CHAPTER EIGHTY-FOUR

Talc

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1.0 Talc

Talc is a natural mineral of the general chemical composition $Mg_3Si_4O_{10}(OH)_2$ (1). The composition varies widely from one geological deposit to another and even within the same deposit. The main component, crystalline hydrated silicate of magnesium, is usually found as plates but rarely may also be found as fibers. In many talc deposits, other silicates such as the amphiboles, tremolite, and anthophyllite, as well as serpentines, antigorite, lizardite, and even chrysotile, may be present. This chapter discusses the health effects associated with talc without asbestos contaminants. Asbestos contaminants are to be distinguished from an asbestiform of talc that is covered in this chapter. However, a number of studies have been conducted to determine the health effects of talc in which the purity of the material was not known. The discussion of asbestos is covered in Chapter 10.

1.0.1 CAS Number

[14807-96-6]

1.0.2 Synonyms

Hydrous magnesium silicate; steatite talc; soapstone

1.0.3 Trade Names for Talc

Agalite; Alpine talc USP; Asbestine; B13 (mineral); B9; Beaver White 200; CCRIS 3656; CI 77718; CP 10-40 and 38-33; Crystalite CRS 6002; Desertalc 57; EINECS 238-877-9; EX-IT; Emtal 500, 549, 596, and 599; FW-XO; Fibrene C 400; Finntalc C10, M05, M15, P40, and PF; French chalk; HSDB 830; hydrous magnesium silicate; IT Extra; LMR 100; Lo Micron talc USP, bc 2755; MP 12-50, 25-38, 40-27, and 45-26; MST; magnesium silicate talc; magnesium silicate, hydrous; Micro Ace K1 and Ace L1; Micron White 5000A, 5000P, and 5000S; Microtalco IT Extra; Mistron 139, 2SC, RCS, Star, frost P, super frost, and vapor; Mussolinite; NCI-C06008; nonasbestiform talc; nonfibrous talc; Nytal 200 and 400; P3 (mineral); PK-C; PK-N; Polytal 4641 and 4725; Sclerosol; Snowgoose; Steawhite; Supreme; Supreme dense; TY 80; Talcan PK-P; Talcron CP 44-31; Talcum; UNII-7SEV7J4R1U (2).

1.1 Chemical and Physical Properties

Talc has a hardness of 1 on the Mohs scale of hardness; a density of 2.58–2.83; is commonly composed of thin tabular crystals up to 1 cm wide; and is usually massive, fine-grained, and compact. It is also found as foliated or fibrous masses or in globular stellate groups (3). Although usually platy, talc less commonly occurs as asbestiform fibers.

Talc is a natural single-phase mineral and in pure form is composed of 31.88% magnesium oxide, 63.37% silicon dioxide, and 4.75% water (Figure 84.1). Formation is said to have occurred by hydrothermal alteration of rocks rich in magnesium and iron and low-grade thermal metamorphism of siliceous dolomites (4). It is an odorless, solid material that varies in color depending upon the minerals that are found with it. Talc may be pale green to dark green or greenish gray; brownish; blue; pink; black; translucent; white to grayish white; or pearly, greasy, or dull.

The term talc in the mineralogical connotation denotes a specific rock-forming mineral of the sheet silicate category. However, when talc is referenced in the industrial or commercial sense, it may represent a varied mixture of associated minerals that have physical properties similar to the mineral talc (5).

Patty's Toxicology, Sixth Edition. Volume 5, Edited by Eula Bingham and Barbara Cohrssen.

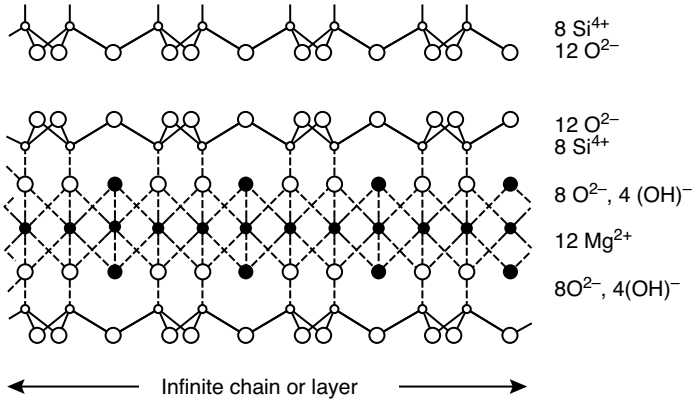

Figure 84.1. Molecular structure of pure talc mineral (1).

Soapstone (steatite) is a form of talc with chlorite and amphibole such as anthophyllite or tremolite.

A number of minerals are commonly associated with talc deposits: calcite, dolomite, magnesite, tremolite, anthophyllite, antigorite, quartz, pyrophyllite, micas, and chlorites (5).

The most common type of talc is of ultramafic origin, formed by the alteration of serpentinite to talc carbonate rock. It is common in Vermont, Quebec, and Finland. Talc of mafic origin, found in Virginia, North Carolina, and Georgia, is formed by hydration of mafic rock to serpentinite, followed by alteration of the serpentinite to talc carbonate. It is usually contaminated with chlorite and silica. Talc of metasedimentary origin is formed by hydrothermal alteration of the dolomitic host rock by silica-containing fluid. This type of talc is commonly found in Montana and Australia. It is usually quite pure and quite white. The fourth type of talc is of metamorphic origin, where siliceous dolomite is first converted to tremolite or actinolite and then partially converted to talc. The New York and California deposits are of this type (1).

1.2 Production and Use

Talc-containing rocks were first used in prehistoric times as utensils and ornaments. The term talc was first applied to this mineral in 869 AD. The abundance of talc, the ease with which it can be mined, and its properties have made it an important industrial mineral.

Talc is typically extracted from open-pit mines, sorted by contact and brightness, and milled using compressed air, steam, and grinding. Talc may be coated or heat treated depending on its use. It may be sold in bags, in bulk as a pellet, or as liquid slurry.

Talc is an extremely versatile mineral that has found a number of uses despite the relative impurity of most of the ores mined. Except for pure steatite grades, hand-picked, platy, cosmetic talcs, and a few products from wet processing plants, industrial products are mixtures of many minerals. The principal uses are as an extender and filler pigment in the paint industry; for coating and filling paper; in ceramic products; and as filler for plastics and roofing products. Miscellaneous uses of talc include binders and fillers in textiles; fillers in integral, foamed, latex rubber backings for carpets, rugs, and parquet hardwood floor panels; filler for upholstery fabric backing and draperies; lubricant in extreme temperature range greases; corrosion proofing composition; 10–15% of dry fire extinguishing powders; loading and bleaching materials such as cotton sacks, cordage, and rope string; cereal polishing; bleaching agents; food odor absorber; floor wax; water filtration; leather treatment; joint fillers and grouts; insecticides; shoe polishes; welding rod coatings; printing inks; encapsulant for acceleration testing artillery shells; coatings for iron ore pellets in direct reduction processes; source of magnesium in plant foods; pigment in white shoe polishes and white glove cleaners; dusting powder for salami; admixture for certain concretes; polishing medium for peanuts, gunpowder grains, and turned wooden articles; to prevent sticking of bottle, rubber, and candy molds; and to impart a finish to wire nails and leather (6).

For example, much of the talc used by the ceramic industry is a mixture of platy talc and tremolite; most of the talc used by the rubber, plastic, and paper industry is at best about 90% talc and the balance is dolomite, calcite, serpentine, chlorite, actinolite, iron- and manganese-containing minerals, and carbonaceous material.

In 2008, the U.S. Geological Survey reported that the worldwide production of talc was 2,240,000 metric tons and that of soapstone was 560,000 metric tons. China produced another 2,200,000 metric tons but it is not specified how much was talc and how much was pyrophyllite, an aluminum silicate ($A1Si_2O_5OH$) that is slightly harder than talc but has similar properties to talc. The United States (Montana, Texas, Vermont, New York, California, and West Virginia in order of production), Finland, France, and India are the largest producers after China. The major mine in New York State where

many of the earlier health studies of talc were performed closed at the end of 2008. In 2008, the total production in the United States was 645,000 metric tons. Consumption in decreasing order for the most common uses of talc was ceramics (31%), paper (21%), paint (198%), roofing (8%), plastics (5%), rubber (4%), and cosmetics (2%) (7).

1.3 Exposure Assessment

The NIOSH Method P&CAM #355 is recommended for determining workplace exposures to talc. This method involves drawing a known volume of air through a MCE filter. Then the sample is ashed and analyzed by X-ray diffraction (8). However, if the sample contains asbestos, several other methods are recommended. These include NIOSH Method 7400 that uses optical counting of asbestos fibers, NIOSH Method 7402 that uses transmission electron microscopy (TEM) for analysis of the sample, or NIOSH Method 9000 that uses X-ray diffraction for analysis. A method recommended for determining the presence of asbestos in talc is NIOSH Method 9002 that analyzes the sample by polarized light microscopy (PLM) (9).

1.4 Toxic Effects

1.4.1 Experimental Studies

1.4.1.1 Inhalation Studies. Inhalation studies have had technical problems due to the lack of methods to determine accurately the amount of talc inhaled by exposed animals.

1.4.1.2 Acute Toxicity. Rats exposed to a "very dense" cloud of talc, whose particle size was less than 5 μm, for 3 h per day up to 12 days may have died because of suffocation (10).

Injection of high but not low doses of talc in the pleural space of rabbits caused systemic inflammatory response with the presence of neutrophils and macrophages in lung tissue, the mediastinum, pericardium, and liver (11). Also after pleural injection, there was a significant increase in blood vascular endothelial growth factor levels and a transient increase in the white blood cell count and the percentage of neutrophils (12).

Injection of talc in the anterior chambers of rabbit eyes caused pseudohypopyon, which persisted for 2 weeks, but disappeared by 4 weeks without the development of granuloma, while in monkeys there was the development of glaucoma (13).

1.4.1.3 Chronic and Subchronic Toxicity. None of a group of rats exposed to 30–383 mg/m^3 of "technical/pharmaceutical grade" talc for 6 h per day, 6 days a week for up to 9 months died as a specific consequence of exposure. However, they developed chronic inflammatory changes, including thickening of the pulmonary artery walls and eventually emphysema (14).

Hamsters exposed by inhalation to 8 mg/m^3 respirable "baby talc" for up to 150 min per day, 5 days a week for 300 days showed no negative effects (15, 16). Hamsters exposed to respirable cosmetic grade talc dust showed no difference in incidence, nature, or pathological lesions compared to those observed in a group of untreated animals (17).

Heavy dosing of rats by inhalation of talc caused severe dyspnea. However, no histological change was observed within 20 days, and talc particles were trapped by alveolar macrophages (10).

Minimal fibrosis was observed in rats exposed by inhalation to 10.8 mg/m^3 of Italian talc (grade 00000, ready milled, mean particle size 25 μm) for 3 months; this did not change during the postexposure period. The rats exposed for 1 year had minimal to slight fibrosis, which increased to moderate fibrosis within 1 year after exposure ceased (18).

However, Syrian golden hamsters exposed to 8 mg/m^3 of talc aerosols for up to 150 min per day, 5 days per week for 30 days showed no histopathological change in the lungs, heart, liver, renal tissues, stomach, or uterus (15, 16, 19).

As part of a carcinogenesis study, conducted by the National Toxicology Program (NTP) (20), groups of 22 male and 22 female rats were exposed and examined for interim pathology or pulmonary function after 6, 11, 18, and 24 months and for lung biochemistry and cytology after 24 months. Absolute and relative lung weights of male rats exposed to 18 mg/m^3 were significantly greater than those of controls at the 6-, 11-, and 18-month interim evaluations and at the end of the lifetime study, whereas those of female rats exposed to 18 mg/m^3 were significantly greater at the 11-, 18-, and 24-month interim evaluations and at the end of the lifetime study. Lung talc burdens of male and female rats exposed to 6 mg/m^3 were similar and increased progressively from 6 to 24 months. Lung talc burdens of females exposed to 18 mg/m^3 also increased progressively from 6 to 24 months, whereas those of males exposed to 18 mg/m^3 remained about the same after 18 months. Lung burdens were generally proportional to exposure concentrations at each interim evaluation. It was also noted that a concentration-related impairment of respiratory function increased in severity with increasing exposure duration. The impairment was characterized by reductions in lung volume, lung compliance, gas exchange efficiency, and nonuniform intrapulmonary gas distribution.

Similarly, the NTP studied groups of 39 or 40 male and 39 or 40 female mice who were examined after 6, 12, and 18 months of exposure for interim pathology, lung biochemistry, and cytology. Lung talc burdens of mice exposed to 6 mg/m^3 were similar between males and females and increased progressively from 6 to 24 months, except for males at 18 months. The lung talc burdens of mice exposed to 18 mg/m^3 were also similar between the sexes at each interim

evaluation. Although the talc burdens of males and females increased substantially from 6 to 24 months, the values at 12 and 18 months were similar. Generally, lung burdens of mice exposed to 18 mg/m^3 were disproportionately greater than those of mice exposed to 6 mg/m^3, suggesting that clearance of talc from the lung was impaired to a greater extent in mice exposed to 18 mg/m^3 than in mice exposed to 6 mg/m^3 (20).

Pickrell et al. studied the lung deposition and effects of inhalation exposure in F344/Crl rats and B6C3F$_1$ mice. The rats were exposed to aerosols containing 2.3, 4.3, or 17 mg/m^3 talc for 6 h a day, 5 days a week for 4 weeks. The mice were similarly exposed to 2.2, 5.7, or 20.4 mg/m^3 talc. The animals were killed 24 h after the last exposure. Talc accumulated in the lungs in a dose-dependent manner. The average talc lung burdens in rats ranged from 0 to 0.72 mg per gram of lung tissue and in mice from 0 to 1.0 mg/g. No exposure-related lung lesions were seen other than slight diffuse increases in the number of free macrophages containing talc particles within the alveolar spaces of rats and mice exposed to the highest doses (21).

Guinea pigs that received single 200 mg intraperitoneal injections of one of the several industrial grade talcs (up to 52% talc, up to 82% tremolite, and traces of quartz) developed nodules consisting of macrophages and giant cells after 10 days on the parietal surface that became smaller after a 15-month period. Fibroblastic proliferation was pronounced in the early phases (22).

There were no treatment-related deaths of rabbits injected daily for 2 weeks with 100 mg of talc in saline (23), or of rabbits that received 50 mg injections of talc two times a week for 10 weeks, or of rats that received injections of talc over a 9-week period, total dose 100 mg (24).

Rats that received a single 50 mg/mL intratracheal injection of talc in water suffered a 79% mortality rate. Subsequently, it was found the rats could tolerate the dose if they were given two 25 mg/0.5 mL injections at weekly intervals (25). Rats injected intratracheally with 25 mg tremolitic talc/mL of water had a 40% mortality rate. In another study of rats, granulomas at the injection site were common, and one small pulmonary adenoma was observed 2 years after the injection of 20 mg of Italian talc into the right pleural cavity, but no other relevant pathology was observed in the lungs (18). Albino rats that received an intraperitoneal injection of approximately 400 mg of talcum powder of the type used on surgical gloves exhibited typical granulomas and numerous foreign body giant cells identified during laparotomy 6 months later (26). Hamilton et al. studied the effects of talc on the ovaries of Sprague–Dawley rats. Animals were sacrificed at 1, 3, 6, 12, and 18 months. They concluded that changes in the ovarian surface may be related to the direct effects of talc or may be due to the buildup of high concentrations of steroid hormones in the distended bursa (27).

Two out of 14 chinchillas given five 40 mg intratracheal injections of talc in saline died (28). Chinchillas that received a single or several 40 mg intratracheal injections of "purified" talc in saline exhibited chronic pulmonary irritation, proliferative pneumonia, giant cell granulomas, and adjacent metaplasia of the alveolar epithelium. The hyperplastic cells subsequently transformed into cuboid cells that formed a continuous lining of the affected alveoli and finally acquired an adenomatous appearance (28).

Cytotoxicity of equal intensity was reported for seven different talc specimens applied *in vitro* to mouse peritoneal macrophages that were exposed to seven different specimens of talc (only one of which contained amphibole) (29).

1.4.1.4 Pharmacokinetics, Metabolism, and Mechanisms. Seven different types of talc were administered *in vitro* to mouse peritoneal macrophages. All of the talcs caused cytotoxicity as determined by the release of lactate dehydrogenase and beta-glucuronidase. All of the talcs were of high purity, except for one talc that contained high amounts of chlorite (30).

Mice that received a sterile subcutaneous injection of talc were studied by measuring the incorporation of radioactive leucine and glucosamine into liver and plasma proteins and the development of talc granuloma at various intervals between 2 and 528 h after injection. Incorporation into plasma proteins indicated a biphasic response with a marked increased incorporation into the perchloric acid insoluble fraction at 21 h, a return to normal values at 45 h, and a similar marked increase into the perchloric acid soluble fraction at 45 h with a gradual return toward normal values. The response was dependent upon the amount of talc injected (31).

Using radioactive tracer techniques in rats, mice, guinea pigs, and hamsters, no intestinal absorption or translocation of ingested talc to the liver and kidneys was detected (32).

In hamsters, the deposition, translocation, and clearance of talc were followed by giving them a single nose-only inhalation exposure to 40–75 mg/m^3 neutron-activated talc for 2 h. High cosmetic talc was used, consisting of 95% platy talc. Alveolar deposition was approximately 6–8% of the inhaled amount. The biological half-life of talc deposited in the alveoli was 7–10 days, and the alveolar clearance was basically complete 4 months after exposure. No translocation of talc to liver, kidneys, ovaries, or other parts of the body was found (15, 33).

Rats that were exposed to aerosols of Italian talc retained 2.5, 4.7, and 12.2 mg per rat following exposures for 3, 6, and 12 months, respectively. These levels were roughly proportional to the cumulative exposures (18). In rats exposed to 2.3, 4.3, and 17 mg/m^3 of respirable talc for 6 h per day, 5 days a week for 4 weeks, the amounts retained in the lung at the end of exposure were 77, 187, and 806 μg talc per gram of lung (34).

In the NTP 2-year study of rats exposed to talc, male rats exposed to 6 mg/m^3 talc had a significant increase in beta-glucuronidase and polymorphonuclear leukocytes after 24 months. Males exposed to 18 mg/m^3 had significant increases in beta-glucuronidase, lactate dehydrogenase, alkaline phosphatase, and total protein in bronchoalveolar lavage fluid. All exposed females had significantly increased alpha-glucuronidase, lactate dehydrogenase, alkaline phosphatase, total protein, and polymorphonuclear leukocytes; females exposed to 18 mg/m^3 also had significantly increased glutathione reductase. Viability and phagocytic activity of macrophages recovered from lavage fluid were not affected by talc exposure. The total lung collagen was significantly increased in rats at both exposure concentrations after 24 months, whereas collagenous peptides in lavage fluid and the percentages of newly synthesized protein from females, but not males, were also significantly increased at the 6 or 18 mg/m^3 levels. In addition, lung proteinase activity, primarily cathepsin D-like activity, was significantly greater in exposed males and females. Rats exposed to talc also had significant increases in collagenous peptides and acid proteinase in lung homogenates (20).

In the NTP study of mice exposed to talc, increases in total protein, beta-glucuronidase, lactate dehydrogenase, glutathione reductase, total nucleated cells, and polymorphonuclear leukocytes in bronchoalveolar lavage fluid were observed primarily in mice exposed to 18 mg/m^3, although some parameters were also increased in mice exposed to 6 mg/m^3. The amounts of collagenous peptides in lavage fluid and total lung collagen were increased in male and female mice exposed to 18 mg/m^3. Acid proteinase activity, principally cathepsin D-like activity of lung homogenate supernatant fluid, was also significantly increased in mice at the 18 mg/m^3 exposure (20).

Phillips et al. studied the effects of tritium-labeled talc fed to male albino Wistar rats, female LACA mice, female guinea pigs, and intravaginally instilled in large white female rabbits. In rats, 75% of the single dose was excreted in feces in 24 h; after 96 h, 95.8% of the dose had been eliminated. Kidneys of rats that received multiple doses had less than 0.02% radioactivity. In the guinea pigs, nearly all of the radioactive dose was excreted in 96 h, and less than 0.2% was in the urine. For the mice, all of the radioactivity was found in the GI tract and feces, and none in other tissues. In rabbits, after 72 h, radioactivity was found only at the site of a single installation and at the site of administration (35).

1.4.1.5 Reproductive and Developmental Toxicity. Talc produced nonspecific abnormalities in chicken eggs at an incidence similar to that induced by thalidomide and sulfadimethoxine (36).

No teratological effects were observed in hamsters, rats, mice, or rabbits after oral administration of the following doses of talc: 1600 mg/kg body weight to rats on days 6–15 of gestation, 1600 mg/kg body weight to mice on days 6–15 of gestation, 1200 mg/kg body weight to hamsters on days 6–10 of gestation, and 900–mg/kg body weight to rabbits on days 6–18 of gestation (37).

Talc was not mutagenic to *Salmonella typhimurium* TA1530, *his* G46, or *Saccharomyces cerevisiae* D3 *in vitro* or in host-mediated assays in mice given 30–5000 mg/kg body weight (38).

In human W138 cells treated with talc at 2–200 μg/mL, chromosomal aberrations were not induced nor were dominant lethal mutations induced in rats following oral administration of 30–5000 mg of talc/kg body weight (38).

Single 20 mg intraperitoneal injections of talc plus 2 mg of particulate prednisolone acetate in saline into mice induced significant numbers of multinucleated giant cells within 48 h. Neither compound alone induced this response. The multinucleated cells arose by cell fusion, and the resultant polykaryons exhibited severe chromosomal abnormalities. Prednisone in combination with talc also elicited the formation of multinucleated giant cells. Polykaryons were not observed when talc was injected in combination with cortesone acetate, cortisone, or testosterone isobutyrate (39).

1.4.1.6 Carcinogenesis. There was no enhancement of unscheduled DNA synthesis or sister chromatid exchanges in *in vitro* cultures of rat pleural mesothelial cells (40).

In the NTP 2-year inhalation study of talc in rats and mice, male and female F344/N rats were exposed to aerosols of 0, 6, or 18 mg of nonfibrous talc/m^3, free of SiO_2 and asbestos minerals, for 6 h per day, 5 days per week for up to 113 weeks (males) and 122 weeks (females). Groups of B6C3F_1 mice were exposed similarly for up to 104 weeks. These exposures resulted in concentration-related chronic inflammation, cell proliferation, and fibrosis in the lungs of both male and female rats, concentration related impairment of respiratory function that increased in severity with duration of exposure, a significant increase in lung tumors in female but not male rats of the high-exposure group, and a significant increase in adrenal medulla pheochromocytomas in both male and female rats. The mice showed limited chronic inflammation and no increased cell proliferative, fibrotic, or tumorigenic responses in their lungs (20).

Neither intraperitoneal nor intrathoracic administration of talc in rats, mice, and hamsters produced an increase in the incidence of tumors, including mesothelioma (41).

The IARC evaluation of studies in experimental animals is that there is limited evidence for carcinogenicity of talc not containing asbestos or asbestiform fibers. IARC's overall evaluation is that inhaled talc not containing asbestos is "not classifiable as to its carcinogenicity in humans" (group 3) (41). This is in contrast to inhaled talc containing

asbestos that is classified as "carcinogenic to humans" (group 1) (42).

1.4.2 Human Experience

Merewether was one of the first to observe that rubber tire workers exposed to French chalk showed "diffuse interstitial fibrosis" by chest X-ray and nothing more than "peribronchial increase in the fibrous tissue" after 30 years. Duration of exposure ranged from 10 to 32 years (6).

Subsequent radiological, pathological, and epidemiological investigations have confirmed the occurrence of lung fibrosis, which is referred to as talc pneumoconiosis. Table 84.1 summarizes reports on nonmalignant respiratory morbidity and Table 84.2 summarizes reports of the earlier mortality studies. More recent studies are described below.

1.4.2.1 Radiology. Radiological findings of individuals with talc pneumoconiosis are typically diffuse small nodules, which may progress to large opacities. Large opacities with talc pneumoconiosis unlike in silicosis, which is typically in the upper lobes, may be throughout the lung. Reports of pleural changes are probably secondary to asbestos contaminants and are not seen after exposure to asbestos-free talc (74). The risk of developing radiographic changes is related to cumulative exposure but may occur years after short-term exposure (75).

1.4.2.2 Pathology. The pathological findings of talc pneumoconiosis are fibrosis, which may be diffuse or more localized and adjacent to vessels and bronchi, foreign body granulomas and foreign body giant cells containing birefringent needle-shaped particles, and ill-defined nodules, which contain little collagen but have birefringent needle-shaped particles (76, 77). The pathology of talcosis from i.v. drug use can be distinguished from talc pneumoconiosis from inhalation by the histology and the larger particle size of the talc particles in the lung after i.v. drug abuse (78).

1.4.2.3 Clinical Findings. Health effects found in workers who have inhaled talc vary, depending upon the composition of the talc inhaled. When silica exposure is significant, the lesions resemble those in silicosis. When fibrous materials such as tremolite are present, diffuse interstitial fibrosis and pleural thickening, changes of asbestosis have been seen.

Respiratory symptoms of talc pneumoconiosis are similar to the other pneumoconioses and may range from being asymptomatic to severe debilitating respiratory impairment. Similarly physical findings may be absent or in advanced disease the individual may be cyanotic, have clubbing and signs of cor pulmonale. Restrictive, obstructive, or mixed changes may be found on pulmonary function testing.

Two epidemiology studies have reported an association with cumulative dust exposure and radiological and pulmonary function changes (79, 80). A recent study did not find an adverse effect on respiratory function in workers with exposure levels below 2 mg/m^3. The lack of effect in this study may have been due to the absence of an effect below 2 mg/m^3 or insufficient latency from onset of exposure or inadequate sample size to show an effect at exposure below 2 mg/m^3 (80).

Unusual presentations include a case report of bronchiolitis in a Finnish talc miner (81), a case of tuberculosis from the atypical *Mycobacterium xenopi* organism complicating talc pneumoconiosis in a Belgian talc miller (82), and hypercalcemia in a former worker with talc pneumoconiosis who was exposed to talc while making molds for porcelain insulators (83).

1.4.2.4 Mortality Studies. Over 20 mortality studies have been published on talc-exposed cohorts. Nine of these studies were on talc miners from upstate New York where the mined mineral was contaminated with asbestos minerals (i.e., 25% talc and 40–60% tremolite) (84). Results of studies on upstate New York talc miners have identified cases of mesothelioma and increased mortality from both lung cancer and nonmalignant respiratory disease (67, 68, 85–92). However, a follow-up case-control study of this cohort only identified a dose–response relationship with mortality from nonmalignant respiratory disease but not for lung cancer (88). Similarly, an exposure response study of this cohort also only identified a dose–response relationship with mortality from nonmalignant respiratory disease but not for lung cancer (92).

A significant increase in mortality has been consistently found for nonmalignant respiratory disease in all talc-exposed cohorts, especially pneumoconiosis and obstructive lung disease (80, 92–94). In the two studies, where a dose–response evaluation was performed there was an association between cumulative exposure to talc and nonmalignant respiratory mortality (92, 93).

There have been 12 mortality studies of talc-exposed workers of non-upstate New York talc miners (73, 93–103). The one study of talc-exposed workers that showed a statistical increase in lung cancer mortality where it was clear that there were no asbestos or other confounding exposures was of talc miners and millers in Vermont. Three hundred ninety-two workers from five facilities in Vermont who had worked at least 1 year from 1940 until 1970 were followed up until the end of 1975. Two lung cancer deaths were observed among millers when 1.96 were expected and 5 lung cancer deaths were observed among miners when 1.15 were expected (SMR $= 4.35$, $p < 0.05$) (96).

Table 84.1. Morbidity Studies of Older Nonmalignant Respiratory Disease

Occupation	Focus of Study	Length of Exposure	Exposure Concentration	No. of People	Findings	Date (Reference)
Mining and milling	Talc pneumoconiosis		17–1672 mppcf of Georgia talc	66	Of 33 patients exposed to high concentrations of dust, 22 had pneumoconiosis of varying severity. Persons with low exposures showed no signs of pneumoconiosis.	1935 (43)
Mining and milling	Talc pneumoconiosis	15 to > 30 years	Tremolitic talc; 6–5000 mppcf in mines; 20–215 mppcf in milling	221	Fibrosis was found in 32 people. All of them had been exposed for at least 10 years. The highest incidence, 40.6%, occurred with those who had been exposed for 15–19 years. Of the eight workers who had worked > 30 years, six had fibrosis.	1943 (44), 1947 (45)
Rubber worker	Talc pneumoconiosis	37 years	Norwegian or Canadian varieties of talc	1	At autopsy, both lungs were found to be moderately pneumoconiotic.	1949 (46)
	Talc pneumoconiosis	28 years		1	X-ray revealed two, dense, homogeneous, opaque masses with round irregular contours in the upper portion of the pulmonary field.	1950 (47)
Millers	Talc pneumoconiosis		Talc containing tremolite	32	Talc plaques observed in all but one case. Six of the 11 electrocardiographic configurations were abnormal. Four persons died who ranged in age from 48 to 84 years.	1955 (48)
Soapstone workers	Talc pneumoconiosis	16–60 months		8	Extent of disease varied with the time of exposure. Clinical signs included cough, mucopurulent sputum with talc bodies, dyspnea on exertion, and weakness.	1955 (49)
Rubber workers	Talc pneumoconiosis	19 years average		12,000	During TB screening, 16 cases of symmetrical, nodular foci of the lungs without swelling of the hilar glands, 9 cases of definite talcosis (19 years exposure), and 7 cases of slight talcosis (12 years exposure) were found.	1959 (50)

(*continued*)

Table 84.1. (*Continued*)

Occupation	Focus of Study	Length of Exposure	Exposure Concentration	No. of People	Findings	Date (Reference)
Lead casters	Talc pneumoconiosis	15–39 years		7	One death from cor pulmonale and talc pneumoconiosis after 15-year exposure. Chest X-rays of all patients showed the presence of scattered opacities throughout the lungs that coalesced to form larger masses with indefinite margins and uneven density.	1960 (51)
Miners	Talc pneumoconiosis	> 20 years		60	All had pneumoconiosis; those with greater exposure had more severe disease.	1963 (52)
Miners	Talc pneumoconiosis	> 12 years		260	First radiographic signs of pneumoconiosis appeared in 89% after 12 years; after 22 years, it was 100%.	1963 (53)
Grinders	Talc pneumoconiosis	10–20 years		25	Incidence of pneumoconiosis was 52% after 10–20 years.	1963 (53)
Rubber workers	Talc pneumoconiosis	Unknown		72	Exhibited linear pneumoconiosis in 11% of workers.	1963 (52)
Miners/Millers	Talc pneumoconiosis	24 years average		6	The most frequent pathological change was diffuse fibrosis containing macrophages with absorbed dust particles. Also found were diffuse or localized emphysema and granulomatous formation made up of focal areas of epithelioid and foreign body giant cells.	1963 (54)
Miners/millers	Pulmonary function	23 years average	Talc admixed with tremolite, anthophyllite, and free silica: > 50 mppcf	20	Changes in pulmonary function indicate a restrictive or obstructive breathing disorder. No consistent correlation exists between degree of functional lung impairment and clinical symptoms or X-ray findings.	1964 (55), 1964 (56)
Miners/millers	Pulmonary function	> 10 years	62.3 mppcf	43	Predominant symptoms were dyspnea, cough, basilar crepitations, and clubbing. Poor correlation between impairment and clinical and X-ray results.	1965 (57)

Electrical fitter	Talc pneumoconiosis	15 years	Pharmacy talc	1	Thoracic radiography revealed large nodular trabecular images with fairly abundant rounded spots in both lungs.	1966 (58)
Rubber workers	Talc pneumoconiosis	20–40 years		5	Granular pneumoconiosis resulting from long-term or intense exposures.	1968 (59)
Milling	Talc pneumoconiosis	<5 to >25 years	$>$MAC for talc	50	Sixteen cases of talc pneumoconiosis diagnosed.	1970 (60)
Miners/Millers		16.2 years	Commercial talc with tremolite and anthophyllite	39	One worker showed a chest X-ray consistent with pneumoconiosis. Talc containing tremolite and anthophyllite may be less fibrogenic than chrysotile or amosite at the same exposure levels.	1973 (61)
Rubber workers	Respiratory function			80	Workers exposed below 20 mppcf showed a greater prevalence of productive cough and positive criteria for COPD than control workers. Workers with <10-year exposure showed decreased FEV_1. TWA exposures below 25 mg/m^3 are recommended.	1976 (62)
Miners/millers	Morbidity study	NY State talc with tremolite		121	With <15 years, increased prevalence of cough and dyspnea; with >15 years, increased prevalence of pleural calcification. Radiographic findings occur primarily after 15 years.	1979 (63)
Grinding (milling)	Talc pneumoconiosis		U.S., Australian, and French talc	6	Large amounts of talc and talc bodies were found in the BAL fluid of all of the workers 21 years after last exposure. The authors suggest that examination of BAL fluid can provide information about talc exposure.	1987 (64)
Talc factory	Respiratory health		1.87–15 mg/m^3	139	Increased exposure decreased FVC and FEV_1	1995 (65)
Latex glove manufacturing	Respiratory function		7.7 mg/m^3 total dust; 1.9 mg/m^3 respirable dust	17	FVC and FEV_1 were lower in latex workers than controls.	1998 (66)

Table 84.2. Older Mortality Studies

Occupation	Focus of Study	Length of Exposure	Exposure Concentration	No. of People	Findings	Date (Reference)
Miners	Mortality	10 months to 27 years		8	Causes of death: five died of cor pulmonale or TB; one of congestive cardiac failure; one of nephritis with cardiac complications; and one unknown.	1955 (24)
Miners/millers	Mortality	>15 years	Talc mixed with serpentine and tremolite	91	Nine lung carcinomas, one fibrosarcoma of the pleura, two stomach cancers, one case each of colon, rectal, and pancreatic cancer; 25 cardiac arrests and 28 deaths from pneumoconiosis.	1967 (67)
	Mortality	>15 years		260	The overall proportional mortality due to carcinoma of the lung and pleura was four times that of the general population. The carcinogenic effect was significant in workers exposed for 15–24 years.	1974 (68)
Rubber workers	Stomach cancer			17,000	There was an association between exposure to talc materials and 100 cases of stomach cancer.	1979 (69)
Talc miners	Mortality			1260	Death was due primarily to pneumoconiosis and tuberculosis.	1979 (70)
Talc millers	Mortality	22 years	11 mppcf	218	Radiographic evidence of pneumoconiosis after 22 years of exposure but little cancer.	1979 (70)

Mining/milling	Mortality/morbidity	13 years	N.Y. State talc	398	Significant increase in mortality due to bronchogenic cancer, nonmalignant respiratory disease, and respiratory tuberculosis. Four of 10 bronchogenic cancer deaths occurred in individuals with less than 1 year of exposure.	1979 (71), 1980 (72)
Mining	Morbidity/mortality (cancer)	> 1 year (1944–1972)	Talc with <1% quartz	94	27 deaths, with 15 cases of cancer; cancers were of the stomach, prostate, and lung.	1990 (73)
Milling	Morbidity/mortality (cancer)	> 2 years (1935–1972)	Talc with <1% quartz	295	90 deaths, with 31 cases of cancer; cancers of the bladder and kidney were elevated.	1990 (73)

Nonsignificant increases in lung cancer mortality were reported among 1070 talc miners and millers from the French Pyrenees (SMR = 1.23, 95% CI 0.76–1.89) and 542 workers from three Austrian talc mines and mills (SMR = 1.06, 95% CI 0.43–2.19) (93). In a follow-up case-control study using cumulative exposure to talc, there was no association between talc exposure and lung cancer mortality although there was an association between the same exposure metric and nonmalignant respiratory mortality (93).

One thousand seven hundred ninety-five talc miners and millers who had worked at least 1 year at a facility in Turin, Italy, from 1946 to 1995 were followed up until the end of 1995. The talc was free of asbestos contaminants. No increase in lung cancer was found in this cohort. Increased mortality from oral and esophageal cancer was found in this cohort. This excess was attributed to alcohol ingestion, as increased mortality from cirrhosis was also observed in the cohort (94).

Studies in users of talc not only require knowledge about the source of the talc used but also need to control for workplace exposures other than talc. A study of 2055 men who worked for at least 1 year between 1939 and 1966 at one of the three ceramic plumbing fixture manufacturing facilities found an increased risk of mortality from lung cancer. There was a statistically significant 2.54 risk of lung cancer mortality in individuals with high silica exposure and nonfibrous talc exposure as casters with increasing risk in individuals with increased duration of nonfibrous talc exposure. The authors concluded that "although the role of silica cannot be ruled out these data suggest that nonfibrous talc exposure is associated with lung cancer risk" (95, 97).

Other mortality studies in industries using talc have not adequately addressed the source of the talc nor controlled for nontalc exposures. For example, studies in the rubber industry have reported increased mortality from lung and stomach cancer (98, 100, 101). Other potential carcinogenic exposures in the rubber industry include asbestos, carbon black, and nitrosamine. Both lung and stomach cancer mortality were increased in a study of 8933 German rubber workers from five facilities who were hired in 1950 or later and were alive as of January 1, 1981. No information is provided about the purity of the talc and analyses for the adjusted risk of mortality were presented only with asbestos and talc exposure combined (101). Similarly, in a study of 1624 Chinese rubber workers, increased mortality for lung cancer was found among workers in the curing area and the inner tire tube area. Mention is made of the use of talc but no further information is provided about the source of the talc or levels of exposures to talc or other substances in these two work areas (98).

Additional articles included in a review article on talc and lung cancer (84) include a study of workers from a U.S. fiberglass manufacturer that showed a small nonstatistically significant increase (odds ratio = 1.36, 95% CI 0.41–4.52) in lung cancer mortality in analyses that used exposure assessment to quantify talc exposure (99); a statistically increased risk of the incidence of ovarian cancer (SIR = 1.5, 95% CI 1.07–2.09) but not in the incidence of lung cancer among women workers from a Norwegian paper and pulp mill (both talc and asbestos were used in the pulp and paper mill and no analysis by exposure was presented) (103); and increased risk of esophageal (SMR= 2.7, 95% CI 1.1–5.4), ovarian (SMR = 2.9, 95% CI 1.5–5.0), and stomach cancer (SMR = 2.2, 95% CI 1.0–4.2) mortality among workers from two large Russian printing plants where there is mention of exposure to talc fillers contaminated with asbestos but no analyses were performed by exposure (102).

The IARC review of these mortality studies is that talc not containing asbestos is "not classifiable as to its carcinogenicity in humans" (group 3) (41).

1.4.2.5 Nonoccupational Health Effects. The International Agency on Research of Cancer reviewed one cohort study and 19 case-control studies on the use of talc in feminine hygiene products and the risk of ovarian cancer. The increase in risk ranged from 30% to 60% across the various studies and the perineal use of talc-based body powder has been categorized as "possibly carcinogenic to humans (Group 2B)" (41).

Acute inhalation of a large amount of baby powder by babies during a diaper change has caused acute severe respiratory disease requiring hospitalization, intubation, and even death (104). Overuse or abuse of talcum powder by adult consumers has caused radiological and pathological changes of talc pneumoconiosis (105, 106) and a reported death from talc pneumoconiosis (107).

Intravenous drug abusers who inject drugs either intended for oral consumption or diluted with talc may develop talc granulomatosis with radiological and pathological changes (108, 109).

Talc is injected into the pleural space (pleurodesis) as a therapeutic procedure to cause scarring in the pleural space to treat malignant pleural effusions, and prevent recurrent bleeding or pneumothorax. The association of acute respiratory failure with death in 2% of treated patients and systemic and pulmonary inflammation after its use has increased the regulation of its use as a therapeutic agent in Great Britain (110).

1.5 Standards, Regulations, and Guidelines of Exposure

A number of countries have standards, regulations, and guidelines for regulating exposure to talc in the workplace. The exposure limits vary depending upon whether the talc

contains asbestos or silica or if it is total dust or respirable dust only. Total dust exposures for talc are 10 mg/m^3 in Switzerland and the United Kingdom, 5 mg/m^3 in Finland, 2.5 mg/m^3 in Australia, and 2 mg/m^3 in Belgium and Germany. Respirable dust exposures for talc are 2 mg/m^3 in Bulgaria, Columbia, Jordan, Korea, New Zealand, Singapore, and Vietnam, and 1 mg/m^3 in the United Kingdom (111).

In the United States, the OSHA PEL for talc not containing asbestos and containing less than 1% quartz is 20 mppcf. For talc containing no asbestos but 1% or more of quartz, the OSHA PEL is calculated from the formula for silica. For talc containing asbestos, the asbestos limit is used (112). The NIOSH REL is 2 mg/m^3 (respirable). A TLV-TWA has been developed by ACGIH (113).

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