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Chapter 16

THE HEALTH EFFECTS OF MINERAL DUSTS

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PROLOGUE

"Everything is a poison, nothing is a poison, the dose alone makes the poison." (Paracelsus 1493–1541).

As a consequence of environmental and health consciousness that began in the 1970s and continues unabated to this day, several common minerals have become suspect as agents of cancer and other diseases. Many mine dumps have been placed on the Environmental Protection Agency's (EPA) Superfund list for future cleanup, because some of the minerals contained in these dumps are assumed to be hazardous to human health. Better environmental controls were certainly needed in many of our basic mining, smelting, steel, and chemical industries, and much progress has been made in recent years in reducing industrial emissions. However, some of the newly instituted (and excessively restrictive in the view of many) regulatory controls are the result of an extreme overreaction to perceived health risks that are in fact insignificant or nonexistent.

The very stringent Federal regulations promulgated in the United States are based on a health policy that appears to require a risk-free living environment. The prevailing cancer dogma in the United States espouses the "no threshold" theory of cancer induction. It is stated repeatedly by influential health specialists that, since no one knows the minimum amount of a carcinogen required to initiate the growth of a tumor, it must be assumed that any amount of a carcinogen is unsafe. Thus, the public is led to believe that exposure to just one molecule of a chemical carcinogen can cause cancer. In regard to exposure to asbestos and other mineral dusts, this paradigm becomes "one mineral fiber or particle can kill." What the public has not been told is that simply living on Earth exposes us to innumerable naturally-occurring carcinogens. It should be recognized that naturally occurring carcinogens (as defined by animal experiments) are ubiquitous in foods we eat; we ingest at least 10,000 times more of nature's carcinogens than of man-made carcinogens (Ames et al., 1987). For example, in California's Silicon Valley, 35 water wells were shut down because the water contains concentrations as high as 2,800 parts per billion (ppb) of trichloroethylene (a man-made organic solvent that causes cancer in animals when administered in large doses), even though this water is at least 1,000 times **less** carcinogenic than an equal volume of cola, beer, coffee, or wine; these beverages contain animal carcinogens such as hydrogen peroxide, methylglyoxal, formaldehyde, nitrosamines, and ethyl alcohol. Naturally occurring chemical carcinogens at concentrations of 50,000 ppb or greater are found in such common foods as apples, strawberries, cauliflower, cabbage, peaches, celery, lettuce, potatoes, bananas, carrots, nutmeg, broccoli, and mushrooms (Ames et al., 1987; 1990a). In summary, an extraordinary variety of chemicals, many proven to be animal carcinogens, are found in edible plants; they are part of the plant's natural defense mechanism against pests such as fungi, bacteria, and insects. The same can be said about mineral carcinogens, for we are exposed to asbestos and other mineral-bearing dusts in the ambient environment every day of our lives; some of these dusts can cause lung disease after heavy exposure of long duration in the work place but seldom affect those experiencing low workplace exposure or exposure outside the occupational setting. As we shall see, *the dose makes the poison.*

INTRODUCTION

Ore and gangue minerals that are presently classified by world health organizations as human carcinogens include chrysotile, amosite, crocidolite, anthophyllite, tremolite, and actinolite asbestos; minerals containing arsenic, cadmium, chromium, nickel, and beryllium; radioactive minerals; quartz; tridymite; and cristobalite. Many workers, including asbestos workers, miners, millers, quarry workers, sandblasters, stone masons, tunnel drivers, and agricultural workers, are exposed to mineral dusts from a variety of sources, but particularly through the inhalation of powders arising from the fragmentation of rocks and their constituent minerals in the mine and mill. These workers may develop pneumoconiosis (a disease of the lung caused by the inhalation of foreign particles) and, in some instances, malignant neoplasms (new tissue not serving any necessary physiologic function), particularly lung cancer, as a result of such exposures. These diseases are also found in working populations which process or handle rock and mineral products in secondary capacities, for example in the smelter, foundry, and construction environments (note that workers in these occupations are also exposed to other toxic agents, such as, various metals and synthetic compounds). Although mankind has been exposed to many different types of mineral dusts, there are only a few minerals to which exposure was of sufficient density and duration that definitive medical evidence of injury is documented. In addition to defining the nature of the disease or lesion in the exposed worker through the practice of clinical medicine, epidemiological studies of a group (cohort) of workers exposed to the same type or types of mineral dust should be made so as to clearly describe the causative agent(s) and to define a "dose-response" relationship between the amount of exposure and degree of injury. The basic principles of the science of epi-

demiology are given by Morris (1975) and Shy (1986).

Miners are generally exposed to rock dusts containing several minerals. For example, granite workers are exposed to large amounts of quartz, feldspars, amphiboles, pyroxenes, and micas; coal miners are exposed to quartz, carbonaceous material, and small amounts of other minerals including various clays, carbonates, sulfides, and silicates; taconite iron ore miners are exposed to quartz, iron oxides, carbonates, amphiboles, and various layer silicates; and chrysotile asbestos miners are exposed to the three serpentine minerals (chrysotile, and asbestiform lizardite and antigorite) and to minor amounts of other minerals. These multiple exposures often make it difficult to describe the exact etiology (cause) of a worker's disease. For example, there is still disagreement as to the relative importance of quartz versus carbonaceous compounds to the development of coal worker's pneumoconiosis (black lung) and quartz versus layer silicates (micas, chlorites, etc.) to the origin of slateworkers' pneumoconiosis. In the following I will give a general review of the health effects from occupational exposure to mineral dusts where there is definite clinical evidence of disease that is supported by some epidemiological data defining the origin of the disease. Since workers are often exposed to more than one type of dust, comparative epidemiology and pathology are necessary to isolate the dust or dusts responsible for injury. For example, if workers such as the Gauley Bridge tunnel drivers who were exposed to sandstone dusts composed almost entirely of quartz (Cherniack, 1986) show the same health effects as granite workers, then quartz can be considered to be the important contributor to disease, with the other minerals in the granite (feldspars, amphiboles, micas, etc.) being much less important. As another example, asbestos workers exposed to amphibole asbestos show much greater amount of disease than do those exposed only to chrysotile asbestos.

The health effects of the following mineral and rock dusts will be reviewed: the three commercially important asbestos minerals (chrysotile, amosite, and crocidolite), three polymorphs of silica (quartz, cristobalite, and tridymite), coal (predominantly carbonaceous material plus minor amounts of other minerals), and several silicate minerals (including talc, pyrophyllite, sepiolite, kaolinite, bentonite, attapulgite, sepiolite, palygorskite, mica, vermiculite, and erionite).

THE ASBESTOS MINERALS

Mineralogy of asbestos

Standard references published over the last 50 years list six forms of asbestos (all belonging to the "silicate" group of minerals) that are used in commerce: the serpentine variety is chrysotile, and the amphibole varieties are amosite, crocidolite, anthophyllite, actinolite, and tremolite. Detailed understanding of the structure and chemistry of these minerals came later than their discovery, thus some of the older literature can be confusing with regard to mineral identifications.

Chrysotile [$Mg_3Si_2O_5(OH)_4$], one of the three polymorphs of serpentine, is generally fibrous and is found in serpentinites and kindred rocks; the two other serpentine minerals, lizardite and antigorite, are nonfibrous. About 90 to 95% of the past and present world production of asbestos was or is of the chrysotile type. Amosite [$(Fe,Mg)_7Si_8O_{22}(OH)_2$] is the very rare asbestiform variety of grunerite amphibole. It is mined only in South Africa in metamorphosed banded iron formations and in the past comprised 2 to 3% of the total world production of asbestos. Crocidolite [$Na_2(Fe^{2+},Mg)_3Fe_2^{3+}Si_8O_{22}(OH)_2$] is the asbestiform variety of riebeckite amphibole, and has been mined in only four localities: (1 and 2) in the banded iron formations of the Transvaal and Cape Provinces of South Africa, (3) in the iron formations of the Hammersley Range of Western Australia, and (4) in the Cochabamba area of Bolivia. Only the South African mines are still active. Crocidolite composes about 3% of the world asbestos production. The only other form of asbestos that has been mined on a significant scale is anthophyllite [$(Mg,Fe)_7Si_8O_{22}(OH)_2$] from the Paakkila area of East Finland. With the Finnish mines closed, there is now very little anthophyllite mined anywhere in the world. Minor amounts of tremolite [$Ca_2Mg_5Si_8O_{22}(OH)_2$] and actinolite [$Ca_2(Mg,Fe)_5Si_8O_{22}(OH)_2$] asbestos have been mined but were of little economic importance. However, these two forms of asbestos may be associated as minor contaminants in chrysotile-bearing rocks and other types of ores and as such have been of some concern to those studying the health effects of miners and other workers.

Deposits of asbestos are found in four types of rocks: (a) Type I—alpine-type ultramafic rocks, including ophiolites and serpentinites (chrysotile, anthophyllite, actinolite, and tremolite); (b) Type II—stratiform ultramafic intrusions (chrysotile, actinolite, and tremolite); Type III—serpentinized limestone (chrysotile); and Type IV—banded iron formations (amosite and crocidolite). Type I deposits are by far the most important and account for approximately 90% of the asbestos ever mined. Reviews of asbestos mineralogy and the geological occurrences of commercial asbestos are given by Ross (1978, 1981).

Diseases related to exposure to asbestos fibers

Three principal diseases are related to exposure to one or more of the asbestos minerals. These are: (1) *lung cancer,* which includes cancer of the trachea, bronchus, and lung proper; (2) *mesothelioma,* a cancer of the pleural and peritoneal membranes, which invest the lung and abdominal cavities, respectively; and (3) *asbestosis,* a nonmalignant diffuse interstitial fibrosis of the lung tissue, often leading after long exposure to severe loss of lung function and respiratory failure. The occurrence of lung cancer in asbestos workers is complicated by its strong association with use of tobacco, which leads to considerable difficulty in assigning the relative risks of asbestos exposure to smokers. For complete reviews of asbestos-related disease, the reader is referred to Craighead et al. (1982), Dement et al. (1986), and Skinner et al. (1988).

Lung cancer

There are four major histological types of lung cancer, all of which are prevalent in asbestos workers: *squamous cell carcinoma* is the most prevalent lung tumor followed by *adenocarcinoma, small cell carcinoma,* and *large cell carcinoma,* respectively (Skinner et al., 1988, p. 138). These four tumors account for approximately 85% of all primary neoplasms of the lung. The lung cancers may be generally classified as hilar types (presumed to originate within the bronchial wall) or peripheral types (presumed to originate in the small airways of the lung). Squamous cell carcinomas are of the hilar type, arising from the major and segmen-

tal bronchi. Adenocarcinomas may arise in the hilar or peripheral region of the lung, the latter arising from cells lying distal to the terminal bronchioles. The small cell carcinomas arise in both major bronchi and in the lung periphery. Microscopically, the small cell type may be divided into oat cell and intermediate cell carcinomas, or a combination of the two. Large cell carcinomas are composed of undifferentiated malignant cells showing no special features. Included in this category are tumors showing clear cells or giant cells that tend to arise from the more distal bronchi (Green and Vallyathan, 1986). The prognosis for bronchial carcinoma is poor and survival rates have changed little over the last 30 years. Overall, 5-year survival rates are less than 10%, but those asymptomatic patients who undergo surgical resection of small peripheral carcinoma can expect a 5-year survival rate of 50% (Hodous and Melius, 1986). The distribution of the four main types of lung cancer among asbestos workers is similar to that found in lung cancer patients who were unexposed to asbestos, the only difference is that the cancer tends to appear in the lower lobes of the lung in the asbestos workers (Skinner et al., 1988). In asbestos worker cohorts a significant increase of lung cancer death rate appears 10 to 14 years after first exposure to asbestos and the rate peaks 20 to 25 years later (Selikoff et al., 1980).

Mesothelioma

Mesothelioma is a rare tumor that arises from the mesothelial membrane that lines the pleural, peritoneal, and pericardial cavities. The tumor is usually, but not always, associated with exposure to asbestos, and particularly to crocidolite asbestos. The macroscopic features of pleural mesothelioma are those of a gray-white mass or yellow-gray mass that may cover part of the lung surface, or may completely encase the lung. Microscopically, the mesothelioma tumor can be classified into tubo-papillary, sarcomatous, and mixed types. The tumor spreads along the interlobar fissures and often invades the superpleural portions of the lungs. Direct invasion of adjacent organs, such as the heart, diaphragm, and liver often occur, as well as metastases to local lymph nodes. Peritoneal mesothelioma tends to spread along the peritoneal cavity and to invade the abdominal organs, becoming so widespread that surgery is ineffective in controlling it (Brenner et al., 1981). Mesothelioma generally appears 20 to 40 years after first exposure to asbestos, but once it appears there is a very rapid growth. Death usually occurs within a year after the first symptoms appear. Mesothelioma is difficult to diagnose for the nature of the clinical course of this disease and its location mimics peripheral bronchogenic carcinoma of the lung parenchyma, a tumor that may spread to the pleura. Pleural mesothelioma is approximately five times more common than peritoneal mesothelioma, except in some of the cohorts exposed to asbestos (HEI.AR, 1991).

Asbestosis

Asbestosis, a nonmalignant disease, is a diffuse interstitial fibrosis of the lung tissue resulting from the inhalation of large amounts of asbestos fibers, often leading after long exposure to severe loss of lung function and respiratory or cardiac failure. The disease is often associated with thickening of the pleura (pleural fibrosis), pleural calcification, and the appearance of asbestos bodies (asbestos fibers that are coated with collagen and ferritin). The earliest lesion related to asbestos exposure involves the respiratory bronchioles where deposition of asbestos fibers on the walls of the bronchioles and adjacent air sacs (the alveoli) stimulate macrophage response that promotes deposition of reticulin and collagen in the walls of the bronchioles. As the disease progresses, the fibrosis extends to the walls of the alveoli and eventually the fibrosis leads to the destruction of the alveolar spaces. This fibrous scar tissue causes the lung tissue to stiffen, narrows the airways, and causes reduced efficiency of gas exchange resulting in shortness of breath (dyspnea) and requiring the patient to expend more effort in breathing. Pulmonary hypertension is frequently associated with advanced asbestosis, and resultant *cor pulmonale* (right-sided heart failure) may be the cause of death.

Epidemiological studies of occupational cohorts exposed to asbestos

Three common forms of asbestos, chrysotile, amosite, and crocidolite, were used extensively throughout the industrialized world from the late 1800s to the present. Ross (1984, pp. 58–60) gives historical data on asbestos use in the United States in terms of tonnages imported of the three common forms of asbestos and the commercial applications of each type. The specific use of chrysotile, amosite, and crocidolite is of great importance in understanding the health history of specific asbestos worker cohorts.

The asbestos trades-workers

A very significant increased incidence, in relation to the general male population, of lung cancer, mesothelioma, and asbestosis is found in men who were employed in the "asbestos trades"—the asbestos insulation of pipes, steam boilers, and buildings and the production of asbestos textiles, roofing materials, friction materials, tiles, wall boards, packings, gaskets, etc. These "trades" workers generally worked with chrysotile, amosite, and crocidolite during their working careers. Ross (1984, Tables 3a,b) gives the observed and expected mortality of 21 cohorts of asbestos trades workers. Of these epidemiological studies, 12 are of asbestos factory workers, 8 are of insulation workers, and 1 of asbestos construction workers. These 21 cohorts comprised 50,143 individuals and of these 7,166 were deceased. Death due to lung cancer was reported for 1,198 (16.7%) workers and 402 (5.61%) deaths were reported as due to mesothelioma. There was also very large excess of mortality (over the control cohorts) due to nonmalignant respiratory disease, including asbestosis. These epidemiological studies show that most asbestos trades worker cohorts showed a large excess death due to lung cancer, mesothelioma, and asbestosis. Lung cancer mortality was much greater for smokers than for nonsmokers, but there appeared to be no relationship between smoking and mesothelioma mortality. Of the 21 trades cohorts reported by Ross (1984) two were exposed to mostly crocidolite asbestos and one was exposed only to chrysotile asbestos. The mortality picture of these three cohorts is quite different; a large excess of mesothelioma and lung cancer appeared on the crocidolite-exposed cohorts, whereas in the chrysotile-exposed cohort, lung cancer mortality was similar to the control cohort and there were no mesothelioma deaths. In addition to the studies of cited by Ross (1984), there are additional health reports on workers who produced chrysotile-bearing friction materials and cement products, for example see Newhouse and Sullivan

(1989), Thomas et al. (1982), Gardner et al. (1986), and Ohlson and Hogstedt (1985). These four studies show no significant excess asbestos-related disease in workers exposed only to chrysotile. Table 16.1 gives mortality data for the cohort of Swedish chrysotile asbestos cement workers studied by Ohlson and Hogstedt (1985). An explanation of epidemiological nomenclature and data tabulation, as presented in Tables 16.1, 16.4, 16.5, 16.6, 16.7, and 16.8, is given in the appendix.

TABLE 16.1—Observed (Obs.) and expected (Exp.) number of deaths 1951-58 for the total cohort of 1,176 Swedish asbestos cement workers, exposed only to chrysotile asbestos. Table adapted from Ohlson and Hogstedt (1985).

Cause of death*	Obs.	Exp.	SMR*
All causes	220	214	103
Malignant tumors	44	50	88
Lung cancer	11	9	123
Gastric cancer	1	5.9	17
Intestinal cancer	11	5.9	186
Cancer of the pancreas	2	2.2	90
Diseases of the circulatory system	103	98	105
Diseases of the respiratory tract	13	8.5	153
Violent death	34	27	125

*Standardized Mortality Ratio. SMR = 100(Obs.)/(Exp.).
An SMR of 100 indicates there is no increased risk of disease.

The asbestos miners and millers

Unlike the trades workers, the men working in the mining and milling of asbestos are generally exposed to only one type of fiber; a few exceptions occur in the mining regions of South Africa where some workers were employed in crocidolite, amosite, and chrysotile mines. Epidemiological studies of miners and millers exposed to only one type of fiber permit one to ascertain the human health effects of the different forms of asbestos. Ross (1984, Table 4—Studies A, F, G, H, and J) gives mortality data for the five major epidemiological studies of asbestos miners and millers; one is a cohort of anthophyllite asbestos miners, one is a cohort of crocidolite miners, and three are cohorts of chrysotile miners. The mortality patterns noted on comparing the trades and mines cohorts makes it clear that there are very significant differences in the human health effects of the different asbestos minerals.

Comparative epidemiology of the asbestos-exposed cohorts

Those groups exposed only to chrysotile asbestos experienced much less disease than those who were exposed to amphibole asbestos (most of the trades cohorts were exposed to amphibole as well as chrysotile asbestos). The long term studies of chrysotile miners and millers from the asbestos mining towns of Québec, Canada (McDonald et al., 1980; Ross, 1984, pp. 72–77) show that those experiencing exposures of less than 20 fibers/cm^3 for a working lifetime are not at increased risk of developing asbestos-related disease. A similar mortality profile is reported for the Italian chrysotile miners (Ross, 1984, Table 4). In contrast, epidemiological studies of crocidolite miners and trades workers show that short term heavy exposure or long term moderate-to-light exposure to this type of fiber causes excessive mortality due to lung cancer, mesothelioma, and asbestosis. There are only two mining regions of the world where mesothelioma is a statistically significant cause of death—the crocidolite mining districts of the Cape Province of South Africa and Wittenoom, Western Australia. Study of the trades workers exposed mostly to amosite asbestos show that this fiber too can cause severe disease. In contrast to chrysotile, where exposure thresholds can be prescribed to prevent disease (<10 fibers/cm^3), there is little exposure data to make a similar estimate to protect the crocidolite or amosite worker. Mossman et al. (1990) present data that shows that exposure to chrysotile asbestos in buildings, schools, and homes (including structures with spray-on chrysotile asbestos coatings) is not a health risk. They state "clearly, the asbestos panic in the U.S. must be curtailed."

THE SILICA MINERALS AND AMORPHOUS SILICA

Mineralogy of silica

The six naturally occurring crystalline silica minerals are composed mostly of silicon and oxygen (SiO_2); only small amounts of Al, Fe, Mn, Mg, Ca, and Na are contained in the crystal structures of these minerals. These minerals (generally referred to in the mineralogical literature as the *silica minerals*) are quartz, cristobalite, tridymite, melanophlogite, coesite, and stishovite. Micro-crystalline varieties of quartz include chalcedony, chert, jasper, agate, prase, onyx, and flint. The silica minerals are all composed of SiO_4 tetrahedra, each linked to four like tetrahedra to form the three-dimensional crystal structure. However, the orientation of the tetrahedra are different in each of these six minerals. Quartz is the second most common mineral (after feldspar) in the Earth's crust; for example, common rocks such as granite rocks contain 25 to 40% quartz, shales average 22% quartz, and sandstones 67% quartz (Clark, 1924). Cristobalite and tridymite are much less common than quartz and occur in cavities in volcanic rocks and as products of devitrification of volcanic glasses. Melanophlogite, coesite, and stishovite are very rare minerals and need not be considered here. General reviews on the nature of the crystalline silica minerals are given by Frondel (1962), Ampian and Virta (1992), and USBM (1992a).

In the health reports of SiO_2-exposed workers the mineral names quartz, cristobalite, etc. are seldom used. Instead the term *silica*, *crystalline silica*, or less often (and improperly) *free silica* is substituted for the correct mineral name. In most of the health studies of silica-exposed workers the exposure has been to quartz, but since the mineral name is often not explicitly stated in the reports, we must in this review continue to use the term *silica*. There are very few studies of workers exposed to cristobalite and there are no studies of workers exposed only to tridymite.

The noncrystalline forms of silica *(amorphous silica)* include natural glasses found in various volcanic rocks and synthetic glasses such as fume silica, fiber glass, and mineral wool. Opal is a natural occurring hydrated form of silica; it may be amorphous or nearly amorphous and appears in a variety of geologic localities, especially in hot spring deposits. Opaline materials are also found in diatomaceous earth deposits and in bentonite clays. Many opals have no crystallinity (amorphous) and are sometimes

referred to as amorphous silica or as opal A. Devitrification in some opals may produce very small inclusions of poorly crystallized cristobalite; such material is sometimes referred to as opal C or opal CT. Some crystallites in opal may be disordered structures composed of domains of cristobalite mixed with domains of tridymite. Amorphous silica may, when heated to high temperature, be converted to cristobalite. Dusts composed of amorphous silica (with the exception of fiber glass) have not been implicated with human disease and thus will not be considered further in this review.

Diseases related to exposure to silica dust

Silicosis

Three types of silicosis are defined.

1) *Chronic silicosis* (also referred to as *classical* or *nodular silicosis*) is a progressive obstructive lung disease characterized by the development of fibrogenic tissue. In response to inhalation of quartz particles (and perhaps other forms of crystalline silica) in the median size range of 0.5 to 0.7 μm, macrophages (the cells that scavenge and ingest foreign particulate matter in the lung) generate fibrogenic proteins and growth factors that stimulate the formation of collagen (Craighead, 1988). The hilar lymph nodes tend to be enlarged and silica-containing fibrotic nodules (which form confluent masses 2 to 3 mm in diameter) appear in large numbers in the apical and posterior regions of the upper and lower lobes of the lung. As the silicosis disease progresses, the fibrotic nodules coalesce into larger masses and these may contain the remnants of blood vessels and bronchi. These lesions may vary in size from about 3 mm to a size involving one-third of the lung (Lapp, 1981). Heart or respiratory failure is the ultimate consequence of silicosis.
2) *Acute silicosis* (also referred to as *silicotic alveolar proteinosis*) develops in workers exposed to exceptionally high concentrations of fine particles of silica, usually quartz dust. Here the lining of the airways are damaged and a lipid-rich protein accumulates, obliterating the air spaces. Progressive massive fibrosis appears, usually in the upper regions of the lung, and superinfection by mycobacterial organisms generally occurs. In acute silicosis the lungs are often very heavy and semisolid and microscopic examination on autopsy shows that the air spaces are filled with an amorphous finely granular substance (Craighead, 1988).
3) *Accelerated silicosis* is a condition whereby the progression of disease is intermediate between chronic and acute silicosis. This form of silicosis develops after 5 to 10 years of heavy exposure to crystalline silica dust and is especially seen in sandblasters who were exposed to fine particulates of almost pure quartz. The victim of accelerated silicosis often shows no clinical abnormalities other than breathlessness, but X-ray shows irregular upper zone fibrosis associated with numerous nodules. This form of silicosis is progressive with a continuing decrease of lung function even in the absence of further dust exposure. Death by cardiopulmonary failure within 10 years of onset of symptoms is often the outcome of this form of silicosis (Craighead, 1988).

Silicotuberculosis

There has long been noted an association between silicosis and *tuberculosis* and in the past tuberculosis was a major cause of death of those with silica-damaged lungs; death certificates often listed the cause of death as due to *silicotuberculosis*. For example, in the *1976 Vital Statistics of the United States*, it is reported that there were 215 silicosis deaths (ICD.8, 515.0) and 92 silicotuberculosis deaths (ICD.8, 010); in contrast, only 54 *asbestosis* (ICD.8, 515.2) deaths were listed for 1976. More recently, due to better dust control and chemotherapy, tuberculosis associated with silicosis has much decreased except in the less developed areas of the world. Experimental evidence shows that the presence of silica promotes the growth of *M. tuberculosis* in macrophage cultures. Silicosis appears to modify the progress of tuberculosis but may also change the character of the tuberculosis lesions. Epitheloid cell proliferation, Langhan's giant cell formation, and the lymphocytic reaction seen in the usual tuberculosis patient may be suppressed by the silicosis (Lapp, 1981).

Cancer

Recently, the crystalline silica minerals have been implicated in the pathogenesis of bronchogenic carcinoma. In 1986 a working group of the International Agency for Research on Cancer (IARC) reviewed the scientific data that suggested a relationship between exposure to crystalline silica dust and cancer induction. They published their findings in IARC Monograph 42 (IARC, 1987a), concluding that there was sufficient evidence for carcinogenicity in experimental animals and limited evidence for carcinogenicity in humans. Monograph 42 was followed by IARC's 1987 publication of Supplement 7 (IARC, 1987b) which, upon review of 628 substances, placed the crystalline silica minerals into Group 2A as **probably carcinogenic to humans**. As a result of this IARC decision, the United States Occupational Safety and Health Administration (OSHA) invoked the OSHA Hazard Communication Standard of 1983 to require that **any product** containing any of the crystalline silica minerals in amounts greater than 0.1 wt% be labeled as a possible human carcinogen.

The fibrogenic effects of crystalline silica in animal models are well known (Saffiotti, 1960, 1962, 1986; Reiser and Last, 1979), but there are also a significant number of experimental studies that show that tumors can be produced in rats through the inhalation and intrapleural or intratracheal injection of silica dusts (usually quartz is used in animal experiments). Wagner (1966) and Wagner and Wagner (1972) produced tumors in Alderly Park rats through single intrapleural inoculations of silica. These tumors consisted of malignant histiocytic lymphomas, reticulum cell sarcomas, and lymphoblastic and lymphocytic lymphomas. Holland et al. (1983) noted squamous cell carcinomas and adenocarcinomas in Fischer-344 rats after silica inhalation and in Sprague-Dawley rats after intratracheal instillation of silica.

Saffiotti (1986) in a review of the fibrogenic and carcinogenic activity of silica-bearing dusts on experimental animals, noted that there were significant differences in the pathogenic effects on different animal species. Saffiotti states "the response of the Syrian golden hamster to the introduction of crystalline silica in the respiratory tract (either by inhalation or by intratracheal instillation) is altogether different from that in the rat. In the hamster no respiratory tumors were induced under exposure conditions compara-

ble to those for rats. A consistent association was observed in these two species between the induction of fibrosis and the induction of tumors of the lung." As shown in Table 16.2, the same types of silica that were effectively fibrogenic and carcinogenic in rats failed to produce either type of response in the hamsters.

TABLE 16.2—Tumorgenic and fibrogenic effects of quartz dust on rats and hamsters. Table adapted from Saffiotti (1986).

Test material	Animal species	Route	Tumors	Fibrosis
Quartz (Min-U-Sil)	Rat (Sprague-Dawley)	i.t.* (10 doses, 7 mg each)	yes	yes
Quartz (Min-U-Sil)	Rat (F-344)	Inhalation (24 mos.)	yes	yes
Raw shale (12% quartz)	Rat (F-344)	Inhalation (24 mos.)	yes	yes
Spent shale (8% quartz)	Rat (F-344)	Inhalation (24 mos.)	yes	yes
Quartz (Min-U-Sil)	Rat (F-344)	i.t. (20 mg, once)	yes	yes
Quartz (novaculite)	Rat (F-344)	i.t. (20 mg, once)	yes	yes
Quartz (Min-U-Sil)	Rat (F-344)	Inhalation (24 mos.)	yes	yes
Quartz (Min-U-Sil)	Syrian golden hamster	i.t. (10 doses, 7 mg each)	no	no
Quartz (Min-U-Sil)	Syrian golden hamster	i.t. (3 mg each)	no	no
Raw shale (12% quartz)	Syrian golden hamster	Inhalation (24 mos.)	no	no
Spent shale (8% quartz)	Syrian golden hamster	Inhalation (24 mos.)	no	no
Quartz (Min-U-Sil)	Syrian golden hamster	i.t. (15 doses, 0.7 mg each)	no	no

* i.t., intratracheal instillation

Craighead (1992) questions the validity of such animal experiments in predicting silica induction of cancer in humans. He asks—"Are the neoplasms that develop in rats exposed to silica and asbestos analogous to bronchogenic carcinomas in humans, or are they unique to the laboratory animal and a reaction to chronic irritation and scarring of tissue rather than a neoplastic response to a carcinogen?" But in view of the rat and hamster experiments discussed by Saffiotti, we might ask a question corollary to that of Craighead's: If silica dust levels are reduced to a point were chronic disease (e.g., fibrosis) disappears in a group of workers, will cancer also disappear? Some further insight into this question can be obtained from an epidemiological review of silica-exposed workers.

Epidemiological studies of occupational cohorts exposed to crystalline silica dust

Compared to asbestos workers and coal miners, relatively few epidemiological studies of workers exposed to silica dusts have been completed. However, in the 1980s, perhaps due to the suggestion that silicosis may increase the risk of lung cancer, many new studies were initiated. Early prevalence studies initiated by the U.S. Public Health Service and the U.S. Bureau of Mines (Lanza and Higgins, 1915; Higgins et al., 1917) showed that many miners in the Joplin District of Missouri, who were exposed to high levels of quartz-bearing dusts, suffered from very high rates of nonmalignant lung disease. The first very large and comprehensive study of U.S. hard rock miners exposed to quartz dusts was accomplished by Flinn et al. (1963). This study included over 14,000 employees working at 50 metal mines. The mine dust concentrations (based on 14,480 impinger sample measurements) varied from 0 to 50 million particles per cubic foot (mppcf) and quartz content of the dust varied from 2 to 95%. The medical history, lung function, chest X-rays, occupational histories, and mine dust control methods, were recorded. A strong relationship was found between duration of exposure to silica and prevalence of silicosis. The health of those having less than 5 years exposure was unaffected whereas 60% of those exposed for 30 or more years showed evidence of silicosis. These and earlier studies clearly demonstrated the need to limit exposure to silica-bearing dust and were the basis to institute more comprehensive state and federal regulations to protect the worker.

One of the problems of measuring the effects of silica dusts is that miners, millers, foundry workers, etc. are exposed to a variety of dusts, both natural and man made. Thus, it has been very difficult to mount an epidemiological study of such workers where the degree and types of exposure to dusts, chemicals, radon, etc. are accurately evaluated. More recently, as funds became more readily available and epidemiological techniques greatly improved, scientists have made progress in defining the effects of these more complex workplace exposures. In the following we will review some of the newer studies of silica exposure in specific occupational groups provided below.

Minnesota iron ore miners (magnetite-bearing rock)

Taconite is a term used particularly in the Lake Superior region of Minnesota for certain rock from the Biwabik Iron-formation. A high-grade iron ore concentrate is obtained from commercial grade taconite that contains enough magnetite (Fe_3O_4) to be economically processed by fine grinding and magnetic separation. During the period from 1989 to 1991 about 43 million metric tons of taconite iron ore concentrate were processed each year in Minnesota (USBM, 1992). Taconite is a hard, dense, fine-grained metamorphic rock that contains major amounts of quartz (20–50%) and magnetite (10–20%), in addition to various other mineral constituents including hematite, carbonate minerals, amphiboles (of the cummingtonite-grunerite series), greenalite, chamosite, minnesotaite, and stilpnomelane (French, 1968). The average mineral composition the Biwabik Iron-formation taconite is: quartz (31.9%), minnesotaite (19.3%), magnetite (18.4%), siderite (9.3%), stilpnomelane (8.7%), plus minor amounts of other silicates and carbonates (Lepp, 1972, p. 275).

The mineral content of the dusts emitted from the mining and milling of taconite rock collected at the mine and mill sites of the Reserve Mining Company, near Babbitt and Silver Bay, Minnesota, respectively, are given in Table 16.3. Clark et al. (1980) report that the quartz content of the rock dust for two groups of Reserve miners varied from 0.21 million to 7.74 million particles per cubic foot with a mean of 2.7 mppcf. Based on the quartz content of the rock, the threshold limit value (TLV) for total dust in the work area is given as 5 mppcf. The TLV is the maximum number of airborne quartz particles allowable in the work place by state or federal regulations. The Minnesota taconite miners work in open pits, thus there should be no health effects due to inhalation of radon gas.

TABLE 16.3—Cohort categories by job and extent of exposure to mineral dust at the mine and mill sites of the Reserve Mining Company, Babbitt and Silver Bay, Minnesota. Table adapted from Clark et al. (1980).

Group	Processing activity	Dust composition* Quartz (wt%)	Silicates (wt%)	Magnetite (wt%)
1	Mining, crushing	25–40	25–35	25–40
2	Pelletizing, shipping	2–5	6–25	65–90
3	Railroad, power plant	0	0	0
4	None, school system employees	0	0	0

*Percentages based on total airborne dust data obtained from industrial hygiene surveys conducted by the Trudeau Institute, Saranac Lake, New York.

Analysis of the mortality among men who were employed by the Reserve Mining Company from 1952 to 1976 has been reported by Higgins et al. (1983). This study was initiated in the 1970s in response to suggestions that "asbestos" was released into the air and water during processing of the taconite rock and posed a risk to the miners as well as to the general public. The town and city drinking water (obtained from Lake Superior and into which Reserve had deposited the pulverized waste rock from the mill) was thought to be a particular hazard to the residents. It was alleged that the amphibole in the waste rock (cummingtonite-grunerite series) was "asbestos" and this asbestos would cause gastrointestinal-intestinal cancer through ingestion and lung cancer from inhalation of the air-born particles (a complete review of this controversy and the ensuing court case is given by Schaumburg, 1976; see also Ross, 1984, p. 72–78). The Reserve cohort consisted of 5,751 men, of whom 298 were deceased and 907 had worked for the company for more than 20 years. The men were exposed to respirable dust concentrations from a low of 0.02 mg/m^3 to a high of 2.75 mg/m^3, the modal range being 0.2 to 0.6 mg/m^3. The mineral "fiber" content of the dust was occasionally higher than 0.5 "fibers"/ml in the crushing department, but usually concentrations were much lower (these "fibers" were actually cleavage fragments of cummingtonite and grunerite amphibole). The observed and expected deaths and standardized mortality ratios (SMRs) for all men who had worked more than one year or longer from 1952 to 1976 are given in Table 16.4. Overall mortality was less than expected (SMR=87) when compared to the male mortality in Minnesota, as was mortality from cardiovascular disease, all cancer, respiratory cancer, and selected nonmalignant respiratory diseases including pneumoconiosis. There was no relationship between mortality and lifetime exposure to silica dust, nor was there any suggestion that deaths from cancer increased after 15 to 20 years of latency. No mesothelioma or asbestosis cases that might be suggestive of a risk from asbestos were recorded (it is clear that the amphibole in the taconite rock is **not asbestos**).

A second epidemiological study of Minnesota taconite miners and millers, who were employed by the Erie Mining Company (Erie mine) and the U.S. Steel Corporation (Minntac mine), is reported by Cooper et al. (1992). This study cohort, followed from 1947 through 1988 with a minimum observation period of 30 years for all participants, was composed of 3,431 men of which 1,058 were deceased. Dust levels in the two mines are reported as containing 28 to 40% crystalline silica in one and 20% in the other (Sheehy and McJilton, 1987). Mineral "fiber" counts at the two mines were nearly all below 2 fibers/ml and nearly all fibers were shorter than 5 μm in length (Wylie, 1990). Note that fibers less than 5 μm in length are not considered hazardous and thus are not included in the total count. The total number of deaths (Table 16.5) of these taconite workers was significantly less than expected, SMR=83 (based on U.S. male rates) and 91 (based on Minnesota male rates). SMRs for all cancer, respiratory cancer, diseases of the circulatory system, and nonmalignant respiratory disease were also fewer than expected when compared to both control groups. Slightly elevated, but not statistically significant, SMRs were found for colon cancer, cancer of the kidney, and lymphopoietic cancer. There was one reported case of mesothelioma in a 62-year old worker whose exposure to taconite had begun only 11 years before his death. He had previously been employed as a locomotive fireman and engineer, an occupation where he may have been exposed to amosite or crocidolite asbestos that was used as boiler insulation. Analyses of mortality of the Minnesota iron ore workers with varying lengths of service, exposure to varying amounts of dust, and with a minimum potential latency period of 30 years, provide no evidence to indicate an increased risk of lung cancer or nonmalignant respiratory disease. Thus, there is no evidence to suggest that exposure to quartz, amphibole "fibers," or any other agent has affected the health of these miners.

TABLE 16.4—Selected causes of mortality for men who worked one year or longer for the Reserve Mining Company. Table adapted from Higgins et al. (1983).

Cause of death	ICD, 8th*	Deaths Observed	Expected	SMR**
All causes	000-E999	298	343.65	87
Cardiovascular disease	402, 404, 410–429	112	123.79	90
All cancer	140–209	58	63.38	92
Respiratory cancer	160–163	15	17.94	84
Digestive cancer	150–159	20	17.57	114
Urinary cancer	188–189	3	2.97	101
Genital cancer	180–187	3	3.31	91
Selected nonmalignant respiratory diseases	470–474, 480–486, 490, 491, 493, 510–519	4	6.80	59
Most trauma	E800–E978	76	72.76	104
Motor vehicle accidents	E810–E823	38	31.12	122

*International Classification of Diseases, Eighth Revision.
**Standardized Mortality Ratio, based on white male mortality in Minnesota, 1952–1976.

Iron ore miners (hematite-bearing rock)

The Biwabik iron formation of Minnesota is composed of both hard rock taconite (the present source of most Minnesota iron ore and discussed above) and soft rock iron ore, which formed by late-stage alteration of the primary taconite. Oxidation changed the iron-bearing minerals of the taconite to hematite (Fe_2O_3) and goethite [FeO(OH)]. This soft ore was a primary source of U.S. iron ore in the past and was mined in the area of the Mesabi Range located between the towns of Hibbing and Mesaba. At present only a small amount of the soft ore is mined. The Mesabi ore contains major amounts of iron oxides, and several percent fine-grained quartz as well as minor amounts of other minerals, including kaolinite, sulfides, residual carbonates, and silicates (Gruner, 1946). Lawler et al. (1985) studied a population of 10,403 workers employed by a large steel company engaged in mining hematite

iron ore in St. Louis County, Minnesota. Of these, 4,708 worked under ground and 5,695 worked above ground. The interval of follow-up was from 1937 through 1978 and at the end of this period 2,642 under ground and 2,057 above ground workers were deceased. Quartz content of the ore was 7 to 10% and radon daughter levels were low (<60 pCi/L or 0.3 working levels). This mortality study (Table 16.6) found no excess risk of lung cancer in the total cohort (SMR=94), in the under ground miners (SMR=100), or in the above ground miners (SMR=88), contrary to the reports of excess of this disease in hematite miners from Sweden, France and England. In the Minnesota hematite miners, there was also a deficiency of nonmalignant respiratory disease (SMR=79, total cohort; 72, under ground; 89, above ground). Significant excess mortality due to stomach cancer was observed in both groups of miners when compared to U.S. males, but this excess disappeared, except for Finnish-born miners, when comparison was made to local county rates. Lawler et al. (1985) suggest that the apparent lack of significant radon exposure, under ground smoking prohibition, and absence of under ground diesel fuel may explain why the under ground miners do not show the cancer risk seen in hematite miners of Europe. However, since both groups of miners have very similar health histories (Table 16.6), any additional health effects of under ground mining are not apparent.

TABLE 16.5—Observed and expected deaths by major causes (1948-1988) in taconite miners and millers employed by the Erie Mining Company and the U.S. Steel Corporation who were exposed to taconite mineral dusts for 3 months or more prior to January 1, 1959. Table adapted from Cooper et al. (1992).

Cause of Death (ICD, 7th Revision, 1955)	Deaths		SMR*
	Observed	Expected	
All causes (001–998)	1058	1272.5	83
All malignant neoplasms (140–205)	232	267.7	87
Digestive organs and peritoneum (150–159)	66	70.5	94
Stomach (151)	11	12.0	92
Large intestine (153)	26	23.9	109
Respiratory system (160–164)	65	97.0	67
Bronchus, trachea, lung (162–163)	62	92.2	67
Kidney (180)	12	6.8	177
Lymphopoietic (200–205)	29	25.8	112
All diseases of circulatory system (400–468)	477	575.1	83
Arteriosclerotic heart disease (420)	368	481.8	76
Cirrhosis of liver (581)	24	35.5	68
Nonmalignant respiratory disease (470–527)	55	77.2	71
All external causes of death (800–998)	114	112.3	102
All accidents (800–962)	79	74.4	106
Motor vehicle accidents (810–835)	32	33.4	96
Suicides (963, 970–979)	32	27.3	117
Cause unknown	19		
Number of workers	3,431		
Number of person-years	101,055		
Deaths per 1,000 person-years	10.5		
Adjustment of cause-specific SMRs for missing certificates	+1.8%		

*Standardized mortality ratio.

TABLE 16.6—Observed and expected deaths of total cohort of St. Louis County, Minnesota iron ore (hematite) miners, 1937 to 1978. Table adapted from Lawler et al. (1985).

Cause of death	ICD*	Obs.	Exp.	SMR**
All causes	001–999	4,699	5,058.6	93
All cancers	140–209	854	879.1	97
Respiratory system	160–163	230	242.3	95
Larynx	161	12	13.7	88
Lung	162–163	212	225.8	94
Digestive organs	150–159	329	295.5	111
Tuberculosis	010–019	33	74.0	45
Arteriosclerotic heart disease	410–413	1,783	1,743.3	102
Vascular lesions of CNS	430–438	405	444.7	91
Respiratory disease	460–519	234	295.5	79
Pneumonia	480–486	95	133.1	71
Emphysema	492	59	63.4	93
Asthma	493	8	13.5	59
Digestive system	520–577	178	228.8	78
Cirrhosis	571	69	92.2	75
Genitourinary system	580–629	46	118.9	39
Chronic nephritis	582	19	39.9	48
Symptoms, senility, and ill-defined	780–799	17	43.0	40
Accidents	800–949	297	274.9	108
Motor vehicle	810–827	97	112.2	86
Suicide	950–959	102	87.4	117

*International Classification of Diseases (8th revision).
**Standardized Mortality Ratio.

European iron ore miners

Epidemiological studies have reported excess malignant and nonmalignant lung disease in European iron ore miners—for example, the studies of the iron ore miners of Kiruna, Sweden (Jörgensen, 1984); Kiruna and Gällivare, Sweden (Damber and Larsson, 1985); Cumberland, England (Boyd et al., 1970); and Lorraine, France (Pham et al., 1983). The excess disease in the English and French studies was variously attributed to radon, silica, and iron oxides, but the quality of the studies was not sufficient to define the etiology of the miners' diseases. The recent Swedish reports, however, implicate radon exposure and tobacco use as the important factors in causing excess lung cancer in the Swedish under ground iron ore miners. There were 15 cases of lung cancer (4.6 expected) among the Kiruna miners who were in the past exposed to radon concentration greater than 60 pCi/L or 0.3 working levels (Jörgensen, 1984). The average radon level reported in the study of Damber and Larsson (1985) was 50 pCi/liter. There were 42 lung cancer cases (38 were smokers); the lung cancer risk was calculated by Damber and Larsson to be about 45% from radon exposure during under ground mining and about 80% from smoking. Possible effect of mineral dusts to both cohorts of Swedish miners was not mentioned. Stokinger (1984), in a review of the world literature on exposure to iron oxides in the under ground mining environment, finds that ionizing radiation "might be an etiological factor." He exonerates iron oxides as carcinogenic, both in the mine and factory workplace. Stokinger also brings to question the nature of the disease "siderosis," a pneumoconiosis thought to be caused by inhalation of iron oxide dusts. Nonmalignant disease attributed to these dusts may be due to

exposure to other mineral dusts, especially quartz dusts. Iron oxide particles, being opaque to X-rays, are prominent in chest X-ray photographs of iron ore workers and produce a picture of reticulation without the presence of fibrosis; the patients are essentially symptom free (Stokinger, 1984, p. 129). Among under ground iron ore miners of Cumberland, England there were, over a 20 year period, 42 deaths attributed to lung cancer; 21 deaths from this disease were expected. There was a substantial radon hazard associated with mining of the hematite-bearing ore in Cumberland, for radon in the mine air averaged 100 pCi/liter. In addition, some of the miners developed silicosis, indicating that quartz dust was an etiological factor, as was tobacco use, in promoting disease. It would appear that a combination of high radon levels, cigarette smoking, and quartz-bearing mine dust were cofactors in the increased health risks to these miners.

Granite workers (Vermont)

The granite industry located in the Barre area of central Vermont includes 60 quarrying and manufacturing companies employing more than 1,700 workers (USBM, 1989, p. 490). The average mineral composition (mineral mode) of the Barre granite is as follows (Chayes, 1952): quartz (27.2 vol%), potash feldspar (19.1%), plagioclase (35.2%), biotite (8.1%), muscovite (8.3%), opaque accessories (metal oxides and sulfides, 0.2%), and non opaque accessories (0.8%). This area has a long history of granite quarrying, milling, and carving—occupations that have employed a large portion of the residents of Barre township. For many years, especially in the 1920s and 1930s, there was a great prevalence of silicosis and tuberculosis among the Vermont granite workers. Dust control measures were instituted between 1937 and 1940, so that granite dust levels were reduced from average values of 40 to 60 mppcf to levels below 10 mppcf (Russell, 1941).

Costello and Graham (1986) followed a cohort of 5,414 Vermont granite workers from 1950 through 1982 to determine the causes of mortality. Many of these workers were employed well prior to 1940 when dust levels were very high. Of the total cohort of 5,414 workers, 1,532 were deceased by 1982. Preliminary results show that silicosis, tuberculosis, and lung cancer accounted for 24.4% of the deaths, with silicosis alone accounting for 8% of the deaths. Lung cancer was the cause of death for 102 workers, with an additional 25 lung cancers cited as an "additional cause of death." The Standard Mortality Ratio (SMR) for the total cohort is: silicosis (586.6), tuberculosis (473.8), and lung cancer (104.9). High quartz dust levels did not appear to be a significant factor in the induction of lung cancer in these workers. Costello and Graham (1986) also examined the mortality data for those employed after 1940 when dust levels were greatly reduced. As can be seen in Table 16.7, the health experience for post-1940 workers is superior to that of the control group (SMR<100). The SMRs for silicosis, tuberculosis, and lung cancer are all less than 100 indicating that dust control was effective in minimizing these diseases as important causes of death.

Slateworkers (Vermont and North Wales)

Slate is a compact, fine-grained metamorphic rock and is particularly characterized by a well-defined cleavage—thus its usefulness for such purposes as roofing shingles. The two most important minerals contained in slate are mica (usually muscovite or sericite) and quartz; lesser amounts of chlorite, hematite, carbonates, rutile, pyrite, magnetite, and carbonaceous matter are often found in slate. Dale (1914) gives the following percentages for slate from Ardennes, France: muscovite (38–40%), quartz (31–45%), Chlorite (6–18%), hematite (3–6%), and rutile (1–1.5%). In the United States slate is quarried particularly in Virginia, Maryland, Pennsylvania, New York, and Vermont. About 35% of the total work force of the U.S. slate industry is employed in a 10 x 25 mile area of western Vermont and adjacent New York. Black slate from Benson, Vermont has the following mineral constituents in order of abundance: muscovite, quartz, chlorite, carbonate, rutile, pyrite, and magnetite (Dale, 1914, p. 144). The quartz in this slate is very fine-grained with particles varying in width from 0.013 mm to 0.03 mm. The workers who quarry and process this slate are thus exposed to very fine dust particles.

Craighead et al. (1992) made a detailed mineralogic and patho-

TABLE 16.7—Selected caused of death and Standard Mortality Ratios (SMR) for Vermont granite workers by date of first employment. Table adapted from Costello and Graham (1986).

Cause of death*	Year of first employment									
	Before 1930		1930–1939		1940–1949		1950–1959		1960–1969	
	Obs.	SMR	Obs.	SMR	Obs.	SMR	Obs.	SMR	Obs.	SMR
All causes of death	891	96	209	78	250	70	135	54	38	42
All tuberculosis	116	764	6	137	2	40	0	-	0	-
All malignant neoplasms	152	96	54	105	49	73	28	58	9	54
Respiratory cancer	53	128	21	124	20	89	9	54	5	88
Lung cancer	49	128	20	125	20	95	8	51	5	91
All circulatory system diseases	399	75	83	58	120	66	37	31	9	25
Arterial and coronary heart diseases	266	80	63	64	82	64	25	29	6	22
All respiratory diseases	86	147	17	102	10	49	7	53	1	24
All pneumonia	10	38	2	32	3	38	1	21	0	-
Emphysema	19	166	4	97	5	104	2	60	0	-
Silicosis	34	919	4	421	1	90	0	-	0	-
Suicide	16	132	7	133	7	83	10	129	2	45

*International Classification of Diseases (ICD, 8th revision).

logic examination of lung tissue of 12 western Vermont slateworkers who had developed pneumoconiosis while employed in their trade. Lung tissue study revealed vascular and bronchial lesions, interstitial fibrosis, and macules, the latter scattered diffusely in the lung tissue. These lesions were associated with a variable number of silicotic nodules. X-ray diffraction analysis of four lung tissue residues from low temperature ashing show the ash to be composed mostly of quartz and muscovite. Energy dispersive X-ray spectrographic analysis of the inorganic residues of the other tissue samples showed the presence of major amounts of various aluminum silicates and silica, consistent with the X-ray diffraction results.

Pneumoconiosis in slateworkers has been reported sporadically in many parts of the world. Many of these cases were diagnosed as silicosis clinically; histologic examination of lung tissue revealed a large number of silicotic lesions. In a comparative study, however, Craighead et al. (1992) found that silicotic lesions were more prominent in the lungs of the Welsh slateworkers (Glover et al., 1980) than in those of the Vermont slateworkers. In addition, chest X-rays of the Vermont slateworkers reveal a diffuse interstitial pulmonary disease, not the nodular lesions characteristic of silicosis. Concluding, Craighead et al. (1992) state "slateworkers are exposed to respirable airborne dust that has the capacity to produce a pneumoconiosis that differs from the classic silicosis." It appears that excessive exposure to mica dusts can cause a pneumoconiosis that is somewhat different from silicosis.

Sandblasting

The occupation of sand blasting exposes the worker, unless carefully protected, to large quantities of quartz dust. The health danger of this trade was particularly brought to the attention of medical scientists in the Gulf Coast area of Louisiana when the emerging petrochemical and ship building industries required a large increase in sandblasting to protect metal surfaces. Respirable quartz dust levels were measured at 318 times the threshold limit value (TLV) in samples taken outside protective hoods during sandblasting (Samimi et al., 1974). Hughes et al. (1982) described the health history of a cohort of silicotic sandblasters. There were 83 patients with a mean age of 44 years and an average silica exposure of 11.3 years. Complicated disease, as defined by the presence of large opacities in the lung and distortion of the intrathoracic organs, sometimes accompanied by tuberculosis, was present in 64% of the cohort. By 1982, 11 members of the cohort had died. They further state that accelerated silicosis and the now rare acute silicosis kills many Gulf Coast sandblasters in the 30–40 year age group. In a review of several health studies of those in the sandblasting trades, Jones et al. (1986) state that this occupation can be extremely hazardous, in theory it could be safe, but in practice it is unsafe and should be stopped unless the workers can be adequately protected.

Cohort studies of certified silicotics

The classification of the crystalline silica minerals as "probably carcinogenic to humans" presented in a report of the International Agency for Research on Cancer (IARC, 1987b) has generated much additional concern about the health effects of these minerals. Conventional epidemiological studies of occupational cohorts, such as those presented above, do not show that workers exposed to silica dust have a significantly increased risk of dying of lung cancer. However, in the last 6 years there have been fifteen or more studies of "certified silicotics"—groups of workers within a specific regional area who were occupationally exposed to silica and are or were drawing workers' compensation for diagnosed silicosis. For example, Kurppa et al. (1986) reported on 961 diagnosed cases of silicosis in Finnish men for the period 1935 and 1977. In this Finnish cohort, as expected, there was a very significant excess of nonmalignant respiratory disease (silicosis, tuberculosis, bronchitis, etc.), but there was also a 3-fold excess of lung cancer. Mortality data for this cohort is given in Table 16.8. In a similar study of 2,399 certified silicotics in Switzerland it was estimated that the risk of lung cancer was 2.2 times that expected from national mortality statistics (Schüler and Rüttner, 1986). In addition, Westerholm et al. (1986) found a 2- to 5-fold risk of lung cancer in Swedish silicotics, Zambon et al. (1986) reported a 2-fold risk of lung cancer in silicotics from the Veneto region of Italy, and a 2-fold risk of this disease was reported by Finkelstein et al. (1986) for miners from Ontario, Canada. However, Hessel and Sluis-Cremer (1986) reported on a case-control study of 127 pairs of South African gold miners; the cases were miners who died of lung cancer and the controls were miners who died of some other cause. A carefully documented history of smoking habits for cases and controls was made. The results of this study indicated that there was no association between lung cancer and silicosis.

TABLE 16.8—Mortality data for 961 Finnish men diagnosed as having silicosis. Table adapted from Kurppa et al. (1986).

Cause of death	Obs.	Exp.	SMR*
Total deaths, all causes	667	335.2	199
Cancer, all sites (ICD 140–209)	122	68.9	177
Lung (trachea, bronchus, pleura) (ICD 162)	80	25.6	312
Esophagus, stomach, colon-rectum (ICD 150–154)	21	19.9	106
Larynx (ICD 161)	-	1.4	-
Oropharynx (ICD 140–149)	1	0.8	128
Leukemia, lymphosarcoma and other neoplasms of lymphatic and haemapoietic system (ICD 200–207)	6	3.7	161
All other sites	20	19.5	103
All cardiovascular disease (ICD 390–458)	203	183.1	111
All pulmonary disease (ICD 460–519)	165	23.4	704
Pneumoconiosis (silicosis) (ICD 515)	120	0.0	infinity
Pneumonia, influenza (ICD 470–474, 480–486)	13	10.2	127
Chronic bronchitis, emphysema, and asthma (ICD 490–493)	27	5.6	478
Other respiratory disease	5	7.5	66
All renal disease (ICD 580–593)	7	5.9	117
Accidents, violent deaths (ICD800–999)	20	23.9	84
Tuberculosis (ICD 010–012)	130	17.6	738
All other causes	20	24.2	83

*Standardized Mortality Ratio

Because many of the conventional cohort studies do not show a statistically strong risk of lung cancer in silica-exposed workers, it is difficult to interpret the studies of silicotics that do suggest a relationship between silicosis and lung cancer. There is a difficulty in properly evaluating the contribution of tobacco use to disease within an occupational cohort if smoking habits are unknown or if the regional or national populations used as controls do not have the same smoking habits as the occupational cohort. For example, cigarette smoking was prevalent among the U.S. male blue collar trades workers and commonly 75 to 85% of the workers smoked. On the other hand, only about 50% of the total male population of the United States were smokers. If 80% of the men in a particular occupational cohort smoke, but who have no other health risks, on the average 8.5% will die of lung cancer. For a "control" cohort in which 50% smoke, on the average 5.5% will die of this disease (Ross, 1984, fig. 2). If the occupational cohort of 80% smokers is erroneously assumed to be composed of 50% smokers, as in the control cohort, an over estimate of lung cancer mortality for smoking habits would be calculated (8.5x100/5.5=155). The 55% excess lung cancer would thus be attributed to some type of occupational hazard rather than to smoking habits.

Other problems with interpreting the studies of silicotics is that they are not true cohorts; that is, they are not well defined occupational groups because the men usually come from several industries. Also, the types and lengths of exposure to dusts, chemicals, radon, etc. were generally unknown in these studies. Craighead (1992) makes the important observation that cancer in silicotics may be a tissue response to lung fibrosis. This is exactly what Hughes and Weill (1991) observed in their study of 839 men employed in the manufacture of asbestos cement products. They reported that no excess of lung cancer was found among workers without radiographically detectable lung fibrosis, whereas those with positive X-ray evidence of fibrosis had a significantly increased risk of lung cancer. Hughes and Weill conclude, "because detectable asbestosis is not likely to result from current occupational and general environmental asbestos exposures, the prevention of the effect of exposure on lung fibrosis is likely also to prevent the excess risk of lung cancer."

COAL

Mineralogy

Several dozen minerals are reported to occur in coals, although most occur only sporadically or in trace amounts. Most of the minerals in coal fall into four groups: (1) aluminum silicates, (2) carbonates, (3) sulfides, and (4) silica, mainly quartz. Aluminum silicates commonly found in coal are clay minerals, including montmorillonite, illite-sericite, kaolinite, halloysite, chlorite, and mixed-layer clays. Principle sulfide minerals are: pyrite, marcasite, galena, chalcopyrite, pyrrhotite, arsenopyrite, and millerite. Carbonate minerals include calcite, dolomite, siderite, ankerite, and witherite. In a study of 65 Illinois coals, Rao and Gluskoter (1973) found the mineral matter content to vary from 9.4 to 22.3 wt%, with 15% being an average value. Harvey and Ruch (1986) give the following variation in mineral content of Illinois Basin coals: quartz (1.2 to 3.1 wt%), calcite (0.9 to 2.3%), pyrite (2.8 to 5.9%), and clay minerals (6.6 to 11.2%). Extensive reviews of the mineralogy and petrology of coal are given by Gluskoter et al. (1981) and Stach et al. (1982).

Diseases related to exposure to coal dust

Coal workers' pneumoconiosis

Coal workers' pneumoconiosis is caused, most importantly, by fine-grained coal dust composed of carbonaceous material. One form of this disease, *simple coal workers' pneumoconiosis*, is characterized by the coal macule, a lesion 1–4 mm in diameter and composed of dust laden macrophages that form a mantel around the first and second order respiratory bronchioli. In lung sections the macules appear as black areas; the smaller macules are usually circular, the larger ones are more irregular and often stellate. The cause of simple pneumoconiosis is considered to be an overwhelming of normal lung particle clearance mechanisms by the large amounts of coal dust entering the respiratory passages. The fibrosis and emphysema may be due to the damaging effects of enzymes released by the macrophages (Merchant et al., 1986; Lapp, 1981).

A second type of lesion, a nodular lesion similar to that seen in the chronic silicotic, also occurs in coal workers' pneumoconiosis. These nodules are gray or black in color, are often rounded, but may have irregular prolongations penetrating the surrounding tissue and may be associated with scar emphysema. The major difference between the macular and nodular lesions is that the fibrous protein collagen is present in the latter. The nodular lesions, which are thought to have developed from the macules, contain bundles of collagen that are usually arranged in an irregular pattern. This arrangement of collagen is useful for distinguishing these lesions, formed by an accumulation of carbonaceous particles, from the fibrotic nodules of the silicotic where the collagen is concentrically arranged. Merchant et al. (1986, p. 354–361) present optical photomicrographs of lung sections that contain macules and nodules caused by the inhalation of carbonaceous dust and sections that contain silicotic nodules caused by inhalation of quartz dust. *Complicated coal workers' pneumoconiosis* or *progressive massive fibrosis* is characterized by extensive fibrosis of the lung tissue; often the nodular lesions coalesce so as to replace a major portion of the upper lobes of the lung. There is a strong association between tuberculosis and progressive massive fibrosis, particularly in the coal miners of South Wales (Merchant et al., 1986).

The onset of simple coal workers' pneumoconiosis, which takes many years to develop, is related to the amount and duration of coal dust exposure; however, unlike silicosis there is no convincing evidence of progression of this disease in the absence of further exposure (Lapp, 1981). Complicated coal workers' pneumoconiosis is a more serious condition in that it is generally progressive even after exposure to coal dust ceases. Severe cases of "black lung" disease lead to airway obstruction, the coughing of large volumes of inky black sputum; death occurs in about 10 to 15 years as a result of cardiopulmonary failure.

Coal workers' silicosis

Coal workers' lung disease may be complicated by exposure to other minerals associated with coal, but particularly from exposure to quartz dust in coal and (more importantly) from quartz in the country rock enclosing the coal beds. Evidence for silicosis has been found particularly in those who are primarily engaged in surface drilling of quartz-bearing country rock (Lapp, 1981). Merchant et al. (1986) observed silicotic nodules in the lungs of

some coal workers (their fig. II-29), but they state that good evidence is lacking that quartz dust plays a significant role in coal miners' disease.

Epidemiological studies of occupational cohorts exposed to coal dust

Historical accounts of miners' "black lung" were reported as early as 1831 and since then many studies have been published which described coal workers' pneumoconiosis and its associated morbidity and mortality. Merchant et al. (1986) review twenty-five of the mortality studies and thirteen morbidity studies of coal miner cohorts which were published between 1936 and 1981.

Pneumoconiosis mortality and morbidity

Coal workers' pneumoconiosis (CWP), often referred to as "black lung" or "anthracosilicosis," is prevalent in coal miners as presented in a vast literature. This is a chronic and incapacitating disease due to progressive loss of lung function. There is a clear dose-response relationship between the severity of lung disease and the number of years working under ground—the surrogate for dose. Jacobsen et al. (1971) give the probability of developing simple CWP over a 35 year working life with mine dust levels varying from an average of 1 to 7 mg/m^3. For a dust level of 6 mg/m^3 the probability of developing simple to more severe pneumoconiosis is approximately 10%. Bronchitis and associated respiratory infections are associated with CWP and seriously impaired lung function is often found in coal workers who have advanced pneumoconiosis, especially progressive massive fibrosis. One of the largest and most extensive mortality studies of coal miners is that of Rockette (1977). He examined a cohort of 22,998 miners, a 10% sample of the qualified members of the United Mine Workers of America Health and Retirement Fund (UMWA cohort). The major findings of the study are given in Table 16.9. The overall Standard Mortality Ratio (SMR) is 101.6 and is not significantly different from the control value of 100. The SMR's for influenza (189.6), emphysema (143.7), asthma (174.9), and tuberculosis (145.5) were significantly elevated. However, major cardiovascular diseases were not elevated in this cohort (SMR=95.2).

Cancer mortality

Overall cancer mortality in the UMWA cohort of Rockette (1977) was slightly less than that of the control (the 1965 total male U.S. population) with an SMR of 97.7. There was a small but statistically insignificant increase in stomach cancer and lung cancer. A study by Enterline (1964) of U.S. coal miners gives an elevated SMR for lung cancer (1.92), however many other health studies of coal miners do not demonstrate that lung cancer is a significant factor in coal miner mortality (Merchant et al., 1986, Table II-20; Bridbord et al., 1979, Table 1). The report by Bridbord et al. (1979) reviews nine epidemiological studies of coal miners; four cohorts show an increased risk of stomach cancer, one shows an increased risk of prostate cancer, one shows an increased risk of lung cancer (Enterline, 1964, cited above) and six show a decreased risk of lung cancer. Rosmanith and Schimanski (1986) report that bronchial cancer seldom develops in cases of severe coal workers' pneumoconiosis in coal miners from the Czechoslovakian and West German coalfields (Ostrava and Ruhr). Breining (1986) reports that during the last 10 years he examined the lung tissue of more than 1,000 diseased coal workers from the Ruhr area of West Germany who had anthracosilicosis; only five cases were found with silicotic scar carcinomas. As yet, there does not appear to be compelling evidence that coal workers have a significant risk for increased lung cancer incidence.

TABLE 16.9—Observed and expected deaths for cohort of 22,998 U.S. coal miners for selected causes. Data from Rockette (1977).

Cause of death	Observed	Expected	SMR*
All causes	7,628	7,506.1	101.6
All malignant neoplasms	1,223	1,252.2	97.7
Benign and unspecified neoplasms	14	14.4	97.5
Major cardiovascular diseases	4,285	4,501.2	95.2
Bronchitis	27	31.5	84.8
Influenza	28	14.8	189.6
Pneumonia	217	232.3	93.4
Emphysema	170	118.3	143.7
Asthma	32	18.3	174.9
Tuberculosis	63	43.3	145.5
Syphilis	16	13.1	122.3
Other infective and parasitic disease	13	17.6	74.1
Diabetes mellitus	64	110.2	58.1
Peptic ulcer	42	58.7	71.6
Cirrhosis of the liver	64	104.9	61.0
Cholelithiasis, cholecystitis, and cholangitis	22	16.7	132.0
Nephritis and nephrosis	42	46.2	91.0
Accidents	408	283.0	144.2
Suicides	81	81.3	99.6
Homicides	30	26.1	115.1
Ill-defined causes	162	86.2	187.9
All other causes	625	459.5	136.0

*Standardized Mortality Ratio.

THE SILICATE MINERALS (OTHER THAN ASBESTOS)

Mineralogy of the silicates

Silicates form the largest chemical class in the mineral system and they comprise a large portion of the Earth's crust. The silicates are structurally and chemically complex and are characterized by the presence of essential amounts of tetrahedrally coordinated silicon. These minerals also have essential amounts of one or more other elements that are found in various coordination schemes within the crystal structures. In addition to Si, the most common elements found in the silicates are Na, K, Ca, Al, Mg, and Fe. Important mineral groups within the silicate class include feldspars, pyroxenes, amphiboles (including amphibole asbestos), micas, chlorites, serpentines (including chrysotile asbestos), the aluminum silicates (sillimanite, kyanite, andalusite), talcs, clay minerals, zeolites, nephelines, garnets, humites, olivines, and epidotes. Workers, particularly miners and millers, are exposed to the dusts of many of these minerals as they process various types of rocks to extract particular mineral commodities. Some of these silicate minerals are mined for a particular use; examples are talc,

wollastonite, kaolinite, attapulgite, amphibole and serpentine asbestos, bentonite, mica, vermiculite, and zeolites. Exposure to a few of the silicates (especially to asbestos) by occupational groups has been great enough to produce clinical evidence of disease and to permit epidemiological studies to be made. The silicates most implicated with disease (chrysotile and amphibole asbestos have already been discussed) are reviewed below.

Health effects of selected silicate minerals

Talc and pyrophyllite

Talc [$Mg_3Si_4O_{10}(OH)_2$], which commonly forms by hydrothermal alteration of ultrabasic rocks rich in magnesium, is mined in many countries and processed in numerous manufacturing industries for use in paints, ceramics, rubber products, roofing materials, paper, insecticides, cosmetics, and pharmaceuticals. In the United States 1,172,000 metric tons of talc was mined in 1989 (Virta, 1991). There have been numerous health studies of talc workers (Gamble, 1986; IARC, 1987a,b), but the results of these studies have often been ambiguous. Talc workers exposed to talc dust may exhibit symptoms of *talc pneumoconiosis*, sometimes referred to as *talcosis*, as well as bronchitis, emphysema, abnormal chest X-rays, and increased risk of tuberculosis. Clinically, talc workers' pneumoconiosis resembles silicosis or asbestosis and since the talc exposed worker may have been exposed to quartz and other silicates, including chrysotile, anthophyllite, and (or) tremolite asbestos, the true etiology of this disease is difficult to describe. One study (Hogue and Mallette, 1949) reported that rubber workers exposed to high levels of talc dust show no disease and thus they concluded that talc dust was benign. However, examination of lung tissues of some of the persons exposed to talc show diffuse pleural thickening, fibrous adhesions, pleural plaques, and large fibrotic masses (Gamble, 1986). The several epidemiological studies of talc workers are in disagreement over whether talc causes lung cancer. Excess cancer may be related to underestimation of smoking habits or to previous exposure to commercial asbestos. Rubino et al. (1976) studied 1,514 miners and millers from the Piedmont in Italy who were exposed to asbestos-free quartz-bearing talc dust and found elevated pneumoconiosis (described as silicosis) and associated tuberculosis. Lung cancer mortality was much less than expected. A study of New York talc miners and millers (Brown et al., 1979) indicated that there was excessive lung cancer (SMR=270); the SMR for nonmalignant lung disease was 277. Stille and Tabershaw (1982) studied nearly the same cohort of New York miners and millers as examined by Brown et al. (1979) and found a lesser risk of lung cancer (SMR=157). The epidemiological studies of talc workers thus far completed have not proven that talc is a human carcinogen, because the cohorts studied were not large enough to produce statistically significant data, smoking habits are not well defined, and the workers were often exposed to other mineral dusts that could produce disease. There is no doubt, however, that heavy exposure to talc dust can cause nonmalignant respiratory disease.

Pyrophyllite [$Al_2Si_4O_{10}(OH)_2$] has similar uses as talc but is produced in much smaller quantities (U.S. production was 81,000 metric tons in 1989; Virta, 1991). Little health data have been obtained on pyrophyllite workers. Hogue and Mallette (1949) report no apparent disease in pyrophyllite-exposed rubber workers.

The clay minerals, micas, and vermiculite

Kaolinite [$Al_2Si_2O_5(OH)_4$], a common clay mineral (also known as "china clay"), is mined for many uses and particularly for ceramics and filler in papers, paints, and plastics. The kaolinite-bearing rock (referred to as "kaolin") generally contains variable amounts of other minerals including quartz. In 1989 the United States produced 8,973,669 metric tons of this mineral (Ampian, 1991). Kaolinite workers who have been heavily exposed to kaolinite dust may develop pneumoconiosis—sometimes referred to as *kaolinosis.* Simple kaolinosis is similar to other mineral dust pneumoconiosis that are characterized by the presence of rounded opacities in the lung. Complicated kaolinosis is similar to progressive massive pneumoconiosis of the coal worker (Gamble, 1986). If the kaolinite worker is also exposed to silica dust, as often may be the case, his lung disease may appear to be typical silicosis. An increased lung cancer risk has not been reported in kaolinite worker cohorts.

Bentonite is a soft plastic rock composed primarily of silicates belonging to the montmorillonite group of clay minerals having the general composition [$(Na,Ca)_{0.33}(Al,Mg)_2Si_4O_{10}(OH)_2 .nH_2O$]. Bentonite deposits are generally associated with other minerals including very fine-grained quartz and amorphous silica. Bentonite is used as drilling mud, as a bleaching clay, as a foundry sand bond, as an iron ore pelletizer, and for many other uses. In 1989 the United States mined 3,112,365 metric tons of bentonite (Ampian, 1991). A study of a random sample of Wyoming bentonite workers revealed that 44% had silicosis, including 2 cases of progressive massive fibrosis (Phibbs et al., 1971). Silica content (which included both quartz and cristobalite) of the Wyoming bentonite clays ranged from 0 to 24%. Surveys of bentonite processing plants showed that silica comprised between 5 and 10% of the mineral matter in the airborne dust, and the TLV for silica was exceeded 3 to 10 times (Gamble, 1986).

Fuller's earth is a general term for a soft fine-grained earthy rock that contains large amounts of hydrous aluminum silicates belonging to the montmorillonite and (or) palygorskite clay mineral group as well as quartz and other minerals. Palygorskite has the composition [$(Mg,Al)_2Si_4O_{10}(OH).nH_2O$] and is chemically and structurally similar to attapulgite and sepiolite. Fuller's earth has many uses, for example, in drilling mud, as an adsorbent and bleach, and as a paint thickener. In 1989 the U.S. production of fuller's earth was 1,881,511 metric tons (Ampian, 1991). There have been a few reports of pneumoconiosis among fuller's earth workers.

The common minerals of the mica group are muscovite [$KAl_2(AlSi_3O_{10}(OH)_2$] and phlogopite and biotite [$K(Mg,Fe)_3AlSi_3O_{10}(OH)_2$]. The micas have numerous uses, particularly in electrical devises and as fillers in plastics, tiles, etc. Mica can cause pneumoconiosis in workers exposed to mica dust from various occupational categories. However, health studies are confounded by the fact that the mica dusts often contain other minerals including quartz.

Vermiculite [$(Mg,Ca)_{0.35}(Mg,Fe,Al)_3(Al,Si)_4O_{10}(OH)_2.nH_2O$] is essentially a hydrated mica with water molecules located between the silicate layers. On heating, this mineral expands to form a light weight product so useful as insulation, a soil conditioner, and filler for many products. Vermiculite workers, particularly those working in the enclosed areas where the product is expanded and in loading areas, were exposed to elevated dust levels. Pulmonary effusions have been reported in some workers. At

the Libby, Montana vermiculite mine and mill an excess of lung cancer (SMR=2.45) and 4 deaths from mesothelioma were reported among the workers (McDonald et al., 1986). The excess lung cancer and mesothelioma incidence at Libby may be related to the fibrous amphibole that is associated with the vermiculite ore. McDonald et al. (1988) studied the health history of South Carolina vermiculite miners and millers who had a low exposure to fibrous amphiboles. They report that there was no evidence for excess respiratory cancer or any cases of mesothelioma, but there was a slightly elevated incidence of nonmalignant disease.

Zeolites

Among this large group of hydrated aluminum silicates there are several fibrous varieties, one of which (erionite) is implicated in respiratory disease in residents of the towns of Karain and Tuzköy located in the Cappadocia region of Turkey. Erionite [$NaK_2MgCa_{1.5}(Al_8Si_{28}O_{72}).28H_2O$] is prevalent in the local ash-flow tuffs and interbedded lacustrine deposits that contain reworked tuffs. Mesothelioma is a very common disease in these towns and is practically unknown in other areas of Turkey. In Karain, over the period 1970 to 1978, there were 76 deaths, of which 50 were due to pleural mesothelioma (Saracci et al., 1982). The mineral implicated in this epidemic is extremely thin and fibrous (comparable to crocidolite asbestos in dimensions) and is found in the rocks, soils, and air samples of the two towns. Such fibers have also been reported in the lung tissues of the diseased residents (Rohl et al., 1982). Wagner et al. (1985) report that intrapleural inoculation of rats with fine-fibered erionite from Oregon produced mesothelial tumors in 100% of the animals, a much larger percentage than found in rats similarly treated with crocidolite asbestos. A second group of rats inoculated with "Karain rock fiber" from Turkey showed a 95% tumor incidence. There is good reason to believe that very thin (<0.5 μm) and long (>10 μm) fibers of some of the silicate minerals and certain inorganic compounds have the potential to cause mesothelioma, lung cancer, and asbestosis when exposures are significantly elevated.

DISCUSSION

In reviewing the health effects of a large variety of mineral dusts, we have seen examples of extreme injury to workers exposed to high levels of certain mineral dusts. Crocidolite asbestos and erionite appear to be particularly potent in inducing mesothelioma both in man and animals. Very high dust levels of all forms of asbestos cause excessive respiratory cancer and nonmalignant lung diseases, although chrysotile asbestos is much less potent in this respect than amphibole asbestos. Quartz, one of the most common minerals in the crust of the Earth, has probably during the course of human existence caused more morbidity and mortality than any other mineral species, including the asbestos minerals; and yet most people are exposed to this substance everyday of their lives without measurable effect. Those living in dry desert-like areas of the world and those employed in agricultural activities are exposed to relatively high levels of mineral dusts including quartz-bearing dust. Do these people suffer from lung disease? From a review of the literature, apparently not much, although there are scattered references in the medical literature for "silicate pneumoconiosis" in the agricultural occupations. Sherwin et al. (1979) report of lung inflammation and fibrosis in California farm vineyard workers and Zolov et al. (1967) noted "pleural asbestosis" in Bulgarian farmers, although these farmers may have been exposed to asbestos-containing soils. Bazas et al. (1985) report of pleural calcification in the lungs of rural villagers living in northwest Greece, but state that there was no evidence of any lung dysfunction; the agent responsible for this apparently benign condition was not identified. We also have good scientific evidence that lower exposure to mineral dusts that are dangerous at high levels, does not cause significant disease. For example, moderate exposures to chrysotile asbestos (<20 fibers/cm^3) by Québec miners and millers show no increased risk of cancer or respiratory disease. Minnesota taconite miners and millers, after exposure to mine dust averaging 2.7 mppcf or 0.2 to 0.6 mg/m^3, did not experience any silica related disease even though the dust contained significant amounts of quartz. However, there is ample reason to believe that **any mineral dust** when inhaled in large enough doses will cause nonmalignant respiratory disease and in some instances cancer. Thus, one should not be surprised that workers heavily exposed to dusts from serpentinite, granite, taconite, slate, coal, bentonite, fuller's earth, diatomaceous earth, and so forth may show a greater than expected morbidity and mortality.

The causes of cancer

In context with the above review of mineral-related disease, it is informative to discuss the work of Bruce Ames and coworkers. They studied the toxic nature of synthetic chemicals as compared to that of natural chemicals, the latter representing the vast bulk of chemicals to which humans are exposed. They find that in high-dose animal tests, a large proportion of both natural and synthetic chemicals are carcinogens, mutagens, teratogens, and clastogens (Ames et al., 1990a). About 50% of the chemicals tested, both natural and synthetic in origin, are carcinogenic in high-dose animal tests. For example, of the 52 natural pesticides that occur in plants and which were tested in animals, 27 were proven to be carcinogenic (Ames et al., 1990b). Ames and Gold (1990) consider why so many animal tests are positive for cancer induction. They postulate that the administration of chemicals at the maximum tolerated dose (MTD), as is done in standard animal cancer tests, causes increased cell death that in turn promotes increased cell division and thus increases cell proliferation (mitogenesis). Mitogenesis in turn increases the rates of mutagenesis, the process of producing mutations in genetic material (DNA) that is particularly enhanced during cell division (see also, Cohen and Ellwein, 1990). An increased rate of mitogenesis and mutagenesis causes an increased rate of carcinogenesis in the test animals. Ethyl alcohol is a human carcinogen and if it were invented today the Food and Drug Administration would never allow it to be marketed. However, epidemiological studies show that alcoholic drinks cause an increased risk of liver cancer only if enough is consumed over the years to so damage the liver that cirrhosis develops. Alcohol is not a significant human carcinogen provided one keeps consumption low enough to prevent liver disease. A similar observation is noted with viral infections. For example, hepatitis B virus can produce chronic hepatitis causing massive liver cell damage and much increased cell division, thus promoting an increased risk of liver cancer. Human papilloma virus 16 is a major risk factor for cervical cancer whose main effect on cells is to increase cell division (Ames and Gold, 1990, p. 7775).

Human cohorts that are exposed to mineral dusts but are free of non malignant lung disease (as noted in the Minnesota iron ore miners exposed to quartz-bearing dusts and the chrysotile asbestos-exposed cement workers) do not show an increased risk of lung cancer. In fact, the epidemiological data of Hughes and Weill (1991) indicate that asbestosis is the **precursor** to lung cancer. Similarly, silicosis may also be a precursor to respiratory cancer, for it is observed that some silicotic cohorts have an increased risk of this disease (Kurppa et al., 1986). As mentioned above, in studies of asbestos-induced lung disease in animals after long term exposure to high concentrations of asbestos dusts, it is observed that cancer appears only in those animals that first develop lung fibrosis. Craighead (1992) suggests that the formation of lung tumors in mineral dust-exposed animals is a reaction to the chronic irritation and scarring of tissue. In a review of inhalation experiments on animals exposed to quartz dust, Saffiotti (1986) states "if the fibrogenesis mechanisms observed in rats are indeed linked to the carcinogenic response in that species, it is interesting to consider that the human lung produces a marked fibrogenic response to silica comparable to rats." It thus appears that the mechanisms of cancer induction by high dose exposure to chemicals, as proposed by Ames and Gold (1990), can be extended to high dose exposure to mineral dusts.

In 1959 U.S. congressman Delaney introduced an amendment to the "Food, Drug and Cosmetics Act" that in part requires that food not contain **any amount** of a carcinogen. At the time this amendment was passed, naturally occurring carcinogens were not known to exist, but now through the work of Ames and many others we know that naturally formed carcinogens are ubiquitous in our environment. If the Delaney amendment is applied to all chemical carcinogens, natural and synthetic, little food could be sold legally. With respect to minerals, we are now in the unfortunate position of having to label **anything** that contains more than 0.1% quartz (rock products, beach sand, cement, fillers, etc.) as a possible human carcinogen. If the Delaney amendment is applied to mineral dusts we might be hard pressed to mine anything for a myriad of minerals and inorganic substances are proven to be carcinogenic when administered to animals in high doses. Common sense requires us to discard the idea of a "no threshold" for cancer induction and look for another way to control materials that may cause human disease. In examining the epidemiological studies of those exposed to mineral dusts, it is noted that if there is no significant evidence of nonmalignant respiratory disease, cancer risk is very low. In cohorts where there is significant excess of nonmalignant lung disease there is often observed an elevation in respiratory cancer mortality. If nonmalignant respiratory disease is eliminated from the workplace through adequate dust control, then lung cancer will become an insignificant health problem. We do see that *the dose does make the poison.*

APPENDIX (EPIDEMIOLOGY)

Epidemiological mortality studies involved the determination of the cause of death of a specially selected group of individuals—the "exposed cohort." Such cohorts are generally composed of workers who were be exposed a substance that presents a particular health risk—for example, asbestos trades workers exposed to asbestos and miners exposed to quartz dust. Cause of death must be determined by accurate death certificates, ideally based on autopsy. The specific disease is numerically coded to the specifications of a particular revision of the *International Classification of Diseases* (IDC). For example, mortality due to respiratory cancer (includes cancer of the trachea, bronchus, and lung) is coded as 162; death due to silicosis is coded as 515.0 (IDC, 8th Revision). Not all epidemiological studies report the codes in addition to the disease type. The mortality profile of the exposed cohort must then be compared to a second group, the "control cohort." Ideally, the control cohort should be as nearly identical to the research cohort as possible—in age distribution, ethnicity, sex, dietary and smoking habits, and other social characteristics, but with the exception that the control group was not exposed to the risk factor under study. Generally, however, the control cohort is not specially selected on these criteria, but rather is composed of the total male (or female) county, state, or national population. Use of such a control cohort can introduce significant error, particularly in the case of lung cancer, if the smoking habits of the control cohort differ from those of the exposed cohort. A *Standardized Mortality Ratio* (SMR) is calculated for each particular cause of death by the relation SMR=100 (observed deaths in the exposed cohort)/(expected deaths in the control cohort), with suitable statistical adjustments for age distribution and age at death. The statistical accuracy of a particular mortality study is of course dependent on the number of deaths within each disease category; SMRs for small numbers of deaths have little meaning. Generally, SMRs less than 150 are not considered as significant. SMRs greater than 200, especially when there are a large number of deaths in a particular category, show that the workers were at significant risk to some substance. As an example, a cohort of North American asbestos trades workers exposed to three types of asbestos dust has a respiratory cancer SMR (IDC 162) of 452, indicating an extreme occupational risk (Ross, 1984, Table 3a, study, IV).

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