led to adhesion formation. When long fiber dusts were finely ground and sieved, only small, distinct lesions without adhesions were formed. Longer fibers may clump and attract more cells, producing larger lesions. Susceptibility of dust to clearance may be the most important factor affecting fibrosis.

Recent studies using electron microscopic procedures would seem to indicate that small uncoated fibers are the most fibrogenic (Miller et al., 1965). However, definitive conclusions regarding fiber length and fibrosis are still to be made.

4.4.1.3.4 Miscellaneous effects--An interesting technique for the production of fibrosis was used by Stanton et al. (1969). These workers used an asbestos-saturated, fibrous-glass pad applied to the pleura and pericardium of rats to induce fibrosis and cancer. Although this method of exposure was unlike any exposure man might encounter, it was

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a rapid and consistent way to induce cancers in the rats. The fibrous-glass pad alone produced a slight initial tissue reaction with complete healing; however, when saturated with crocidolite (40 mg in 2 ml of 10-percent gelatin), there was extensive and progressive fibrosis in all animals.

4.4.2 Carcinogenesis

As will be disucssed in the human section (5.0), lung cancer and mesothelioma have been positively associated with asbestos exposure. This association was found by studying data from many epidemiological investigations and obviously could not be obtained through direct experimentation. Animal models, however, permit a direct approach, not only to finding an association, but to possibly discovering how asbestos causes cancer.

4.4.2.1 Mesothelioma--When injected intrapleurally into rats, chrysotile, crocidolite, amosite, and silica have all been shown to cause mesothelioma (Wagner and Skidmore, 1965). This finding seems to indicate that the ability of a fiber to reach a target tissue is the most important factor; however, the chemical composition, trace metal contaminants, and oil content of an asbestos type could be involved in its quantitative carcinogenicity.

An example of both the ability of asbestos types other than crocidolite to cause mesothelioma and of the different carcinogenicity of asbestos types is shown in the following report.

SPF-Wistar rats and Standard rats were injected intraperitoneally with 20 mg of amosite, crocidolite, chrysotile, or chrysotile with oil extracted (Wagner and Berry, 1969). The incidence of mesothelioma induction is shown in Table 4.1.

Extracting the oil from crocidolite did not change its carcinogenicity, although oils extracted from asbestos do have some carcinogenic potential. Oils extracted from amosite and crocidolite were shown to cause papilloma formation when applied to mouse skin (Poe et al., 1966).

Several other studies have been directed at mechanisms of mesothelioma induction by asbestos. The structural shape, rather than physicochemical properties, was implicated in the following report. Fiberous-glass pads saturated with UICC crocidolite, amosite, or chrysotile were applied to the pleura of rats (Stanton and Wrench, 1972). All three asbestos samples caused mesothelioma (incidence of

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TABLE 4.1 INCIDENCE OF MESOTHELIOMA INDUCTION IN RATES INJECTED INTRAPERITONEALLY WITH ASBESTOS (in %)[a]

Asbestos type	SPF Rats	Standard Rats
Amosite	40	31
Crocidolite	64	69
Chrysotile	59	68
Oil-extracted chrysotile	59	64
Saline control	0	0

[a] Source: modified from Wagner and Berry, 1969.

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58 to 75%): no mesotheliomas occurred from the pad alone. When glass fibers were reduced to a size comparable to asbestos fibers (0.06 to 3 micrometers in diameter), a 12 to 18 percent incidence of mesothelioma resulted. In addition, when asbestos was milled to clumps of submicroscopic fibrils, carcinogenicity was lost. Extracting oil from crocidolite did not reduce its carcinogenicity.

The needle shape of chrysotile fibers longer than 2 or 3 micrometers was considered to be the decisive factor in tumor induction in a study comparing UICC chrysotile (95% of fibers less than 5 micrometers long) and powdered chrysotile (95% less than 3 micrometers long) (Pott et al., 1972). The tumor incidence was the same for both samples, but the latent period was longer with powdered chrysotile.

Rhodesian chrysotile was injected intraperitoneally into rats, resulting in a 48-percent incidence of mesotheliomas (Hunter and Thomson, 1973). Vermiculite, which has many of the same components as asbestos, did not produce tumors. The authors concluded that the carcinogenic properties were due to the chemical-physical nature of the fibers and/or the chemical composition of organic materials associated with the asbestos.

SPF Wistar rats were intrapleurally injected with one of the following types of asbestos: superfine chrysotile, crocidolite, UICC standard reference samples of amosite, anthophyllite, Canadian chrysotile, Rhodesian chrysotile, or crocidolite, UICC samples with oil removed, or other dusts (Wagner et al., 1973). There was a high incidence of mesothelioma from all types, with risk proportional to dose. Crocidolite was the most carcinogenic of the UICC samples. Carcinogenicity was not related to trace metal content. Finer fibers were more carcinogenic.

Mesotheliomas have been produced in rats exposed to asbestos through inhalation (Wagner et al. 1974 and Reeves et al. 1974). However, uptake of tritiated thymidine by pleural mesothelial cells (indicating DNA synthesis) was greatly increased following intratracheal infusion of natural chrysotile into rats. Synthetic chrysotile, which had submicroscopic fibers, or saline did not increase the labeling index.

A synergistic effect was found between chrysotile and $^{239}PuO_2$ with respect to mesothelioma induction in rats (Sanders, 1972).

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4.4.2.2 Lung Cancer--Lung cancers are also induced by asbestos. A direct association hetween lung cancer and chrysotile was reported by Gross et al. (1966). Rats, hamsters, and guinea pigs were exposed to 42 to 146 mg chrysotile dust per cubic meter for 62 weeks. Thirty-five percent of the rats surviving 16 months or more from the end of exposure developed lung cancer. No hamsters or guinea pigs exposed at the same time developed lung cancer.

The cancer rate in rats pretreated with 5-percent NaOH to reduce clearance of asbestos from the lungs was 48 percent, compared to 24 percent in those not pretreated with NaOH (Gross et al., 1967b).

Sixty-four other rats received intratracheal injection of chrysotile dust; of the 19 that survived 16 months or longer, 16 percent developed lung cancer (Gross et al., 1967b). Of all the cancers in the rats, 71 percent were adenocarcinomas, 14 percent were squamous cell carcinomas, and 25 percent were fibrosarcomas. The authors attributed the high cancer rate to trace metal contaminants from the hammer milling (Gross et al., 1967b), but later studies did not support this conclusion (Wagner et al., 1973).

Lung cancers and mesotheliomas were induced in rats inhalaing UICC amosite, anthophyllite, crocidolite, Canadian chrysotile, or Rhodesian chrysotile (Wagner et al., 1974; Reeves et al., 1974). Mean dose varied from 1,880 mg per cubic meter-hour for a 5-week exposure to 33,400 mg per cubic meter-hour for a 24-month exposure. No tumors occurred within the first 300 days from start of exposure, but all dusts eventually induced tumors. Sixteen of 20 metastasized tumors resulted from chrysotile exposure.

The hypothesis that asbestos may serve a passive role in tumor induction by adsorbing a chemical carcinogen such as benzo(a)pyrene was tested by Miller et al. (1965). The effect of chrysotile (which efficiently adsorbs BP) and amosite (which does not adsorb BP as well) on the carcinogenicity of BP in the hamster respiratory tract was examined. Chrysotile promoted BP carcinogenesis, whereas amosite had no effect.

Tumors have also been induced in white leghorn chickens by injection of crocidolite into the air sac (Peacock and Peacock, 1963). Tumors appeared in two of 30 birds that survived 1 year or more. One developed 1 year, and the other 3 years after injection.

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4.4.2.3 In Vitro Studies--Dixon et al. (1970) used an in vitro technique to examine the role of asbestos-associated trace metals in cancer induction. They hypothesized that either asbestos played a passive role as a metal carrier in cancer induction with benzo(a)pyrene (a potent carcinogen), or that a related polycyclic aromatic hydrocarbon assumed the major active role (Dixon et al., 1970).

Assuming that the longer benzo(a)pyrene remains in the lung, the greater the cancer risk, then any agent that slows or prevents the activity of benzo(a)pyrene hydrolase should increase the carcinogenic risk. Therefore, to test this assumption, the effect of various metals on the benzo(a)pyrene hydrolase activity of the microsomal fraction of rat lung homogenates was measured (Dixon et al., 1970). When added to the homogenates in concentrations comparable to those attainable in human lungs from industrial exposure, Co^{2+}, Cu^{2+}, Fe^{2+}, Mg^{2+}, Ni^{2+}, and Zn^{2+} all could either stimulate or inhibit BP hydrolase activity, depending on concentration. In general, all metals depressed activity at the higher concentrations used, but Be^{2+}, Cr^{6+}, and Fe^{3+} were the predominant inhibitors. When tested as a group, the metals extracted from chrysotile (nickel, cobalt, chromium, and manganese) reduced the BP hydrolase activity by 73 percent. The authors also pointed out that BP hydrolase activity and the concentration of metals normally present in hydrolase-stimulating concentrations (copper, magnesium, and zinc) decrease with age, permitting the inhibitory metals in asbestos to be more competitive. Although the BP content of asbestos is quite low (1 mg per kg for some asbestos types), many other sources exist in the environment, tobacco smoke being a prime example.

4.4.3 Cytotoxicity

One of the first in vitro observations of the cytotoxic nature of asbestos was unplanned. House (1964) found that a factor toxic to baby hamster kidney cells was eluted from asbestos filter pads by Eagle's tissue culture medium. A similar observation was made by Kogan and Dorinovskaya (1966) when they unexpectedly got a much reduced virus yield from either pig or baby hamster kidney cells grown in medium that had been filtered through a Seitz E.K. asbestos pad. To further clarify this observation, low-phosphate or Eagle's medium was filtered through a Seitz or Ford's asbestos pad (Kogan and Dorinovskaya, 1966). Virus yield was reduced in both pig and baby hamster kidney cells. Filtration of Eagle's medium through a cellulose acetate membrane filter did not change the virus yield in baby hamster kidney cells; however, it did decrease the virus

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yield in pig kidney cells. The reduced yields were due to a toxic factor rather than to removal of a necessary nutrient: prewashing of a filter pad would reduce or eliminate toxicity, and the first batch of medium filtered through a pad would be more toxic than later batches filtered through the same pad. The toxic factor was not identified.

Both nonfibrous serpentine and asbestos were found to inhibit growth, migration, and the early phases of cell mitosis in a culture of human embryo pulmonary tissue (Kogan and Dorinovskaya, 1966). Asbestos dust was more inhibitory. Particle size of both dusts was mostly under 4 micrometers with 80 percent below 2 micrometers.

The cytotoxicity of various asbestos dusts on guinea pig peritoneal macrophages in vitro was determined by measuring the production of lactic acid and the release of lactate dehydrogenase and acid phosphatase from the cells, and by loss of fluorochromasia (Parazzi et al., 1968). Both Balangero chrysotile and South African crocidolite were cytotoxic. The toxic effect of crocidolite was evident in 100 percent of the cells within 30 minutes, while chrysotile was somewhat less toxic, affecting only 60 percent of the cells. The toxic activity was related primarily to the fiber content of the dusts rather than to the particulate matter, which was only slightly toxic. Pretreatment of the asbestos dusts with polyvinylpyrrolidone-N-oxide (PVPNO) or ethylenediaminetetraacetic acid (EDTA) did not reduce the cytotoxicity, leading the authors to conclude that the physical characteristics rather than the chemical composition were involved in cytotoxicity.

Release of cellular components may be the result of cell leakage during phagocytosis of asbestos fibers and not a reflection of cell damage (Bain et al., 1973).

Another study on the cytotoxic effects of asbestos on guinea pig peritoneal macrophages gave somewhat different results (Beck et al., 1971b). Toxicity was measured by O_2 respiration and nigrosine staining. Chrysotile B was most toxic, damaging 85 percent of the cells; chrysotile A damaged 65 percent; anthophyllite 49 percent, crocidolite 38 percent, and amosite 38 percent. Addition of 5% serum did not reduce the cytotoxicity. Heating chrysotile to 600 C gradually increased cytotoxicity with respect to O_2 respiration, suggesting that the crystalline and electronic structure were related to the biological effects.

Asbestos dusts were also found to be cytotoxic to peritoneal macrophages from rats (Koshi et al., 1968).

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Changes in lactic acid production, acid phosphatase activity, and triphenyltetrazolium chloride (TTC) reducing power were measured. Four different chrysotile samples caused increased release of acid phosphatase from cells. Antigorites and orth-serpentines had no toxic effect; and the amphiboles, including crocidolite, had little effect (unlike the results reported in the preceding study on guinea pig peritoneal macrophages). Triphenyltetrazolium chloride-reducing capacity was decreased only by the chrysotile samples. Lactic acid production was decreased by the same samples that caused an increase in acid phosphatase release. PVPNO reduced the toxic effects of the chrysotile group and eliminated the toxic effect of the sepiolite-polygroskite group. There was a strong correlation between hemolytic activity against rat red blood cells and cytotoxic activity.

The toxicity of asbestos dusts to rat peritoneal macrophages was modified by protein in the growth medium and by pretreatment of the asbestos particles with 30 percent rat serum protein solutions (Koshi and Sakabe, 1972). Toxicity was measured by lactic dehydrogenase (LDH) release, acid soluble nucleotide content of cells, and 14C-leucine uptake into cell protein. Crocidolite and amosite, previously reported to have no cytotoxic effects, were found to be cytotoxic, but to a lesser degree than chrysotile. Koshi and Sakabe (1972) showed that shortly after addition of "naked" chrysotile, amosite, or crocidolite to serum-free cell cultures, large amounts of LDH were released into the medium, and the content of acid soluble nucleotides in the cells decreased; 14C-leucine incorporation was also decreased. When serum-coated asbestos was added, the LDH release was much less and required a longer incubation time. There was no effect on lactic acid production or 14C-leucine uptake when serum-coated asbestos was added to macrophages in serum-free medium, or when "naked" asbestos was added to cells in serum-containing medium. Two studies showed chrysotile dust to be toxic to hamster peritoneal macrophages; but at equivalent concentrations, amosite and crocidolite were not (Bey and Harington, 1971; Miller and Harington, 1972). Weight rather than surface area of chrysotile determined its toxicity (Bey and Harington, 1971).

Conning et al. (1971) found a direct relationship between the fibrogenicity in vivo of several dusts and their cytotoxicity to peritoneal and alveolar macrophages in culture. There was no relation to particle size, shape, concentration, or to phagocytic potential of the cultured cells. Chrysotile was the most toxic dust used.

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Another aspect of asbestos toxicity that has been examined in some detail is hemolysis. Chrysotile was shown to be as hemolytic as silica powder towards sheep erythrocytes (MacNab and Harington, 1967). Under identical conditions crocidolite and amosite were inactive; however, after prolonged incubation with sheep erythrocytes, the latter two asbestos types did cause some lysis. The hemolytic action of chrysotile was prevented by disodium versenate and simple phosphates, but PVPNO and aluminum, two agents that prevent lysis by silica, are only partially active against lysis by chrysotile. This observation suggested that the nature of the hemolytic activity differed between silica and chrysotile. Mechanical action was ruled out as a cause of lysis. The authors concluded that magnesium ions on the surface of the fibers were responsible for the lytic action of chrysotile.

Similar results were reported in later studies (Schnitzer and Pundsack, 1970; Schnitzer and Bunescu, 1970), but it was concluded that the lytic action related to the surface area and openness of the fibers.

The hypothesis that magnesium is the principal agent in hemolysis by asbestos was supported by experiments reported by Harington et al. (1971). Sialic acid prevented hemolysis to a greater degree than EDTA, but poly-2-vinylpyridine-1-oxide had little effect. The authors also reported that chrysotile was much more active hemolytically than amosite or crocidolite. The surface area of asbestos fibers was not related to hemolytic activity, except possibly in asbestos forms with low magnesium content.

4.4.4 Nutritional Requirement

There is no known nutritional requirement for asbestos in animals.

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ACL Doc 19184 · Page 52 of 114 asbestosclaims.law/library/19184/52

4.5 REFERENCES

1. Beck, E. G., J. Bruch, K. H. Kriedrichs, W. Hilscher, and F. Pott. Fibrous Silicates in Animal Experiments and Cell Culture--Morphological Cell and Tissue Reactions According to Different Physical Chemical Influences. Proc. Int. Symp. Inhaled Particles III. 1:477-487, 1971a.

2. Beck, E. G., P. F. Holt, and E. T. Nasrallah. Effects of Chrysotile and Acid-Treated Chrysotile on Macrophage Cultures. Brit. J. Ind. Med. 28(2):179-185, April 1971b.

3. Bey, E., and J. S. Harington. Cytotoxic Effects of Some Mineral Dusts on Syrian Hamster Peritoneal Macrophages. J. Exp. Med. 133(5):1149-1169, May 1971.

4. Botham, S. K., and P. F. Holt. Asbestos-Body Formation in the Lungs of Rats and Guinea-Pigs After Inhalation of Anthophyllite. J. Pathol. 107(4):245-252, August 1972a.

5. Botham, S. K., and P. F. Holt. The Effects of Inhaled Crocidolites from Transvaal and North-West Cape Mines on the Lungs of Rats and Guinea-Pigs. Brit. J. Exp. Pathol. 53(6):612-620, December 1972b.

6. Botham, S. K., and P. F. Holt. The Mechanism of Formation of Asbestos Bodies. J. Pathol. Bacteriol. 96(2):443-453, 1968.

7. Brian, J. D. The Effects of Increased Particles on the Number of Alveolar Macrophages. Proc. Int. Symp. Inhaled Particles III. 1:209-225, 1971.

8. Bryks, S., and F. D. Bertalanffy. Cytodynamic Reactivity of the Mesothelium. Arch. Environ. Health. 23(6):469-472, 1971.

9. Burger, B. F., and F. M. Engelbrecht. The Biological Effects of the International Standard Reference Asbestos Samples (UICC) on the Lungs of Rats. S. Afr. Med. J. 44(44):1271-1274, November 1970.

10. Conning, D. M., M. J. Hayes, J. A. Styles, and J. A. Nicholas. Comparison Between *in Vitro* Toxicity of Dusts of Certain Polymers and Minerals and Their Fibrogenicity. Proc. Int. Symp. Inhaled Particles III. 1:499-506, 1971.

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NOT FOR QUOTATION

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DOW 02057

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 53 of 114 asbestosclaims.law/library/19184/53

11. Cunningham, H. M., and R. D. Pontefract. Asbestos in Beverages, Drinking Water and Tissues: Their Passage Through the Intestinal Wall and Movement Through the Body. Symposium on Industrial Chemicals as Food Contaminants. J. AOAC. 56(4):976-981, 1973.

12. Cunningham, H. M., and R. D. Pontefract. Placental Transfer of Asbestos. Nature. 249(5453):177-178, May 1974.

13. Davis, J.M.G. The Calcification of Fibrous Pleural Lesions Produced in Guinea-Pigs by the Injection of Chrysotile Asbestos Dust. Brit. J. Exp. Pathol. 52(3):238-243, 1971.

14. Davis, J.M.G. An Electron Microscopy Study of the Effects of Asbestos Dust on the Lung. Brit. J. Exp. Pathol. 44(4):454-464, 1964.

15. Davis, J.M.G. The Fibrogenic Effects of Mineral Dusts Injected Into the Pleural Cavity of Mice. Brit. J. Exp. Pathol. 53:190-201, 1972.

16. Davis, J.M.G. Further Observations on the Ultrastructure and Chemistry of the Formation of Asbestos Bodies. Exp. Mol. Pathol. 13(3):346-358, 1970b.

17. Davis, J.M.G. The Long Term Fibrogenic Effects of Chrysotile and Crocidolite Asbestos Dust Injected Into the Pleural Cavity of Experimental Animals. Brit. J. Exp. Pathol. 51(6):617-618, 1970a.

18. Davis, J.M.G., P. Gross, and R.T.P. De Treville. "Ferruginous Bodies" in Guinea Pigs: Fine Structures Produced Experimentally From Minerals Other Than Asbestos. Arch. Pathol. 89(4):364-373, 1970.

19. Dixon, J. R., D. . Lowe, D. E. Richards, L. J. Cralley, and H. E. Stokinger. The Role of Trace Metals in Chemical Carcinogenesis: Asbestos Cancers. Cancer Res. 30(4):1068-1074, April 1970.

20. Duma, R. J. Particulate Matter of Particular Interest. Ann. Intern. Med. 78:146-147, January 1973.

21. Evans, J. C., R. J. Evans, A. Holmes, R. F. Hounam, D. M. Jones, A. Morgan, and M. Walsh. Studies on the Deposition of Inhaled Fibrous Material in the Respiratory Tract of the Rat and Its Subsequent

DRAFT
NOT FOR QUOTATION

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DOW 02058

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ACL Doc 19184 · Page 54 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/54

Clearance Using Radioactive Tracer Technique. 1. UICC Crocidolite Asbestos. Environ. Res. 6(2):180-201, June 1973.

22. Ford, J. E. The Effect of Pulmonary Macrophage Suppression in Developing Asbestos. Diss. Absts. Intern. (b). 32, 1972.

23. Striedrichs, K. H., W. Hilscher, and S. Sethi. Staub- und Gewebeuntersuchungen an Ratten nach Intraperitonealer Injektion von Asbest (Study of Tissue Reaction and Fibers Distribution in Abdominal Granulomas and Lymph Nodes of the Rat Following Intraperitoneal Administration of Various Amphiboles). Int. Arch. Arbeitsmed. 28(4):341-354, 1971.

24. Gross, P., L. J. Cralley, and R.T.P. De Treville. Asbestos Bodies: Their Nonspecificity. Amer. Ind. Hyg. Assoc. J. 28(1):541-542, 1967a.

25. Gross, P., and R.T.P. De Treville. Experimental Asbestosis. Arch. Environ. Health. 15:638-649, November 1967.

26. Gross, P., R.T.P. De Treville, E. B. Tolker, M. Kaschak, and J. A. Babyak. Experimental Asbestosis. Arch. Environ. Health. 15(3):343-355, 1967b.

27. Gross, P., R. A. Harley, L. M. Swinburne, J.M.G. Davis, and W. B. Greene. Ingested Mineral Fibers: Do They Penetrate Tissue or Cause Cancer: Arch. Environ. Health. 29(6):341-347, December 1974.

28. Hain, E., H. Bohlig, W. Klosterkoetter,A. Schutz, and H. J. Wotowitz. Asbestos: Health Hazard, Limiting Values, Prevention. Ataub. 33(2):51-57, 1973.

29. Harington, J. S., K. Miller, and G. MacNab. Hemolysis by Asbestos. Environ. Res. 4(2):95-117, 1971.

30. Holmes, A., and A. Morgan. Leaching of Constituents of Chrysotile Asbestos in Vivo. Nature. 215(5099):441-442, July 1967.

31. Holt, P. F., and J. Mills. Experimental Asbestosis in Guinea Pigs. In: Fourteenth Int. Congress Occup. Health (Madrid, 1963). Exerpta Medica Found., N.Y. 2:667-670, 1964.

DRAFT
NOT FOR QUOTATION

ST0066268

DOW 02059

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 55 of 114 asbestosclaims.law/library/19184/55

32. Holt, P. F., J. Mills, and D. K. Young. The Early Effects of Chrysotile Asbestos Dust on the Rat Lung. J. Pathol. Bacteriol. 87(1):115-23, 1964.

33. Holt, P. F., J. Mills, and D. K. Young. Experimental Asbestosis with Four Types of Fibers: Importance of Small Particles. Ann. N.Y. Acad. Sci. 132(1):87-97, 1965.

34. Holt, P. F., J. Mills, and D. K. Young. Experimental Asbestosis in the Guinea Pig. J. Path. Bact. 92(1):185-195, 1966.

35. House, W. Toxicity of Cell Culture Medium Due to Filtration Through Asbestos Pads. Nature. 201(4925):1242, March 1964.

36. Hunter, B., and C. Thomson. Evaluation of the Tumorigenic Potential of Vermiculite by Intrapleural Injection in Rats. Brit. J. Ind. Med. 30(2):167-173, 1973.

37. Jagatic, J., M. E. Rubnitz, M. C. Godwin, and R. W. Weiskopf. Tissue Response to Intraperitoneal Asbestos with Preliminary Report of Acute Toxicity of Heat-Treated Asbestos in Mice. Environ. Res. 1:217-230, November 1967.

38. Kanazawa, K., M.S.C. Birbeck, R. L. Carter, and F.J.C. Roe. Migration of Asbestos Fibres from Subcutaneous Injection Sites in Mice. Brit. J. Cancer. 24:96-106, 1970.

39. Karacharova, V. N., R. A. Ol'shvang, and F. M. Kogan. Changes in Certain Organs After Experimental Intraperitoneal Injection of Asbestos-Containing Dust. Bull. Eksp. Biol. Med. 67:117-120, May 1969.

40. Kiviluoto, R. Pleural Plaques and Asbestos: Further Observations on Endemic and Other Nonoccupational Asbestosis. Ann. N.Y. Acad. Sci. 132:235, 1965.

41. Kogan, F. M., and A. P. Dorinovskaya. Effects of Asbestos and Serpentine Dust and Pulmonary Tissue Culture. J. Hyg. San. 31:37-41, 1966.

42. Koshi, K., H. Hayashi, and H. Sakabe. Cell Toxicity and Hemolytic Action of Asbestos Dust. Ind. Health (Japan). 6(1-2):69-79, 1968.

DRAFT
NOT FOR QUOTATION

ST0066269

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ACL Doc 19184 · Page 56 of 114 asbestosclaims.law/library/19184/56

43. Koshi, K., and H. Sakabe. Effect of Asbestos Dust on the Cultured Macrophages. Ind. Health (Japan). 10:16-23, 1972.

44. MacNab, G., and J. S. Harington. Hemolytic Activity of Asbestos and Other Mineral Dusts. Nature. 214(5087):522-523, April 1967.

45. Miller, K., and J. S. Harington. Some Biochemical Effects of Asbestos on Macrophages. Brit. J. Exp. Pathol. 54(4):397-405, August 1972.

46. Miller, L., W. E. Smith, and S. W. Berliner. Tests for Effect of Asbestos on Benzo(a)pyrene. Carcinogenesis in the Respiratory Tract. Ann. N.Y. Acad. Sci. 132(1):489-500, 1965.

47. Morgan, A., A. Holmes, and C. Gold. Studies of the Solubility of Constituents of Chrysotile Asbestos in Vivo Using Radioactive Tracer Techniques. Environ. Res. 4(6):558-570, 1971.

48. Motlagh, F., and W. G. Falor. Asbestos-Penicillin Induced Pleurodesis: An Experimental Study. Dis. Chest. 53(1):89-92, 1968.

49. Parazzi, E., B. Pernis, G. C. Secchi, and E. C. Vigliani. Studies on in Vitro Cytotoxicity of Asbestos Dust. Medicina del Lavoro. 59(10):561-576, 1968.

50. Peacock, A., and P. R. Peacock. Asbestos as a Potential Carcinogen for Fowls. Brit. Emp. Cancer Campaign 1963. Part 2: Sci. Rept. British Empire Cancer Campaign Research. London, S.W.I., 534-535, 1963.

51. Pott, F., F. Huth, and K. H. Friedrichs. Tumors of Rats after I.P. Injection of Powdered Chrysotile and Benzo(a)pyrene. Zentrabl. Bakteriol. Parasitenk. 155(5-6):463-469, 1972.

52. Reeves, A. L., H. E. Puro, and R. G. Smith. Inhalation Carcinogenesis from Various Forms of Asbestos. Environmental Research. 8:178-202, 1974.

53. Roe, F.J.C., R. L. Carter, M. A. Walters, and J. S. Harington. The Pathological Effects of Subcutaneous Injections of Asbestos Fibres in Mice: Micration of Fibres to Submesothelial Tissues and Induction of

DRAFT
NOT FOR QUOTATION

ST0066270

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Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 57 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/57

Mesotheliomata. Int. J. Cancer. 2(6):628-638, November 1967.

54. Roe, F.J.C., M. A. Walters, and J. S. Harington. Tumour Initiation by Natural and Contaminating Asbestos Oils. Int. J. Cancer. 1(5):491-495, 1966.

55. Sanders, C. L. Production of Abdominal Mesotheliomas in Rats with 239PuO2 and Chrysotile Asbestos. Health Phys. 23(3):418, Abstract P/71, 1972.

56. Schnitzer, R. J., and G. Gunescu. Polymers as Selective Antagonists of Hemolytic Asbestos Fibers. Arch. Environ. Health. 20:481-482, April 1970.

57. Schnitzer, R. J., and F. L. Pundsack. Asbestos Hemolysis. Environ. Res. 3(1):1-13, 1970.

58. Schreiber, G. Ingested Dyed Cellulose in the Blood and Urine of Man. Arch. Environ. Health. 29:39-42, 1974.

59. Schuster, N. H. Pulmonary Asbestosis in a Dog. J. Pathol. Bacteriol. 34:751-757, 1963.

60. Shin, M. L., and H. I. Firminger. Acute and Chronic Effects of Intraperitoneal Injection of Two Types of Asbestos in Rats with a Study of the Histopathogenesis and Ultrastructure of Resulting Mesotheliomas. Amer. J. Pathol. 70(3):291-314, 1973.

61. Smith, W. E., L. Miller, J. Churg, and I. J. Selikoff. Mesotheliomas in Hamsters Following Intrapleural Injection of Asbestos. J. Mt. Sinai Hosp. N.Y. 32(1):1-8, 1965a.

62. Smith, W. E., L. Miller, J. Churg, and I. J. Selikoff. Pleural Reaction and Mesothelioma in Hamsters Injected with Asbestos. Proc. Amer. Assoc. Cancer Res. 5(1):59, 1964.

63. Smith, W. E., L. Miller, R. E. Elsasser, and D. D. Hubert. Tests for Carcinogenicity of Asbestos. Ann. N.Y. Acad. Sci. 132:456-487, 1965b.

64. Stanton, M. F., R. Blackwell, and E. Miller. Experimental Pulmonary Carcinogenesis with Asbestos. Amer. Ind. Hyg. Assoc. J. 30(3):236-244, 1969.

DRAFT
NOT FOR QUOTATION

ST0066271

DOW 02062

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 58 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/58

65. Stanton, M. F., and C. Wrench. Mechanisms of Mesothelioma Induction with Asbestos and Fibrous Glass. J. Nat. Cancer Inst. 48(3):797-821, 1972.

66. Suzuki, Y., and J. Churg. Formation of the Asbestos Body. A Comparative Study with Three Types of Asbestos. Environ. Res. 3(2):107-118, 1969b.

67. Suzuki, Y., and J. Churg. Structure and Development of the Asbestos Body. Amer. J. Pathol. 55(1):79-91, 1969a.

68. Suzuki, Y., J. Churg, and T. Ono. Phagocytic Activity of the Alveolar Epithelial Cells in Pulmonary Asbestosis. Amer. J. Pathol. 69(3):373-388, 1972.

69. Suzuki, Y., J. Churg, and W. Smith. Pnagocytosis of Asbestos Fibers by Epithelial Cells. Lab Investi. 18:335, 1968.

70. Szymczykiewicz, K. Some Aspects of Pathogenesis of Asbestosis. Pol. Med. Sci. Hist. Bull. 13(3):115-119, 1970.

71. Timbrell, V. Assessment of Airborne Particles. In: Proceedings of the Third Rochester International Conference on Environmental Toxicity, Rochester, 1970. Mercer. T. T., P. E. Marrow, and W. Stoker (eds). Thomas, Springfield, IL. 1972.

72. Timbrell, V. The Inhalation of Fibers. In: Proceedings of an International Conference on Pneumoconiosis (Johannesburg, 1969). Shapiro, H. A. (ed.) Oxford University Press, New York. 1970.

73. Volkheimer, G. Persorption, Acta-Hepato-Gastroenteral. 20:361-362, 1973.

74. Wagner, J. C. Asbestosis in Experimental Animals. Brit. J. Ind. Med. (London). 20:1-12, 1963.

75. Wagner, J. C., and G. Berry. Mesothelioma in Rats Following Inoculation with Asbestos. Brit. J. Cancer (London). 23(3):567-581, 1969.

76. Wagner, J. C., G. Berry, J. W. Skidmore, and V. Timbrell. The Effects of the Inhalation of Asbestos in Rats. Brit. J. Cancer, 29:252-269, 1974.

DRAFT
NOT FOR QUOTATION

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DOW 02063

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
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Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/59

77. Wagner, J. C., G. Berry, and V. Timbrell. Mesotheliomata in Rats After Inoculation with Asbestos and Other Materials. Brit. J. Cancer. 28(2):173-185, 1973.

78. Wagner, J. C., and J. W. Skidmore. Asbestos Dust Deposition and Retention in Rats. Ann. N.Y. Acad. Sci. 132(1):77-86, 1965.

79. Webster, I. Asbestosis in Non-Experimental Animals in South Africa. Nature. 197(4866):506, 1963.

80. Westlake, G. E., H. J. Spjict, and M. N. Smith. Penetration of Colonic Mucosa by Asbestos Particles; An Electron Microscope Study in Rats Fed Asbestos Dust, Lab. Invest., 14(11):2029;2033, 1965.

81. Zaidi, S. H., R. Shanker, and R.K.S. Dogra. Experimental Infective Pneumoconiosis: Effect of Asbestos Dust and Candida albicans Infection on the Lungs of Rhesus Monkeys. Environ. Res. 6(3):274-286, 1973.

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NOT FOR QUOTATION

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5.0 PHYSIOLOGICAL AND PATHOLOGICAL ASPECTS OF ASBESTOS IN HUMANS

5.1 Summary

Clinical and epidemiological studies of persons occupationally exposed to asbestos have established a causal relationship between asbestos inhalation and a high incidence of asbestosis, lung cancer, gastrointestinal cancer, and mesotheliomas of the pleura or peritoneum. Asbestosis is a chronic, progressive pulmonary disease characterized by impaired lung function, lung fibrosis, and the presence of asbestos bodies in fibrotic tissue. It is estimated that 50 percent of the persons who develop asbestosis also develop lung cancer. However, asbestosis is probably not a necessary prerequisite for cancer induction. Pleural and peritoneal mesotheliomas are rare, malignant primary tumors of the serosa. Most epidemiological studies show that 80 percent of the mesotheliomas occur in persons exposed to asbestos. Gastrointestinal malignancies have also been attributed to extensive asbestos exposure. Despite the numerous studies involving the pathogenic effects of asbestos in humans, dose-response data are essentially nonexistent because dust exposure in most cases is not measured quantitatively; consequently, the minimum amounts required to produce asbestosis or cancer remain undefined.

The mechanisms of carcinogenicity and fibrogenicity are undetermined for asbestos, but it appears that different types and sizes of asbestos fibers cause varying responses. Cigarette smoking may act synergistically with asbestos in causing cancer and fibrosis.

5.2 Human Metabolism

5.2.1 Uptake, Distribution, and Retention

The deposition, distribution, and retention of inhaled asbestos dust in the respiratory tract are related closely to the physical characteristics of the fibers. Penetration by and retention of short, straight, amphibole fibers are significantly greater than for chrysotile fibers, which are long and curved (Timbrell, 1970a). Both curvature and increased length reduce the efficiency of passage by fibers, especially in narrow airways where they are deposited high in the respiratory tract by interception (Timbrell 1970b; Timbrell, et al., 1970). The magnitude of deposition for

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fibers of a given length increases with decrease in airway diameter (Timbrell, 1965). Consequently, in human and animal lungs, the long fibers generally concentrate in respiratory bronchioles and alveolar ducts, and shorter fibers are transported more deeply into air sacs (Timbrell et al., 1970). Fibers deposited higher in the respiratory tract are removed more readily by mucociliary lung clearance mechanisms (Timbrell, 1965; Thomson and Short, 1969).

To a great extent, the deposition of fibers in the lung is proportional to the particle free-falling speed as a function of fiber diameter; therefore, differences in fiber diameter among various asbestos types influence the efficiency of passage to the lung (Timbrell, 1965; Timbrell et al., 1969). In both animals and humans, asbestos fibers with diameters greater than 3 micrometers are deposited readily in the upper respiratory tract by sedimentation and inertial impact; fibers with smaller diameters have lower free-falling speeds and succeed in penetrating terminal air sacs (Timbrell, 1970b; Timbrell, 1965; Timbrell et al., 1970). By these mechanisms, some long fibers (up to 200 micrometers) are able to penetrate the lung efficiently. For example, chrysotile may penetrate deeply because the fibers consist of bundles that divide into numerous fibrils with small diameters (approximately 0.016 micrometer) and low free-falling speeds (Timbrell, 1970a).

5.5.2 Fate of Asbestos in the Lungs

5.2.2.1 Cellular Response--Study of the cellular reaction of human lung tissue to inhaled asbestos dust revealed that small particles (up to 0.5 micrometer long and 0.1 micrometer in diameter) are phagocytosed directly by alveolar macrophages and deposited in cytoplasmic phagosomes (Morgenroth, 1973). Larger particles (up to 5.0 micrometers long and 0.7 micrometer in diameter), either coated or uncoated, locate in the alveoli and connective tissue septa.

5.2.2.2 Asbestos Body Formation--Asbestos fibers inhaled into the lungs may become coated with a segmented deposit of protein-iron granules, forming club-shaped asbestos bodies (Milne, 1971; Davis, 1964). Embedding sites are located intracellularly in macrophages and fibroblasts or seated among collagen tissues (Davis, 1964). Asbestos bodies may vary in length from 10 micrometers to more than 200 micrometers (Pooley, 1972). In early stages, the body coating is a thin, beaded yellow shape that thickens with progressing maturity and changes from yellow to brown (Milne, 1971).

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The coating of mature bodies develops a more granular, segmented form and may fragment into smaller bodies that are phagocytosed and incorporated into macrophages (Milne, 1971). Segmentation of the body coat in humans may be produced by the deposition of the iron-protein complex, ferritin, as separate globules, or by splitting a previously smooth coat (Davis, 1964).

The mechanisms of asbestos body formation are poorly understood. Amino acid analyses of asbestos bodies from human lungs support evidence that the coating is formed from the cytoplasm of alveolar macrophages by the adsorption of iron and protein by the fibers (Blount et al., 1966). Histochemical studies indicate that the body coating forms from intercellular components that are deposited around the fiber in three basic layers (Governa and Rosanda, 1972; Governa and Vadala, 1972). Initially, proteins, hematoidin (blood crystals without iron), and ferric iron are deposited. Governa and Vadala (1972) suggest that these may be products of hemoglobin breakdown. Mucopolysaccharides, especially hyaluronic acids, make up the second layer. And finally, ferric iron particles impregnate the hyaluronic acid molecules (Governa and Rosanda, 1972; Governa and Vadala, 1972). According to electron diffraction patterns, the major crystalline component of the coating is structurally similar to ferritin extracts formed by human and animal tissues; phosphorus and calcium also are constituents (Pooley, 1972). Calcium probably accounts for the structural stability of the body and acts as an aggregating agent for ferritin or hemosiderin in the early stages of body formation (Pooley, 1972).

The deposition of body coating may be a function of the physical characteristics of the fibers (Pooley, 1972). Electron microscopic examination of human asbestos bodies indicates that bodies more frequently form on straight amphibole fibers longer than 10 micrometers than on curved chrysotile fibers, and they vary in shape according to the asbestos variety (Timbrell, 1965).

No etiological significance has been attributed to asbestos body formation. Asbestos bodies commonly are found in the lungs of persons who are not occupationally exposed to asbestos, but their presence has not been associated with disease in these cases.

It appears that, though the presence of asbestos bodies in pleural plaques and fibrotic lung tissue establishes the diagnosis of asbestosis, the occurrence of asbestos bodies

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alone merely indicates exposure to asbestos (Milne, 1971; Longley, 1969).

5.2.2.3 Uncoated Fibers--Chemical analyses of uncoated amosite, anthophyllite, and chrysotile fibers from human lungs show that significant alteration in fiber chemistry occurs in the lung tissue, probably because of biochemical interactions (Langer et al., 1970; 1972). It has been suggested that the smallest uncoated fibers are the most fibrogenic (Gaensler, 1969, Miller et al., 1975). Predominant changes include the depletion of magnesium and an increase in iron content (Langer, et al., 1970; 1972). In biologic environments, chrysotile fibers are considered to be chemically unstable (Miller et al., 1975). Magnesium is lost from the surface exposing the silica layer to chemical degradation. The biological and etiological implications of in vivo magnesium loss from asbestos fibers are unknown; iron gain possibly reflects the incipient early stages of asbestos body formation (Langer, et al., 1972).

5.2.3 Transport

The presence of asbestos bodies, fragments, and dust particles in the hilar and mediastinal nodes, in pleural lymphatics, and in the spleen, abdomen, and intestinal mucosa of mesothelioma patients indicates that asbestos is transported via lymphatic channels and is widely distributed throughout the body (Godwin and Jagatic, 1970). The lymphatic transport of foreign particles from lungs is a physiological mechanism of pulmonary clearance whereby small fibers and dust particles penetrate the alveolar membrane into the lung interstitium; from there they are transported to satellite lymph nodes by tissue fluids (Gross et al., 1973). Electron microscope studies have estimated lymph node fiber concentrations as high as 125 million per g of dry tissue in fiber glass workers and 60 million per g of dry tissue in nonoccupationally exposed females; approximately 6 percent of the fibers were chrysotile (Gross et al., 1973). The transport of asbestos from the lungs to pleural tissue via lymphatic vessels may explain the formation of pleural abnormalities by small asbestos fibers less than 5 micrometers in length (Taskinen, et al., 1973).

Gravity and constant motion of the lungs can induce downward lateral movement of inhaled asbestos fibers that are too long to be phagocytosed by lung macrophages; eventually, these fibers may reach the pleura and peritoneum by direct penetration through soft lung tissue (Thomson, 1970).

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5.2.4 Metabolic Alterations

Changes in serum amino acid patterns of 29 asbestos workers with clinical and radiological signs of asbestosis imply that asbestos inhalation results in disruption of protein metabolism (El-Sewefy and Hagazi, 1971). Compared to a healthy group of workers, the diseased group showed significant increases in serum concentrations of free and total amino acids, including aspartic acid, tryptophan, glutamic acid, serine, glycine, alanine, threonine, lysine, arginine, valine, leucine, and tyrosine. In addition, reduced levels of albumin and increased levels of globulin resulted in decreased albumin/globulin ratios in exposed workers. These effects have been observed in diseases associated with protein catabolism (El-Sewefy and Hagazi, 1971). No other metabolic changes with asbestosis have been documented.

5.3 Human Effects

5.3.1 Asbestosis and Related Pathological Changes

Asbestosis is a chronic, progressive, pulmonary disease resulting from prolonged asbestos inhalation. It is characterized mainly by interstitial fibrosis with functional impairment of the lungs, pleural lesions, and symptoms including dyspnea, cough, rales, weight loss, and finger clubbing (Scott and Hodge, 1971; Kleinfield, 1970; Dutra and Carney, 1965). Although it has been recognized as an industrial disease for almost 50 years, there is no effective treatment for asbestosis or its complications; prevention depends solely on the elimination of hazardous airborne asbestos concentrations by dust control methods (Smither, 1971). The detection of asbestosis is difficult because the condition produces inconspicuous lung effects, except in extremely severe cases (Otto, 1973). Where they penetrate the lung tissue, asbestos fibers induce sclerotic, diffuse fibrosis on a microscopic scale, primarily in the lower parts of the lungs. Diagnosis of asbestosis is confirmed mainly by the histological identification of asbestos bodies and fibers in biopsy or necropsy specimens of fibrotic lung tissue (Otto, 1973). Fibrosis alone is not diagnostic because it is indicative of numerous pulmonary diseases (Gough, 1965). The accurate detection of small numbers of asbestos particles in the lung tissue of occupationally exposed workers continues to be a major problem in the diagnosis and study of asbestosis and related disease (Gough, 1965).

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5.3.1.1 Pulmonary Changes--Interstitial lung fibrosis may develop as early as 3 to 6 years after initial asbestos exposure (Solomon, 1970a). At first it involves thickening of the interlobular septa in subpleural, posterior portions of the lower lobes; gradual progression causes distortion of terminal bronchioles and distal air spaces (MacKenzie, 1971). Early radiological signs frequently are manifested as a ground glass appearance with clouding of lower lung fields (Hurwitz, 1961). More definite stages show fine, striated, fibrillar changes in lung structure, resulting in progressive reduction of radiolucency and blurring of vascular lung markings (Hurwitz, 1961). The types of radiological changes that are manifested in asbestosis are highly variable and difficult to classify into development stages (Gelfand and Morton, 1970). Solomon (1970b) and Blum (1962) defined numerous radiological patterns of asbestos lung fibrosis as follows:

a. Bead-like disruption of normal basal vascular patterns in early stages;

b. Simple, diffuse fibrosis consisting of fine, linear, fibrillary changes;

c. Nodular changes that give a mottled appearance to the parenchyma;

d. Pneumonitic fibrosis producing localized, irregularly shaped areas of solid fibrosis;

e. Coarse fibrosis, made up of broad, linear, fibrotic bands with gross, vascular distortion; and

f. Massive fibrosis resulting from the confluence of nodulations.

Nodular, pneumonitic, and massive fibrotic changes often occur in combination (Solomon, 1970b). In South African miners exposed to high asbestos dust concentrations for more than 10 years, the basic pathological pattern of fibrotic lesions was diffuse hyaline fibrosis with areas of concentric fibrosis (Solomon et al., 1971).

5.3.1.2 Benign Pleural Changes--Pleural abnormalities commonly accompany asbestotic lung fibrosis and often are the only radiological manifestations of the disease (Hurwitz, 1961; Solomon, 1969). In many roentgenological studies of asbestos workers, pleural lesions such as

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lamellar thickening, accentuation of fissures, effusion, fibrosis, adhesions, hyaline plaques, and nonspecific reactions are observed more frequently than fibrotic lung changes (Hurwitz, 1961; Solomon, 1970b; Freundlich and Greening, 1967). The primary reason is that pleural changes may develop when only minor histological signs of the lung fibrosis are evident (Hurwitz, 1961; Solomon, 1970b). The main pleural lesions observed in asbestosis are hyaline pleural plaques; they develop within the costal or diaphragmatic pleura and may completely surround the lower lung lobes (Ulrich, 1971; Lesobre et al., 1973). Pleural plaques are layers of hyalinized fibrin formed by the slow proliferation of fibroblasts and fibrocytes in collagenous connective tissue (Thomson, 1970; Ulrich, 1971). Lesion development continues after exposure to asbestos has ceased (Lesobre et al., 1973). This fibrotic response is attributed to the continual abrasive action of asbestos fibers that penetrate the parietal pleura, although the exact mechanism of plaque formation by asbestos is unclear (Roberts, 1971). The selective distribution of plaques in the posterior, lower half of the pleural cavity in most asbestos-related cases suggests that mechanical factors, such as the varying pressures and stretching of the pleura during respiration, influence the localization of plaques (Roberts, 1971).

Calcified pleural plaques are the most striking and characteristic lesions in asbestosis, but they are rarely manifested in fewer than 20 years from the onset of asbestos exposure (Solomon, 1969; Fletcher and Edge, 1970; Rusby, 1968; Selikoff, 1965). Calcification of hyaline pleural plaques usually develops bilaterally in the middle and lower areas of the parietal pleura through the deposit of calcium in linear plates at the base of the plaques or in linear to nodular patches on the surface (MacKenzie, 1970). Occasionally they also involve diaphragmatic and mediastinal pleura (Hurwitz, 1961). Calcification of pleural plaques is a dystrophic process originating in the center of the older plaques where collagen is degenerated and devoid of nuclei (Thomson, 1970). Histological evidence indicates that the degenerative change is due to poor nourishment in the center of the plaque; subsequent calcification of degenerated areas may result from repeated stretching of the plaques during respiration (Roberts, 1971).

Except for the presence of calcium, there is no histological difference between calcified and noncalcified pleural plaques.

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The significance of pleural plaques in the development of mesotheliomas is not known (Hourihane et al., 1966; Dalquen et al., 1970). However, it has been suggested that both are caused by similar dust conditions, since they frequently coexist with or without asbestosis (Dalquen et al., 1970): they also develop within the same latency period and are macroscopically similar (Hourihane et al., 1966). Though it is possible that benign plaques are forerunners of mesotheliomas, transitional stages between the two have never been observed.

5.3.1.3 Physiological effects--The primary physiological alteration resulting from asbestos inhalation and asbestosis involves the impairment of pulmonary function as a result of structural changes in the lung tissue. Lung function abnormalities related to asbestos exposure represent a restrictive rather than obstructive ventilatory defect, as reflected by reduction in carbon monoxide diffusing capacity, lung compliance, residual volume, vital capacity, and total lung capacity, along with impaired ventilation-perfusion relationships (Thomson et al., 1965; Gandevia, 1967; Kleinfield et al., 1966; Regan et al., 1971; Jodoin et al., 1971).

Lung function defects may be manifested independently of clinical and radiological signs of asbestosis (Smither, 1971) and may not reflect the progression of fibrosis, particularly in the early stages (Busser et al., 1971; Hunt, 1965). The following studies demonstrate this fact. Results of function tests conducted on 17 asbestos workers by Bader et al. (1961) showed that although all patients with radiological abnormalities had functional impairment, six patients with only minimal radiological involvement exhibited severe functional impairment. Among 21 workers exposed to chrysotile and amosite for 14 to 55 years, vital capacity, total lung capacity, and diffusion capacity were significantly lower in those with radiological abnormalities; however, lung function did not reflect the degree of pulmonary infiltration (Kleinfield et al., 1966). In a 10-year study of 13 asbestos workers who were exposed for 4 to 24 years, reduced vital capacity correlated well with radiological changes in half of the cases; but the rest showed reduced values in the absence of radiological signs (Bader et al., 1965). Busser et al. (1971) studied 100 asbestos workers for several years by chest x-ray and lung function diagnostic procedures; early phases of asbestosis were represented by decreased vital capacity and lung compliance, accompanied by less rapid development of radiological changes.

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Although most authors agree that pulmonary function tests are not specifically diagnostic for asbestosis (except in the presence of characteristic radiological abnormalities and a history of asbestos exposure), reduced vital capacity and carbon monoxide diffusing capacity are potent indicators of lung disease and appear to be the most sensitive functional changes resulting from asbestos inhalation (Regan et al., 1971; Becklake et al., 1970; Murphy et al., 1972; Langlands et al., 1971).

The degree of functional impairment may or may not correlate with the duration and level of asbestos exposure (Bader et al., 1961). However, Hunt (1965) observed that men who are removed from occupational exposure during early stages of asbestosis maintain a reasonable functional level, whereas those who remain do not.

Examination of patients with asbestosis indicates a good correlation between functional changes during life and pathological findings at necropsy (Heard and Williams, 1961). Fibrous obliteration of fine air spaces, narrowing of small arteries by fibroelastic thickening, and formation of dense pleural adhesions or plaques are consistent with reduced inspiratory volume and total lung capacity. Decrease in vital capacity is associated with reduction in diffusing capacity as a result of fibrosis and probably arises from decrease in the total area of alveolar membrane available for diffusion, or from reduction in membrane permeability (Heard and Williams, 1961).

5.3.2 Other Nonmalignant Effects

5.3.2.1 Rheumatoid disease--Rheumatoid disease has been associated with asbestosis in several cases (Morgan, 1964; Tellesson, 1961). Though this syndrome closely resembles progressive, massive fibrosis, it is characterized by multiple nodular lesions, diffuse, dense parenchymal fibrosis in both lungs, and the presence of numerous asbestos bodies (Morgan, 1964; Tellesson, 1961). This extensive form of fibrosis may represent an abnormal response to asbestos by lungs predisposed to the rheumatoid state (Tellesson, 1961). In a case involving a 33-year-old male with rheumatoid arthritis, biopsy disclosed rheumatoid pneumoconiosis associated with asbestosis in the absence of characteristic radiological changes (Tellesson, 1961). The patient was occupationally exposed to low concentrations of amosite, crocidolite, and chrysotile for 15 years. Estimated exposure approached an average density of 8 thousand particles per cubic meter or 0.3 million particles per cubic foot; the total cumulative exposure approximated

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113 thousand particles per cubic meter years or 4 mppcf yrs (Telleson, 1961). Signs of rheumatoid pneumoconiosis in a 49-year-old man included multiple nodular rheumatoid lesions, massive fibrosis (asbestosis), and asbestos bodies in the lung parenchyma, but no symptoms of rheumatoid arthritis were present. The patient was exposed to asbestos for 20 years as a pipe welder in the interior of ships (Morgan, 1964).

Immunological analyses (Turner-Warwick and Parkes, 1970) have demonstrated rheumatoid (antiglobulin) and antinuclear factors in 46.5 percent of 80 patients who had a history of asbestos exposure; this represents a fourfold increase over the incidence in random populations. Similar results often are manifested in connective tissue disorders such as rheumatoid arthritis. In asbestosis cases, both diffuse interstitial fibrosis and large necrobiotic nodules were observed, and circulating rheumatoid factor was demonstrated in one-fourth of these patients. Polyarthritis was present in four of the 17 cases with rheumatoid factor. Though the pathogenic role of these antibodies is unknown, they appear to correlate with severe, progressive, radiologic lung changes rather than with duration of asbestos exposure.

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5.3.2.2 Possible Effects of Intravenous Injection--Certain intravenous preparations, especially antibiotics, contain excessive amounts of particulates, including asbestos fibers (Duma, 1973). Contamination arises from asbestos filters used in the pharmaceutical industry to remove foreign material from the final preparations. Human autopsies and animal experiments have shown that the intravenous infusion of particles exceeding 7 to 12 micrometers in length can produce inflammation of the pulmonary arteries, microemboli, thrombosis, foreign body granulomas, and pulmonary hypertension. Since numerous intravenous fluids contain 500 to 2,000 particles (larger than 5 micrometers) per liter of fluid, patients receiving intravenous medications for long periods of time are particularly susceptible to this health hazard (Duma, 1973).

5.3.2.3 Heart Abnormalities--In a study by Emara and El-Ghawaki (1969), electrocardiograms of 29 patients with asbestosis showed left axis deviation in 9 cases (31 percent) and abnormalities in ventricular conduction in 16 cases (55 percent) because of complete or partial bundle blockage related to asbestos cardiopathy. Radiological irregularities in cardiac outline are associated with abnormalities in ventricular conduction. Asymmetrical radiological findings in the left side of the chest are consistent with left axis deviations observed in electrocardiograms.

5.3.2.4 Cytotoxicity--In vitro investigations of hemolysis in human erythrocytes demonstrate that chrysotile is a potent hemolytic agent, whereas crocidolite, amosite, and anthophyllite are inactive or weakly lytic (Secchi and Reggonico, 1968). When incubated with red cell suspensions, chrysotile adsorbed two erythrocyte enzymatic proteins--acetyl cholinesterase and lactate dehydrogenase. Secchi and Reggonico (1968) hypothesize that the hemolytic activity of chrysotile relates to its capacity to adsorb the erythrocyte membrane components.

5.3.3 Dose-Response Relationships

Dose-response relationships between asbestos inhalation and associated respiratory diseases are poorly defined because most epidemiological or clinical studies do not express dust exposure in quantitative terms (National Institute for Occupational Safety and Health, 1972). Usually, length of employment or duration of exposure is used as the best measure of asbestos exposure, since dust concentrations are measured in few instances. When environmental data are included, they frequently have been

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collected by nonstandardized techniques and expressed in terms that cannot be compared from study to study; furthermore, they fail to determine the spectrum of fiber length and types of asbestos encountered. Consequently, only a low correlation between human epidemiological data and environmental asbestos exposure exists, and even this reflects the noticeable lack of definitive information concerning the etiologic role of asbestos (Gilson, 1965). In the following review of dose-response studies, quantified exposure levels usually were not available but were included whenever possible.

In general, the development of asbestosis appears to be closely related to the dose and duration of asbestos exposure and to the length of asbestos residence in the lung, as shown in the results of the following investigations.

In a 1970 study of South African amosite miners, the incidence of asbestosis increased with employment time (Sluis-Cremer, 1970). 1970).

Among 252 insulation workers in Belfast, the proportion of men with abnormal chest x-rays increased with age and duration of exposure; the frequency of lung or pleural abnormalities increased from 13 percent in workers employed for less than 10 years to 85 percent for those employed for at least 30 years (Langlands et al., 1971). Radiographs showed 62 workers with lung field abnormalities; fibrosis or calcification was detected in 67 percent of these. Ten men who had been exposed for a minimum of 25 years exhibited both pleural fibrosis and calcification in the presence of lung fibrosis. Reduction in vital capacity and carbon monoxide diffusing capacity indicated impairment of lung function in 40% of the men with radiological lung abnormalities and in only 3 percent of the men with normal chest x-rays. A summary of results is shown in Tables 5.1 and 5.2.

Chest roentgenograms of 39 workers exposed to tremolite and anthophyllite in commercial talc dust revealed only one individual with pneumoconiosis; mean exposure time was 16.2 years, with a range of 11 to 22 years (Kleinfield et al., 1973). Mixed dust concentrations ranged from 171 to 1370 thousand particles per cubic meter (6 to 48 mppcf) with asbestos fiber counts of 8 to 260 per ml for fibers longer than 5 micrometers. In another talc plant, 35 workers exposed to higher concentrations 57 to 2,000 thousand particles per cubic meter or 62 to 371 fibers per ml for

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Table 5.1 RELATION OF EMPLOYMENT TIME TO ABNORMAL CHEST X-RAYS IN INSULATION WORKERS [a]

Years as an insulator	Number of x-rays				
	Total	With pleural abnormality only	With lung field abnormality + pleural lesions	Total abnormal Number	Percent
0-9	55	5	2	7	13
10-19	103	12	16	28	29
20-29	75	10	29	39	52
Over 30	19	1	15	16	85

[a] Source: modified from Langlands et al., 1971.

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Table 5.2 RELATION OF EMPLOYMENT TIME TO TYPE OF CHEST X-RAY ABNORMALITY IN INSULATION WORKERS[a]

Years as an insulator			No. of men	Lung field abnormality	Pleural abnormality	
No. of men	Mean	Range			Calcification	Fibrosis
23	18	9-44	28	No	No	Yes
5	13	6-23	5	No	Yes	Yes/No
21	21	7-39	21	Yes	No	No
31	25	10-45	31	Yes	No	Yes
10	35	25-48	10	Yes	Yes	Yes

[a]Source: modified from Langlands et al., 1971.

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similar durations demonstrated an increased frequency of dust pneumoconiosis.

In pulmonary studies (Jodoin et al., 1971) of 25 mine workers with normal radiographs and asbestos exposure ranging from 6 months to 24 years, those with the greatest exposure (220 thousand particles per cubic meter or 8 mppcf) showed reduced vital capacity, low static pulmonary compliance, and 30 percent increase in static recoil pressures. Effects of exposure to less than 100 thousand particles per cubic meter (3.5 mppcf) were not as severe (Jodoin et al., 1971). Wegman et al. (1973) showed a significant correlation between restrictive loss in pulmonary function and the duration of asbestos exposure in a wallboard manufacturing operation. Although periodical environmental sampling conducted in the plant from 1952 through 1968 detected average dust concentrations of 17.4 to 134 thousand particles per cubic meter (0.6 to 4.7 mppcf) an unannounced inspection in 1972 showed actual values ranging from 6.4 to 11.5 fibers/ml; apparently, earlier results were attained by cleaning the work areas and lowering production on the day of inspection (Gross et al., 1973). This case demonstrates one of the problems involved in using epidemiological surveys to determine dose-response effects of asbestos exposure.

One study demonstrates the pathogenic effects of exposure to low doses of asbestos over a long period. A 38-percent incidence of asbestosis was observed among 101 shipyard pipecoverers who were exposed to low asbestos concentrations (approximately 142 thousand particles per cubic meter or 5 mppcf) for more than 20 years. The cumulative dose exceeded 2,800 thousand particles per cubic meter-yrs (100 mppcf-yrs) of exposure (Murchy et al., 1971). The earliest case developed after 13 years of exposure at a total cumulative dose of 1,710 thousand particles per cubic meter-yrs (60 mppcf-yrs). Compared to a matched, nonexposed control group with similar smoking habits, the incidence of asbestosis among pipecoverers was 11 times greater. The incidence increased both with age and with duration of exposure as a function of cumulative dose; 20 percent of those exposed for 2,000 to 2,800 thousand particles per cubic meter-yrs (70 to 100 mppcf-years) developed asbestosis. These results strongly indicate that prolonged exposure to low concentrations of asbestos is hazardous (Murphy et al., 1971). They demonstrate the need to lower the current recommended threshold limit value (TLV) of 5 fibers per ml (greater than 5 micrometers long) (American Conference of Governmental Industrial Hygienists, 1971). Presumably, the NIOSH-recommended (National Institute for

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Occupational Safety and Health) level of 2 fibers per cubic centimeter (greater than 5 micrometers in length), determined as a time-weighted, average exposure for an 8-hour work day, reflects a deepening concern for this hazard (National Institute for Occupational Safety and Health. 1972).

Weill, et al. (1973) studied the health effects of asbestos and silica dust exposure in 908 asbestos cement workers. The frequency of irregular and linear opacities increased as the cumulative dust exposure was increased. The incidence of diffuse radiological changes correlated better with total dust exposure than with duration of employment in the industry. Although it was not possible to distinguish between constituent exposures to asbestos or silica in the study, results suggest that irregular opacities were due primarily to asbestos exposure.

A similar study was conducted on 347 workers exposed to asbestos silica in an Egyptian pipe factory (El-Sewefy et al., 1970). The percentage of persons with positive chest symptoms and signs increased proportionally with the duration of exposure; 73.4 percent of the cases with dyspnea, 91 percent of those having finger clubbing, and 74.4 percent of the cases with positive x-ray findings had been employed for 10 to 20 years. Cigarette smoking and age did not account for the high incidence of chest symptoms and signs. Dust counts in factory locations where asbestos was mixed ranged from 19.7 to 626.3 mg per cubic meter; it is significant to note that, like the previous study, this one also did not distinguish between the silica and asbestos as components of the counts.

Not all studies correlate the development of asbestosis with long durations of exposure. In 247 cases of asbestosis that developed between 1955 and 1963 in Great Britain, age at initial employment was not a factor in the development of asbestosis, and the disease manifested itself following exposures of less than ten years (McVittie, 1965). Lung biopsy revealed asbestosis in a 47-year-old man 16 years after he was exposed to crocidolite (Goff and Gaensler, 1972). He handled raw asbestos for only 9 months in a cigarette filter manufacturing process. Pulmonary insufficiency resulting from advanced pleural and pulmonary fibrosis, progressed to total disability within 2 years. This case suggests that the inhalation of large doses for limited durations may be as harmful as the cumulative effect of low concentrations over many years of exposure.

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In a study of pleural plaques and asbestosis in Germany, Dalquen et al. (1970) determined that pleural plaques formation depended on initial dose and the latency period from the time of initial exposure, rather than the duration of exposure. The latency period was 40.2 years for the development of plaques, 36.1 years for asbestosis with plaques, and 26.1 years for asbestosis without plaques. Moreschi et al. (1970) observed a latent period of at least 15 years for the development of pleural calcification in asbestotic patients.

Clinical surveys at dockyards in Plymouth, England, showed that young workers exposed to asbestos develop extensive pleural reactions that frequently include effusion and ventilatory defects (MacKenzie and Harries, 1970). Calcified pleural plaques developed in older men who were exposed to "low concentrations" for many years; lung function in these cases shows little impairment.

MacPherson and Davidson (1969) correlated asbestos counts in lung tissue with radiological evidence of asbestosis to determine the dose effects of asbestos. Among 100 cases examined, positive counts were detected in 44. Radiological features of asbestosis were observed in eight of nine cases in which the asbestos counts at necropsy ranged from 44 to 205 fibers per 1.5 square centimeters of lung tissue (lower lobe). Abnormalities included calcified and/or noncalcified pleural plaques in eight cases, interstitial lung fibrosis in three, shaggy diaphragm in seven, and bronchial carcinoma in one. One study demonstrates a relationship between the number of asbestos bodies in the lungs and the incidence of pleural plaques (Thomson, 1970). Plaques were present in 15.8 percent of 57 cases in which fewer than five bodies were detected in the lungs, in 32.6 percent of 52 cases with 55 asbestos bodies, and in 100 percent of eight cases showing more than 100 asbestos bodies. The number of asbestos bodies observed in pleural plaques was not related to the degree of pleural fibrotic response.

The extent of asbestos inhalation may not be the only significant factor responsible for the development of asbestosis. Badr and El-Sewefy (1971) observed that approximately 20 percent of the workers in an Egyptian pipe factory never developed clinical or radiological signs of asbestosis, regardless of the duration of exposure. The resistance implied may be attributed to inherent genetic resistance or to defense mechanisms induced by specific extrinsic factors (Badr and El-Sewefy, 1971). Serum from 33 asbestos workers with signs of asbestosis and 10 to 23 years

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of exposure showed elevated concentrations of the immunoglobulin fractions IgM, IgG, and IgA in more than 50 percent of the samples. The increase in IgM and IgG is a characteristic response to chronic inflammatory disease; the IgA increase may reflect an autoimmune response (El-Sewefy and Hassan, 1971). These changes were not related to the duration of exposure or to the degree of asbestosis.

Cigarette smoking and asbestos inhalation may have an additive or synergistic effect on the incidence and severity of pulmonary fibrosis in occupationally exposed workers (Langlands et al., 1971; Weiss, 1971; McDonaldd et al., 1972). Langlands et al. (1971) observed that impairment of lung function in 252 insulation workers was more closely related to the amount of cigarette smoking than to radiological abnormalities. Statistical analysis of the age, sex, smoking habits, duration of asbestos exposure, and radiological evidence for 98 asbestos textile workers clearly implicates both asbestos exposure and cigarette smoking as causes of pulmonary fibrosis. The incidence was 40 percent in smokers, compared with 24 percent in nonsmokers, and it rose with increasing amounts and duration of smoking and asbestos exposure (Weiss, 1971). The results are summarized in Table 5.3.

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5.3.4 Carcinogenicity

Asbestos has been implicated as the causative agent of several types of human cancers. The most predominant are lung cancer and pleural and peritoneal mesotheliomas. Cancer of the gastrointestinal tract (Stumphius and Meyer, 1968; Gerber, 1970; Selikoff et al., 1965b, 1968, 1972a; Newhouse et al., 1969) and ovarian cancer (Graham and Graham, 1967) have also been associated with asbestos exposure.

5.3.4.1 Cancer Types

5.3.4.1.1 Lung cancer--The first report of a relationship between asbestosis and lung cancer was as early as 1935, by Lynch and Smith (Stumphius and Meyer, 1968). A report in 1965 estimated that asbestosis progressed to malignant neoplasms in 10 to 15 percent of the cases (Telischi and Rubenstone, 1965); later figures postulate that more than 50 percent of the persons who develop asbestosis will also develop lung cancer (Roe, 1968). The first statistical review was that of Merewether (1947) who reported finding lung cancer in 13.2 percent of 235 necropsies on patients with asbestosis (Merewether, 1947). The majority of

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Table 5.3 RELATION OF PRELIMINARY FIBROSIS IN 98 ASBESTOS MILL WORKERS TO CIGARETTE SMOKING STATUS AND DURATION OF ASBESTOS EXPOSURE[a]

Smoking status and asbestos exposure (years)	Number of workers	Pulmonary fibrosis			
		Mild (no.)	Severe (no.)	Total No.	Total %
Nonsmokers					
20	11	0	0	0	0
20+	14	5	1	6	43
Total ----	25	5	1	6	24
Smokers					
20	45	12	1	13	29
20+	28	12	4	16	57
Total ----	73	24	5	29	40

[a]Source: modified from Weiss (1971)

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recorded lung carcinomas associated with asbestosis have been the squamous cell type (Cordova et al., 1962).

5.3.4.1.2 Mesothelioma--Mesotheliomas are rare primary tumors of the serosa. These ordinarily are associated with asbestos exposure via the presence of asbestos bodies in the lungs. Asbestos bodies have been found in lung sections in more than 25 percent of mesothelioma cases (Selikoff et al., 1965a) and epidemiological studies show that 80 percent of mesotheliomas occur in persons exposed to asbestos (Anonymous, 1973a). Detection of asbestos bodies and naked fibers in the mesothelioma itself is very difficult. Incineration of the sample along with HCl treatment, evaporation, filtration, microscopic examination, and selected area electron diffraction (SAED) analysis are required in this type of analysis (Le Bouffant et al., 1969; Langer et al., 1972; Pooley, 1972).

5.3.4.1.2.1 Pleural mesothelioma--Pleural mesothelioma occurs primarily in the male population after the age of 40 (Heller et al., 1970) and has been diagnosed with increasing frequency in recent years (Hitchock, 1970). Possibly the only primary malignant tumor of the pleura is the pleural mesothelioma (Solomon, 1970c).

The most common symptom is dyspnea, followed in frequency by nonspecific chest pain (Heller et al., 1970). The lung parenchyma can be invaded by pleural mesothelioma, and with tumor progression, the entire thoracic cavity may become encased.

5.3.4.1.2.2 Peritoneal mesothelioma--Ascites commonly occur in peritoneal mesothelioma. Tumor growth is unevenly distributed, consisting of a main large mass with scattered, smaller deposits (Smith et al., 1968). Common signs and symptoms of peritoneal mesothelioma are:

a. Bilateral pleural thickening and calcifications;

b. basal pulmonary parenchymal changes; and

c. abdominal pain, vomiting, and distention with x-ray evidence of intraabdominal tumefaction and/or obstruction of varying degrees (Smith 35 al., 1968; Enticknap and Smither, 1964; Adelman et al., 1972; Roberts and Irvine, 1970).

The abdominal cavity may eventually become obliterated by confluent growth. Obviously, the prognosis for either type of mesothelioma is poor.

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5.3.4.1.3 Gastrointestinal tract cancer--Data associating gastrointestinal cancer with employment in asbestos insulation work were first reported in 1963 (Selikoff et al., 1964). Persons with asbestosis also have an increased incidence of cancer of the gastrointestinal tract; asbestos inhalation appears to enhance the risk of cancer in the stomach and colon (Selikoff et al., 1965a). Inhalation exposure to asbestos results in ingestion of many fibers cleared from the lungs. The passage of fibers through the gastrointestinal tract wall may result in the excess gastrointestinal and peritoneal cancer observed. Various particles such as starch granules and dyed fibers have been found in human blood and urine after ingestion, indicating that the human intestinal mucosa can be penetrated by particles up to 120 micrometers in diameter (Volkheimer, 1973; and Schreiber, 1974).

Between 1962 and 1963, Japanese men had the highest rate of stomach cancer of all nations--seven times the rate for men in the United States, or 66.96 per 100,000 male population (Merliss, 1971). Asbestos-contaminated rice is suspected as a factor in promoting cancer. Rice prepared for the Japanese consumer is milled and treated with glucose and talc (normally containing some asbestos) to preserve flavor. Microscopic examination of the ash of store-bought rice treated in this manner displayed 3.7×10^6 asbestos-form fibers per g of rice. The incidence of stomach cancer decreases in immigrant Japanese who remain in the West long enough to drastically change their diet. Women and children were not mentioned in this report. A recent study using transmission and scanning electron microscopy and energy-dispersive x-ray analysis could not detect asbestos fibers within the gastric cancer cells--only talc crystals (Matsudo, et al., 1974). These crystals were found in cells of six of seven Japanese with gastric adenocarcinomas. The significance of these studies remains undetermined.

Fibers of a type of amphibole asbestos, cummingtonite-grunerite, have entered the water supply of Duluth, Minnesota since 1955. This continuing pollution has been the target of a recent lawsuit (United States of America et al. vs. Reserve Mining Company et al., No. 5-72, Civ. 19) filed by the Environmental Protection Agency against the Reserve Mining Company, whose waste products (iron ore tailings containing asbestos) are the source of the contamination (Cook et al., 1974). So far, no effects are apparent in the patterns of cancer mortality in any portion of the population (Masson et al., 1974); however, because of the long induction time required for most cancers, more time is necessary before a final conclusion can be drawn.

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Information on the effects of asbestos ingestion in humans is severely limited.

5.3.4.2 Exposure Level and Duration--The greatest risk from asbestos occurs with heavy exposure for long periods, which is most likely to occur in industrial situations. The younger the individual when first exposed, the earlier the development of the pulmonary carcinoma (Cordova et al., 1962).

Most lung cancer requires an average induction time of 25 years (Roe, 1968). One report indicated that individuals who had been exposed to asbestos and had developed carcinoma of the lung had an average exposure time of 15 years, ranging from 3 to 27 years (Cordova, et al., 1962). The latent period, or induction time, varied from 15 to 22 years. One exception--an individual who developed pulmonary carcinoma approximately 20 years after exposure--had been exposed to asbestos dust for only 12 months.

The induction time for mesotheliomas averages 35.5 years, with a range of 16 to 55 years (Smith et al., 1968). Individuals with peritoneal mesothelioma may have a considerable amount of asbestos in their lungs without the presence of a pleural or intrapulmonary tumor (Gold, 1971). Lungs in persons with pleural mesothelioma can contain relatively little asbestos, whereas lungs with bronchial carcinoma tend to have a high asbestos content. Mesotheliomas may occur at exposure levels below those required for prevention of radiologically evident asbestosis (National Institute for Occupational Safety and Health, 1972). Cases of mesothelioma have been reported in persons indirectly exposed to asbestos--particularly through contact with clothing of a person occupationally exposed to asbestos--or in persons environmentally exposed by living in the vicinity of asbestos industries (National Institute for Occupational Safety and Health, 1972; Smith et al., 1968).

5.3.4.3 Mechanism of Action--The mechanism of carcinogenic activity remains undetermined; however, several associated possibilities have been suggested (Harington and Roe, 1965):

a. the organic materials associated with the fibers, either naturally or as a result of contamination of the asbestos during processing,

b. the presence of certain carcinogenic metals or metal complexes in asbestos, and

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c. the prolonged tissue residence of chemically inert material that is incapable of being rapidly removed by phagocytosis.

The cancer risk associated with asbestos exposure appears to be a function of the shape, length, and, most importantly, the diameter of the fibers, which apparently are most dangerous when straight and very fine (Anonymous, 1973b). There is still some confusion over whether the longer fibers (40 to 320 micrometers) or the shorter fibers (under 20 micrometers) are more likely to produce mesothelial tumors (Anonymous, 1973a).

Evidence that all commercial types of asbestos except anthophyllite may be responsible for mesothelioma is increasing. The risk is greatest with crocidolite, less with amosite, and apparently less with chrysotile (McDonald et al., 1971).

Investigation of crocidolite asbestos mining districts in the North Western Cape, Africa, reported deaths from lung cancer to be three times as high as those from adjoining districts or control districts with similar population and degree of urbanization (Harington and Roe, 1965). Data similarly compiled from chrysotile and amosite mining areas revealed no excess mortality from any form of cancer; however, the relative proportion of the population exposed is considerably less than the North Western Cape. Although this study could suggest that crocidolite is much more carcinogenic than amosite, even though their mineral composition is very similar, more information is needed for definite conclusions.

Two metals known to be carcinogenic--nickel and chromium--may occur in relatively high concentrations (e.g., 0.5 percent Ni and 0.1 percent Cr) in chrysotile. In addition, crocidolite and amosite contain iron concentrations that well exceed those in certain macromolecular complexes of iron known to be highly carcinogenic in animals (Harington and Roe, 1965).

The natural oils found in crocidolite and amosite asbestos contain benzo(a)pyrene and related polycyclic hydrocarbons (Harington and Roe, 1965; Wagner, 1963). One sample of crocidolite oil contained 1 microgram benzo(a)pyrene per 100 g of fiber, whereas the amosite oil sample contained 5 micrograms benzo(a)pyrene per 100 g of fiber (Harington and Roe, 1965). Unprocessed chrysotile fibers do not contain polycyclic hydrocarbons; however, all three types of asbestos contain secondary oils possibly

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encountered during transport and industrial treatment (Harington and Roe, 1965). Analysis of 12 materials containing chrysotile revealed that a third of the samples contained benzo(a)pyrene, benzo(a)anthracene, and dibenzo(a,h)anthracene (Boiteau et al., 1972). These compounds apparently are not present in concentrations large enough to be strongly carcinogenic; however, the possibility exists that the asbestos oils possess incomplete carcinogenic activity of either the tumor-initiating or tumor-promoting type (Harington and Roe, 1965).

5.3.4.4 Cocarcinogenesis--Asbestos exposure combined with cigarette smoking has been shown to markedly increase the incidence of lung cancer over that observed with either factor alone (Churg and Kannerstein, 1970). Cigarettes have also been suggested as a cofactor in the development of mesothelioma (Whitwell and Rawcliffe, 1971), although other data indicate no apparent relationship (Selikoff et al., 1970).

For asbestos workers who smoke, the risk of dying from bronchogenic carcinoma is reportedly 92 times greater than for men who neither work with asbestos nor smoke cigarettes (Selikoff et al., 1968). However, surveys of three naval dockyards--Portsmouth, Chatham, and Rosyth--showed no evidence that smoking habits were involved in the incidence of parenchymal or pleural disease associated with asbestos exposure (Harries et al., 1972). Another study indicated that a significant excess in mortality from lung cancer occurred in smokers who were heavily exposed to asbestos but not in smokers or nonsmokers with only low to moderate exposure (Berry, 1972).

5.3.5 Mutagenesis and Teratogenesis

There is no available literature on the mutagenic or teratogenic effects of asbestos exposure in humans.

5.3.6 Epidemiological Studies

Several types of asbestos exposure occur as the result of air pollution (Selikoff et al., 1971): direct and indirect occupational exposure, exposure of families, neighborhoods, entire communities, and random (close) exposures.

5.3.6.1 Cancer Mortality and Occupational Exposure--A survey (1936-67) of over 1,000 anthophyllite asbestos miners in Finland who were exposed from 3 months to more than 20 years revealed the following causes of death in 33 cases

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exposed for more than 20 years: carcinoma of the lung in eight; carcinoma of the gastrointestinal tract in two; asbestosis and corpulmonale in five; asbestosis in two; cardiac in eight; cerebral in four, and other causes in four (Kiviluoto and Meurman, 1970).

Another survey of 1,348 retired men over age 65 and previously exposed occupationally to asbestos for an average of 25 years (ranging from 3 to 50 years) showed a mortality rate 14.7 percent higher than the counterpart male population of the United States (Enterline et al., 1973). The major causes of death were respiratory cancer and respiratory diseases, but some excess was found in other cancers, particularly cancer of the digestive system. Excess mortality from other respiratory diseases was due entirely to pneumoconiosis and pulmonary fibrosis. Time-weighted calculations of asbestos exposure indicated that large increments in respiratory cancer appear at a cumulative asbestos dust exposure of somewhere between 35 and 70 million particles per cubic meter years (100 & 200 mppcf-years). Table 5.4 summarizes dose-response relationships between asbestos exposure and mortality from malignant respiratory diseases among retired asbestos workers (Enterline et al., 1973). Table 5.5 presents observed and expected deaths and standardized mortality ratios (SMRs) of the 1,348 retired male workers for selected causes of death by age, Table 5.6 shows the average cumulative dust exposure, observed and expected deaths, and SMR's for respiratory cancer in men exposed to three types of asbestos. Table 5.6 suggests that crocidolite asbestos may be more carcinogenic than either amosite or chrysotile (Enterline and Henderson, 1973).

Insulation and textile workers have higher than normal levels of asbestosis, lung cancer, and mesothelioma. Mesothelioma cases studied in South Africa and the United Kingdom revealed that 80 percent have an occupational or paraoccupational association with asbestos fibers. An excess of bronchogenic cancer was demonstrated among 632 asbestos insulation installers observed from 1943 to 1967 (National Institute for Occupational Safety and Health, 1972). There were 99 deaths above that expected on the basis of the U.S. white male population for three types of malignancies: bronchogenic, 63; gastrointestinal, 26; and all other sites combined, 10.

Among 392 insulation workers exposed to asbestos for more than 20 years in New York and New Jersey, 339 exhibited asbestosis, and 11 had pleural cancer (Selikoff et al., 1965a). Among 307 consecutive deaths in this group, the

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TABLE 5.4 RELATION OF TOTAL DUST EXPOSURE TO DEATHS AND STANDARD MORTALITY RATIOS (SMR) FOR RESPIRATORY CANCER IN ASBESTOS WORKERS[a]

Total Dust Exposure				No. of Men	Respiratory Cancer		
Range		Mean					
Metric Equivalent[b]	(English Equivalent)[c]	Metric Equivalent	(English Equivalent)		Observed Deaths	Expected Deaths	SMR
Under 708	(25)	314	(11.1)	75	2	1.3	153.8
708-1766	(25-62.4)	1248	(44.1)	181	8	3.1	258.1
1769-3535	(62.5-124.9)	2522	(89.1)	277	5	4.6	108.7
3538-7047	(125-249)	5122	(181.0)	305	12	4.8	250.0
7075-14122	(250-499)	9933	(353)	328	17	5.2	326.9
14150-21197	(500-749)	17153	(606.1)	126	9	1.8	500.0
21225 and over	(750)	27175	(960.2)	56	5	0.9	555.6

a. Study of 1348 men retired from the asbestos industry 1941 to 1967 and observed through 1969. Source: Modified from Enterline et al., 1973.
b. In thousand particles per cubic meter of air per year (TPPCM/yr).
c. In million particles per cubic foot of air per year (MPPCF/yr).

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TABLE 5.5 DEATHS AND STANDARD MORTALITY RATIOS (SMR) IN ASBESTOS WORKERS, BY CAUSE OF DEATH AND AGE[a]

Cause of Death and International List Number	Deaths											
	All Ages			Age 65 to 69			Age 70 to 74			Age 75+		
	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
Cancer (140-205)	167	109.4	152.6[b]	59	42.9	137.5[b]	56	35.4	158.2[b]	52	31.1	167.2[b]
Digestive (150-159)	53	41.8	126.8	15	16.0	93.7	19	13.6	139.7	19	12.2	155.7
Respiratory (162-163)	58	21.7	267.3[b]	27	10.5	257.1[b]	18	7.1	253.5	13	4.1	317.1[b]
All other cancers	56	45.9	122.0	17	16.4	103.7	19	14.7	129.3	20	14.8	135.1
Respiratory disease (470-527)	67	36.8	182.1[b]	27	11.5	234.8[b]	20	11.1	180.2[b]	20	14.2	140.8
Pneumoconiosis and pulmonary fibrosis (523-525)	29	---	---	14	---	---	10	---	---	5	---	---
Asbestosis (523.2)	18	---	---	9	---	---	6	---	---	3	---	---
Other respiratory diseases	38	36.8	103.3	13	11.5	113.0	10	11.1	90.1	15	14.2	105.6

a. Study of 1,348 men retired from the asbestos industry 1941 to 1967 and observed through 1969. Source: Modified from Enterline and Henderson, 1973.

b. SMR is significantly different from 100 at the 5-percent level.

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TABLE 5.6 DUST EXPOSURES, DEATHS, AND STANDARD MORTALITY RATIOS (SMR) FOR RESPIRATORY CANCER IN ASBESTOS WORKERS, BY TYPE OF ASBESTOS[a]

Type of asbestos	No. of men	Average cumulative dust exposure: Metric equivalent[b]	Average cumulative dust exposure: English equivalent[c]	Total deaths	Respiratory Cancer: Observed deaths	Respiratory Cancer: Expected deaths	Respiratory Cancer: SMR	Respiratory Cancer: Adjusted SMR
Amosite only	59	9430	(330.2)	47	4	0.9	444.4	390.7
Chrysotile only	1,013	6980	(244.4)	572	39	16.5	236.4	237.7
Amosite and chrysotile	102	7600	(266.3)	50	3	1.7	176.5	171.2
Chrysotile and crocidolite	120	5960	(208.6)	54	10	1.9	526.3	563.0
Amosite, chrysotile and crocidolite	54	7810	(273.4)	31	2	0.8	250.0	239.8
Any amosite	215	8160	(285.6)	128	9	3.4	264.7	249.0
Any chrysotile	1,289	6970	(244.0)	707	54	20.9	258.4	260.0
Any crocidolite	174	6540	(228.9)	85	12	2.8	428.6	442.5

a. Study of 1,348 men retired from the asbestos industry 1941 to 1967 and observed through 1969. Source: Modified from Enterline and Henderson, 1973.

b. In thousand particles per cubic meter of air per year (tppcm/yr).

c. In million particles per cubic foot of air per year (mppcf/yr).

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incidence of lung cancer was seven times greater than expected; cancer of the gastrointestinal tract was three times the expected rate, and ten mesotheliomas were found.

5.3.6.2 Nonoccupational Exposure--Until 1969, disease associated with asbestos exposure (primarily scarring of the lungs or asbestosis) was considered an occupational hazard exclusively (Selikoff et al., 1971). More recently, investigators have begun to realize the possibility of health risks to the general public from asbestos exposure, especially in urbanized areas.

5.3.6.2.1 Incidence of asbestos bodies--Structures identified as similar to asbestos bodies (commonly seen in persons known to have an extensive exposure to asbestos fibers) are found in 25 percent or more of the adult general population by direct examination of lung tissue or of the fluids pressed from such tissue (Wright, 1969). The incidence of asbestos bodies is obviously increasing, as shown by a London hospital study of lung tissue from 100 necropsies: 0 percent in 1936, 3 percent in 1946, 14 percent in 1956, and 20 percent in 1966 (Chang-Hyum, 1971).

Persons living in urbanized areas or in the vicinity of asbestos mines apparently are more likely to encounter an asbestos-polluted atmosphere than those who do not. One study revealed several hundred persons with radiological evidence of pleural calcification among rural people living near two open cast anthophyllite asbestos mines (Newhouse, 1973). Chrysotile asbestos is commonly found in the lungs of people autopsied in New York City, and similar observations have been recorded in London (Selikoff, et al., 1971; Langer and Selikoff, 1971). Asbestos content in the air near building sites in Manhattan where asbestos was being sprayed was calculated by Selikoff et al. (1972). The maximum concentration downwind of the source was 80 X 10^{-9} g per cubic meter. This figure was calculated before the implementation of New York City's regulation banning the spraying of asbestos fireproofing in 1972. Since chrysotile asbestos fibers fragment easily, 10^{-9} g of chrysotile could represent more than a million fibrils.

Lung base smears from 500 consecutive autopsies (over age 15) in two cities--Cape Town, South Africa and Miami, Florida--show that 30 percent of the males and 20 percent of the females have evidence of asbestos fiber inhalation (Thomson, 1965). The higher figure for males is probably the result of an occupational factor. Asbestos bodies were scanty in 85 percent of the positive cases, were not

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associated with pulmonary changes, and were regarded as the result of contamination of urban atmosphere.

5.3.6.2.2 Significance of nonoccupational exposure--Data are presently insufficient to determine the significance of the amounts of asbestos generally detected in lung tissues of urban residents (Selikoff et al., 1971). Currently, no direct evidence suggests that the presence of asbestos dust particles or similar materials--either coated or uncoated--in the lungs of persons not occupationally exposed to these particles is making any contribution to pulmonary disease, either inflammatory or neoplastic (Utidjian et al., 1968).

The Advisory Committee on Asbestos Cancers (1973) supports the above statements concerning low levels of asbestos exposure to the general public and also states that no evidence exists showing increased risk of cancer from asbestos contamination of water, beverages, or food. However, in neighborhoods with a source of asbestos dust, mesothelial tumors, as well as asbestos bodies or calcified asbestos pleural plaques, do occur in the general population (Newhouse, 1973).

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5.4 REFERENCES

1. Adelman, H., P. Berkson, and J. P. Sackler. Partial Intestinal Obstruction Due to Peritoneal Mesothelioma in Chronic Asbestos Exposure. N.Y. State J. Med. 72(18):2322-2334, September 1972.

2. Advisory Committee on Asbestos Cancers. Biological Effects of Asbestos - Report to the Director of the International Agency for Research on Cancer. Ann. Occup. Hyg. 16:9-17, October 1972.

3. American Conference of Governmental Industrial Hygienists. Documentation of the Thresnold Limit Values for Substances in Workroom Air, Third Edition, ACGIH, Cincinnati, OH. p. 17-19, 1971.

4. Anonymous. Asbestos as an Industrial Hazard. Med. J. Aust. (Australia). 1:92, January 1973a.

5. Anonymous. Asbestos-Lung Cancer-Mesothelioma. Lancet. 1(7807):815-816, April 1973b.

6. Bader, M. E., R. A. Bader, and I. J. Selikoff. Pulmonary Function in Asbestosis of the Lung. Amer. J. Med. 30:235-242, January-June 1961.

7. Bader, M. E., R. A. Bader, A. S. Tierstein, and I. J. Selikoff. Pulmonary Function in Asbestosis: Serial Tests in a Long-Term Prospective Study. Ann. N.Y. Acad. Sci. 132(1):391-405, December 1965.

8. Badr, F. M., and A. Z. El-Sewefy. The Association between Asbestosis and ABO Blood Groups. Ann. Occup. Hyg. (England). 14:35-40, 1971.

9. Becklake, M. R., G. G. Fournier-Massey, J. C. McDonald, J. Siemiatycki, and C. E. Rossiter. Lung Function in Relation to Radiographic Changes in Quebec Asbestos Workers. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, p. 233-236, 1970.

10. Berry, G. Combined Effect of Asbestos Exposure and Smoking on Mortality from Lung Cancer in Factory Workers. Lancet. 2(7775):476-479, September 1972.

DRAFT
NOT FOR QUOTATION

ST0066304

DOW 02095

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 91 of 114 asbestosclaims.law/library/19184/91

11. Blount, M., P. F. Holt, and A. A. Leach. The Protein Coating of Asbestos Bodies. Biochem. J. (England). 101(1):204-207, 1966.

12. Blum, C. K. Radiology of Some Rarer Dust Diseases. Scot. Med. J. (Scotland). 7:478-487, 1962.

13. Boiteau, H. L., M. Robin, and S. Gelot. Polycyclic Hydrocarbins in Various Materials Containing Asbestos. Arch. Mal. Prof. Med. Trav. Secur. Sociale. 33(6):271-286, 1972.

14. Borow, M., A. Conston, L. Livornese, and N. Schalet. Mesothelioma Following Exposure to Asbestos: A Review of 72 Cases. Chest. 64:641-646, 1973.

15. Busser, E., F. Dorschner, and A. A. Bohlmann. Zur Fruhdiagnase der Asbestose (Early Diagnosis of Asbestosis). Schweiz. Med. Wschr. (Germany). 101(47):1687-1692, 1971.

16. Chang-Hyum, U. Study of the Secular Trend in Asbestos Bodies in Lungs in London 1936-66. Brit. Med. J. 2:248-252, 1971.

16. Churg, J., and M. Kannerstein. Occupational Exposure and Its Relation to Type of Lung Cancer. In: Morphology of Experimental Respiratory Carcinogenesis, U.S. Atomic Energy Commission Symposium Series, No. 21, Nettesheim, P., M. G. Hanna, Jr., and J. W. Deatherage, (eds.). U.S. Atomic Energy Commission, Division of Technical Information, Springfield, Va., p. 105-120, 1970.

18. Cook, P. M., G. E. Glass, and J. H. Tucker. Asbestiform Amphibole Minerals: Detection and Measurement of High Concentrations in Municipal Water Supplies. Science. 185:853-855, 1974.

19. Cordova, F., H. Tesluk, and P. Knudtson. Asbestosis and Carcinoma of the Lung. Cancer. 15:1181-1187, 1962.

20. Dalquen, P., I. Hinz, and A. F. Dabbert. Pleura Plaques, Asbestose und Asbestexposition, eine Epidemiologische Studie aus dem Hamburger Raum (Pleural Plaques, Asbestosis and Exposure to Asbestos, an Epidemiological Study of the Hamburg Area). Pneumologie (Germany). 143:23-42, 1970.

DRAFT
NOT FOR QUOTATION

ST0066305

DOW 02096

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 92 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/92

21. Davis, J.M.G. The Ultrastructure of Asbestos Bodies from Human Lung. Brit. J. Exp. Pathol. (England). 45(6):642-646, 1964.

22. Duma, R. J. Particulate Matter of Particular Interest. Ann. Intern. Med. 78:146-147, January 1973.

23. Dutra, F. R., and J. D. Carney. Asbestosis and Pulmonary Carcinoma. Arch. Environ. Health. 10(3):423-426, 1965.

24. El-Sewefy, A. Z., S. Awad, and M. S. Abdel-Salam. Chest Symptomology in an Eguiptian Cement-Asbestos Factory. J. Egypt. Med. Assoc. (Egypt). 53:84-92, 1970.

25. El-Sewefy, A. Z., and S. M. Hagazi. Serum Proteins and Amino Acids in Asbestosis. Ann. Occup. Hyg. (England). 14:29-33, 1971.

26. El-Sewefy, A. Z., and F. Hassan. Immunoelectrophoretic Pattern Changes in Asbestosis. Ann. Occup. Hyg. (England). 14:25-28, 1971.

26. Emara, A., and S. El-Ghawaki. Correlation Petween the Electrocardiogram and Radiological Picture in 29 Cases of Asbestosis. J. Egypt. Med. Assoc. (Egypt). 52:561-570, 1969.

28. Enterline, P., P. DeCoufle, and V. Henderson. Respiratory Cancer in Relation to Occupational Exposure Among Retired Asbestos Workers. Brit. J. Ind. Med. 30(2):162-166, 1973.

29. Enterline, P., and V. Henderson. Types of Asbestos and Respiratory Cancer in the Asbestos Industry. Arch. Environ. Health. 27:312-317, November 1973.

30. Enticknap, J. B., and W. J. Smither. Peritoneal Tumours in Asbestosis. Brit. J. Ind. Med. 21:20-31, 1964.

31. Fletcher, D. E., and J. R. Edge. The Early Radiological Changes in Pulmonary and Pleural Asbestosis. Clin. Radiol. (London). 21(4):355-365, 1970.

32. Freundlich, I. M., and R. B. Greening. Asbestosis and Associated Medical Problems. Radiology. 89(2):224-229, July-December 1967.

DRAFT
NOT FOR QUOTATION

ST0066306

DOW 02097

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 93 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/93

33. Gaensler, E. A., and Addington, W. W. Asbestos or Ferrunqinous Bodies. N. Engl. J. Med. 280:488-492, 1969.

34. Gandevia, B. Pulmonary Function in Asbestos Workers. Amer Rev. Resp. Dis. 96(3):420-427, 1967.

35. Gelfand, M., and S. Morton. Asbestosis in Rhodesia. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, p. 204-208, 1970.

36. Gerber, M. A. Asbestosis and Neoplastic Disorders of the Hematopoietic System. Amer. J. Clin. Pathol. 53:204-208, 1970.

36. Gilson, J. C. Problems and Perspectives: The Changing Hazards of Exposure to Asbestos. Ann. N.Y. Acad. Sci. 132(1):696-705, December 1965.

38. Godwin, M. C., and J. Jagatic. Asbestos and Mesotheliomas. Environ. Res. 3(5-6):391-416, 1970.

39. Goff, A. M., and E. A. Gaensler. Asbestosis Following Brief Exposure in Cigarette Filter Manufacture. Respiration. 29(1):83-93, 1972.

40. Gold, C. Asbestos in Tumours. J. Clin. Pathol. 24:481, 1971.

41. Gough, J. Differential Diagnosis in the Pathology of Asbestosis. Ann. N.Y. Acad. Sci. 132(1):368-372, December 1965.

42. Governa, M., and C. Rosanda. A Histochemical Study of the Asbestos Body Coating. Brit. J. Ind. Med. (London). 29(2):154-159, April 1972.

43. Governa, M., and C. R. Vadala. Histochemical Demonstration of Hematoidin in the Innermost Layers of Human Asbestos Body Coating. Int. Arch. Arbeitsmed. (West Germany) 30:273-282, 1972.

44. Graham, J., and R. Graham. Ovarian Cancer and Asbestos. Environ. Res. 1:115-128, 1967.

45. Gross, P., J.M.G. Davis, R. A. Harley, and R.T.P. De Treville. Lymphatic Transport of Fibrous Dust from the Lungs. J. Occup. Med. 15(3):186-189, March 1973.

DRAFT
NOT FOR QUOTATION

ST0066307

DOW 02098

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 94 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/94

46. Harington, J. S., and F.G.C. Roe. Studies of Carcinogenesis of Asbestos Fibers and Their Natural Oils. Ann. N.Y. Acad. Sci. 132(1):439-450, 1965.

46. Harries, P. G., F.A.F. MacKenzie, G. Sheers, J. H. Kemp, T. P. Oliver, and D. S. Wright. Radiological Survey of Men Exposed to Asbestos in Naval Dockyards. Brit. J. Ind. Med. 29(3):274-279, 1972.

48. Heard, B. E., and R. Williams. The Pathology of Asbestosis with Reference to Lung Function. Thorax. 16:264-281, 1961.

49. Heller, R. M., M. L. Janower, and A. L. Weber. The Radiological Manifestations of Malignant Pleural Mesothelioma. Amer. J. Roentgenol. Radium. Ther. Nucl. Med. 108(1):53-59, January 1970.

50. Hitchcock, H. T. Mesothelioma of the Pleura. Irish J. Med. Sci. 3(10):453-456, 1970.

51. Hourihane, D., T. Tessof, and P. C. Richardson. Hyaline and Calcified Pleural Plaques as an Index of Exposure to Asbestos: A Study of Radiological and Pathological Features of 100 Cases with a Consideration of Epidemiology. Brit. Med. J. (London). 1:1069-1074, April 1966.

52. Hunt, R. Routine Lung Function Studies on 830 Employees in an Asbestos Processing Factory. Ann. N.Y. Acad. Sci. 132(1):406-420, December 1965.

53. Hurwitz, M. Roentgenologic Aspects of Asbestosis. Amer. J. Roentgenol. 85(2):256-262, February 1961.

54. Jodoin, G., G. W. Gibbs, P. T. MacKlem, J. C. McDonald, and M. R. Becklake. Early Effects of Asbestos Exposure on Long Function. Amer. Rev. Resp. Disease. 104:525-535, 1971.

55. Kiviluoto, R., and L. Meurman. Results of Asbestos Exposure in Finland. In: Pneumoconiosis. Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, p. 190-191, 1970.

56. Kleinfield, M. J. Industrial Pulmonary Disease: Clinical and Experimental Observations. Trans. N.Y. Acad. Sci. 32(1):107-126, January 1970.

DRAFT
NOT FOR QUOTATION

ST0066308

DOW 02099

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 95 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/95

57. Kleinfield, M., J. Messite, and A. M. Langer. A Study of Workers Exposed to Asbestiform Minerals in Commercial Talc Manufacture. Environ. Res. 6(2):132-143, June 1973.

58. Kleinfield, M., J. Messite, and J. Shapiro. Clinical, Radiological, and Physiological Findings in Asbestosis. Arch. Intern. Med. 117:813-819, January-June 1966.

59. Langer, A. M., I. Rubin, and I. J. Selikoff. Electron Microprobe Analysis of Asbestos Bodies. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, p. 57-69, 1970.

60. Langer, A. M., I. B. Rubin, I. J. Selikoff, and F. D. Pooley. Chemical Characterization of Uncoated Asbestos Fibers from the Lungs of Asbestos Workers by Electron Microprobe Analysis. I. Histochem. Cytochem. 20(9):735-740, 1972.

61. Langer, A. M., and I. J. Selikoff. Chrysotile Asbestos in Lungs of Residents of New York City. In: Proceedings of the Second International Clean Air Congress, H. M. Englund and W. T. Berry (eds.). New York, Academic Press, p. 161-165, 1971.

62. Langlands, J.H.M., W.F.M. Wallace, and M.J.C. Simpson. Insulation Workers in Belfast. 2. Morbidity in Men Still at Work. Brit. J. Ind. Med. (England). 28(3):217-225, 1971.

63. Le Bouffant, L., H. Daniel-Moussard, S. Durif, J. C. Martin, C. Normand, and A. Policard. Research and Characterization of Asbestos Particles in Pleural Mesotheliomas. Compt. Rend. Ser. D. (Paris). 268:2269-2274, 1969.

64. Lesobre, R., A. Hadengue, and M. Legrand, Les Manifestations Pleurales de l'Asbestose (Pleural Changes in Asbestosis). Presse Med. (France). 222:1491-1494, June 1973.

65. Longley. E. O. The Many Faces of Asbestos Disease. Med. J. Aust. (Australia). 56-2(21):1063-1066, November 1969.

66. MacKenzie, F.A.F. The Radiological Investigation of the Early Manifestations of Exposure to Asbestos Dust.

DRAFT
NOT FOR QUOTATION

ST0066309

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 96 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/96

Proc. Roy. Soc. Med. (London). 64(8):834-837, August 1971.

67. MacKenzie, F.A.F., and P. G. Harries. Changing Attitudes to the Diagnosis of Asbestos Disease. J. Roy. Nav. Med. Serv. (England). 56:116-123, 1970.

68. MacPherson, P., and J. K. Davidson. Correlation Between Lung Asbestos Count at Necropsy and Radiological Appearances. Brit. Med. J. (London). 1(5640):355-357, January-March 1969.

69. Masson, T. J., J. W. McKay, and R. W. Miller. Asbestos-Like Fibers in Duluth Water Supply: Relation to Cancer Mortality. J. Amer. Med. Assoc. 228(8):1019-1020, May 1974.

70. Matsudo, H., N. M. Hodgkin, and A. Tanaka. Japanese Gastric Cancer. Arch. Pathol. 97:366-368, June 1974.

71. McDonald, J. C., M. R. Becklake, G. Fournier-Massey, and C. N. Rossiter. Respiratory Symptoms in Chrysotile Asbestos Mine and Mill Workers of Quebec. Arch. Environ. Health. 24:358-363, May 1972.

72. McDonald, J. C., A. D. McDonald, G. W. Gibbs, J. Siemiatycki and C. Rossiter. Mortality in the Chrysotile Asbestos Mines and Mills of Quebec. Arch. Environ. Health. 22:677-686, June, 1971.

73. McVittie, J. C. Asbestosis in Great Britain. Ann. N.Y. Acad. Sci. 132(1):128-138, December 1965.

74. Merewether, E.R.A. Annual Report of the Chief Inspector of Factories for the Year 1947. H.M.S.O., London, England, p. 15-17, 1946. In: Keal, E. E. Asbestosis and Abdominal Neoplasms. Lancet. 2:1211-1216, December 1970.

75. Merliss, R. R. Talc-Treated Rice and Japanese Stomach Cancer. Science. 173:1141-1142, September 1971.

76. Miller, A., A. Langer, A. Tierstein, and I. Selikoff. Nonspecific Interstitial Pulmonary Fibrosis. New Eng. J. Med. 292:91-93, January, 1975.

77. Milne, J.E.H. Development Changes in Asbestos Bodies and Their Significance. Trans. Soc. Occup. Med. (London). 21(4):118-121, October 1971.

DRAFT
NOT FOR QUOTATION

ST0066310

DOW 02101

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 97 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/97

78. Moreschi, N., G. Farina, and A. Cardini. Le Calcificazione Pleuriche Nella Asbestosi E. Nella Tuberculosi: Elementi Di Diagnostica Differeziale. (Pleural Calcifications in Asbestosis and in Tuberculosis: Elements of Differential Diagnosis.) Med. Laboro (Italy). 61(3):141-153, 1970.

79. Morgan, W.K.C. Rheumotoid Pneumoconiosis in Association with Asbestosis. Thorax. 19:433-435, 1964.

80. Morgenroth, K. Cellular Reaction in the Human Lung Caused by Inhalation of Asbestos Dust Over Long Periods. Beitr. Pathol. (West Germany). 148:199-210, 1973.

81. Murphy, R.T.H., B. G. Ferris, W. A. Burgess, J. Worchester, and E. A. Gaensler. Effects of Low Concentrations of Asbestos: Observations in Shipyard Pipe Coverers and Controls. New Engl. J. Med. 285(23):1271-1278, December 1971.

82. Murphy, R.T.H., E. A. Gaensler, R. A. Redding, R. Betteau, P. J. Keelan, A. A. Smith, A. M. Goff, and B. G. Ferris. Low Exposure to Asbestos. Arch. Environ. Health. 25(4):263-264, October 1972.

83. National Institute for Occupational Safety and Health. Criteria for a Recommended Standard. Occupational Exposure to Asbestos. U.S. Department of Health, Education and Welfare, Washington, D.C., 1972.

84. Newhouse, M. L. Asbestos in the Work Place and the Community. Ann. Occup. Hyg. 16:97-107, 1973.

85. Newhouse, M. L., and J. C. Wagner, Br. J. Ind. Med. 26:302, 1969.

86. Otto, H. The Risk of Asbestosis from a Pathological-Anatomical Viewpoint. Staub Reinhalt. Luft (West Germany). 33(2):58-60, 1973.

87. Pooley, F. D. Asbestos Bodies, Their Formation, Composition and Character. Environ. Res. 5(4):363-379, December 1972.

88. Regan, G. M., B. Tagg, J. Walford, and M. T. Thomson. The Relative Importance of Clinical, Radiological, and Pulmonary Function Variables in Evaluating Asbestosis and Chronic Obstructive Airway Disease in Asbestos Workers. Clin. Sci. 41(6):569-582, 1971.

DRAFT
NOT FOR QUOTATION

ST0066311

DOW 02102

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP...
ACL Doc 19184 · Page 98 of 114
Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/98

89. Roberts, G. H. The Pathology of Parietal Pleural Plaques. J. Clin. Pathol. (London). 24(4):348-353, 1971.

90. Roberts, G. H., and R. W. Irvine. Peritoneal Mesothelioma; A Report of Four Cases. Brit. J. Surg. 57(0):645-650, September 1970.

91. Roe, F. J. C. Some Recent Developments in the Field of Cancer Causation. In: The Veterinary Annual, Pool, W. A. (ed.). John Wright and Sons, Ltd., Bristol, England, p. 170-178, 1968.

92. Rusby, N. T. Pleural Manifestations Following the Inhalation of Asbestos in Relation to Malignant Change. J. Roy. Nav. Med. Ser. (England). 54(2):142-148, 1968.

93. Schreiber, G. Ingested Dyed Cellulose in the Blood and Urine of Man. Arch. Environ. Health. 29:39-42, 1974.

94. Scott, J. K., and H. C. Hodge. Nonabsorbable Dusts. In: Drill's Pharmacology in Medicine, DiPalma, J. R. (ed.). New York, McGraw-Hill Book Company, p. 1249-1255, 1971.

95. Secchi, G. C., and A. Reggonico. Hemolytic Activity of Asbestos Dusts. Med. Lavoro (Milan, Italy). 59(1):1-5, 1968.

96. Selikoff, I. J. The Occurrence of Pleural Calcification Among Asbestos Insulation Workers. Ann. N.Y. Acad. Sci. 132(1):351-367, 1965.

97. Selikoff, I. J., J. Churg, and E. C. Hammond. Asbestos Exposure and Neoplasia. J. Amer. Med. Assoc. 18822-26, 1964.

98. Selikoff, I. J., J. Churg, and E. C. Hammond. The Occurrence of Asbestosis Among Insulation Workers in the United States. Ann. N.Y. Acad. Sci. 132(1):139-155, 1965a.

99. Selikoff, I. J., J. Churg, and E. C. Hammond. Relation Between Exposure to Asbestos and Mesothelioma. New Engl. J. Med. 272(11):560565, March 1965b.

100. Selikoff, I. J., E. C. Hammond, and J. Churg. Asbestos Exposure, Smoking and Neoplasia. J. Amer. Med. Assoc. 204(2):106-110, April 1968.

DRAFT
NOT FOR QUOTATION

ST0066312

DOW 02103

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for EP... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 99 of 114 asbestosclaims.law/library/19184/99

101. Selikoff, I. J., E. C. Hammond, and J. Churg. Carcinogenicity of Amosite Asbestos, Arch. Environ. Health. 25:183-185, 1972.

102. Selikoff, I. J., E. Hammond, and J. Churg. Mortality Experiences of Asbestos Insulation Workers. In: Pneomoconiosis: Proceedings of the International Conference (Johannesburg, 1969). Shapiro, H. A. (ed.). New York Oxford University Press, p. 180-186, 1970.

103. Selikoff, I. J., E. C. Hammond, and H. Heimann. Critical Evaluation of Disease Hazards Associated with Community Asbestos Air Pollution. In: Proceedings of the Second International Clean Air Congress, H. M. Englund, and W. T. Berry (eds.). New York, Academic Press, p. 165-171, 1971.

104. Selikoff, I. J., W. J. Nicholson, and A. M. Langer. Asbestos Air Pollution. Arch. Environ. Health. 25:1-13, July 1972b.

105. Sluis-Cremer, G. K. Asbestosis in South African Miners. Environ. Res. 3:310-319, November 1970.

106. Smith, P. G., P. McR. Higgens, and W. D. Park. Peritoneal Mesothelioma Presenting Surgically. Brit. J. Surg. 55:681-684, September 1966.

107. Smither, W. J. Asbestos and Health. Occup. Health. 23(6):181-187, June 1971.

108. Solomon, A. Radiological Features of Diffuse Mesothelioma. Environ. Res. 3:330-338, 1970c.

109. Solomon, A. Radiological Features of Diffuse Mesothelioma. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, p. 261-265, 1970a.

110. Solomon, A. Radiology of Asbestosis. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, 1970b. p. 190-192.

111. Solomon, A. The Radiology of Asbestosis. S. Afr. Med. J. (South Africa). 43(27):847-851, July 1969.

DRAFT
NOT FOR QUOTATION

ST0066313

DOW 02104

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for E... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 100 of 114 asbestosclaims.law/library/19184/100

111. Solomon, A., B. Goldstein, I. Webster, and G. K. Sluis-Cremer. Massive Fibrosis in Asbestosis. Environ. Res. 4(5):430-439, November 1971.

113. Stumphius, J., and P. B. Meyer. Asbestos Bodies and Mesothelioma. Ann. Occup. Hyg. 11:283-293, 1968.

114. Taskinen, E., K. Ahlman, and M. Wiikeri. A Current Hypothesis of the Lymphatic Transport of Inspired Dust to the Parietal Pleura. Chest. 64(2):193-196, August 1973.

115. Telischi, M., and A. E. Rubenstone. Pulmonary Asbestosis. Arch. Pathol. 72:234-243, 1961. In: Dutra, F. R., and J. D. Carney. Asbestosis and Pulmonary Carcinoma. Arch. Environ. Health. 10(3):416-423, March 1965.

116. Tellesson, W. G. Rheumatoid Pneumoconiosis (Caplan's Syndrome) in an Asbestos Worker. Thorax. 16:372-377, 1961.

117. Thomson, J. G. Asbestos and the Urban Dweller. Ann. N.Y. Acad. Sci. 132(1):196-214, 1965.

118. Thomson, J. G. The Pathogenesis of Pleural Plaques. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, p. 138-141, 1970.

119. Thomson, M. L., A. Pelzer, and W. J. Smither. The Discriminant Value of Pulmonary Function Tests in Asbestosis. Ann. N.Y. Acad. Sci. 132(1):421-436, December 1965.

120. Thomson, M. L., and M. D. Short. Mucociliary Function in Health, Chronic Obstructive Airway Disease, and Asbestos. J. Appl. Physiol. 26(5):535-539, May 1969.

121. Timbrell, V. Inhalation and Biological Effects of Asbestos. In: Assessment of Airborne Particles, Third Rochester International Conference on Environmental Toxicity, T. T. Mercer, P. E. Morrow, and W. Stoker (eds.). Springfield, Illinois, Charles C. Thomas, Publishers, p. 425-429, 1970a.

122. Timbrell, V. The Inhalation of Fibers. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, p. 3-9, 1970b.

DRAFT

NOT FOR QUOTATION

ST0066314

DOW 02105

Union Carbide trial exhibit UC-4636: Dinger, Whitfield, Hammons and Huff (Oak Ridge National Laboratory) for E... Published by AsbestosClaims.Law
ACL Doc 19184 · Page 101 of 114 asbestosclaims.law/library/19184/101

123. Timbrell, V. The Inhalation of Fibrous Dusts. Ann. N.Y. Acad. Sci. 132(1):255-273, December 1965.

124. Timbrell, V., D. M. Griffiths, and F. D. Pooley. Possible Biological Importance of Fibre Diameters of South African Amphiboles. Nature. 232:55-56, July 1969.

125. Timbrell, V., F. Pooley, and J. C. Wagner. Characteristics of Respirable Asbestos Fibers. In: Pneumoconiosis: Proceedings of the International Conference (Johannesburg, 1969), Shapiro, H. A. (ed.). New York, Oxford University Press, p. 120-125, 1970.

126. Turner-Warwick, M., and W. Parkes. Circulating Rheumatoid and Antinuclear Factors in Asbestos Workers. Brit. Med. J. (London). 3:492-495, July-September 1970.

127. Ulrich, P. Pathologische Anatomie de Hyalinen Pleurplatten (Pathological Anatomy of Hyaline Pleural Plaques). Pneumologie, 146(3):159-177, 1971.

128. Utidjian, M. D., P. Gross, and R. T. P. De Treville. Ferruginous Bodies in Human Lungs. Arch. Environ. Health. 17(3):327-333, 1968.

129. Volkheimer, G. Persorption. Acta-Hepato-Gastroenteral. 20:361-362, 1973.

130. Wagner, J. C. Asbestos Dust Exposure and Malignancy. In: International Congress of Occupational Health, Vol. 3, International Congress Series No. 62, Madrid, Spain, p. 1066-1066, 1963.

131. Wagner, J. C. Epidemiology of Diffuse Mesothelial Tumors: Evidence of an Association from Studies in South Africa and the United Kingdom. Ann. N.Y. Acad. Sci. 132(1):575-578, 1965.

132. Wegman, D. H., G. P. Theriault, and J. M. Peters. Work-Sponsored Survey of Asbestosis. Arch. Environ. Health. 27:105-109, August 1973.

133. Weill, H., C. Waggenspack, W. Bailey, M. Ziskind, and C. Rossiter. Radiographic and Physiologic Patterns Among Workers Engaged in Manufacture of Asbestos Cement Products: A Preliminary Report. J. Occup. Med. 15:248-252, March 1973.

DRAFT
NOT FOR QUOTATION

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134. Weiss, W. Cigarette Smoking, Asbestosis and Pulmonary Fibrosis. Amer. Rev. Resp. Dis. 104:223-227, 1971.

135. Whitwell, F., and R. M. Rawcliffe. Diffuse Maliqnant Pleural Mesothelioma and Asbestos Exposure. Thorax. 26:6-22, 1971.

136. Wright, G. W. Asbestos and Health in 1969. Amer Rev. Respirat. Dis. 100(4):467-479, October 1969.

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6.0 ENVIRONMENTAL DISTRIBUTION AND PROCESSES

6.1 SUMMARY

Asbestos has manifold applications in today's industrialized society and is often referred to as the "mineral of a thousand uses." One result of its industrial popularity has been a widespread dissemination into the environment.

Emission into the environment results from losses during manufacture, transportation, or use of the product, and from industrial waste disposal. Contamination probably also occurs as a result of natural processes, including erosion of asbestos outcrops, farming of asbestos-laden soils, and passage of water through asbestiform rocks.

Asbestos fibers are easily disseminated by wind and water and are generally regarded as being persistent in the environment. Degradation occurs under extremes of heat, mechanical stress, or acidity. When these minerals are broken into fine fibers, a large surface area is exposed to chemical degradation. However, conditions severe enough to cause alteration of the mineral usually are not encountered in the normal human environment.

A drawback to establishing a hazardous level of asbestos in the environment is the apparent lack of standardized sampling and detection techniques for collecting, identifying, and quantifying the fibers in air, water, and soil. Although many tests of varying sensitivity are now used, standard methods that are reliable, rapid, and economically feasible have not been established. Measurements made with the same analytical procedure, preferably by the same laboratory, can be used to compare asbestos concentrations in different samples.

6.2 FATE OF ASBESTOS IN THE ENVIRONMENT

6.2.1 Distribution

It generally is acknowledged that asbestos is commonly present in water and ambient air, particularly in urban areas. However, there is a noticeable lack of published

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data concerning the amounts that are present (Selikoff et al., 1972). Sample collecting and quantification of asbestos in the environment are difficult and require elaborate, time-consuming techniques that as yet are neither standardized nor commercially feasible (Selikoff et al., 1972; Pattnaik and Meakin, 1973). Although many techniques for environmental monitoring have been used, the main problem in each case lies in identifying a very small number of asbestos fibers among numerous other particulates in the same sample (Pattnaik and Meakin, 1973). As a result, the few environmental studies that exist present unquantified or approximate concentrations, with no information about the size distribution of asbestos fibers and fibrils in air, soil, and water.

6.2.1.1 Air--Air samples collected from nine international cities by Millipore filter techniques contained "small" concentrations of asbestos fibers; most occurred as single fibers, but some were agglomerates consisting of numerous fibers (Holt and Young, 1973).

X-ray diffraction analysis of air samples taken near an asbestos textile factory in Great Britain indicated an asbestos content of less than 0.1 microgram per cubic meter (Rickards and Badami, 1971).

Ambient air concentrations of chrysotile measured at various sites in New York City ranged from 10 to 60 X 10^{-9} g per cubic meter; these concentrations may be significant in view of the possibility that 10^{-9} g of chrysotile could divide into 1 million fibrils.

Preliminary air analyses by ultrasonification and electron microscopy methods demonstrated asbestos levels of approximately 2 g per cubic meter at a point source, 0.15 to 15 ng per cubic meter at urban sites, and 0.1 ng per cubic meter at nonurban sites (Thompson and Morgan, 1971).

6.2.1.2 Water--Contamination of North American water resources by asbestos or asbestos-like particles may be widespread. Preliminary findings using optical methods (Robeck's personal communication, 1975) indicate the presence of asbestos-like particles in drinking water samples in Atlanta, Boston, Chicago, Dallas, Denver, Duluth, Kansas City, New York City, Philadelphia, San Francisco, and Seattle (Anonymous, 1974b). At present, the presence of asbestos has been confirmed for San Francisco's water only. Contamination has also been reported in Canada (Cunningham and Pontefract, 1971, 1973). Cunningham and Pontefract (1973) determined that filtered Ottawa tap water contains

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approximately 2.0 million fibers per liter, river water concentrations range from 8.1 to 9.5 million fibers per liter, and melted snow from Ottawa contains 33.5 million fibers per liter.

Attention concerning the problem has been focused primarily on Duluth, where asbestos contamination is the result of industrial effluent discharge into Lake Superior, the city's water supply. Duluth water samples taken on August 28, 1973 were analyzed by seven different laboratories. An average fiber concentration of 12 million amphibole fibers per liter was measured. When adjusted for seasonal fluctuations, it is estimated that the average concentration in Duluth's drinking water is 43 million amphibole fibers per liter. Daily and seasonal fluctuations in amphibole concentrations have been determined by x-ray diffraction (Cook et al., 1974). Concentrations as high as 8 billion fibers per liter have been estimated for turbid Duluth tap water (United States of America et al. vs. Reserve Mining Company et al., No 5-72, Cov. 19).

There is an indication that the San Francisco water supply contains as much or more asbestos than Duluth, although the source of contamination is natural rather than industrial (Anonymous, 1974a,d). Other municipal water systems may be contaminated as a result of leaching of asbestos fibers into the water supply from asbestos-cement pipe contained within the system (Anonymous, 1974b).

Asbestos fiber concentrations are higher in water near points of emission than in areas remote from such points (Anonymous, 1974c). For example, water sample concentrations of fibers in Silver Bay, Minnesota (the site of the industrial source) were determined as 1.10 million fibers per liter but samples taken near Superior, Wisconsin (approximately 80 miles south, but served by the same water supply) contained only 0.37 million fibers per liter (Anonymous, 1974c).

6.2.1.3 Soil--Asbestos is a component of many fibrous silicate minerals. These minerals are divided into two groups: (a) serpentine, which contains chrysotile, and (b) amphibole, which contains anthophyllite, amosite, crocidolite, tremolite, and actinolite (May and Lewis, 1970). Asbestiform, amphibole, and serpentine occur in metamorphic rocks, which are distributed over much of the United States (Anonymous, 1974c).

Major commercial deposits of asbestos are found in Vermont, California, Arizona, and North Carolina (May and

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Lewis, 1970; Anonymous, 1972). Smaller asbestos outcrops are found in other States, but at present, production from these is negligible.

Soils produced through the weathering of fibrous silicates may contain asbestos. Studies in agricultural regions of Bulgaria have shown that asbestos particles may make up as much as 5 percent of individual soil samples collected from farm land where dispersed outcrops occur. Soil from similar farmland without asbestos outcrops contained no fibers (Burilkov and Michailova, 1970).

6.2.1.4 Contamination of Foods, Beverages, and Drugs--Asbestos fibers are ingested with foods and beverages that have been processed through asbestos filters (Anonymous, 1971). Asbestos fibers have been detected in Canadian and American beer, imported sherry, port wine, vermouth, and Canadian soft drinks at concentrations ranging from 1.1 to 12.2 million fibers per liter (Cunningham and Pontefract, 1971).

Chrysotile filters are widely used to remove foreign material from parenteral drugs and solutions used for intravenous, intramuscular, and intraperitoneal therapy in the United States (Nicholson, et al., 1972). Measurable amounts (above background levels) of chrysotile have been detected in one-third of the samples analyzed over a 1-year period (Nicholson et al., 1972). Amounts estimated in some of the samples exceeded 1 microgram. Fibrils typically observed in drugs approximate 0.04 micrometer in diameter and 0.1 micrometer in length; 10^{-9} g of chrysotile can fragment into 106 fibrils of this size.

6.2.2 Mobility

6.2.2.1 Air--Tabershaw (1968) estimates that from 10 to 15 percent of processed asbestos becomes airborne. He cites indirect evidence that asbestos is carried over long distances from industrial and natural emission sources: (a) analysis of deposits on the surface of the earth, snow, etc. (b) evidence that significant numbers of people with mesothelioma worked or lived near asbestos mines or plants and (c) evidence that a significant number of the population have asbestos bodies in their lungs at autopsy.

A preliminary study in Finland indicates that asbestos dust from mining and milling sources is deposited on surrounding areas. The rate of deposition is dependent on the distance from the source and meteorological conditions such as wind and rain (Lamanen et al., 1965). Winds are

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capable of widely dispersing industrial emissions and entraining weathered fibers from natural outcrops. Precipitation removes particles from the atmosphere (Sullivan and Athanassiadia, 1969).

6.2.2.2 Water--No studies specifically concerned with the water mobility of asbestos were found in the literature. However, testimony in a Duluth-related court case revealed that a 1.4-micrometer taconite tailing (a source of asbestos) deposited in Lake Superior in the vicinity of Silver Bay at a depth of 98 feet would travel 120 miles before settling to the bottom (that is, assuming a current speed of 1 centimeter per second and no vertical turbulence). If vertical turbulence is considered, the same particle would travel 294 miles before settling. In still water, a 2-micrometer particle will settle to a depth of 600 feet in approximately 1 year (Anonymous, 1974a). Particles which have settled, however, can easily reenter the water currents if the settling point is disturbed by water movement such as that caused by wind or thermal gradients.

6.2.2.3 Soil--No specific studies concerning the mobility of asbestos within soil have been located in the literature. It is probable that asbestos is transported on and within the soil by natural processes such as weathering, erosion, movement of wind or water, and by human activity such as farming or construction (Burilkov and Michailova, 1970).

6.2.3 Persistence in Air, Water, and Soil--No study was found that would indicate that biological transformation or degradation of asbestos occurs in the environment. Asbestiform minerals are subject to chemical degradation in extreme conditions that would rarely occur at the earth's surface: the magnesium hydroxide layers are soluble at low pH and in boiling water, the fibers decompose at around 1,000 c, and they are converted to other minerals under severe mechanical degradation (Speil and Leniweber, 1969). Since the conditions for degradation are so severe, it may be assumed that asbestos would persist in the normal human environment.

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ACL Doc 19184 · Page 108 of 114 asbestosclaims.law/library/19184/108

6.3 REFERENCES

1. Anonymous. Asbestos. Food Chem. News 16(7):2, 1974a.

2. Anonymous. Asbestos in the Water: Temporizing with Cancer. Consumer Reports 6:438, 1974b.

3. Anonymous. A Preliminary Report on Asbestos in the Duluth, Minnesota Area. Office of Technical Analysis, Office of Enforcement and General Counsel, Environmental Protection Agency, 1974c.

4. Anonymous. Safety of Food Additives and Solvents. World Health Organ. Chron. 25:409-411, September 1971.

5. Anonymous. Schmidt Queries Train About Duluth Water Supply. Food Chem. News 16(8):50-51, 1974d.

6. Anonymous. Supplementary Notes Supplied to the Attendees of the IITRI Seminar on Asbestos, April 4-7, 1972. IIT Research Institute, Chicago, Ill., 1972.

7. Burilkov, T., and L. Michailova. Asbestos Content of the Soil and Endemic Pleural Asbestosis. Environ. Research 3:443-541, 1970.

8. Cook, P. M., G. E. Glass, and J. H. Tucker. Asbestiform Amphibole Minerals: Detection and Measurement of High Concentrations in Municipal Water Supplies. Science 185:853-855, 1974.

9. Cunningham, H. M., and R. D. Pontefract. Asbestos Fibers in Beverages and Drinking Water. Nature. 232:332-333, 1971.

10. Cunningham, H. M., and R. D. Pontefract. Asbestos Fibers in Beverages, Drinking Water, and Tissues: Their Passage Through the Intestinal Wall and Movement Through the Body. J. Assoc. Offic. Anal. Chem. 56(4):976-981, 1973.

11. Holt, P. F., and D. K. Young. Asbestos Fibres in the Air of Towns. Atmos. Environ. 7:481-483, 1973.

12. Lamanen, A., Leo Noro, and V. Raunio. Observations on Atmospheric Air Pollution Caused by Asbestos Ann. N.Y. Acad. Sci. 132(1):240-245, 1965.

13. May, T. C., and R. W. Lewis. Asbestos. In: Mineral Facts and Problems, Bureau of Mines Bull. 650, 1970.

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NOT FOR QUOTATION

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DOW 02113

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Washington, D. C., Bureau of Mines, U.S. Department of the Interior. p. 851-863.

14. Nicholson, W. J., C. J. Maggiore, and I. J. Selikoff. Asbestos Contamination of Parenteral Drugs. Science 177:171-173, 1972.

15. Pattnaik, A., and J. D. Meakin. Development of an Instrument Monitoring Method for Measurement of Asbestos Concentrations in or Near Sources. Report no. EPA-650/2-73-016. Environmental Protection Agency, Office of Research and Development, Washington, D.C., June 1973.

16. Rickards, A. T., and D. V. Badami. Chrysotile Asbestos in Urban Air. Nature 234(5321):93-94, November 1971.

17. Robeck, G. Personal Communication, February 21, 1975.

18. Selikoff, I. J., W. J. Nicolson, and A. M. Langer. Asbestos Air Pollution. Arch. Environ. Health. 25L-13, July 1972.

19. Speil, S., and J. P. Leniweber. Asbestos Minerals in Modern Technology. Environ. 2:166-208, 1969.

20. Sullivan, R. J., and Y. C. Athanassiadia. Preliminary Air Pollution Survey of Asbestos--A Literature Review. National Air Pollution Control Administration Publication No. APTD 69-27, 1969.

21. Tabershaw, I. R. Asbestos As An Environmental Hazard. J. Occup. Med. 10(1):32-37, 1968.

22. Thompson, R. F., and G. B. Morgan. Determination of Asbestos in Ambient Air. In: International Symposium on Identification and Measurement of Environmental Pollutants (Ontario, Canada), Westly, B. (ed.), p. 154-155, 1971.

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NOT FOR QUOTATION

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7.0 ENVIRONMENTAL INTERACTIONS AND THEIR CONSEQUENCES

7.1 SUMMARY

Information on the environmental cycling of asbestos and related biological effects was not found in the available literature. However, the probable flow of asbestos through environmental media could be projected using information about its chemical and physical properties, emission sources, and natural occurrences.

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7.2 MOBILITY AND DISTRIBUTION

7.2.1 Sources

Asbestos is found naturally in many fibrous silicate minerals and is released into the atmosphere directly from mineral outcroppings and indirectly from soils produced during weathering processes. Rates of release can be altered by human activity such as road building, tilling of the soil, and construction (National Academy of Sciences, 1971).

Asbestos also enters the atmosphere via

--mining and milling of asbestos and of asbestos-contaminated talc

--transportation of materials containing asbestos

--manufacture and use of products containing asbestos

--demolition of buildings with asbestos incorporated into the building material

--solid waste disposal (National Academy of Sciences, 1971; U.S. Environmental Protection Agency, 1974).

Asbestos mines and mills are estimated to contribute 85 percent of the total emissions of asbestos from stationary

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sources. The potential for emissions from wet-process milling is much less than that of typical dry milling operations (U.S. Environmental Protection Agency, 1973). No land-use conflicts seem likely to inhibit the production of asbestos (May and Lewis, 1970). Virtually all of the deposits are in rugged country far removed from populated areas. The mining operations are on privately owned or leased lands. Waste rock is hauled to nearby dumps,and, as the pile builds up, a bulldozer spreads it out. Water sprays allay the dust as the tailings are discharged. The milling of asbestos is generally a dry operation, and all the screens are hooded and operate under a slight negative pressure for dust control (May and Lewis, 1970).

Atmospheric asbestos dust settles or is washed out by precipitation, returning to the soil and to waterways and thereby contributing to the contamination of ground and surface waters. Some industrial wastes containing asbestiform fibers are dumped directly into surface waters (e.g., Reserve Mining Company, Duluth, Minnesota) (Cook et al., 1974). Some fibers have been found in various public drinking water systems (see Section 6.2.1.2).

Available data are inadequate to determine the contribution that asbestos-cement pipes make to the amount, size, and persistence of the asbestos fibers found in potable water distribution systems (American Water Works Association, 1974).

Environmental asbestos concentrations are highest in urbanized areas and near asbestos mines; however, asbestos fibers are easily resuspended by wind and water and can be redistributed widely. Asbestos differs from many other pollutants in that it is stable with respect to decomposition (U.S. Environmental Protection Agency, 1973). Because of this stability, asbestos fibers are regarded as persistent in the environment.

7.2.2 Food Chains

No data were found to suggest the transfer of asbestos in food chains. Some foods and beverages, however, are contaminated with asbestos fibers through certain food processing procedures (see Section 6.2.1.4).

7.3 EFFECTS OF ASBESTOS POLLUTION

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The hazard of inhaling asbestos fibers is well documented for long-term, heavy exposure (see Section 6.0). But effects of inhaled asbestos are not well understood when exposure levels are low, as in most environmental circumstances.

Data implicating asbestos as a serious hazard when ingested are inconclusive. Most of the information concerning the health effects of asbestos exposure is limited to occupational and paraoccupational exposure, which constitutes a combination of inhalation and ingestion. Physical mechanisms do exist through which fibers could migrate from the lungs to the peritoneum without entering the gastrointestinal tract (American Water Works Association, 1974). It is possible, then, that the excess of peritoneal mesotheliomas in certain occupations with asbestos exposure is the result of inhalation and not ingestion.

One must assume that inhaling or ingesting asbestos fibers under any circumstances is a significant health hazard.

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Published by AsbestosClaims.Law
asbestosclaims.law/library/19184/113

7.4 REFERENCES

1. American Water Works Association. A Study of the Problem of Asbestos in Water. American Water Works Association Journal. Part 2:1-22, September 1974.

2. Cook, A. M., G. E. Glass, and J. H. Tucker. Asbestiform Amphibole Minerals: Detection and Measurement of High Concentrations in Municipal Water Supplies. Science. 185:853-855, 1974.

3. Cunningham, H. M., and R. Pontefract. Nature. 232, July 30, 1971.

4. May, T. C., and R. W. Lewis. Asbestos. In: Mineral Facts and Problems, Bureau of Mines Bull. 650. Washington, D.C., Bureau of Mines, U.S. Department of the Interior, p. 851-863, 1970.

5. National Academy of Sciences. Asbestos--the Need for and Feasibility of air Pollution Controls. Washington, D.C., 40 p., 1971.

6. U.S. Environmental Protection Agency. Asbestos and Mercury--Proposed Amendments to National Emission Standards for Hazardous Air Pollutants. Fed. Reg. 39(208):38064-38073, October 25, 1974.

7. U.S. Environmental Protection Agency. Control Techniques for Asbestos Air Pollutants. Reasearch Triangle Park, N.C. AP-117. EPA Office of Air Quality Planning and Standards. Feb., 1973.

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NOT FOR QUOTATION

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